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Contents

„Immortalis est ingenii memoria"

Seneca

Original Article

Bladder dysfunction in pelvic urinary tract obstructions Congenital posterior urethral stenosis in boys. Part I

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Abstract

Disfuncția vezicii urinare în obstrucțiile tractului urinar pelvin
Stenoza congenitală uretrală posterioară la băieți. Partea I

Stenoza congenitală a uretrei posterioare se întâlnește frecvent și duce la tulburarea întregului tract urinar - uretra suprastenotică, colul vezicii urinare, vezica urinară, ureterohidronefroză, mai frecvent bilateral. Având origine congenitală, această malformație rezultă din dezvoltarea incompletă a membranei urogenitale - limita pasajului uretral posterior și anterior și spasmul muscular al tractului urinar pelvin.
Diagnosticul include ultrasonografie, urografie, cistouretrografie micțională, renoscintigrafie dinamică, cistometrie, urofluometrie radionuclidică, uretroscopie, calibrarea uretrei cu buj cu olivă, examen neurologic, miografie musculară perineală. A fost elaborată clasificarea clinico-radiologică a acestui tip de stenoze, fiind descrise diferite grade, care necesită un tratament diferențiat în funcție de fazele clinic-radiologice. Stenoza neurogenă se dezvoltă la copiii mai mici cu un tablou clinic mai sever comparativ cel forma congenitală.
Rezecția transuretrală a peretelui anterior al uretrei stenotice este metoda de elecție în tratamentul stenozei uretrale.

Cuvinte cheie: afecțiune renală cronică, valvă uretrală, diagnostic imagistic, ablația valvei

Abstract

Congenital posterior urethral stenosis is common and leads to disorder of the entire urinary tract - suprastenotic urethra, bladder neck, bladder, ureterohydronephrosis, more often bilaterally.
It can be congenital as a result of incomplete development of the urogenital membrane - the limit of the posterior and anterior urethral passage and the muscular spasm of the pelvic urinary tract.
Diagnosis includes ultrasound, urography, micturating cystourethrography, dynamic renoscintigraphy, cystometry, radionuclide uroflowmetry, urethroscopy, calibration of the urethra with olivary bougies, neurological examination, perineal muscle myography. The clinical-radiological classification of stenosis was developed, which is more didactic. There are different degrees of stenosis as suprastenotic resonance that requires a differentiated treatment depending on the clinical radiological phases. Neurogenic stenosis develops in younger children with a more severe clinical picture than the congenital one.
Transurethral resection of the anterior wall of the stenotic urethra is the method of choice in the treatment of stenosis.

Keywords: chronic kidney disease, congenital obstructive uropathy, urethral valve, imaging diagnosis, valve ablation

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Introduction

Restoration of the upper urinary tract by antireflux surgery is performed after removing the obstruction, carrying out intravesical surgery; in neurogenic stenosis spasmolytics are administered, neurological observation and treatment is required [5, 6].

Obstructive bladder dysfunction is a urodynamic disorder of the urinary tract. An in-depth study of congenital posterior urethral stenosis performed by Stefens F. (1963), Sow (1968), and especially Moormon J. (1976), etc., was based on the interpretation of the etiology, clinic and diagnosis of obstruction. This is of paramount importance in establishing the tactics, the use of either one or another method of treatment.

There are still a number of unresolved questions so far, regarding early diagnosis, therapeutic tactics, prognosis of complications, consequences. There is lack of data on the clinical-anatomical picture of congenital stenosis in the literature, concerning the degree of stenosis and changes in the suprastenotic sectors of the urinary system. Moorman (1977) described the radiological phases of congenital stenosis of the bulbar urethra, considering only changes in the upper urinary tract. However, Moorman did not provide data on changes revealed by cystourethrography, which depend on the degree of stenosis and the compensatory capacities of the suprastenotic segment of the urethra, bladder neck, etc. The reciprocal relationship between the timely diagnosis and differentiated surgical correction according to the case help control the pathological process [3].

Purpose of the paper: to elaborate a complex of diagnostic tests and differentiated surgical management for the correction of congenital stenosis of the posterior urethral spasm and its consequences in children.

If the disorders are persistent, especially if they are associated with urinary tract infections, it is necessary to determine the anatomical and neurological causes [4].

The work is based on the results of clinical observation, methods and results of complex surgical treatment of a group of 265 boys with congenital urethral stenosis, the age ranging in newborns, infants and 15-year old adolescents, treated in the Department of Urology and Neonatal Surgery of the Republican Clinical Hospital „E. Coțaga" and HCF IM and C during 1970-2018.

Patients were examined pre-, intra- and postoperatively according to a pre-established protocol. The "Patient Observation Sheet" and the "Patient Outpatient Sheet" were used as sources of information. It hould be mentioned that the only selection criterion was the diagnosis of infravesical obstructive syndrome. A thorough urological examination was performed in newborns with dilation of the upper urinary tract detected intrauterinely.

If there are 3 cases of correctly diagnosed urinary tract infection in girls and 2 cases in boys, it is necessary to carry out a thorough examination (many years of experience) of urodynamics in order to reveal the factors involved in filling, storing, transporting and evacuation of a part of the lower urinary tract. In some cases ultrasound, micturating cystourethrography, i/v urography, dynamic renoscintigraphy, and radionuclide cystourethrography with the examination of bladder and urethra urodynamics as well as cystometry are carried out.

If the urethra cannot be examined by the cystourethrography, in girls the urethra is calibrated with normal diameter bougies according to age, in boys with olivary bougies, to exclude meatal stenosis in girls or posterior membranous urethra in boys.

Congenital posterior urethral stenosis (CPUS) is often confused with form III valves, the treatment of which differs. Frequently, open perineal urethrotomy does not detect any mucosal folds in the urethral lumen that can lead to obstruction.

There were attempts to introduce new terms and new methods of treatment. Thus, Dewan and Ransley (1992) proposed a new term "Obstructive posterior urethral membrane". Courajos B.M. (2019) - Congenital posterior urethral stenosis, incomplete development of the urogenital membrane - the limit of the posterior urethral passage to the anterior one, Cobb`s collar (Moorman`s ring) -1975. Muscle spasm of the pelvic urinary tract.

Material analysis

Based on the data presented as well as the clinical examination data, it was made an attempt to demonstrate the mechanism of evolution of suprastenotic changes of the entire urinary system, the latter being dependent.

However, suprastenotic disorders in urethral obstruction are manifested by urodynamic disorders and infection association. In urethral obstruction, the more marked congenital stricture is, the more forced urination is. In most cases this fact is overlooked by both parents and children. As a reaction to stricture, the urethra dilates, the urine flow becomes turbulent, the retrograde parietal movement occurs, causing urethritis and cystitis. The bladder infection penetrates the upper urinary tract, thus causing chronic pyelonephritis. The bladder becomes hypertrophied, the infravesical pressure is increased, manifesting clinically by pollakiuria and enuresis. This represents the urination left in the first stage of its evolution. The striated sphincter does not intervene at all and involuntary urination occurs diurnally. Decompensation of the bladder and bladder neck subsequently causes forced urination, with residual urine and *ischuria paradoxa.*

Particular attention is paid to vesicoureteral reflux, which can accompany chronic cystitis, hyper- and hypotonia of the bladder. This causes chronic pyelonephritis and dilation of the upper urinary tract. It should be mentioned that in case of bilateral vesico-renal reflux, the suprastenotic disorders of the urethra, bladder neck and upper bladder are not so marked even if stenosis has a pronounced character.

It was found that in the suprastenotic segment of the posterior urethra during urination, the tension increases and the urethra dilates, initially the posterior wall, then the entire posterior urethra does. The retrograde parietal turbulent movement in the urethral lumen favors urethral dilation, bringing about urethritis, prostatitis or cystitis. The turbulent urine flow can only be observed in isotope uroflowmetry.

The upper urinary tract undergoes the same changes as the bladder, namely, lesions that can be detected sonographically, urographically and by radionuclide scanning. The ureter, the renal pelvis and the calyx system become hypertrophied, trying to overcome the vesicoureteric hypertension, then become hypercontracted, producing ureterohydronephrosis that distorts the structure of the renal parenchyma.

The longer the duration and degree of hypertension, the more impaired the kidney function is, and it does not depend only on the child`s age. This condition can be temporarily remedied by the presence of an extrarenal pelvis, acting as an expansion vessel. Impaired kidney function occurs as a consequence of the two mechanisms - ischemia and infection. It should be mentioned that the initial kidney injuries are reversible, and advanced injuries do not have the chance to recover.

The ureters undergo morphological changes that represent the pathophysiological mechanisms of high resonance of the posterior urethral stricture (fig. 1).

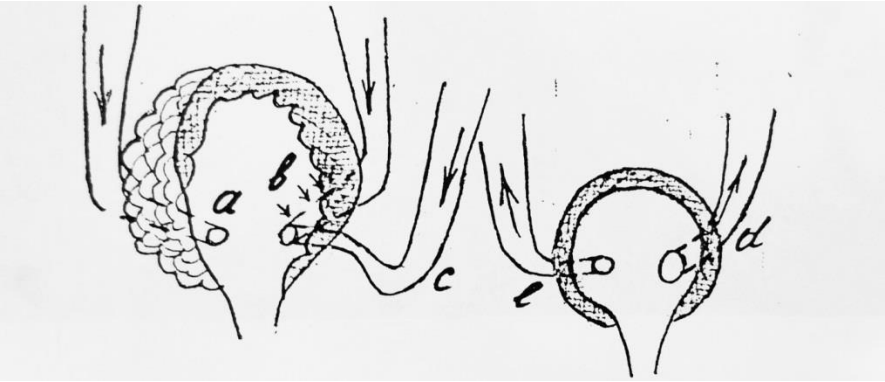

Fig. 1. Mechanism of urethral disorders in infravesical obstruction:
a - compression of intramural ureters by hypertrophy, the detrusor spasm (initial mechanism);
b - difficult ureteral discharge, caused by intravesical hypertension following urine stagnation in the bladder;
c - fishhook ureters - bladder dilation and trigone lifting cause the ascent of the terminal part of the ureters, which angles at the vas deferens crossing

Retrograde reflux is due to:

- meatal insufficiency in intravesical hypertension;
- insufficiency of the vesicoureteral junction in the phase of bladder distension and shortening of the intramural part of the ureter in chronic cystitis;

Clinical manifestations of CPUS

1. The clinical symptoms of CPUS depend on the degree of obstruction, the child's age and the time of seeking medical care.

Congenital urethral stenosis is an abnormal embryological development, being a spasm of the external urethral sphincter with fibrosis, which at birth has a symptomatology defined by the degree of stenosis and suprastenotic resonance of the urinary tract.

In newborns and infants, the clinical picture is severe, being characterized by general signs, such as fever, anemia, rickets, digestive disorders (anorexia, nausea, vomiting, diarrhea), which lead to acute dehydration, the neurological picture being more severe. Urinary disorders are present, such as weak urine flow, urinary retention, bladder distension, etc. On palpation, the kidneys are usually enlarged and painful, although on CUGM the bladder is virtually unchanged.

In children and adolescents, the clinical picture is characterized by urological signs, mainly micturition disorders, depending on the degree of obstruction. Dysuria, pollakiuria and nocturnal urination are the most common, subsequently followed by diurnal urinary incontinence. The urinary flow continuity as well as the caliber and projection force are reduced. In severe cases, urination is painful and requires effort, which can only be achieved by compressing the hypogastric region. Finally, detrusor hypotonia develops with false urinary incontinence (overfull urination) and ischuria paradoxa.

The evolution of these cases is sometimes torpid, other times the urinary signs remain constant for years. Getting used to them, the child seeks medical assistance in the advanced stages of the disease, when, anticipated by imperative urination. Thus, acute urinary retention develops, accompanied by abdominal pain, febrile seizures, sometimes with severe renal failure.

Urethroscopy - stenosis of the distal part of the posterior urethra is detected as well as an annular prolapse in the urethral lumen with a centric or eccentric foramen. Depending on the obstruction severity, the posterior urethral dilation is observed, the dimensional increase of the verumontanum, sometimes with edema, and the bladder neck being opened. In the bladder there are columns, trabeculae and pseudodiverticula.

A difference in supra- and substenotic transit can be revealed on radionuclide uroflowmetry. This test allows exclusively the recording of the turbulent urine flow in the supra-stenotic segment.

Clinical-radiological classification of CPUS

Summarizing the symptomatic evolution of CPUS depending on the pathophysiological substrate, four clinical-radiological phases have been highlighted;

Phase I - compensated

Phase II - undercompensated

Phase III - decompensated

Phase IV - refluxing ureterohydronephrosis

The highlighted phases are strictly didactic, as they cannot be delimited from each other. They have been classified as such, because there are different degrees of stenosis as suprastenotic resonance requiring a differentiated treatment.

Depending on the clinical-radiological phases, micturating cystourethrography and urographic examination found the following (fig. 2).

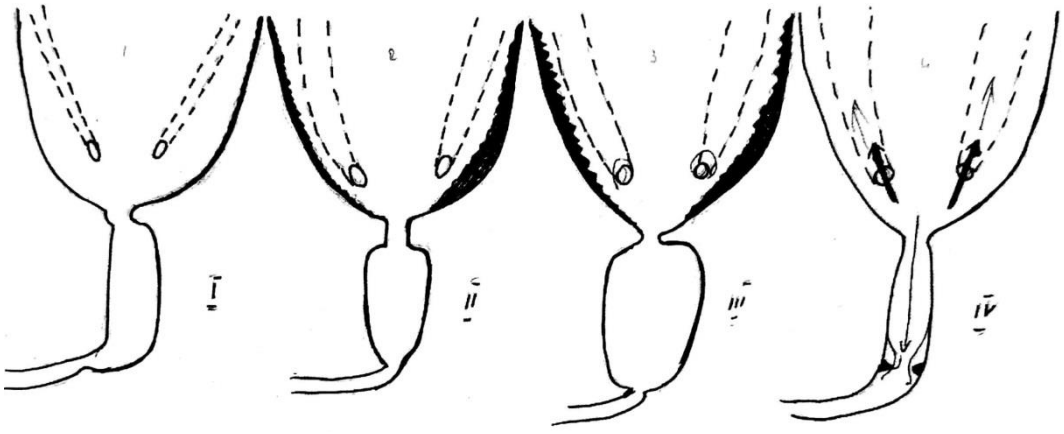

Fig. 2. Clinical-radiological phases of congenital posterior urethral stenosis. Scheme

Phase I - annular stenosis of the distal portion of the posterior urethra with insignificant suprastenotic urethral dilation on account of the posterior wall. In the region of the bladder neck there is a prominence in the lumen of the posterior wall. The bladder is slightly deformed with trabeculae on the posterior wall (fig. 3). Ureters and kidneys do not have any marked disorders (75 patients).

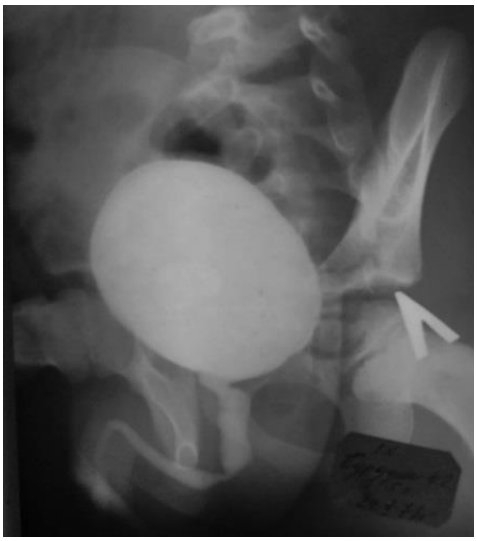

Fig. 3. Child C., 6 years; Micturating cystourethrography - posterior urethral stenosis, phase I

Phase II - annular stenosis of the distal posterior urethra, with marked dilation of the suprastenotic urethra. The bladder neck is narrowed and elongated. The bladder is deformed, with trabeculae on all walls, dilation of the upper urinary tract (46 patients).

Phase III – marked annular stenosis with exaggerated suprastenotic dilation. Dilated and short bladder neck. Enlarged bladder with trabeculae and pseudodiverticula. Refluxing megaureter on the right (fig. 4).

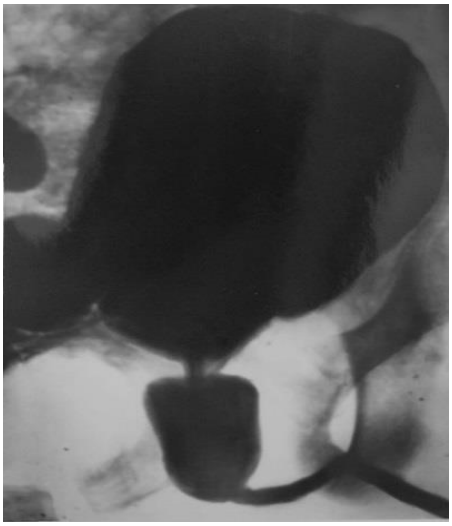

Fig. 4. Micturating cystourethrography - posterior urethral stenosis, phase III

Phase IV – It should be mentioned that in case of bilateral vesico-renal reflux the suprastenotic changes of the urethra, bladder neck and bladder are not marked, even in significant stenosis. This is due to urine flow which encounters an increased hypertension, obstructively, more easily returns to the ureters and renal pelvis. The bladder in this case does not look like a fight bladder.

In newborns and infants there are changes highlighting stenosis of the membranous urethra, suprastenotic dilation of the posterior urethra; the bladder and bladder neck are without essential changes. In these patients, it is necessary to calibrate the urethra with olivary bougies, which either confirm or not stenosis.

The principles of treatment of CPUS depending on the clinical and radiological phases

Treatment of patients with congenital stenosis of the posterior urethra is difficult, because once the obstacle (stenosis) is removed, it is necessary to correct the resonance of suprastenotic urinary tract - bladder disorders, vesico-renal reflux, ureterohydronephrosis, chronic urinary tract infection and kidney failure even in infants.

Considering the pathophysiology of suprastenotic disorders of the urinary system and the changes that take place in the bladder neck in urethral obstruction, after the `80s of the 20th century, no intervention on the bladder neck was performed. According to the literature, in about a quarter of patients, vesico-renal reflux gr. I-II disappeared during the first year after removing the obstruction.

Vesico-renal reflux should be closely monitored. If there is no spontaneous improvement over an adequate period of time after surgery, careful assessment of the renal function is required. Nephroureterectomy of the refluxing unit may be considered when no function is marked. If the function is maintained, urethral reimplantation can be individually considered.

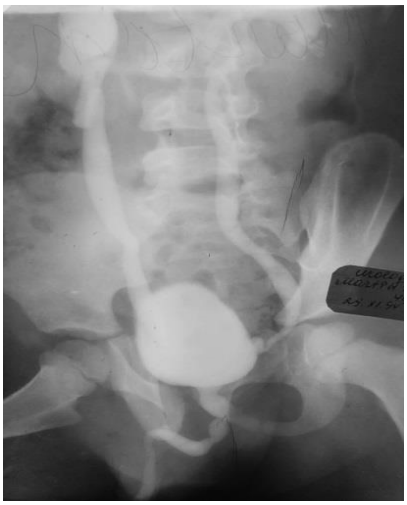

Fig. 5. Posterior urethral stenosis. Bilateral reflux. The bladder has no signs of "fight bladder"

Over several years the treatment of urethral stenosis entailed different procedures and methods. In the `70s of the 20th century, the dilation of the strictured segment was performed with metallic bougies under anesthesia.

The vast majority of the results of these procedures were unsatisfactory and sometimes stricture progression was recorded. Later, dilation with a mechanical urethral dilator or blind urethrotomy along with *commissurotomy* was performed.

Because the treatment results were not satisfying, in more severe cases of stricture, transperineal plastic surgery was performed, with a longitudinal incision and transverse suturing of the anterior wall of the stenotic or transperineal segment, namely, Holtsov procedure – resection of the stenotic segment and termino-terminal anastomosis.

Although these treatment methods have good results, in recent years they haven`t been used because they are laborious surgeries with anesthesia lasting 1.5-2 hours and a postoperative hospitalization period lasting for 10-12 days. During transperineal surgery, there is the risk of injuring the external urethral sphincter and perineal nerves, which can lead to urinary incontinence and impotence. In recent years, obstruction has been removed with an original urethrotome that allows us to resect transurethrally the anterior wall of the stenotic segment of the posterior urethra with good results (fig. 6).

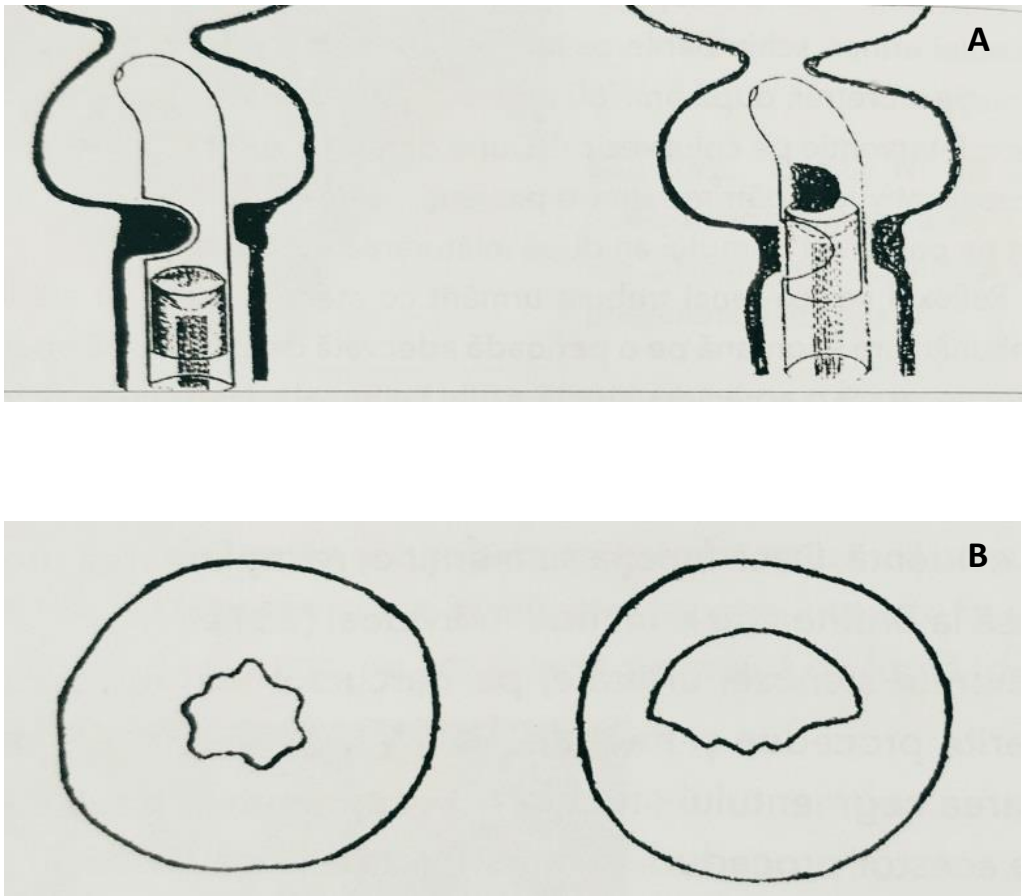

Fig. 6. A - Resection of the stenotic segment with an original urethrotome: before and after resection
B - Stenotic segment before and after resection: before and after resection

Macroscopically, the removed material has whitish tissue of hard elastic consistency with areas of fibrosis, the mucosa being pale pink and well differentiated. Microscopically, the urethral mucosa is lined with multilayered epithelium, in some places with proliferative phenomena in the submucosa, vast connective tissue with edema and infiltration, as well as dispersed lymphocytosis is revealed. In some sections, ectopy of the multilayered epithelium in the submucosa is determined. The muscle tunic is almost completely replaced by the connective tissue, which shows atrophied muscle fibers, being hypertrophied here and there.

Blood and lymphatic vessels show lesions manifested by mucoid and fibrinoid intumescence, in some places with hyalinization phenomena, deformation of thickened and sclerosed walls. Lymphatic vessels are in the form of deformed caverns. There is vast lymphocytosis. Nerve fibers are irregularly thickened and deformed. Analysis of histological results confirms the congenital genesis of obstruction.

Based on experience of over 20 years, the principles of treatment in disease phases have been developed, because patients in different phases require differentiated treatment.

Other diseases with infravesical obstruction are treated depending on the clinical picture of urodynamic disorders, urinary tract infection and neurological disorders.

In phase I – compensatory stage, changes in the suprastenotic urinary tract are not marked. In most cases it is necessary only to remove the obstruction, less often to balance the bladder tone and administration of uroseptics for a short time.

If urodynamic changes with signs of overactive bladder are not obvious, no drug treatment is required. Initially, urination reeducation should be carried out (behavioral urotherapy aimed at normalizing bladder function and preventing functional disorders). If the desired effect is not obtained, the therapy of stimulation of the presacral nerve roots is applied. Treatment with anticholinergic medication also has some side effects, such as: constipation, dryness of the mucous membranes, increased residual urine (Oxybutynin 0.1 - 0.15mg / kg)

In phase II - subcompensatory, the resonance of suprastenotic urinary tract is more pronounced, often with a marked urinary tract infection. Initially, cystostomy is performed, then the obstruction is removed, then the muscular tone of the bladder should be balanced with a longer treatment of the urinary tract infection. If after 6 months - 1 year there is no clinical improvement, the infection, vesico-renal reflux, and ureterohydronephrosis are present, the reconstruction of the upper urinary tract should be performed (antireflux surgery, ureteroplasty, pelvic plasty, etc.), after which the conservative treatment is prescribed.

In phase III - decompensation, refluxing phase, the treatment is aimed at achieving three goals. If the general condition of the patient allows, the obstruction is removed, the treatment of bladder tone balancing is performed, the treatment of the urinary infection is carried out, and in 6 months - 1 year the upper urinary tract plastic surgery should be performed with a prolonged conservative treatment.

In phase IV - with obvious dilation of the urinary tract, the patient's condition is severe with exacerbation of the urinary tract infection, a permanent probe is applied to the bladder (preferably a catheter smaller than the urethral lumen), cystostomy and percutaneous nephrostomy, after which the condition quickly improves and the obstruction is removed. Ureteral interventions are delayed until the patient is stabilized for 2-3 months.

Subsequently, intensive detoxification therapy and antibiotic therapy are performed, and uroseptics are administered. After 10-14 days, when the child's condition improves, cystourethrography is performed along with bladder filling through the stoma, antibiotics and diuretics being added to the contrast medium. It is possible to remove the obstruction 2-3 weeks after admission. Prolonged conservative treatment is prescribed, and plastic surgery of the suprastenotic urinary tract is performed after 6 months - 1 year with the conservative treatment – anti-reflux surgery. Surgery for neurogenic stenosis includes ureteral resection, even if the distal ureter is not spasmed, there is also obstruction of the intramural segment with intravesical neoimplantation. Ureterostomy is an additional burden for the patient, physician and parents.

Neither ureterostomy, nor probing, nor vesicostomy were applied to any patient. It is necessary to monitor the functional dynamics of the bladder, ureters, and kidneys. Sometimes cholinolytics, physiotherapy and phytotherapy should be administered.

If there is marked dilation of the ureters and renal pelvis, as well as megaureterohydronephrosis with impaired kidney function, antireflux surgery should be performed. If the kidney function is unilaterally disrupted, with the function preserved less than 25-30%, nephroureterectomy should be performed and ureter removed, to prevent reflux into the ureteral stump.

The X-rays of 105 newborns and infants with reflux megaureter were selected and studied from the archive data. There were radiological signs of posterior urethral obstruction in 38 patients, due to posterior urethral valve. Of 7 children with obstruction, neurological disorders were detected in 5 patients.

In phase IV - patients are usually hospitalized with exacerbation of the urinary tract infection. In parallel with antibacterial treatment and detoxification, the urethro-bladder probe or cystostomy is applied. In 7-10 days, after the condition improves, voiding cystourethrography should be performed where the urethra is practically

unchanged, but bilateral vesico-renal reflux is present, sometimes very pronounced or having an advanced degree. The bladder does not look like a *fight bladder*.

If the condition allows, the antireflux surgery should be performed, preferably transvesically (to capitalize on the increased intravesical pressure - Cohen, Leadbetter - Politano, *Bischoff* methods, etc.) on the most affected part of the kidney (after urography, scintigraphy). After 3-6 months, CUM should be repeated, where usually posterior urethral stenosis is clearly manifested and the obstruction is removed and antireflux surgery on the opposite side.

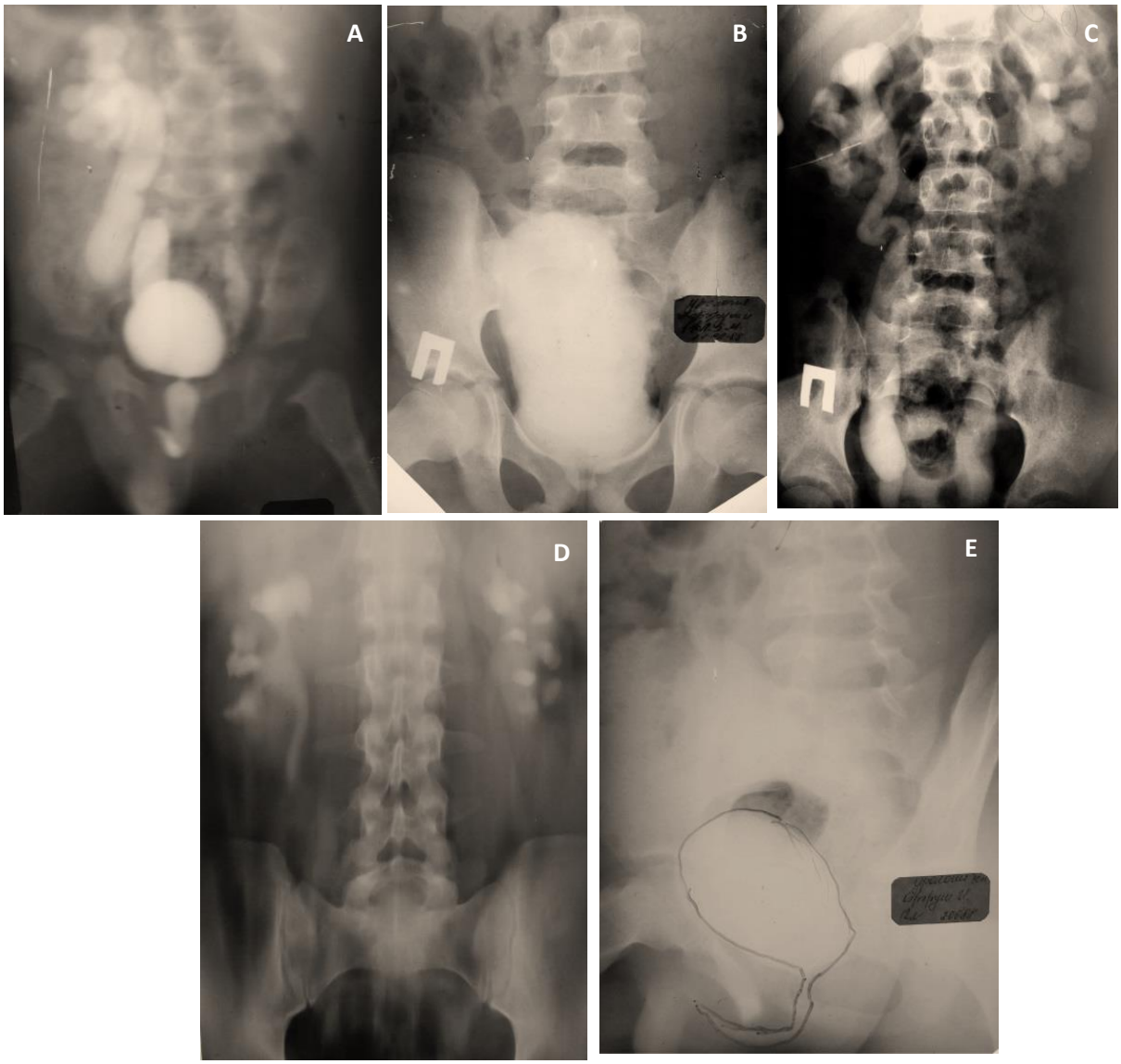

Fig. 7. A - Child C., 11 months; Cystourethrography - posterior urethral stenosis, undercompensated form. Bilateral vesico-renal reflux, marked megaureter on the right; B - The same child, 11 years Cystourethrography - marked urine retention, very large bladder with marked trabeculae; C - The same child urography: marked bilateral megauretero-hydronephrosis; D - 1 year after obstruction removal; urography - preserved renal function, dilation of the left renal cavities with nephrosclerosis signs; E - Cystourethrography - bladder with clear outline, normal size, permeable urethra

According to the literature, on urethrotomy there are recurrences of strictures, the recovery rate of subsequent urethrotomy decreasing by 10%, being almost zero for the following procedures (Heynes, 1998); this being a palliative treatment, often burdened by traumatic and infectious complications, progressively aggravating urethral lesions in length and depth [1].

The urethral stent or augmented anastomosis is one of the solutions. Urethrotomy originally excises the sclerotic wall and perforation is excluded because the tube is at the level of the urethral wall.

Antireflux surgery is performed no later than 6-12 months after removing the obstruction and only after normalization of micturition, suppression of bladder disorders, treatment of recurrent urinary tract infection and reduction of intravesical pressure as much as possible. Intravesical antireflux surgeries (Cohen, Leadbetter - Pollitano) are recommended to capitalize on the intravesical pressure and to form a stable antireflux procedure.

If urinary tract infection develops slowly, without exacerbation, patients with reflux are monitored for a longer time (1-2 years).

the intrauterine muscle spasm.

In one case the distal part of the posterior urethra is affected and the external urethral sphincter, in another case (neurogenic) along with the damage to the urethra, the muscles of the juxtavesical ureter (Waldeyer`s segment) are also affected, pelvic urinary tract muscles are hypertrophied, and there is increased intravesical pressure. In neurogenic stenotic urethra, children are restless, can not stand the urinary catheter. The physiological contracture of skeletal muscles maintains for a long time, strong urine stream (when urinating the stream reaches the face). In congenital stenosis, children bear calmly the urinary catheter. The urination is free and more frequent, sometimes at older age children have diurnal urinary incontinence.

In case of antireflux surgery, if the obstruction was not removed, and reflux was not detected on examination, ureterohydronephrosis maintains.

If urethral obstruction is removed, the overlying urinary tract returns to normal, in other cases, after removing the urethral obstruction, the urinary tract urodynamics is disturbed, although the vesico-renal reflux is not recorded, the *ureterovesical* segment is removed, renal parenchymal fibrosis and urinary tract,

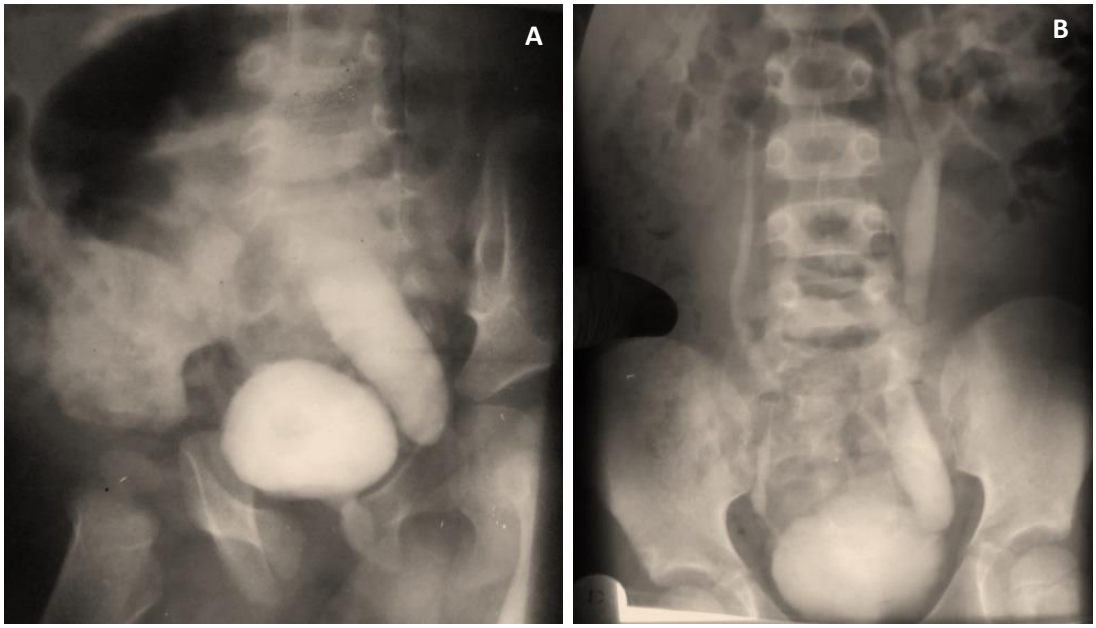

Fig. 8. Child C., 3 months. A – Micturating cystourethrography: bilateral vesico-renal reflux, megaureter on the left. Posterior urethral stenosis; B – urography after surgery: bilateral antireflux, infravesical obstruction was not removed – bilateral ureteral dilation.

Posterior urethral stenosis in some boys may be a consequence of muscle spasm in the intrauterine period with subsequent fibrosis.

It cannot be said that infravesical obstruction is absolutely a congenital organic or neurogenic abnormality. In both organic and neurogenic obstruction there is fibrosis of the urinary tract muscles as a result of

infection persist, but with less frequent exacerbations. On scintigraphy, there are sometimes marked evacuation disorders, caused by the spasm of bladder muscles, obstructing the intramural ureter as well as increasing the intravesical pressure, which is indicative of the persistence of the obstruction in the pelvic urinary tract.

There are also neurological signs after removing the

organic obstruction, which persist and require additional treatment. According to the literature, 5-6 years after removing the obstruction, neurological signs appear, which are likely present from birth but have not been detected. Thus, of 7 newborns and infants with megaureter, neurological manifestations were detected in 5 of them. Posterior urethral stenosis is probably not only an abnormality of organic development, but also a component of prolonged intrauterine muscle spasm with fibrosis of this segment [2]. Regardless of how advanced the urethral obstruction is, the section is maintained. Obliteration of the urethra or distal ureter in the *ureterovesical* segment is not common. This accounts for the fact that CPUS is not only an abnormality such as congenital abnormality of the rectum, namely fistula and atresia, but also represents a prolonged spasm causing its fibrosis. Both forms require surgical resolution.

Conclusions:

1. Annular stenosis of the distal segment of the posterior urethra which is a congenital abnormality or malformation caused by a prolonged intrauterine muscle spasm with fibrosis of the external urethral and intrauterine sphincter cannot be diagnosed and its evolution cannot be influenced, thus requiring surgical treatment.
2. The complications of stenosis are typical and atypical determined by age, degree of obstruction and ability to compensate for suprastenotic urinary tract. Signs of congenital stenosis in patients older than 3 years are urinary disorders, such as pollakiuria, urinary incontinence, difficult urination, abdominal pain, lumbar pain, and recurrent urinary tract infections. In children under 3 years the disease develops severely with difficult urination, bladder distension, leukocytosis, leukocyturia, proteinuria (urinary tract infections, sometimes severe infections).
3. To establish the diagnosis some diagnostic tests are used, such as micturating cystourethrography, urethroscopy, urethral calibration with olivary bougies (it is superior to radiological examination in children up to 3 years).
4. There are 4 phases from the evolutionary, clinical and radiological perspectives. Phase I is frequently characterized by pollakiuria and enuresis; phases II and III are marked by difficult urination, nocturnal / diurnal urinary incontinence, recurrent urinary tract infections with suprastenotic urinary tract dilation; phase IV is characterized by frequent refluxing ureterohydronephrosis and recurrent urinary tract infections.
5. The treatment of choice is partial transurethral excision of the anterior stenotic wall, satisfactory results up to 100% being recorded in the compensated phase and 47-70% in the decompensated phase.
6. Functional changes in the suprastenotic urinary tract are reversible and regress after surgical treatment, requiring only conservative *maintenance* treatment. Advanced changes, such as ureterohydronephrosis, vesicular-renal reflux grade III-IV, will require surgical correction but not earlier than 6-12 months, after normalization of urination and detrusor function.
7. Initially, the suprastenotic urethra, bladder neck and bladder are restored postoperatively. In the early stages of the disease, after surgery, the upper urinary tract recovers definitively, but the dilation is persistent in the decompensation phase, which is idicative of the presence of general dysplasia of the pelvic urinary tract.
8. The patient should be monitored pre- and postoperatively by a pediatric neurologist.

REFERENCES

1. Curajos B. Diagnosticul și tratamentul chirurgical diferenciat al stenozei congenitale a uretrei posterioare și consecințelor ei la copii. Autoref. dis. dr. hab. șt. med. Chișinău. 1997.
2. Curajos B., Petrovici V., Curajos A.” Muscular spasm of the bladder and urodinamic abnormalities in newborn and infants with refluxing megaureter” Moldav. J. Pediatr. Surg. 2019. 4:41-51.
3. Козырев Г.В., Черкашина Е.Н. Тактика лечения детей ранего возраста с уретерогидронефрозом. Вест. Росс. Гос. Мединст. 2010. 2:310-1.
4. Николаев В.В., Козырев Г.В, Черкашина Е.Н. Клапаны задней уретры у мальчиков как причина дисфункции мочевого пузыря. Дет. Бол. 2010. 1(39):4-8.
5. Гурская А.С. Диагностика и лечение новорождднных и детей раннего возраста с клапанами задней уретры. Андрол. Генит. Хир. 2014. 2:44-7.
6. Печерица Г.Ф., Тахаумдинов Ш.К, Байбусов Р.С. и др. Практическая медицина. 2008. Вып. 30.

Posterior urethral valves in children. Part II

Curajos B.

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Abstract

Valvele uretrei posterioare la copii

Autorul prezintă experiența proprie confruntată cu datele literaturii de specialitate în diagnosticul și tratamentul valvei de uretră posterioară (VUP) la copii. În ultimii 15 ani, în Centrul Național Științifico-practic de Chirurgie Pediatrică Natalia Gheorghiu au fost diagnosticați și tratați 25 de pacienți cu VUP, initial fiind stability diagnosticul de stenoză congenitală a uretrei (290 copii). Severitatea și gradul de obstructive au depins de configurația membrane obstructive. Toți copiii au beneficiat de ablația valvei fiind folosit uretroromul original propus de autor.
Autorul conchide că toți pacienții cu VUP supuși tratamentului chirurgical necesită monitorizare pe termen lung până la adolescent, iar prognosticul depinde de modificările suprastenotice și de gradul de disfuncție a vezicii urinare la adresare.

Cuvinte cheie: valve uretrale, diagnostic, ablație, copii

Abstract

The author presents his own experience confronted with data from the literature in the diagnosis and treatment of posterior urethral valve (VUP) in children. During the last 15 years, in CNȘPCP "Natalia Gheorghiu" 25 patients with urethral valves were diagnosed and treated, initially for which the diagnosis of congenital stenosis of the urethra was established (290 patients). The severity and degree of obstruction depended on the configuration of the obstructive membrane. All children benefited from valve ablation using the original urethrotome proposed by the author, which allowed good results.
The author concludes that all patients with VUP undergoing surgical treatment require long-term monitoring until adolescence, and the prognosis depends on suprastenotic changes and the degree of bladder dysfunction at the address.

Keywords: urethral valves, diagnostic, excision, childrens

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Introduction

Posterior urethral valves (VUP) are defined as a congenital malformation characterized by the presence of semicircular folds of the posterior urethral mucosa, which creates an obstacle to urine evacuation with serious repercussions on the upper urinary tract [27]. VUP is the leading cause of congenital postvesical obstruction of urinary flow in male children, being a significant cause of morbidity, mortality and persistent kidney damage in infants and children of various ages [23].

The incidence of VUP is 1: 5000 - 1: 8000 boys or 1: 25000 live births [25, 26], this malformation representing about 10% of all urinary obstructions diagnosed prenatally [4].

VUP were first described in 1717 by Morgagni, later Langenbeck (1802) reported the presence of valve-like folds during the dissection of corpses. In 1832, Velpeau described the presence of folds in the posterior urethra as houses resemble valves and mentioned that they can cause obstruction when a catheter passes. In 1840, Budd presented the case of a 16-year-old sailor who died, the necropsy found excessive dilation of the ureters similar to the size of an intestinal loop, a dilated and thickened bladder, and in the upper wall of the membranous urethra was observed a fold similar to venous valves. In 1847, Bednar presented the case of a 12-day-old premature newborn, who died after 5 days of urinary retention, at necropsy it was discovered that the lower end of the verumontan was divided into two concave folds facing the bladder, the kidneys being atrophic and hydronephrotic. Later, several authors described the presence of posterior urethral valves, including: Godart (1854), Picard (1855), Jarjavay (1856), etc. The first scientific description of VUPs, their embryology and the role of these valves in urinary tract pathology was presented by Tolmatschew in 1870 [11, 14].

Various disorders associated with congenital urethral obstruction have been reported internationally, including: Cobb collar (1968), Moorman ring (1972), congenital obstructive membrane of the posterior urethra (COPUM), the differences between these concepts of disease remaining unclear [22]. In the early 1990s, Dewan et al. considered the term valve to be incorrect because this condition reflects obstruction in the posterior urethra of a single membrane, proposing the term COPUM. These authors were of the opinion that the type I and III valves after Young are identical, being confused during endoscopy, claiming that there are only 2 distinct entities, with different embryological origin, that cause obstruction of the posterior urethra: COPUM and Cobb collar [18, 22].

Classification

In 1913, Young H.H. and coauthor. published the presentation of a 20-month-old child with successfully treated VUP, and in 1919, trying to unify several developmental theories, described the famous work with the classification of these valves into three different types, including: Type I (90-95 %) - the presence of a ridge, which continues with the vera montanum and which protrudes anteriorly; Type II - retraction of the mucosa, which takes place proximal between the vera montanum and the bladder neck, behaving obstructively; Type III - presents as a diaphragm with a distal opening of the vera montanum, generating an obstruction on the entire circumference of the urethra. Subsequently, this classification was challenged [12, 21].

Although they believed that Tolmatchew's theory explained the development of type 1 valves, and Bazy's theory explained the appearance of type 3 valves, they favored the VUP development theory proposed by Watson (1918), believing that none of the proposed theories explained valves. type 2 [18].

Lately, more and more papers are using the classification proposed by Douglas Stephens, based on findings from urinary cystourethrography and endoscopic examination, according to which there are types 1, 3 and 4 of the posterior urethral valves and congenital bulbar urethral narrowing. Type 1 is defined as a valve structure, which connects directly from the vera montanum or lower ridge; type 3 is a ring-like structure located at the junction of the membranous and bulbar urethra, and a bent urethra associated with the prominence of the anterior wall of the posterior urethra has been classified as type 4. In cases where a ring-like structure has been located in the bulbar urethra, at the junction of the membranous and bulbar urethra is considered a congenital narrowing of the bulbar urethra [17].

In the opinion of some authors, a useful classification would be the one proposed by Hendren (1971), resumed by Caione et al., Who distinguish from the anatomical point of view and the clinical consequences two categories of VUP: "gentle shape" - 2 folds of mucosa with distal origin of vero montanum, forming two folds that partially obstruct the posterior urethra; „Severe form" - 2 wider folds of mucosa, with distal origin of vera montanum, but which join anteriorly, considerably narrowing the urethral lumen [27].

Embryology

The development of the male urethra begins with the expansion of the urogenital sinus cavity on the surface of the genital tubercle during the 6th week of gestation. Subsequently, this groove, which is an endodermal derivative, becomes a solid cell plate, which eventually tubules proximal-distally to form the phallic urethra, at week 14 the male urethra is fully developed [18]. The origin of the urethral plaque and its role in urethral development to date remains a topic of discussion, with some authors arguing that this plaque is the only precursor of the glandular urethra, with the rest of the

penile urethra developing from the urogenital sinus, while others claim that the urethral plaque it is the precursor of the entire penile urethra [16, 19].

VUP embryology is insufficiently understood, several theories have been proposed over the years. The hypothesis of an anomaly in the regression of the Wolf and Muler channel, reaffirmed by Stephens, seems the most accepted. It is claimed that the abnormal, too anterior insertion of the distal orifice of the Wolf canal and the migration anomalies, which occur much more sagittally than laterally, are the origin of the cup-shaped folds at the level of vero montanum and constitute type 1 valves [27, 28].

Clinic and diagnosis

VUP is associated with several morbidities, and the pathology is characterized by a spectrum of serious urological and renal consequences (hydronephrosis, urinary tract infection, urinary incontinence, sepsis, chronic kidney disease), in some cases fatal even in the prenatal or neonatal period [1, 4]. At the same time, in some cases, the condition remains asymptomatic, manifesting later with subtle signs and symptoms [13]. Some studies indicate that 20-65% of VUP patients will develop chronic kidney disease and 8-21% will progress to the final stage of kidney disease during childhood [8].

During the last 15 years, in CNȘPCP "Natalia Gheorghiu" 25 patients with urethral valves were diagnosed and treated, initially for which the diagnosis of congenital stenosis of the urethra was established (290 patients). The severity and degree of obstruction depended on the configuration of the obstructive membrane, the clinical symptoms being dominated by: fever, vomiting, palpable kidneys, bladder, dysuria, hematuria. Pollenuria, urinary incontinence, renal failure, urosepsis, stature-weight and psychomotor retardation have been associated with several young children.

VUP embryology is insufficiently understood, several theories have been proposed over the years. The hypothesis of an anomaly in the regression of the Wolf and Muler channel, reaffirmed by Stephens, seems the most accepted. It is claimed that the abnormal, too anterior insertion of the distal orifice of the Wolf canal and the migration anomalies, which occur much more sagittally than laterally, are the origin of the cup-shaped folds at the level of vero montanum and constitute type 1 valves [27, 28].

In all 25 cases, intrauterine ultrasound was performed, which revealed: bladder distinguished by hypertrophied walls (>3-4 mm), ureters and renal cavities dilated bilaterally, sometimes you could see the dilated urethra. The presence of focal renal parenchymal cystic formations, found in 6 cases, indicated renal dysplasia. At the same time, the presence of ascites and oligohydroamnios was diagnosed (13 cases).

In children of various ages, along with ultrasound, we used micturition cystourethrography, dynamic renoscintigraphy, which allowed us to assess renal function and highlight evacuation disorders, as well as cystoscopy for direct visualization of the valve positioned posteriorly. The early diagnosis in the prenatal period of this malformation is due to the presence of hydroureteronephrosis found on ultrasound examination, subsequently confirmed postnatal by micturition cystourethrography (fig. 1), which remains a method of choice in the diagnosis of VUP. In some cases, the diagnosis of VUP is established quite late: in children of various ages, in adolescence or even in adults [1, 24].

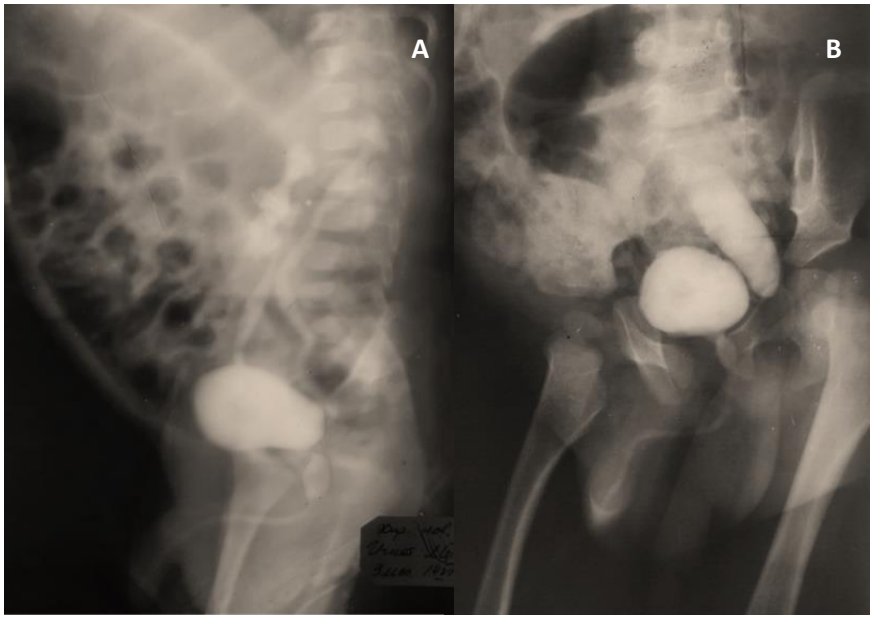

Fig. 1. Urinary cystourethrography: appearance of the posterior urethral valve diagnosed in the newborn (A) and infant (B)

Differential diagnosis includes: neurogenic bladder, Prune-Belly syndrome, bladder neck pathology, congenital stenosis of the posterior urethra, vesicoureteral reflux, primary megaureter, obstructive ectopic implantation of the ureters, stenosis or atresia of the ureters [3, 5, 15].

Cystography and cystocopy are essential in clarifying the diagnosis, more often confusing congenital stenosis with type III VUP, which on cystography presents as obstruction in the upper third of the posterior urethra with dilation of the proximal prostatic urethra, the bladder still having the appearance of "bladder the fight". To take into account the clinical signs present, more pronounced in VUP compared to stenosis, and urinary tract infection is characterized by severe evolution, often ending with renal failure. Usually, children with stenoses with urological accusations are addressed after the age of 1 year with urinary disorders [7, 9]. Urinary cystourethrography indicates obstruction of the distal part of the membranous urethra, dilation of the suprastenotic posterior urethra, bladder with pseudodiverticles, located more frequently on the posterior wall. Some authors describe a picture similar to micturition cystourethrography as stenosis, others as VUP. Until 1975, I also supported the idea promoted in the literature that the obstruction in the distal portion of the posterior urethra is type III valve after Young.

The open surgeries that we performed countless times due to urethral valves forced us to give up this method: during these operations we did not find such valves, mucosal folds, but we found small sectors of sclerotic urethra on a path of 0.2-0.4 cm in the form of a rigid ring.

A more in-depth study of cystourethrographies performed in patients with congenital stenosis and posterior urethral valves identified identical radiological signs for both pathologies, including: obstruction, proximal urethral obstruction dilation, narrowing and lengthening or dilation and dilation and shortening of the bladder neck, enlargement and change in the shape of the bladder, trabeculae and pseudodiverticles on the bladder wall. On cystography, the irregular bladder is observed, the side walls with clear, wavy contours, with prominences. On the lateral cystogram, the posterior wall has a trabecular appearance. At a more pronounced obstruction, at the same time with age, the capacity of the bladder, trabecularity and pseudodiverticles of the bladder walls also advance. Proximal to the obstruction, the prostatic urethra is dilated, the degree of dilation depending on the type and degree of obstruction.

Anatomically, VUPs are located along the proximal segment of the posterior urethra (prostate), in the region of the spermatic colic, upper or lower than it, and congenital stenosis affects the distal segment of the posterior urethra, which is why cystourethrography pathologies will manifest differently.

In micturition cystourethrography, in cases of VUP, the posterior urethra is dilated in the prostate portion, up to the level of the middle third, while in cases of stenosis - throughout, up to the level of the passage in the anterior portion (bulbar). In case of stenosis, the urethra is abruptly interrupted at the level of the obstacle in the form of a ring, while in the case of VUP the dilated urethra is observed above the obstacle, gradually narrows in the form of a funnel and almost constantly a diaphragm is present in the urethral lumen. stretched out. The distal urethra of stenosis can often be slightly dilated, which is never seen in the case of the valve [2, 28].

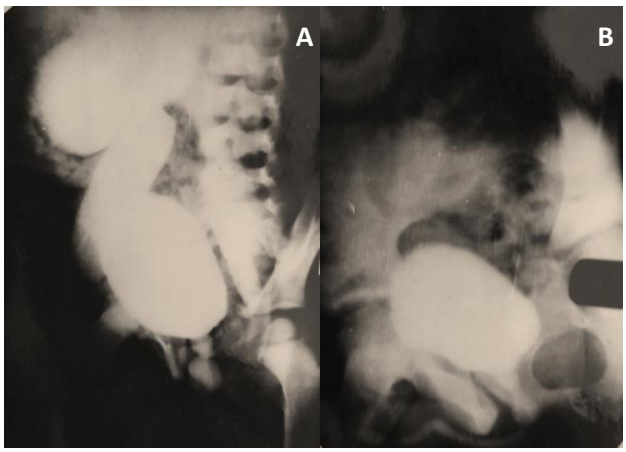

Fig. 2. Patient C., 3 years. Urinary cystourethrography: posterior urethral stenosis, suspicion of VUP, bilateral vesico-renal reflux gr. IV-V on the right, gr. IV on the left (A); B - radiological appearance over 10 after transperineal plasty of the urethra (intraoperatively VUP was not detected, being found urethral stenosis)

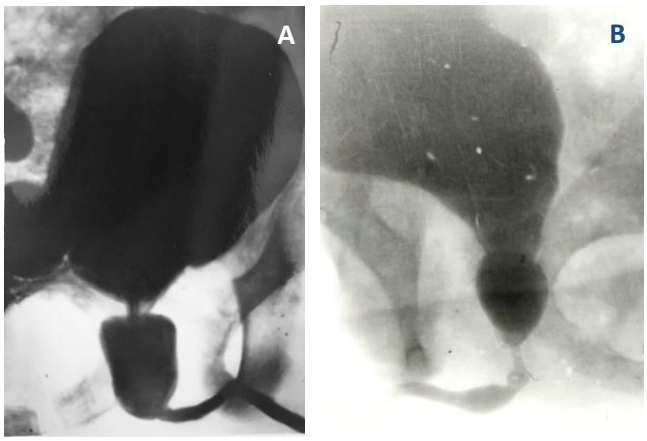

Fig. 3. A – Patient A., 4 years with congenital stenosis of the posterior urethra. B – Patient K., 6 years: posterior urethral valve

Evaluation of urodynamics is the only investigation, which allows to establish with certainty the diagnosis of overactive bladder, determining the direction of therapeutic conduct and timely monitoring of treatment outcomes [2, 28]. If the urodynamic changes are not obvious, the initial drug treatment is not necessary, but micturition education is used with the inclusion of behavioral psychological treatment, which aims to normalize bladder function and prevent functional disorders. In cases of obtaining negative results, it is possible to resort to applications of stimulation of presacral roots.

In some cases, pathophysiological changes in the bladder may develop after VUP ablation, which may be referred to as Valve Bladder Syndrome, first described by Mitchell M.E. (1982) [6]. This syndrome includes disorder of the bladder storage function that develops as a result of overcontractility associated with emptying disorders caused by bladder neck hypertrophy, which can result in ureterohydronephrosis and renal failure. Along with the dilation of the urinary tract, after the ablation of the valve in almost 50% of cases urinary incontinence develops, usually at a critical age of 5-6 years. In patients with ureterohydronephrosis without valves, bladder disorders were not found. I assume that these changes can be categorized into stages of the disease, which are present until ablation, becoming much more expressed after the age of 5-6 years. In some cases, in children with infravesical obstruction can be detected some various neurological disorders, found by us in 7 cases of the study group [10].

I would mention that the neurogenic dysfunction of the bladder, detected after the age of 4-5 years, can be present in younger children, but it is not always established due to an obvious symptomatology. Later, the children become more sociable, they alone can appreciate the urination disorders, the complications become more obvious, the parents addressing themselves with concrete accusations, which at the beginning they did not pay due attention to. The compensatory efforts made by the body to synchronize urinary propulsion reach a phase of exhaustion, followed by the onset of mild symptoms of urodynamic disorders, with chronic kidney disease, recurrence of urinary tract infection, caused by the consequences of neurogenic obstruction, intravesical hypertension, in the bladder and upper urinary tract, with the development of a dilated ureter, vesico-renal reflux.

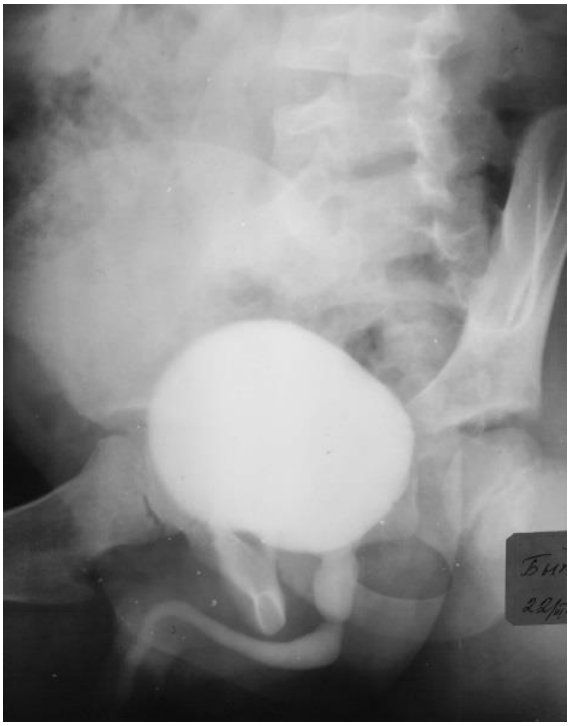

Fig. 5. Patient N., 3 years. Urinary cystourethrography: VUP; the prostate segment of the urethra is clearly dilated

Fig. 6. Patient V., 4 years. Urinary cystourethrography: stenosis of the posterior urethra. Posterior urethra dilated proximally by stenosis of the bulbar segment

Treatment

In the case of the newborn with VUP, it is recommended: to ensure the bladder drainage (gastric tube 5,6,8 Fr., suprapubic catheter); ensuring the venous approach; monitoring of renal function (serum creatinine value); ensuring the hydro-electrolytic balance (monitoring of transient polyuria, correction of metabolic acidosis; prophylaxis / treatment of UTI; endoscopic resection of VUP / temporary urine derivations [27].

Endoscopic valve ablation is the postnatal treatment of choice for VUP, aiming to resolve the obstruction, maintain renal function and achieve adequate urinary flow. However, lower urinary tract dysfunction is a common finding after VUP ablation in children [24]. Although after the correction of the valve and neurogenic dysfunction the kidney function improves, in some cases postoperatively the reflux on the contralateral side can develop. In cases where urethral obstruction predominates, signs of diurnal urination are associated with enuresis. The child tries to prevent this by restraint maneuvers, by voluntary contraction of the pelvic floor, urine is eliminated in small amounts so drink less fluid. Subsequently, muscle spasm, present in the first months of life, is associated with urinary tract infection and urinary tract dilation.

Long-term treatment with anticholinergic medication (oxybutynin 0.1-0.15 mg / kg 2 times / day) can contribute to the development of constipation, increased bladder residue, dry mucous membranes, sometimes aggression

Endoscopic treatment, especially in cases of reflux, did not positively influence the improvement of functional results. For this reason, it is recommended to initially remove the obstruction, then to resort to non-implantation or the simultaneous performance of both procedures. We performed the valve ablation with the urethoma proposed by us, which turned out to be quite safe. Removal of the valve can be performed transvesically with or without sectioning of the pubic symphysis (Gross), transsymphysis with the opening of the posterior urethra (Millin) or with the help of a hard probe with perineal destruction, endoscopic resection or retrograde bladder, balloon catheter crushing. We note that the original urethrotome proposed allows the ablation of the valve practically without complications in 4-5 min. Potential complications may include persistence of the valve and scarring of the resection, in some cases a significant increase in urinary flow.

In severe cases, surgical treatment includes a prior derivation of urine by cystostomy or transcutaneous nephrostomy. After 4-6 weeks, valve excision was used, using one of the suprapubic, perineal or endoscopic resection. In cases of reflux, the ureters were reimplanted, using the anti-reflux procedure after Cohen, Leadbetter Politano, which allowed the shortening and narrowing of the dilated ureters. Nephrectomy was necessary in one kidney with marked hydronephrotic atrophy, the other kidney having a satisfactory function. In the postoperative period, treatment with uroseptics and periodic control is indicated, which will include urine culture, origography, cystography, ultrasound, renoscintigraphy. Assessment of serum urea and creatinine levels is a true prognostic indicator in the postoperative evolution of VUP [24].

Conclusions:

- Posterior urethral valves are considered as one of the most common causes of infravesical obstruction, probably in the top of the valves are included SCUP (organic and neurogenic form) as type IIIa of the valves.
- Stenosis is located in the distal part of the posterior urethra with dilation of the urethra throughout; in cases of VUP the obstruction is located in the proximal, prostatic part of the urethra with dilation of the urethra in the proximal segment.
- Suprastenotic urinary tract disorders are identical. From our experience we found that the clinical evolution in VUP is comparatively more serious, it is highlighted earlier in newborns and infants, while in cases of stenosis - more frequently after 1 year.
- Also due to the inclusion of SCUP as valves, neurological signs appear in these patients at 5-6 years of age. According to our data, they are also present in newborns and infants, not being pronounced, we do not diagnose them, we do not treat them.
- These neurological signs with age worsen, the child at 5-6 years becomes more sociable, can alone appreciate urinary disorders, on examination the complications are obvious.
- The treatment of choice in VUP is transurethral resection.
- All patients with VUP need long-term monitoring until adolescence. The prognosis depends on the suprastenotic changes and the degree of bladder dysfunction at the address.

REFERENCES

1. Alsaywid B.S., Mohammed A.F., Jbril S.M., Bahashwan M., Mukharesh L., Al Khashan M. Renal outcome among children with posterior urethral valve: when to worry? Urol. Ann. 2021. 13(1):30-5.
2. Androulakakis P.A. Miogenic bladder decompensation in boys with posterior uretral valves may be secondary to bladder neck obstruction BJU Int. 2005. 1:140-3.
3. Bernardes L.S., Aksnes G., Saada J., Masse V., Elie C. et al., Keyhole sign: how specific is it for the diagnosis of posterior urethral valves? Ultrasound Obstet. Gynecol. 2009. 34(4):419-23.
4. Bilgutay A.N., Roth D.R., Gonzales E.T., Janzen N., Zhang W. et al. Posteior urethral valves: rosk gactors for progression to renal failure. J. Pediatr. Urol. 2016. 12(3):179-
5. Bulucea D., Georgmaneanu M. Manual de pediatrie. 2000. Vol. .II. 241 p.
6. Chan E.P., Wang P.Z.T., Dave S. Valve bladder syndrome associated with posterior urethral valves: natural history, work-up, and management. Curr. Bladder Dysfunct. Rep. 2020. 15:76-82. https://doi.org/10.1007/s11884-020-00577-1
7. Ciofu E.P., Ciofu C. Tratat de pediatrie Ed.1. 2001. pp.726-8.
8. Coquillette M., Lee R.S., Pagni S.E., Cataltepe S., Stein D.R. Renal outcomes of neonates with early presentation of posterior urethral valves: a 10-year single center experience. J. Perinatol. 2020. 40(1):112-7.
9. Curajos B. Diagnosticul și tratamentul chirurgical diferenciat al stenozei congenitale a uretrei posterioare și consecințelor ei la copii. Autoref. tezei de doctor hab. în șt. med. Chișinău. 1997. 28 p.
10. Curajos B. Compendiu de urologie pediatrică. Chișinău. 2018. p.202-6.
11. Dewan P.A. Congenital posterior urethral obstruction: the historical perspective. Pediatr. Surg. Int. 1997. 12:86-94.
12. Heikkilä J. Posterior urethral valves. Early features and renal outcome. Academ. Diss. Helsinki 2015. 69 p.
13. Herbs K.W., Tomlinson P., Lockwood G., Mosha M.H., D'Alessandri-Silva C. Survival and kidney outcomes og children with an early diagnosis of posterior urethral valves. Clin. J. Am. Soc. Nephrol. 2019. 14(11):1572-80.
14. Hodges S.J., Patel B., McLorie G., Atala A. Posterior urethral valves. Sci. World J. 2009. 9:1119-26.
15. Hydrycks A., Delatte L. Prenatal diagnosis of congenital renal and urinary tract malformation. Facts View. Vis. Obgyn. 2011. 3(3):165-74.
16. Hynes P.J., Fraher J.P. The development of the male genitourinary system: II. The origin and formation of the urethral plate. Brit. Assoc. Plast. Surg. 2004. 57:112-21.
17. Kihara T., Nakai H., Mori K., Sato R., Kihara S., Yasuda K. Variety of congenital urethral lesions in boys with lower urinary tract symptoms and the results of endoscopic treatment. Int. J. Urol. 2008. 15(3):235-40.
18. Krishnan A., De Souza A., Konijeti R., Baskin L.S. The anatomy and embryology of posterior uretral valves. J. Urol. 2006. 175:1214-20.
19. Levin T.L., Han B., Little B.P. Congenital anomalies of the male urethra. Pediatr. Radiol. 2007. 37:851-62.
20. Manzoni C., Valentini A.L. Posterior urethral valves. Rays. 2002. 27(2):131-4.
21. Mohamed A.O., Eradi B., Owen A., Rajimwal A. Rare associations with posterior urethral valves. Hindawi Case Rep. Urol. 2021. Art. ID 6647692. 4 p. https://doi.org/10.1155/2021/6647692.
22. Nakamura S., Hyuga T., Kawai S., Kubo T., Nakai H. The endoscopic morphological features of congenital posterior urethral obstructions in boys with refractory daytime urinary incontinence and nocturnal enuresis. Eur. J. Pediatr. Surg. 2016. 26(4):368-75.
23. Nasir A.A., Ameh E.E., Abdur-rahman L.O., Adeniran J.O., Abraham M.K. Posterior urethral valve. Word J. Pediatr. 2011. 7(3):205-16.
24. Shields L.B.E., White J.T., Mogamed A.Z., Peppas D.S., Rosenberg E. Delayed presentation of urethral valves: a diagnosis that should be suspected despite a normal prenatal ultrasound. Glob. Pediatr. Health. 2020. 7:2333794X20958918. doi: 10.1177/2333794X20958918.
25. Talabi A.O., Sowande O.A., Etonyeaku A.C., Salako A.A., Adejuyigbe O. Posterior urethral valves in children: pattern of presentation and outcome of initial treatment in lle-Ife, Nigeria. Niger. J. Surg. 2015. 21(2):151-6.
26. Tambo F.F.M., Tolefac P.N., Ngowe M.N., Minkande J.Z. et al. Posterior urethral valves: 10 years audit of epidemiologic, diagnostic and therapeutic aspects in Yaoundé gynaeco-obstetric and paediatric hospital. BMC Urology. 2018. 18:46. https://doi.org/10.1186/s12894-018-0364-1.
27. Țîrlea S., Ionescu S. Considerente privind diagnosticul și tratamentul primar al valvelor de uretră posterioară. Chirurgia. 2012. 107:218-25.
28. Гурская А.С. Диагностика и лечение новорождннных и детей раннего возраста с клапанами задней уретры. Андрол. и Генит. Хир. 2014. 15(2):44-7.

Conflicts of interest: *authors have no conflict of interest to declare*

Research Article

Peculiarities of morphopathological diagnosis of skin mucinosis in children

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Abstract

Particularitățile diagnosticului morfopatologic în mucinoza cutanată la copii

Background: Afecțiunile cutanate sunt frecvente manifestări ale exteriorizării pielii, inclusiv primare în cadrul unor dereglări funcționale sau preexistente metabolice. Diagnosticul metabolismului glucidic prin afectarea pielii poate fi primul semn a evoluției tulburărilor metabolice. Printre grupurile diverse ale afecțiunilor cutanate metabolice se înscriu și mucinozele cutanate, caracterizate prin depozite de mucină focal sau generalizat printre fibrele de colagen în dermul pielii, variind de la focare mici lezionale cosmetice, până la afecțiuni grave sistemice de organe. Ca regulă, acestea sunt mai frecvent diagnosticate la vârsta adultă, datorită precauției personale estetice ale pacientului și mult mai rarisim atestate la copii, dat fiind faptul că este mai dificilă utilizarea diagnosticului prin *panci* biopsie a manifestărilor reactive sau patologice cutanate, precum și complexitatea acestora prin diversitatea frecventă a dermatitelor nemetabiolice polietiologice la această perioadă de vârstă. Diagnosticul și gestionarea mucinozelor cutanate la copii este, de asemenea, o provocare dificilă și confuză din cauza lipsei de cunoștințe științifice adecvate sau a recomandărilor bazate pe dovezi.
Material and methods: Materialul de studiu a servit probele tisulare cutanate prelevate de la o pacientă la vârsta de 17 ani cu apariția erupților cutanate papulomatoase în regiunea lombară în diagnostic clinic prezumtiv de mucinoză papuloasă. Probele tisulare au fost examinate morfologic conform planului de examinare cu aplicarea metodei histologice prin colorație uzuală cu hematoxilină-eozină și histochimice: van Gieson cu picrofuxină, albastru alcian în scopul cercetării particularităților componentei conjunctive fibrilare și atestării depozitărilor de mucină intradermală.
Results: La revizia externă, erupții cutanate multiple în regiunea lombară, unilaterale pe dreapta, dimensiuni 3-4 mm, în formă de papule, culoare roșie-cianotice, durata de expunere 2 luni. La revizia macroscopică a bioptatului cutanat cu dimensiunile de 0,5x0,2x0,2 cm sau atestat papule de culoare cafenie/surie. La examenul microscopic depozite mucinoase printre fibrele de colagen la nivelul stratului papilar, procese fibrosclerotice în stratul reticular al dermului cu reactivitate ușoară proliferativă din partea fibroblastelor, infiltrate limfo-histiocitare perivasculare ale vaselor patului microcirculator cu vasculopatie și reacție pozitivă la mucină la nivelul peretelui vascular.
Conclusions: Biopsia cutanată reprezintă o metodă invazivă cu impact deosebit în diagnosticul diferențiat ale exteriorizărilor cutanate și suspectate în dereglările metabolice, în particular la copii, cu aplicarea metodelor complexe de examinare conform unui procedeu standard. Aplicarea investigației histochimice cu albastru alcian reprezintă o metodă de elecție în determinarea mucinei intradermale ca indice principal histopatologic în dereglările metabolismului glucidic. Importanța cazuisticii raportate a constituit-o atestarea vasculopatiei pozitive la mucină (albastru alcian: ++/+++) concomitent cu testul pozitiv (+++) intradermal.

Cuvinte cheie: mucinoză cutanată, mucină, papule cutanate.

Abstract

Background: Skin conditions are a common exteriorization of diseases, and can be primary in functional or pre-existing metabolic disorders. Skin lesions can induce the suspicion of carbohydrate metabolism disorders and they may be their first sign. Among the various metabolic skin diseases are cutaneous mucinoses, characterized by focal or generalized mucin deposits among collagen fibers in the dermis of the skin; manifestations ranging from small foci of cosmetic lesions to severe systemic organ disease. As a rule, they are more frequently diagnosed in adults, due to the esthetic inconveniences and much rarer in children, given that it is more difficult to use the diagnosis by punch biopsy of reactive or pathological skin lesions and the frequent incidence of non-metabolical polyethiological dermatitis at this age. The diagnosis and management of cutaneous mucinoses in children is also a difficult and confusing challenge due to a lack of adequate scientific knowledge or evidence-based recommendations.

Material and methods: We examined several skin tissue samples taken from a 17-year-old patient with papulomatous rashes in the lumbar region and a presumptive clinical diagnosis of papular mucinosis. Tissue samples were examined morphologically using the histological method which included routine staining (hematoxylin-eosin) and histochemical staining (van Gieson with picrofuchsin, Alcian blue) which allowed to investigate the peculiarities of the fibrillar connective component and detection of intradermal mucin deposits.

Results: Visual inspection revealed multiple rashes in the lumbar region, unilateral, on the right side, 3-4 mm in size, papule-shaped, of a red cyanotic color, which appeared 2 months ago. The skin biopsy was the size of 0.5x0.2x0.2 cm. Its macroscopic examination attested grayish brown papules. During microscopic examination, we found mucin deposits among collagen fibers in the papillary layer, fibrosclerotic processes in the reticular layer of the dermis with mild proliferative reactivity of fibroblasts, perivascular lymphohistiocytic infiltrates of microcirculatory bed vessels with vasculopathy and positive reaction to mucin in the blood vessels' walls.

Conclusions: Skin biopsy is an invasive method with a significant impact on the differential diagnosis of primary skin lesions and secondary lesions in case of metabolic disorders, especially in children, with the application of complex examination methods according to a standard procedure. The application of histochemical investigation with Alcian blue is a method of choice in determining intradermal mucin as the main histopathological index of carbohydrate metabolism disorders. The importance of the presented case was the confirmation of mucin-positive vasculopathy (Alcian blue: ++ / +++) simultaneously with the positive (+++) intradermal test.

Keywords: cutaneous mucinosis, mucin, skin papules.

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Introduction

Skin conditions are a common exteriorization of diseases, and can be primary in functional or pre-existing metabolic disorders. Skin lesions can induce the suspicion of carbohydrate metabolism disorders and they may be their first sign [3]. Among the various metabolic skin diseases are cutaneous mucinoses, characterized by focal or generalized mucin deposits among collagen fibers in the dermis of the skin; manifestations ranging from small foci of cosmetic lesions to severe systemic organ disease [5]. Cutaneous mucinoses are a heterogeneous group of disorders in which there is an abnormal amount of mucin accumulated in the skin with uncertain etiopathogenesis [6]. As a rule, they are more frequently diagnosed in adults, due to the esthetic inconveniences and much rarer in children, given that it is more difficult to use the diagnosis by punch biopsy of reactive or pathological skin lesions and the frequent incidence of non-metabolical polyethiological dermatitis at this age. The diagnosis and management of cutaneous mucinoses in children is also a difficult and confusing challenge due to a lack of adequate scientific knowledge or evidence-based recommendations.

The given work is a report of a rare case of cutaneous manifestations, the only one registered in the last 10-15 years and confirmed by the morphopathological diagnosis. These manifestations can be related to the syndrome of functional disorders and unclear clinical conditions linked to the disrupted carbohydrate metabolism in children.

Aim of the study: To reveal the importance of skin biopsy in case of visible/ suspected skin lesions linked to metabolic disorders in children.

Material and methods

We examined several skin tissue samples taken from a 17-year-old patient with papulomatous rashes in the lumbar region and a presumptive clinical diagnosis of papular mucinosis. Tissue samples were examined morphologically using the histological method which included routine staining (hematoxylin-eosin) and

histochemical staining (van Gieson with picrofuchsin, Alcian blue) which allowed to investigate the peculiarities of the fibrillar connective component and detection of intradermal mucin deposits.

Results

According to the medical records, the very first papulomatous rashes appeared on the body of the child almost 2 months ago. They poped up in the inferior lumbar region on the right side, had a red-cyanotic color, with sizes ranging from 3 to 4 mm. There was no itching. The macroscopic examination of the tissue sample (0.5x0.2x0.2 cm) attested grayish brown papules on the epidermis. We then performed a hematoxylin-eosin staining which revealed prominent bundles of collagen fibers, nodular microfocus of collagen fibers in the reticular layer of the dermis with a wavy irregular appearance, accompanied by a slightly accentuated interfascicular edema (fig. 1).

The papillary layer was moderately thickened, with wavy collagen fibers and a transparent organic mass. The lymphohistiocytic infiltrates were located in the perivascular regions of the microcirculatory bed and were more prominent in the upper layer of dermis. The blood vessels walls were moderately thickened and endothelium was swelled. The staining with van Gieson and picrofuchsin confirmed fibrosclerotic changes of dermis (fig. 2).

We also did a staining with Alcian blue in order to confirm or exclude the presence of any deposits among the collagen fibers. In given case, the detected organic mass had an obvious basophilic staining , more prominent in the papillary layer of dermis. We also detected a positive basophilic reaction in the blood vessels' walls (fig. 3).

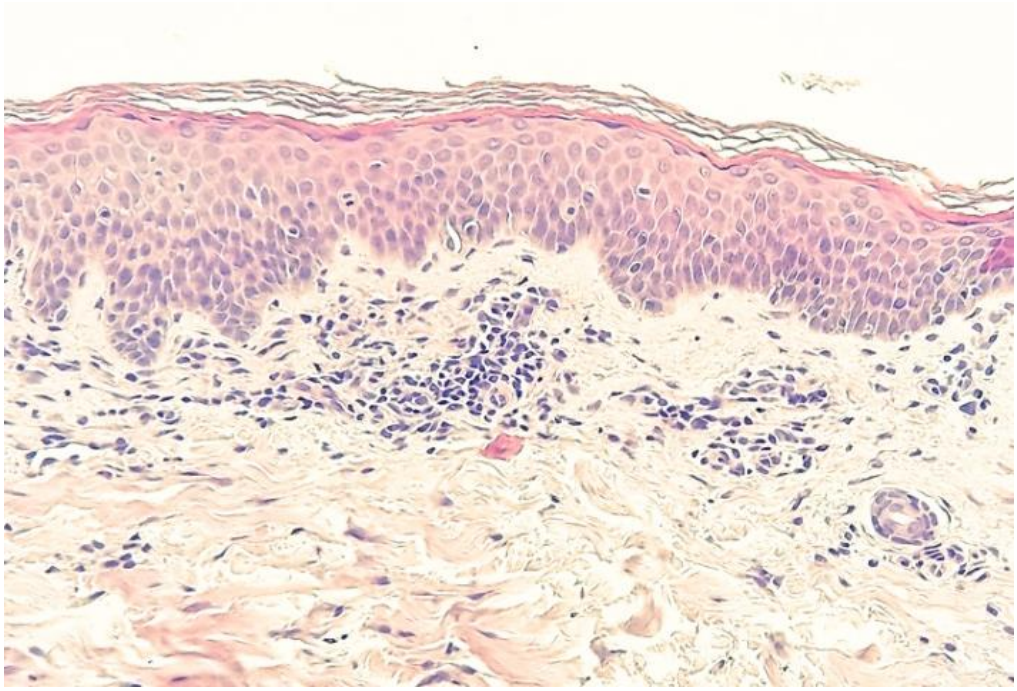

Fig. 1. Skin biopsy. Increased collagenization of dermis layers with a multifocal lymphohistiocytic infiltrate. Staining: hematoxylin-eosin. x100.

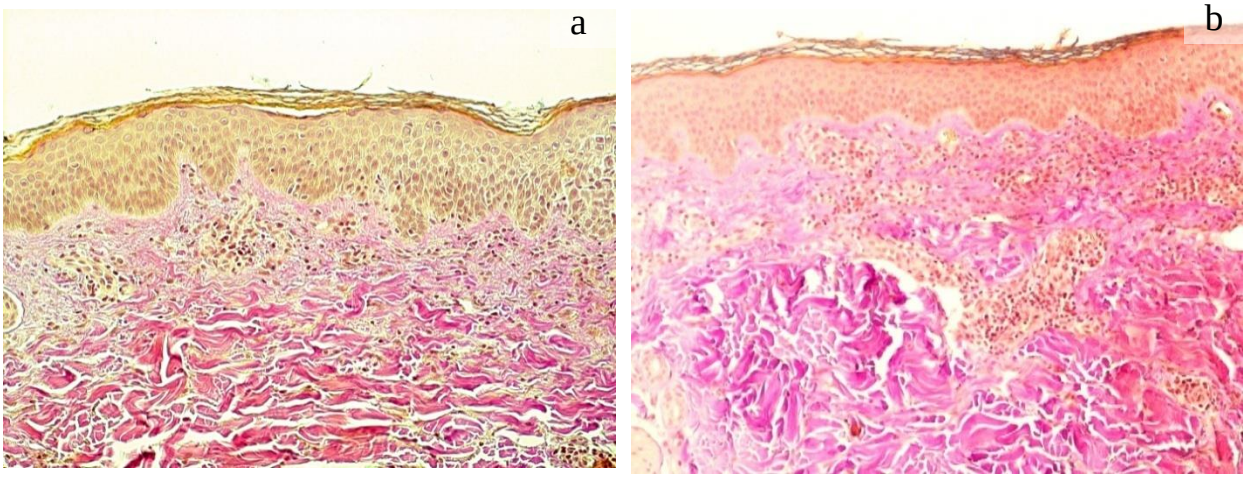

Fig. 2. Skin biopsy: a) Fascicular pattern of collagenization in the reticular layer of dermis. b) Nodular pattern of collagenization in dermis; a, b) Enlarged interfascicular spaces. Staining: van Gieson with picrofuchsin, x 100.

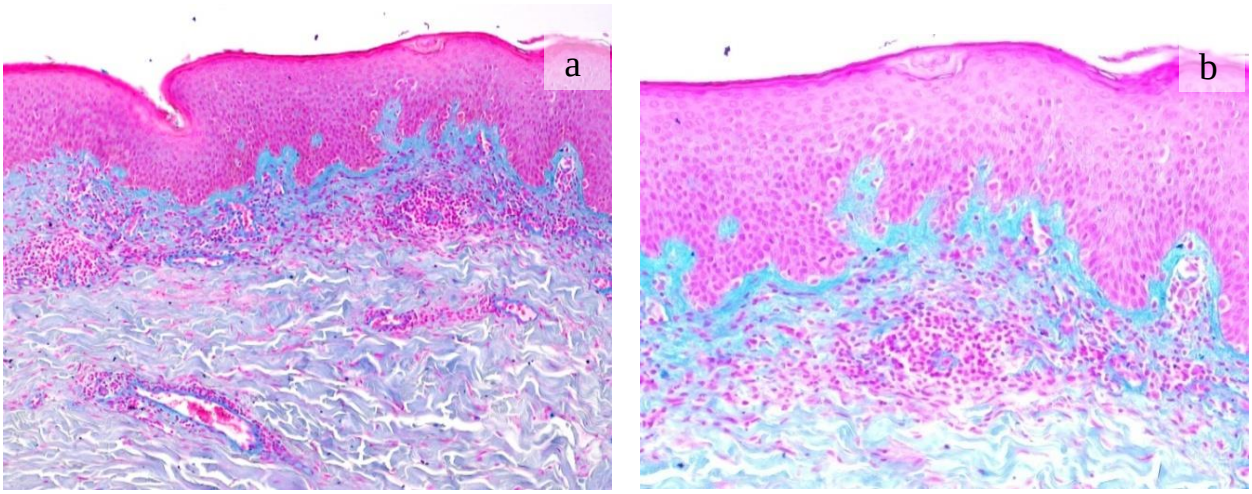

Fig. 3. Skin biopsy. Increased basophilic staining of the papillary layer of dermis. Basophilic staining of blood vessels' walls. Multifocal and perivascular lymphohistiocytic infiltrates. Staining: alcian blue, a) x100, b) x200

Discussion

Skin conditions are a common exteriorization of diseases, and can be primary in functional or pre-existing metabolic disorders. Skin lesions can induce the suspicion of carbohydrate metabolism disorders and they may be their first sign [3]. Among the various groups of metabolic skin diseases are cutaneous mucinoses, characterized by focal or generalized mucin deposition among collagen fibers in the dermis of the skin [6]. Cutaneous mucinoses are a heterogeneous group of disorders in which there is an abnormal amount of mucin accumulated in the skin and their etiopathogenesis is still unknown [3]. Conditionally, cutaneous mucinoses are divided into the following types: primary mucinosis – the storage of intradermal mucin with cutaneous characteristics and secondary mucinosis - attestation of mucin storage as a result of other diseases. The last group includes: endocrinopathies, toxic diseases (toxic oil syndrome), eosinophilic myalgia syndrome, nephrogenic fibrosing dermopathy, diffuse connective tissue diseases (lupus erythematosus, etc.) [1, 2, 5]. The most recent classification of dermal mucinosis was developed by Rongioletti F., Rebora A. in 2001, who differentiated two main groups of dermal mucinosis: scleromixedema

(generalized form) and myxedematous lichen (localized form) [5]. A great importance is attributed to diabetes, which is a common disease involving the skin by disrupting carbohydrate metabolism. Between thirty and seventy percent of patients with diabetes, both type 1 and type 2, will have a skin complication of diabetes at some point in their lives [4]. Thus, early findings of skin changes may provide insight into glycemic control in patients and may be the first sign of metabolic disorders in patients with diabetes. In our case, according to the findings, we tend to mention that diabetic vasculopathy with papular cutaneous expression in children has both generalized and focal character.

Conclusions.

Skin biopsy is an invasive method with a significant impact on the differential diagnosis of primary skin lesions and secondary lesions in case of metabolic disorders, especially in children, with the application of complex examination methods according to a standard procedure. The application of histochemical investigation with Alcian blue is a method of choice in determining intradermal mucin as the main histopathological index of carbohydrate metabolism disorders. The importance of the presented case was the confirmation of mucin-positive vasculopathy (Alcian blue: ++/+++) simultaneously with the positive (+++) intradermal test.

REFERENCES

1. Cervigón-González I., Torres-Iglesias L.M., Palomo-Arellano A., Sánchez-Díaz E. Papules on the dorsum of the hands. Actas Dermosifiliogr. 2008. 99:731-2.
2. Favarato M.H., Miranda S.S., Caleiro M.T., Assad A.P., Halpern I., Fuller R. Cutaneous mucinosis in mixed connective tissue disease. Bras. Dermatol. 2013. 88:635-8.
3. Kang-Ling K., Li-Yu L., Tseng-Tong K. Solitary cutaneous focal mucinosis: A clinicopathological study of 11 cases of soft fibroma-like cutaneous mucinous lesions. Japanese Dermatol. Assoc. 2016. 44(3):335-8.
4. Meurer M., Stumvoll M., Szeimies R-M. Hautveränderungen bei diabetes mellitus. Der Hautarzt. 2004. 55(5):428-35.
5. Rongioletti F., Rebora A. Cutaneous mucinoses. Microscopic criteria for diagnosis. Am. J. Dermatopathol. 2001. 23:257-67.
6. Rongioletti F. A review of cutaneous mucinoses in children. Brit. J. Dermatol. 2020. 182:29-38.

Conflicts of interest: *authors have no conflict of interest to declare*

Case Report

Kidney atrophy after retroperitoneal neuroblastoma resection in children. Clinical case presentation and literature review

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Abstract

Atrofia renală după rezecția neuroblastomului retroperitoneal la copil.
Prezentare de caz clinic și revista literaturii

Neuroblastomul (NB) reprezintă cea mai frecventă tumoră solidă malignă extracraniană la copii. În cazurile unui tratament chirurgical radical asociat cu chimioterapie și/sau radioterapie există riscul dezvoltării unor complicații tardive, inclusiv cele renale ipsilaterale. În acest context autorii prezintă următorul caz clinic.
Pacienta E., în vârstă de 3 ani, a fost internată pentru o formațiune tumorală abdominală depistată la ecografie abdominală și confirmată la CT spiralată cu contrast a abdomenului, diagnosticul imagistic fiind sugestiv pentru o formațiune tumorală retroperitoneală fără semne clare de agresiune, posibil ganglioneurom; pieloectazie stângă moderată.
Copilul a fost supus intervenției chirurgicalet. Sub anestezie endotraheală generală s-a efectuat o laparotomie transrectală stângă, cu îndepărtarea completă a tumorii fără leziunea capsulei tumorii și vasele renale cu păstrarea rinichiul stâng. Ulterior, a fost exciziată a doua formațiune. Tratamentul chimioterapeutic a fost tolerat relativ satisfăcător, cu dezvoltarea agranulocitozei moderate. După a treia serie de chimioterapie, examenul ecografic a constatat micșorarea în volum a rinichiului stâng. La RMN, efectuată după a patra serie de chimioterapie, a pus în evidență lipsa recidivei tumorii, aspectul hipoplazic al rinichiul stâng, care avea dimensiuni de 36 x 15 mm, cu pierderea diferențierii stratului cortico-medular. Secvențele postcontrast au atestat contrastarea slabă a parenchimului renal stâng.
Concluzie. Intervenția chirurgicală radicală urmată de chimioterapie a permis de a asigura un control local benefic în neuroblastomul retroperitoneal slab diferențiat cu metastaze în ganglionii limfatici regionali la un copil cu vârsta peste 18 luni. În cazurile de rezecție radicală a neuroblastomului retroperitoneal de dimensiuni majore există riscul dezvoltării unor complicații postoperatorii renale, inclusiv a atrofiei renale. Dislocarea rinichiului cu comprimarea tumorală a hilului renal, inclusiv a vaselor renale, poate fi considerat un factor de risc predictor de dezvoltare a atrofiei renale postoperatorii ipsilaterale la copiii cu neuroblastom retroperitoneal de dimensiuni majore.

Cuvinte cheie: neuroblastom retroperitoneal, chirurgie, complicații, atrofie renală, copii

Abstract

Neuroblastoma (NB) is the most common extracranial malignant solid tumor in children. In cases of radical surgical treatment associated with chemotherapy and / or radiotherapy there is a risk of developing late complications, including ipsilateral renal complications. In this context, the authors present the following clinical case.

Patient E., aged 3 years, was hospitalized for an abdominal tumor formation detected on abdominal ultrasound and confirmed on spiral CT with contrast of the abdomen, the imaging diagnosis being suggestive for a retroperitoneal tumor formation without clear signs of aggression, possibly ganglioneuroma; moderate left pyeloectasia. The child underwent surgery. Under general endotracheal anesthesia, a left transrectal laparotomy was performed, the tumor was completely removed without injuring the tumor capsule and renal vessels while keeping the left kidney in place. Subsequently, the second mass was excised. Chemotherapeutic treatment was relatively well tolerated with the development of moderate agranulocytosis. After the third cycle of chemotherapy, the ultrasound examination revealed a reduction of the left kidney. On MRI, performed after four courses of chemotherapy, there were not signs of recurrence, the left kidney was hypoplastic, (the size 36 x 15 mm), with loss of cortico-medullary layer differentiation. Postcontrast sequences showed poor contrasting of the left renal parenchyma.

Conclusion. Radical surgery followed by chemotherapy ensured a beneficial local control in poorly differentiated retroperitoneal neuroblastoma with metastases in the regional lymph nodes in a child over 18 months of age. In cases of radical resection of major retroperitoneal neuroblastoma there is a risk of developing postoperative renal complications, including renal atrophy. Dislocation of the kidney with tumor compression of the renal hilum, including the renal vessels, may be considered a predictive risk factor for the development of ipsilateral postoperative renal atrophy in children with major retroperitoneal neuroblastoma.

Keywords: **retroperitoneal** neuroblastoma, surgery, complication, kidney atrophy, children

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Neuroblastoma (NB) is the most common extracranial malignant solid tumor in children [30, 42], this embryonic neoplasm originating from the primitive neuroectodermal cells of the neural crest from which the sympathetic nervous system and adrenal medulla are differentiated [16, 35]. NB can be located in the cervical, intrathoracic, intra-abdominal, retroperitoneal or pelvic regions [5].

This heterogeneous tumor represents about 8-10% of all cases of malignancies and 15% of the total number of deaths in children with various forms of cancer, with an estimated incidence of 1 case per 10,000 live births [4, 17, 24]. The average age of onset of the disease is 18 months [53]. In the morbidity structure of children up to 1 year of age, NB constitutes about 26% of malignant tumors [52]. About 50% of NB cases are diagnosed in children up to the age of 2 years [53], over 90% of cases being found in the first 5 years of life, with different clinical behaviors such as: progressive evolution and metastasis, spontaneous regression or maturation in ganglioneuroma, this phenomenon being first described in 1927 by Cushing H. and Wolbach S.B. [22, 31, 53]. Over 50% of children with NB have metastatic disease [49]. After the age of 15 years and in adults it is described as a rare entity [27, 46]. Usually, neuroblastoma is a sporadic tumor, but 1-2% of patients have a family history of the disease [1]. The prognosis of this neoplasm varies depending on the stage and the biological and morphopathological characteristics of the tumor [26]. Low and intermediate risk forms of NB have been well managed being surgically resolved, long-term survival rates being about 90%, while in high-risk forms the total survival rate of five years after multimodal surgical and non-surgical treatment is about 40% -50% [39]. At the same time, in cases of radical surgical treatment associated with chemotherapy and / or radiotherapy there is a risk of developing of late complications, including ipsilateral renal complications, such as renal hypoplasia or even insidious ipsilateral renal atrophy with the development of renal failure [14, 20, 21]. In this context we present the following clinical case.

Patient E., 3 years old, was consulted at the end of 2019 for intermittent abdominal pain at the PHI Mother and Child Institute consultative center, where an abdominal ultrasound showed an abdominal tumor. The contrasting spiral CT of the abdomen revealed the presence of a massive solid tumor, located retroperitoneally on the left (Th11-L3), was polylobulated, well contoured with the following size - 7.2 cm (vertical) x 6.2 cm (transverse) x 4, 5 cm (anterior-posterior). Texturally heterogeneous, the tumor contained multiple hypodense areas (possibly necrolithic), intrastromal calcinations, without invasion in the spinal canal, the native density being + 40UH with post-contrast amplification in the late phase + 62UH. The afferent and efferent vessels were undetectable. The mass effect was characterized by posterior dislocation of the

left kidney with moderate compression of the renal hilum, moderate dilation of the left renal pelvis. The left renal artery was posteriorly displaced, renal vein - caudally dislocated, and an anterior displaced supernumerary artery participated in vascularization of the lower pole of the kidney. Also the moderate upper displacement of the pancreas, spleen artery and vein was found out, without clear signs of invasion, and CT image was suggestive of a left sided retroperitoneal tumor without signs of aggression, possibly ganglioneuroma; moderate left pyeloectasia (fig. 1).

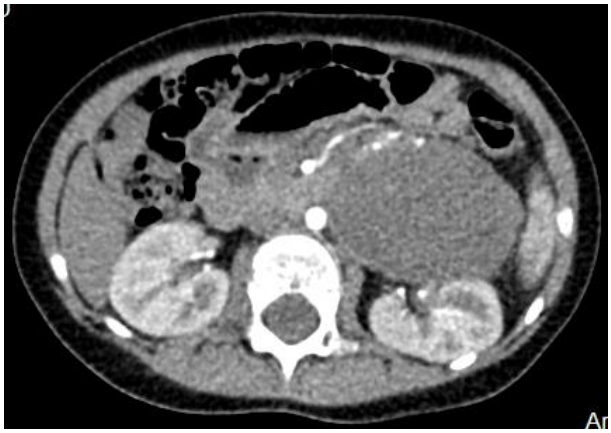


Fig. 1. Patient E., 3 years. Contrasted spiral CT of the abdomen (explanations in text)

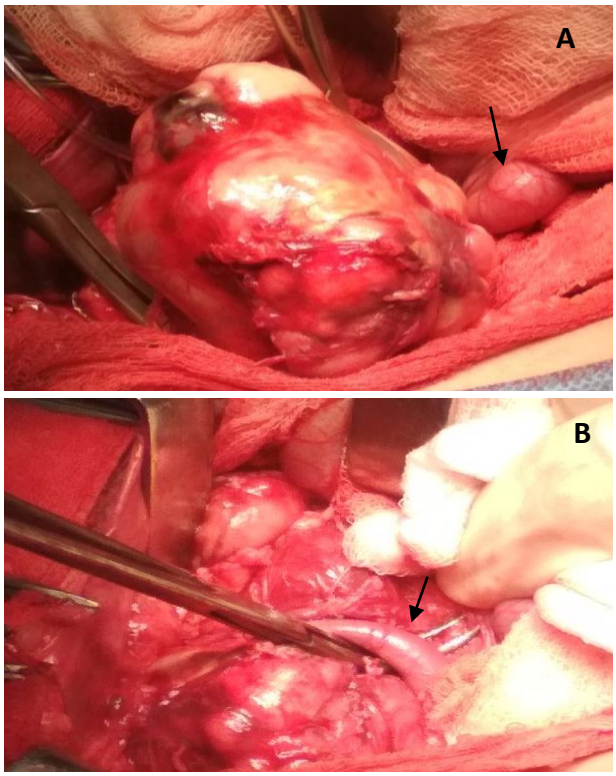


Fig. 2. Intraoperative appearance of retroperitoneal tumor after mobilization (A) with a smaller adjacent mass (arrow); B - blood vessel crossing the lower pole of the tumor (arrow)

With the diagnosis described above, the child was hospitalized. It was found out that the child complained of abdominal pain for half a year. The child was afebrile without vomiting and fever. Other diseases were not diagnosed. On inspection, the abdomen was normal, palpation revealed a hard consistency tumor, which was painless, adherent to the deep planes and located in the left flank. The peripheral lymph nodes were of normal size. Chest radiography didn't show pathological changes, except the fact that in the left axillary fossa, in the lymph nodes were found impregnations of calcium salts which was treated as BCG sequelae. Hematological and urine lab tests were without any significant pathological changes. The child underwent surgery. Under general endotracheal anesthesia, a left transrectal laparotomy was performed. After opening the peritoneal cavity and the left retroperitoneal space, the surgical exploration found an oval encapsulated tumor (fig. 2A), circumferentially vascularized from multiple sources, which compressed the left kidney and renal vessels without involving the adrenal gland. The lower edge of the tumor was crossed by a medium-sized blood vessel, which was participating in the vascularization of the lower pole of the kidney (fig. 2 B). Below the tumor, another mass was observed, measuring 1.2 x 1.0 cm. After careful mobilization of adjacent tissues by combining the blunt dissection and the electrocoagulator, the tumor was completely removed without injuring the tumor capsule and renal vessels, the left kidney was left in place. Subsequently, the second mass was excised. After hemostasis, other retroperitoneal or intra-abdominal masses or enlarged lymph nodes were not identified. The integrity of the peritoneum was restored with the application of a tubular drainage in the abdominal cavity and the restoration of the anatomical planes.

Histopathological examination established the diagnosis of poorly differentiated neuroblastoma (poor in Schwanian stroma), later confirmed by immunohistochemical investigations. Postoperative recovery was without severe complications, except for a pronounced abdominal distension developed on the 2nd postoperative day which was resolved conservatively.

The patient was discharged on the tenth day. Subsequently, the patient underwent chemotherapeutic treatment and regular supervision in the profile institution. Chemotherapeutic treatment was relatively well tolerated with the development of moderate agranulocytosis. After the third cycle of chemotherapy, the ultrasound examination found a reduction of the left kidney size, which was about 48x18 mm. On MRI, performed after the fourth course of chemotherapy, there were not signs of recurrence, the left kidney was hypoplastic, of 36 x 15 mm, with the loss of cortico-medullary layer differentiation. Postcontrast sequences showed poor contrasting of the left renal parenchyma (fig. 3).

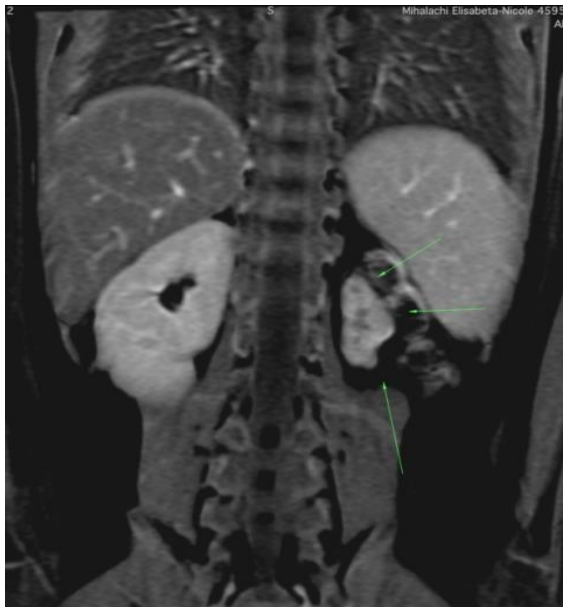
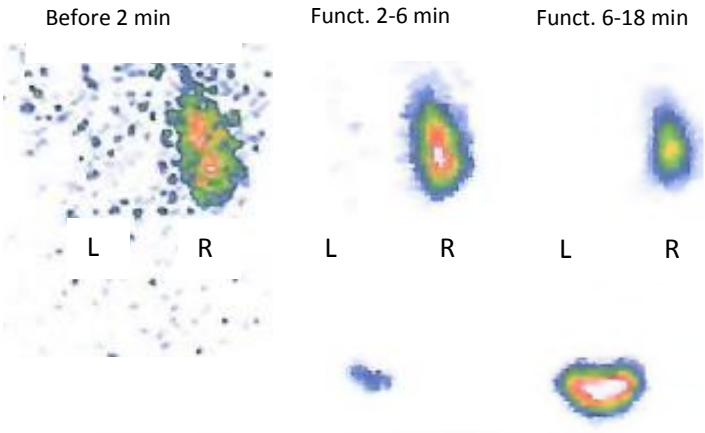


Fig. 3. Patient E., MRI performed at 6 months postoperatively. Left kidney atrophy found (explanations in text)



	Left	Right
T0 (sec):		0
Tmax:		2'30"
Thalf:		14'05"
Wash-out Thalf:		10'10"
Residual Activity:		29.9 %
Norm.Res. Activity:		29.9 %

Fig. 4. Patient E. Dynamic renal scintigraphy performed 1 year after surgery (explanations in the text).

Angiographic reconstruction did not visualize the left renal artery. One year after surgery, CT found no signs of tumor recurrence or metastasis. On dynamic kidney scintigraphy, there was a lack of function of the left kidney. The right kidney was visualized in the typical place, with clear contours and normal sizes. The accumulation of the radiopharmaceutical substance is normal, the glomerular filtration process and the evacuation of the radiopharmaceutical being within normal range (fig. 4).

Discussions. NB was first described in 1864 by Rudolf Ludwig Karl Virchow, who called it "infantile glioma", later in 1891 the German pathologist Felix Marchand found that this neoplasm originates from the sympathetic nervous system and adrenal glands. The stage IV-S of neuroblastoma, which is characterized by liver metastases without bone metastases, was described in 1901 by William Pepper. Only in 1910 that James Homer Wright has used the term of "neuroblastoma", mentioning that some retroperitoneal and posterior mediastinal tumors are morphopathologically similar to immature primitive nerve tissue. [53]

Neuroblastoma usually presents as a solid tumor mass and rarely as a cystic lesion, the latter being located almost exclusively in the adrenal gland and very rarely found in other regions [45]. Molecular and biological investigations found several distinct subtypes of neuroblastoma with genetic changes in MYCN, ALK, PHOX2, PTPN11, ATRX, NRAS, etc. [22].

In 1971, Evans et al. proposed a classification of neuroblastoma in children based on the degree of spread of the neoplastic process, with the stages I, II, III, IV and IV-S [10].

According to the international neuroblastoma staging system (INSS, 1986), 4 clinical stages are distinguished depending on the results of the surgery [29].

Stage I - localized tumor located in the initial area of development; the neoplasm can be completely surgically removed with or without residual microscopic signs; macroscopic - the absence of lymph node involvement on both sides of the spine is confirmed.

Stage 2-A - unilateral tumor with removal of most of the tumor; microscopic - absence of bilateral lymph node involvement.

Stage 2-B - unilateral tumor, completely or mostly removed microscopic - unilateral lesion of the lymph nodes.

Stage 3 - the tumor is spread contralaterally with or without metastatic lesions of the regional lymph nodes; unilateral tumor with metastases in the contralateral lymph nodes; median tumor with metastases in bilateral lymph nodes.

Stage 4 - disseminated tumor with metastases in distant lymph nodes, bone, liver and bone marrow metastases.

Stage 4S (special), described by D'Angio et al. (1971), relates to patients with localized primary tumor in stage I, IIA and IIB but with liver metastases, skin and / or bone marrow [3, 53]. Neuroblastoma in stage IV-S, is

characterized by a comparatively favorable evolution of the disease, with a high rate of spontaneous tumor regression [38].

In 2009, the International Neuroblastoma Risk Group Staging System (INRGSS), developed by a consortium from North America, Europe, Japan and Australia, is based on a preoperative assessment of certain risk factors, according to which are distinguished: *L1 stage* - localized tumor that does not involve the vital structures indicated in the list of imagistically defined risk factors and limited to a single compartment of the body; *L2 stage* - locoregional tumor with the presence of one or more imagistically defined risk factors; *M stage* - distant metastatic disease (except stage MS); *MS stage* - metastatic disease in children under 18 months with metastases in liver, skin, and / or bone marrow [29].

According to Monclair T. et al. (2009) the imagistically defined risk factors in neuroblastic tumors are:

• *Ipsilateral tumor spread inside two compartments of the body*

- Neck-chest, thorax-abdomen, abdomen-pelvis;

• *Neck*

- Tumor involving the carotid and / or vertebral artery and / or the internal jugular vein;
- Tumor that extends to the base of the skull;
- Tumor that compresses the trachea;

• *Cervico-thoracic junction*

- Tumor involving the roots of the brachial plexus;
- Tumor involving the subclavian vessels and / or the vertebral and / or the carotid artery;
- Tumor that compresses the trachea;

• *Chest*

- Tumor covering the aorta and / or major branches;
- Tumor that compresses the trachea and / or main bronchi;
- Inferior mediastinal tumor with infiltration of the costo-vertebral junction between T9 and T12;

• *Thoraco-abdominal location*

- Tumor covering the aorta and / or vena cava;

• *Abdominal-pelvic location*

- Tumor with infiltrative growth in the hepatic hilum and / or hepatoduodenal ligament;
- Tumor involving branches of the superior mesenteric artery at the level of the mesenteric root;
- Tumor involving the celiac axis and / or the superior mesenteric artery;
- Tumor that invades one or both kidney pedicles;
- Tumor covering the aorta and / or vena cava;
- Tumor covering the iliac vessels;
- Pelvic tumor covering the iliac vessels;
- Pelvic tumor that crosses the sciatic notch;

• *Intraspinal tumor extension regardless of location, provided:*

- More than one third of the axial spinal canal is invaded and / or the perimedullary leptomeningeal spaces are not visible and / or the spinal cord signal is abnormal;

• *Infiltration of adjacent organs / structures:*

- Pericardium, diaphragm, kidney, liver, duodeno-pancreatic block and mesentery;

• *Conditions that must be recorded, but which are not considered imagistically defined risk factors:*

- Multifocal primary tumors;
- Presence of pleural fluid, with or without malignant cells;
- Ascites, with or without malignant cells.

Neuroblastoma patients are stratified into very low, low, intermediate, and high-risk groups according to age, imagistically defined risk factors, and tumor biology, including: tumor histology, DNA ploidy, MYCN gene amplification, and chromosome 11q changes, treatment strategies being largely adapted to these groups [11, 32]. It should be noted that the presence of MYCN oncogenic amplification, observed in 20-30% of primary neuroblastoma cases, is a key factor in the INRG (International Neuroblastoma Risk Group) system that designates the high risk neuroblastoma, being one of the main indicators of tumor aggression, resistance to chemotherapy and a poor prognosis [39, 53]. The favorable and unfavorable histological subtypes of neuroblastoma are based on the level of Schwanian stroma present in the tumor, the mitosis-karyorexia index and the patient's age [13, 41].

The factors that determine a *favorable prognosis* are: the patient's age under 1 year, stage I, II or IVS, the absence of MYCN gene amplification and chromosomal segmental aberrations, polysomy. Factors of an *intermediate prognosis* include: the patient's age over 1 year, localized tumor with lymph nodes involvement, bone and bone marrow metastases in children under 1 year, absence of MYCN gene amplification and chromosomal segmental aberrations. *Poor prognosis* of the disease is determined by: patient age over 1 year, bone and bone marrow metastases, chromosomal segmental aberrations, such as deletions of the subtelomeric region (dellp36), long arm of chromosome 11 (del11q), enlargement of the long arm of chromosome 17 (+ 17q), amplification of the MYCN gene, morphologically undifferentiated tumor, high mitotic index [53].

Neuroblastoma treatment strategies include a combination of surgical treatment with chemotherapy, radiotherapy, myeloablative therapy, immunotherapy, stem cell use, therapeutic solutions being based on the stage of the disease, the patient's age, risk groups, etc. [7, 9, 33, 51]. Surgical resection of neuroblastoma has been shown to be effective in most low-risk cases, for intermediate-risk neuroblastoma the goal of surgery is to remove as much of the primary tumor as possible, surgical treatment being associated with pre- and postoperative chemotherapy [7, 18, 34, 49]. A

controversial issue is the role of surgical resection of the primary tumor and regional lymph nodes in patients with high-risk neuroblastoma [6, 8, 23]. Most authors emphasize the importance of resection in favor of a radical operation [8, 12, 48], some authors recommending in these cases the administration of chemotherapy before surgical resection, afterwards - the myeloablative chemotherapy [35, 36].

Surgical treatment of NB, in young children especially, presents significant risks, the rate of postoperative complications being up to 20-29%, and after repeated operations this index is 62.5% [15, 43, 50]. The literature describes postoperative renal atrophy as a complication after neuroblatom resection in children [19, 28, 50], which can have several causes, including: direct injury by kidney invasion, compression of renal vessels or ureter, spasm of renal vessels [37]. Some authors believe that dislocation of the renal artery may cause its spasm, and endothelial lesions may contribute to the stasis of renal blood flow with subsequent thrombosis of the renal artery [40, 47]. The development of renal atrophy is described even in cases of complete separation of renal vessels from the tumor, in order to reduce renal impairment being performed intraoperative monitoring of central venous pressure and urine flow, intravenous administration of electrolyte solutions, mannitol and furosemide, as well as the local application of lidocaine on the renal vessels, measures that can effectively contribute to the prevention of renal damage caused by renal vascular spasm [25]. It has been found that "tumor contact with renal vessels" is a major risk factor for the development of complications related to renal vessels, including renal atrophy [50]. It also needs to consider the nephrotoxic effect of chemotherapy and radiotherapy [42, 44], which in some cases may contribute to renal artery stenosis [2].

Conclusion.

Radical surgery followed by chemotherapy provides a beneficial local control in poorly differentiated retroperitoneal neuroblastoma with metastases in the regional lymph nodes in a child over 18 months of age. In cases of radical resection of a major retroperitoneal neuroblastoma, there is a risk of developing postoperative renal complications, including renal atrophy. Dislocation of the kidney with tumor compression of the renal hilum, including the renal vessels, may be considered a predictive risk factor for the development of ipsilateral postoperative renal atrophy in children with major retroperitoneal neuroblastoma.

REFERENCES

1. Abu-Arja R., Hashem H., El-Sheikh A., Abusin G. Neuroblastoma in monozygotic twins with distinct presentation pathology and outcome: is it familial or in utero metastasis. Pediatr. Blood Cancer. 2014. 61:1124-5.
2. Beckham T.H., Casey D.L., La Quaglia M.P., Kushner B.H., Modak S., Wolden S.L. Renal function outcomes of high-risk neuroblastoma patients undergoing radiation therapy. Int. J. Radiation Oncol. Biol. Phys. 2017. 99(2):486-93.
3. Bernardi B., Di Cataldo A., Garaventa A., Massirio P., Viscardi E. et al. Stage 4S neuroblastoma: features, management and outcome of 268 cases from the Italian Neuroblastoma Registry. Italian J. Pediatr. 2019. 45:8. https://doi.org/10.1186/s13052-018-0599-1.
4. Borriello L., Seeger R.C., Asgharzadeh S., DeClerck Y.A. More than the genes, the tumor microenvironment in neuroblastoma. Cancer Letter. 2016. 380:304-14.
5. Campagna G., Rosenfeld E., Foster J., Vasudevan S., Nuchtern J. et al. Evolving biopsy techniques for the diagnosis of neuroblastoma in children. J. Pediatr. Surg. 2018; 53:2235-9.
6. Dubbers M., Simon T., Berthold F., Fischer J., Volland R. et al. Retrospective analysis of relapsed abdominal high-risk neuroblastoma. J. Pediatr. Surg. 2018. 53:558-66.
7. Dumba M., Jawad N., McHugh K. Neuroblastoma and nephroblastoma: a radiological review. Cancer Imaging. 2015. 15:5. DOI 10.1186/s40644-015-0040-6.
8. Englum B.R., Rialon K.L., Speicher P.J., Gulack B., Driscoll T.A. et al. Value of surgical resection in children with higj-risk neuroblastoma. Pediatr. Blood Cancer. 2015. 62:1529-35.
9. Esposito M.R., Aveic S., Seydel A., Tonini G.P. Neuroblastoma treatment in the post-genomic era. J. Biomed. Sci. 2017. 24:14. DOI 10.1186/s12929-017-0319-y.
10. Evans A.E., D'Angio G.J., Randolph J. A proposed staging for children with neuroblastoma. Children's cancer study group A. Cancer. 1971. 27(2):374-8.
11. Fahy A.S., Roberts A., Nasr A., Irwin M.S., Gerstle J.T. Long term outcomes after concurrent ipsilateral nephrectomy versus kidney-sparing surgery for high-risk, intraabdominal neuroblastoma. J. Pediatr. Surg. 2019. 54:1632-7.
12. Fischer J., Poh A., Volland R., Hero B., Dubbers M. et al. Complete surgical improves outcome in INRG high-risk patients with localized neuroblastoma older than 18 monts. BMC Cancer. 2017. 17:520. DOI 10.1186/s12885-017-3493-0.
13. Fukudome N., Kimura F., Arita S., Atupelage C., Mizuguchi K. Significance of cytological findings of neuroblastomas: rosette arrangement and neuropil structure. J. Cytol. Histol. 2015. 6: 357. doi:10.4172/2157-7099.1000357.

14. Fusaro F., Cecchetto G., Boglino C., Inserra A., Zanon G.F. et al. Measures to prevent renal impairment after resection of retroperitoneal neuroblastoma. Pediatr. Surg. Int. 2002. 18: 388-91.
15. Gunther P., Holland-Cunz S., Schupp C.J., Stockklausner C., Hinz U., Schenk J.P. Signifi cance of image-defined risk factors for surgical complications in patients with abdominal neuroblastoma. Eur. J. Pediatr. Surg. 2011. 21:314-7.
16. Hassan S.F., Mathur S., Magliaro T.J., Larimer E.L., Ferrell L.B. et al. Needle core vs open biopsy for diagnosis of intermediate- and high-risc neuroblastoma in children. J. Pediatr. Surg. 2012; 47:1261-6.
17. Holub J.L., Qiu Y.Y., Chu F., Madonna M.B. The role of nerve growth factor in caspase-dependent apoptosis in human BE (2) C neuroblastoma. J. Pediatr. Surg. 2011; 46:1191-6.
18. Iehara T., Yagyu S., Tsuchiya K., Kuwahara Y., Miyachi M. et al. Residual tumor in cases of intermediate-risk neuroblastoma did not influence the prognosis. Jpn. J. Clin. Oncol. 2016. 46(7):661-6.
19. Iehara T., Yoneda A., Yokota I., Takahashi H., Teramukai S. et al. Results of a prospective clinical trial JN-L-10 using image-defined risk factors to inform surgical decisions for children with low-risk neuroblastoma disease: a report from the Japan Children's Cancer Group Neuroblastoma Committee. Pediatr. Blood Cancer. 2019. e27914. https://doi.org/10.1002/pbc.27914.
20. Kandula S., Sutter A., Prabhu R.S., Jegadeesh N., Esiashvili N. Reassessing dose constraints of organs at risk in children with abdominal neuroblastoma treated with definitive radiation therapy: A correlation with late toxicity. Pediatr. Blood Cancer. 2015. 62(6):970-5.
21. Kubota M., Yagi M., Kanada S., Okuyama N., Kinoshita Y. et al. Long-term follow-up status of patients with neuroblastoma after undergoing either aggressive surgery or chemotherapy - a single institutional study. J. Pediatr. Surg. 2004. 39(9):1328-32.
22. Kurihara S., Hiyama E., Onitake Y., Yamaoka E., Hiyama K. Clinical features of ATRX or DAXX mutated neuroblastoma. J. Pediatr. Surg. 2014. 49:1835-8.
23. La Quaglia M.P. State of the art in oncology: High risk neuroblastoma, alveolar rhabdomyosarcoma, desmoplastic small round cell tumor, and POST-TEXT 3 and 4 hepatoblastoma. J. Pediatr. Surg. 2014. 49:233-40.
24. Lautz T.B., Naiditch J.A., Clark S., Chu F., Madonna M.B. Efficacy of class I and II vs class III histone deacetylase inhibitors in neuroblastoma. J. Pediatr. Surg. 2012. 47:1267-71.
25. Liu Z.L., Xiao Y.H., Chen D.X., Wang Z. The impact of gross total resection on survival in children with stage III/IV neuroblastoma – study of clinical efficacy in 21 cases. Eur. J. Med. Pharmacol. Sci. 2014. 18:2253-7.
26. Luo Y.B., Cui X.C., Yang L., Zhang D., Wang J.X. Advances in the surgical treatment of neuroblastoma. Chin. Med. J. 2018. 131(19)2332-7.
27. Manjunath S., Mouli S., Singh K.R., Rana C., Ramakant P., Mishra A. Neuroblastoma in late adolescence: case report and review of literature. World J. Endoc. Surg. 2018. 10(3):157-62.
28. Mohamed A.H.A., Mahmoud I.H., El Dein H.M.S., Sallam K.R., Wahba H.S. Assessment of the validity of imagedefined risk factors (IDRFs) in abdominal neuroblastoma Egyptian J. Radiol. Nuclear Med. 2020. 51:88. https://doi.org/10.1186/s43055-020-00205-2.
29. Monclair T., Brodeur G.M., Ambros P.F., Brisse H.J., Ceccheto G. et al. The International Neuroblastoma Risk Group (INRG) Staging System: An INRG task force report. J. Clin. Oncol. 2009. 27(2):298-303.
30. Nakaoka T., Uemura S., Nakagawa Y., Yano T., Oda M. Retroperitoneal ganglioneuroblastoma resected 8 years after mass screening: a case report. J. Pediatr. Surg. 2007. 42:E29-E32.
31. Ogura T., Hiyama E., Kamei N., Kamimatsuse A., Ueda Y., Ogura K. Clinical feature of anaplastic lymphoma kinase-mutated neuroblastoma. J. Pediatr. Surg. 2012. 47:1789-96.
32. Phelps H.M., Ndolo J.M., Van Arendonk K.J., Chen H., Dietrich H.L. et al. Association between image-defined risk factors and neuroblastoma outcomes. J. Pediatr. Surg. 2019. 54:1184-91.
33. Pinto N.R., Applebaum M.A., Volchenbaum S.L., Matthay K.K., London W.B. et al. Advances in risc classification and treatment strategies for neuroblastoma. J. Clin. Oncol. 2015. 33(27):3008-17.
34. Qin H., Yang S., Cai S., Ren Q., Han W. et al. Clinical characteristics and risk factors of 47 cases with ruptured neuroblastoma in children. BMC Cancer. 2020. 20:243. https://doi.org/10.1186/s12885-020-06720-9.
35. Rojas Y., Jaramillo S., Lyons K., Mahmood N., Wu M.F. et al. The optimal timing of surgical resection in high-risk neuroblastoma. J. Pediatr. Surg. 2016. 51:1665-9.
36. Simon T., Häberle B., Hero B., von Schweinitz D., Berthold F. Role of surgery in the treatment of patients with stage 4 neuroblastoma age 18 months or older at diagnosis. J. Clin. Oncol. 2013. 31(6):752-8. DOI:10.1200/ JCO.2012.45.9339.
37. Tanabe M., Otinuma N., Iwai J., Yoshida H., Takahash H. Renal impairment after surgical resection of neuroblastoma. J. Pediatr. Surg. 1996. 31(9):1252-5.
38. Tas M.L., Nagtegaal M., Kraal K., Tytgat G., Abeling N. Et al. Neuroblastoma stage 4S: tumor regresion rate and risk factors of progressive disease. Pediatr. Blood Cancer. 2019. e28061. https://doi.org/10.1002/pbc.28061.
39. Taylor J.S., Zeki J., Ornell K., Coburn J., Shimada H. et al. Down-regulation of MYCN protein by CX-5461 leads to neuroblastoma tumor growth suppression. J. Pediatr. Surg. 2019. 54:1192-7.
40. Tokiwa K., Fumino S., Ono S., Iwai N. Results of retroperitoneal lymphadenectomy in the treatment of abdominal neuroblastoma. Arch. Surg. 2003. 138(7):711-5.
41. Van Arendonj K.J., Chung D.H. Neuroblastoma: tumor biology and its implications for staging and treatment. Children. 2019. 6:12. DOI: 10.3390/children6010012.

42. Vollmer K., Gfroerer S., Theilen T.M., Bochennek K., Klingebiel T. et al. Radical surgery improves survival in patients with stage 4 neuroblastoma. World J. Surg. 2018. 42(6):1877-84.
43. Von Allmena D., Grupp S., Diller L., Marcus K., Ecklund K. et al. Aggressive surgical therapy and radiotherapy for patients with high-risk neuroblastoma treated with rapid sequence tandem transplant. J. Pediatr. Surg. 2005. 40:936-41.
44. Warmann S.W., Seitz G., Schaefer J.F., Scheel-Walter H.G., Leuschner I., Fuchs J. Vascular encasements as element of risk stratification in abdominal neuroblastoma. Surg. Onco. 2011. 20:231-5.
45. Watanabe M., Komuro H., Kaneko M., Hori T., Tatekawa Y. et al. A rare case of presacral cystic neuroblastoma in an infant. J. Pediatr. Surg. 2008. 43:1376-9.
46. Wu X.L., Dai Y.J., Sun G.Y., Wang L.K., Han L. et al. Adult neuroblastoma in the retroperitoneum: a case report. Medicine (Baltimore). 2018. 97(51):e13750. doi: 10.1097/MD.0000000000013750.
47. Yamagiwa I., Obata K., Saito H., Washio M. Renal atrophy following removal of a neuroblastoma. Pediatr. Surg. Int. 1994. 9:387-90.
48. Yang X., Chen J., Wang N., Liu Z., Li F. et al. Impact of extent of resection on survival in high-risk neuroblastoma: a systematic review and meta-analysis. J.Pediatr. Surg. 2019. 54:1487-94.
49. Yeung F., Chung P.H.Y., Tam P.K.H., Wong K.K.Y. Is complete resection of high-risk stage IV neuroblastoma associated with better survival? J. Pediatr. Surg. 2015. 50:2107-11.
50. Yoneda A., Nishikawa N., Uehara S., Oue T., Usui N. et al. Can image-defined risk factors predict surgical complications in localized neuroblastoma? Eur.J. Pediatr. Surg. 2016. 26:177-22.
51. Zage P.E. Novel therapies for relapsed and refracrory neuroblastoma. Children. 2018. 5:148. DOI:10.3390/children5110148.
52. Качанов Д.Ю., Шаманская Т.В., Муфтахова Г.М., Варфоломеева С.Р. Нейробластома 4S стадии. Вопр. Гематол./Онкол. Иммунопатол. Педиатрии. 2014. 13(2):9-19.
53. Строганова А.М., Карселадзе А.И. Нейробластома: морфологическая структура, молекулярно-генетические особенности и прогностические факторы. Успехи молекулярной онкологии. 2016; 3(3):32-43.

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Operative Technique

Regarding some elements of surgical anatomy in treatment of pyelo-ureteral segments (PUS) in children

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Abstract

Referitor la unele elemente de anatomie chirurgicală în tratamentul PUS la copii

Frecvența complicațiilor postoperatorii (recurență, fistulă etc.) variază între 3% și 17%, considerându-se că acestea sunt cauzate de întreruperea vascularizării ureterului în timpul intervenției chirurgicale, ne existând date concludente cu privire la prevenirea intraoperatorie a leziunilor vasculare.

Autorul prezintă un studiu ce reflect vascularizarea ureterului, constatând prezența unei teci vasculo-nervoasă (mezo a ureterului), precum și ramuri vasculare și nervoase aferente și eferente situate într-o masă de țesut conjunctiv liber, circumscriind ureterul exterior. Această teacă participă în acoperirea pelvisul renal spre hilul renal și continuă în fascia renală.

Autorul conchide că pentru a preveni trauma ureterală, în timpul mobilizării intraoperatorii a ureterului, peritoneul nu trebuie detașat de ureter, iar ultimul nu trebuie fixat cu nicio ancoră, care să poată aluneca de-a lungul lui și să contribuie la leziunea vasele mezzo. Pentru a evita deteriorarea vaselor mezo se recomandă fixarea ureterului cu forcepsul Allisca. Este necesar de a recurge la mobilizarea doar a segmentului care necesită de a fi eliminate, iar anastomoza trebui să implice învelișul care înconjoară ureterul cu vasele care îl vascularizează.

Cuvinte cheie: segment pielouretereal, anatomie chirurgicală, complicații postperatorii, copii

Abstract

The frequency of postoperative complications (recurrence, fistula, etc.) varies between 3% and 17%, considering that they are caused by interruption of vascularization of the ureter during surgery, there are no conclusive data on the intraoperative prevention of vascular damage.

The author presents a study that reflects the vascularization of the ureter, finding the presence of a vascular-nervous sheath (meso of the ureter), as well as afferent and efferent vascular and nervous branches located in a mass of free connective tissue, circumscribing the outer ureter. This sheath participates in covering the renal pelvis to the renal hilum and continues into the renal fascia.

The author concludes that in order to prevent ureteral trauma, during intraoperative mobilization of the ureter, the peritoneum should not be detached from the ureter, and the latter should not be fixed with any anchor that could slide along it and contribute to the injury of the mezzo vessels. To avoid damage to the meso vessels, it is recommended to fix the ureter with Allisca forceps. It is necessary to resort to the mobilization of only the segment that needs to be removed, and the anastomosis must involve the envelope that surrounds the ureter with the vessels that vascularize it.

Keywords: pyelo-ureteral segments, surgical anatomy, postoperative complications, children

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Introduction

Hydronephrosis is one of the most common kidney diseases requiring surgical treatment (1 in 100 children). After surgery complications occur, sometimes being severe, which according to the data of different authors range from 3% to 17%. In our clinic until 2015 complications accounted for 2-3% of recurrent fistulas (stenosis). There were recurrences (stenoses) with rapid evolution, especially after ureterolysis, the hydronephrotic kidney being nonfunctional during 8-12 months. Currently, ureterolysis is not performed in the clinic, because often the PUS remains devascularized after the stents are removed [1, 2, 7].

Purpose of the paper: to present an original method of PUS plastic surgery with the preservation of vascularization.

The vascular-nervous and fundamental components of the ureter, such as the predominantly loose connective tissue at this level, having an important role in its vascularization, innervation and protection, morpho-functionally constitute a *conjunctival-vascular-nervous sheath* [3].

This sheath is made by the passage of the connective tissue from the muscular-conjunctive sheath to the periphery as well as the passage of the connective tissue from the retroperitoneal cellular-adipose tissue in a loose connective plate, consisting of fine collagen and elastic fibers of varied condensation, anchoring the ureter in the retroperitoneal space [4, 5]. The sheath comprises the renal pelvis towards the renal hilum and continues into renal fasciae. From the renal pelvis segment, it partially becomes part of the external longitudinal muscular layer of ureters, simultaneously dispersing to the urocyst, in the pelvic subperitoneal space, thus serving as a *conjunctival-vascular-nervous sheath* of the ureter.

Normally, this sheath is in close relationship with the ureter (fig. 1), and a distance from the muscular sheath can be observed in malformations due to the distribution of correlation between loose and cellular-adipose tissues (fig. 2). Depending on the ureteral segments, the sheath has a rather varied density, being denser in the pelvic-ureteral, subperitoneal and pre-urocystic region.

Histomorphologically, it has been established that the afferent and efferent vascular-nervous branches are located in a network (rețea) of loose connective tissue, circumscribing the ureter externally.

Although according to the histomorphological peculiarities the sheath is an intimate part of the ureter, between the sheath (conjunctival-vasculo-nervous sheath) and the ureteral muscular layer, the connective tissue is devoid of vascular anastomoses, only afferent and efferent arterio-venous vessels being present, allowing its detachment on insignificant areas.

The results obtained, confirm the existence of a cleavage plane between the sheath and muscular layer, which allows the mobilization of the ureter within various limits. Detachment of the ureteral sheath induces amputation of afferent and efferent arterial and venous branches (fig. 3), with disruption of local circulation in the ureteral meso, including the ureter within the detachment limits, especially in ureteral malformations (fig. 4).

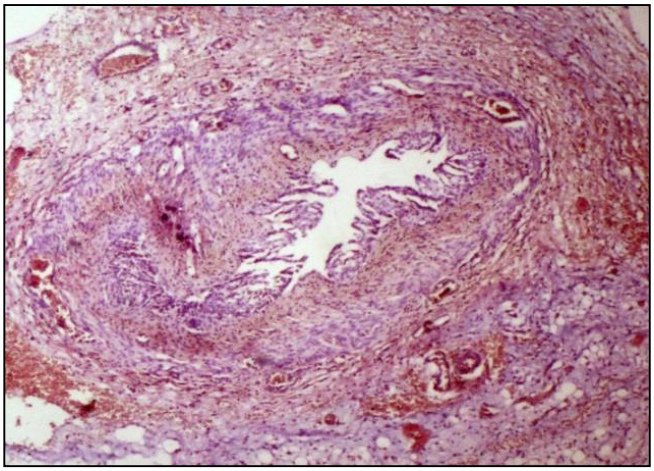

Fig. 1. Conjunctival-vascular-nervous sheath in the middle part of the ureter in a 6-month child. × 25. H&E staining

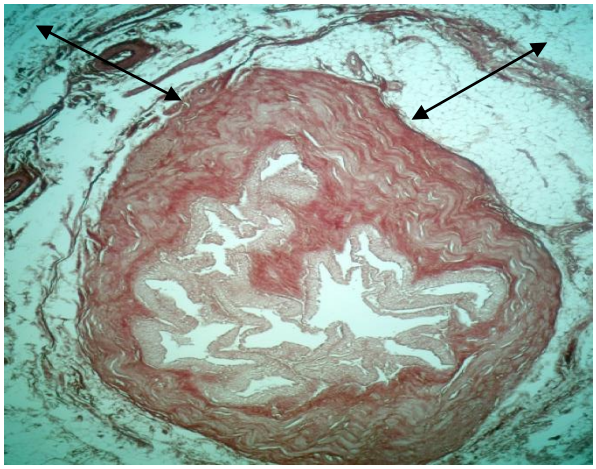

Fig. 2. Conjunctival-vascular-nervous sheath in mega-uretero-hydro-nephrosis of the ureter in the retroperitoneal space in a 1-year-old child

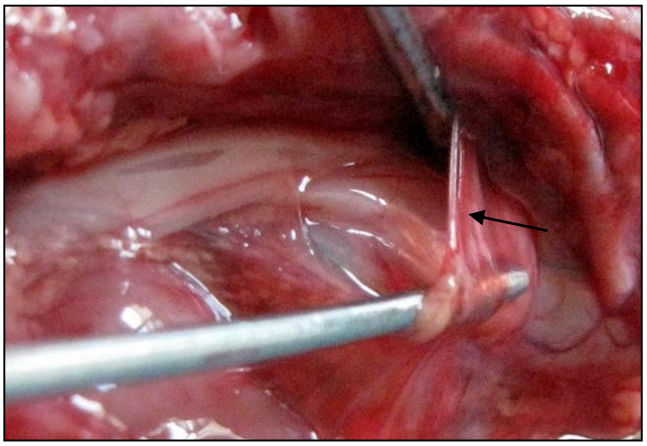

Fig. 3. Detachment of the periureteral conjunctival-vascular-nervous sheath (tunic) with ureter mobilization. Macropreparation.

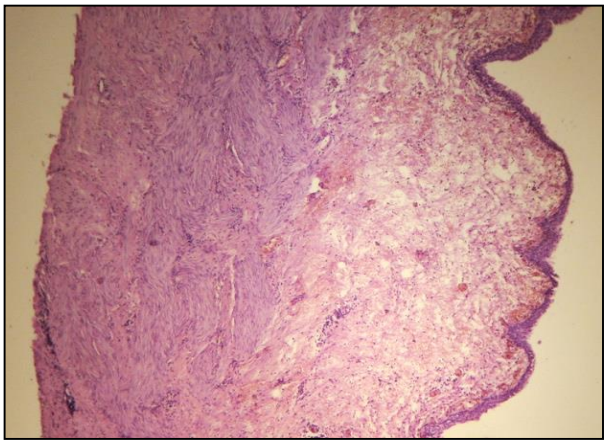

Fig. 4. Severe anemia of the ureter in the resection area after detachment of the conjunctival-vasculo-nervous sheath x25. *H&E staining*

Detachment of the ureter sheath over large areas, 1.0-1.5 cm, especially in malformations or inflammatory processes, generate severe circulatory disorders in the ureteral segments, intended for anastomosis. Therefore, in dissections performed on ureters, the integrity of the conjunctival-vasculo-nervous sheath should be kept maximally in order to avoid the onset of hemorrhage or ischemic and necrolytic processes, which can be direct causes of anastomoses, hernias or anastomotic fistulas. The ureteral conjunctival-vasculo-nervous sheath, due to the prevalence of loose connective tissue, is quite resistant, protecting both the vascular devices of the ureter and the ureter itself from invasive inflammatory processes or retroperitoneal infiltrative neoplasms. This property of the sheath has also been observed in infiltrative tumors of the *nephron* in which the ureter remains intact, crossing the tumor area. Similar observations have been made by other authors [6].

No postoperative complications were practically recorded in the last 3 years. Between 30 and 35 children are annually operated.

Surgery description: By lumbar approach, the PU segment is visualized, the peritoneum is detached from the ureter. The ureter is not mobilized to protect the meso (vessels) that is attached to the peritoneum.

It is recommended mobilizing only the PUS to be excised so as not to devascularize the ureter. According to Handren, a surgery meeting these requirements should be performed. The sheath should be involved in anastomosis.

In most cases, in children the renal pelvis should not be modeled (resected) because after removing the obstruction it returns to normal. Resection is performed only in a large, inflamed, thickened renal pelvis. Stents are applied in infants, while in newborns ureteropyelonephrostomy is performed.

According to Lopatkin N.A. (1973) and our data, drainage-free plastic surgery is indicated if only:

1. Urinary tract infection is absent.
2. On scintigraphy, there are signs of occlusion without disruption of secretion and discharge.
3. The transport of isotope in the parenchyma is disrupted.
4. The function of the contralateral kidney is not disrupted.
5. Normal or slightly disturbed intra-basal pressure.

The vascular-nervous sheath (meso) is also involved in suture-based plastic surgery in underdeveloped young children, being more visible in older children; thus, covering the ureter. In this way, vascularization can be protected, and anastomosis is sealed.

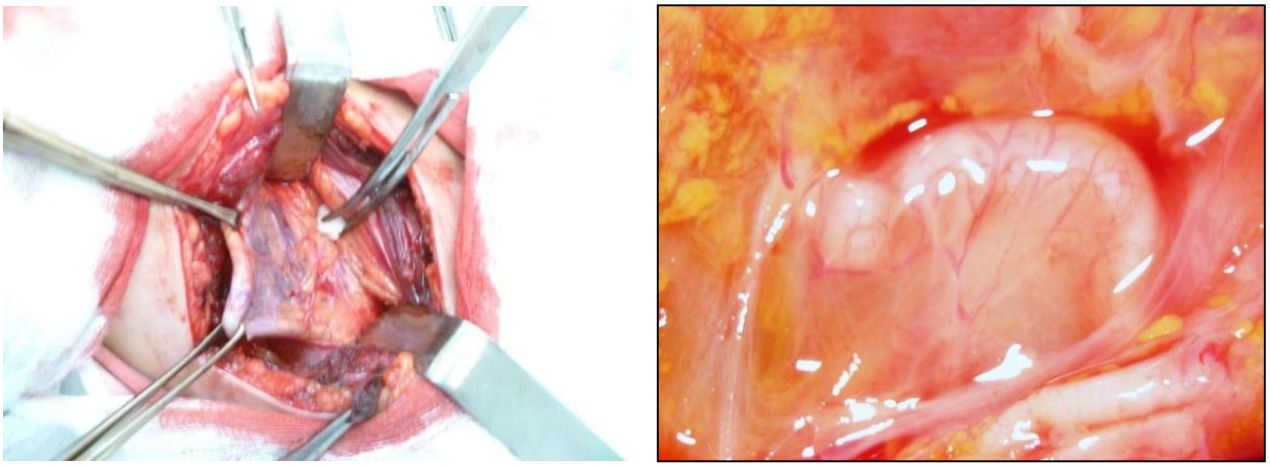

Fig. 5. Macroscopic appearance of the vascular-nervous sheath after detachment of the paranephral adipose layer. Ureter fixed with Alisca forceps

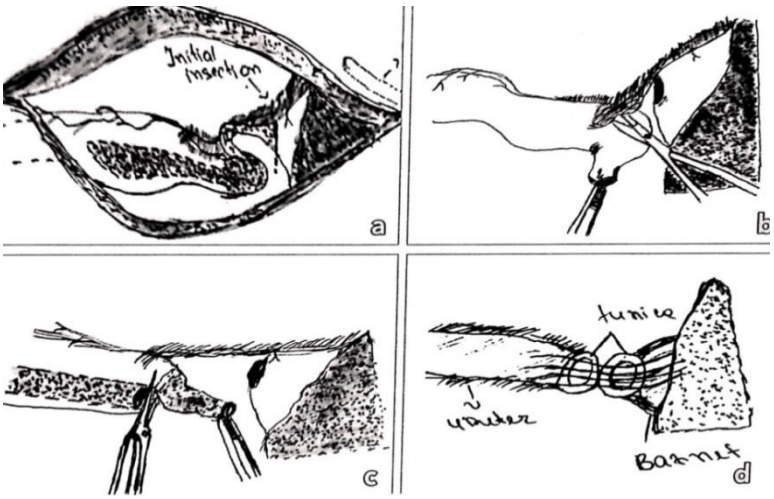

Fig. 6. Scheme. Pyelo-ureteral segment (PUS) plastic surgery. W.H. Hendren - Curajos B.: A- PUS causing hydronephrosis; B - PUS mobilization only within the resection limits; C- PUS resection; D - uretero-pelvic anastomosis with the involvement of the vascular-nervous sheath.

Conclusion.

To improve the results of surgical treatment of obstruction of the pyeloureteral segment, the described method should be extensively used, based on the morphological study and providing good follow-up results.

REFERENCES

1. Andersen J.C., Hynes W.R. Retrocaval ureter a case diagnosed preoperatively and treated successfully by plastic operation Br. Urology. 1949. 209-12.
2. Copolicehio G., Homsy I., L. Houle A.M. Long-term results of percutaneous endopieloctomy in the treatment of children with failed open pieloplasty. J. Urology. 1997. 158(4) : 1531-7.
3. Curajos B., Petrovici V., Bernic J. ș.a. Un nou concept privind morfologia chirurgicală a structurii și vascularizării ureterului în normă la copii. Al VI Congres de urologie, dializă și transplant renal din Republica Moldova. 21-23 octombrie, 2015. P.91-5.
4. Elder J.S. Antenatal hydronephrosis fetal and neonatal management. Ped.Clin. North. Am. 1997. UN. 1299.
5. Malone P. Pediatric urological disorders. Surgery int. 2001. 55:244.
6. Rodriguez L.V., Spielman D. et al. Functional and morphological resonance imaging for the evaluation of hydronephrosis, reflux and renal searing in children. J.Urol. 2001. 166 (3):1023-7.
7. Ulman I., Layanthi UR, Koff S.A. A long-term follow-up o newborn with severe unilateral hydronephrosis initially treated non-operatively. J.Urol. 2000. 164:1101-5.
8. Лопаткин Н.А. Об оперативном лечении нервно-мышечной дисплазии мочеточников. Урология и нефрология. 1973. 3б:25-9.

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Reviews

Characteristics of postoperative complications and their role in the evolution of esophageal atresia in children.

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Abstract

Caracteristica complicațiilor postoperatorii și rolul lor în evoluția atreziei de esofag la copii

Autorii ilustrează varietatea și gravitatea complicațiilor postoperatorii ce se dezvoltă după tratamentul chirurgical primar al atreziei congenitale de esofag, inclusiv dehiscențele anastomotice, recurența fistulei traheoesofagiene, disfuncția coardelor vocale, dismotilitatea postoperatorie, stricturile anastomotice. Se atrage atenția la indicii sporiți de morbiditate și mortalitate în aceste complicații, fiind descrise unele dificultăți diagnostice și opțiuni de tratament. Autorii conchid, că fiecare din potențialele complicații survenite în atrezia de esofag reprezintă o problemă semnificativă și o provocare de gestionare a acestei malformații grave la copii, impunându-se necesitatea elaborării a noi măsuri de prevenire și metode de tratament.

Cuvinte-cheie: atrezia de esofag, fistulă traheoesofagiană, complicații, copii

Abstract

The authors illustrate the variety and severity of postoperative complications that develop after primary surgical treatment of congenital esophageal atresia, including: anastomotic dehiscence, recurrence of tracheoesophageal fistula, vocal cord dysfunction, postoperative dysmotility, anastomotic strictures. Attention is drawn to the increased rates of morbidity and mortality in these complications, describing some diagnostic difficulties and treatment options. The authors conclude that each of the potential complications of esophageal atresia is a significant problem and a challenge in the management of this serious malformation in children, requiring the development of new prevention measures and treatment methods.

Keywords: esophageal atresia, tracheoesophageal fistula, complication, child

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Actuality. Esophageal atresia (EA) is a severe congenital malformation found in the neonatal period, characterized by impaired esophageal continuity, without or with a pathological connection to the trachea, resulting in a tracheoesophageal fistula that has several configurations [17, 82]. The incidence of EA is about 1 in 2500-4500 live births [53].

Documented for the first time in 1670 by William Durston, and the first one-stage operation being successfully performed in 1941 by Cameron Haight [62], this malformation continues to present a challenge for the pediatric surgeon both in regarding the surgical technical procedure, as well as the management of postoperative morbidity [11, 43, 76]. Although postoperative mortality in this malformation has decreased significantly, the literature indicates an increased incidence of postoperative morbidity caused by both anastomotic complications [111, 113] and respiratory and gastrointestinal problems, some of which persist throughout life [37, 45]. Some studies have indicated that the incidence of postoperative complications varies between 20% and 60% [112]. Anastomotic fistulas and strictures, dysphagia, gastroesophageal reflux, motility disorders, epithelial metaplasia, tracheomalacia are frequently documented radiological, scintigraphic and endoscopic [51, 81]. In this context, there is a need for complex prospective histopathological studies in order to describe more details in the pathogenesis of these postoperative consequences, in the literature being described few reports on the histopathology of esophageal atresia with eso-tracheal fistula [1, 30, 45].

Esophageal atresia is a severe problem of pediatric surgery both by the correction of this structural malformation and by the management of its sequelae [20, 101]. Despite the remarkable results obtained in the surgical treatment of esophageal atresia, the incidence of postoperative morbidity remains increased, being identified several factors that influence the prognosis of these patients [65, 71, 111]. According to some studies, respiratory problems (about 37%), anastomotic stenosis (22% - 40%), dysphagia (15% -100%), gastroesophageal reflux requiring antireflux surgery (12%), recurrent fistulas (4% -17%) are quite common. etc. [27, 42, 51, 80].

Anastomotic dehiscence after repair of esophageal atresia continues to encounter difficulties and challenges in management, being characterized by significant mortality and morbidity, caused by the risk of infection, stricture formation, respiratory distress and delayed onset of feeding [44, 61, 74]. Anastomotic dehiscence remains the most serious postoperative complication [23], registering an incidence of 4-36% of patients operated with congenital esophageal atresia [18, 38, 110], the mortality rate being 60-80% in developing countries and up to 25% in developed countries [38, 103].

Several factors significantly involved in the mechanism of development of anastomotic dehiscences are described, such as: friable lower atretic segment, ischemia of esophageal segments, sepsis, excessive mobilization of atretic segments, imperfect suturing technique, type of suture, excessive tension of the anastomotic area, gestational age and birth weight having an impact on survival, but not on healing of anastomosis [5, 38]. Postoperative elective ventilatory support has been shown to be of paramount importance in reducing anastomotic complications by decreasing the tension of the anastomosis area [99].

In cases of anastomotic dehiscence in children with esophageal atresia, management depends largely on the degree of dehiscence and the clinical condition of the child. Anastomotic dehiscences exceeding ¼ from the circumference of the esophagus are considered major [100]. Most anastomotic leaks are found on a routine radiological examination performed 5-7 days postoperatively. The development of this complication can be suspected in cases when some elimination occur through the placed thoracic tube, in such situations it is necessary to perform radiological examination with a water-soluble contrast agent [65].

Anastomotic dehiscence can be solved by conservative methods with placement of the thoracic drainage tube, administration of broad-spectrum antibiotics and proton pump inhibitors, pareneteral nutritional support and oral aspirations [29, 100, 110] or surgically, resorting to an early thoracotomy with reconstruction of the anastomosis [110]. In some cases it may be necessary to apply cervical esophagostomy and gastrostomy with pleural lavage and reanastomosis after a certain period of time, repair with the pleura or pericardium, use of intercostal muscle patches, or gastric transposition or colonic interposition [56, 65, 100].

Chilothorax is a rare complication in children undergoing surgical treatment with esophageal atresia, with an incidence of 3%. This complication develops secondary to thoracic duct lesions following repair of esophageal atresia [26, 65]. Usually, the duct lesion produced above the level of the fifth thoracic vertebra develops in the left chilotorax, while the lesions below this level can develop a chilotorax on the right side [65].

Some pathological conditions such as anastomotic leakage or reflux of gastric contents into the thoracic cavity may mimic a chylothorax after surgery for esophageal atresia, in these cases for the purpose of differential diagnosis, being necessary to perform pleural fluid analysis, with a predominance of lymphocytes and triglycerides (> 110 mg / dl) [73].

Usually, conservative treatment is quite effective in resolving post-traumatic chylothorax (80% of cases) and includes: cessation of enteral feeding or administration of medium-chain triglycerides with or without parenteral nutrition, aimed at reducing lymph flow in the thoracic

duct. In some cases, intravenous administration of somatostatin or octreotide, repeated thoracentesis or, if necessary, the application of thoracic drainage is used. In cases of inefficiency of conservative methods, as a possible alternative stage before surgery may be the use of pharmacological pleurodesis with the instillation of various substances in the pleural space iodopovidone, bleomycin, tetracycline, etc. [86]. Some authors resort to embolization of the thoracic duct with various substances, including Lipiodol or N-butyl cyanoacrylate tissue adhesive [22]. Surgical options for resolving posttraumatic chylothorax include: thoracic duct ligation, surgical pleurodesis, mediastinal electrocoagulation, application of pleuroperitoneal shunts [65].

Recurrent tracheoesophageal fistula (TEFr) is a fairly common postoperative complication in the surgical treatment of esophageal atresia, with an incidence of 5% -10%. In 4% of patients with primary repair of EA / FTE, leaky fistulas can be found, which manifest shortly after surgery [24, 34, 91].

It is considered that in addition to improper ligation, recurrent tracheoesophageal fistula develops as a result of an abscess-shaped anastomotic dehiscence, which subsequently opens into the trachea on the suture line, which is a point with weaker resistance. In this context, some authors indicate that almost 75% of patients successfully treated for an anastomotic discharge subsequently developed tracheoesophageal fistula [34, 49]. Some authors indicate that esophageal strictures, which require force dilation, may contribute to the development of this complication [7].

Clinical symptoms include the presence of a persistent cough caused by salivary aspiration, dyspnea or apnea during feeding, recurrent pneumonia and chronic lung damage. Injection of the contrast agent under pressure through a nasogastric tube that is gradually withdrawn is a fairly sensitive diagnostic method. The diagnosis is confirmed by bronchoscopy or esophagoscopy, which occasionally requires the use of methylene blue [7, 16, 96].

Management of children with TEFr is quite difficult, the endoscopic option of solving evolving as an alternative approach [69]. Endoscopic treatment can be performed by both bronchoscopy and esophagoscopy and includes:

- Injection of an adhesive (eg fibrin or histoacryl adhesive) into the fistula or submucosal tract [32, 107].
- Deepithelialization of the fistula tract by various methods, including: cauterization, chemocauterization, sclerosis, etc. [54, 65].
- The combined method [39].

Surgical treatment of TEFr is quite difficult due to the adhesion process and mediastinal fibrosis, and the failure rate is quite high, the incidence of refistularization being about 21% and a mortality of 3% -10% [14, 91].

Vocal cord dysfunction (VCD) is a complication found in patients with esophageal atresia (unilateral or bilateral) that develops as a result of congenital or iatrogenic dysfunction of the laryngeal nerve or vagus nerve from which the laryngeal nerve originates, this complication having an incidence of 4% -50% [50, 65, 70].

More commonly, VCD is found in cases of isolated closed tracheoesophageal fistula by surgical approach [108]. The use of diathermy can cause transient or permanent damage to the vagus nerve or laryngeal nerve fibers, especially in cases where these nerves have not been clearly identified [68]. In this context, the use of thoracoscopy offers several advantages [104].

The diagnosis of VCD is made by flexible laryngoscopy or by direct laryngoscopy on spontaneous breathing [70], the identification of congenital forms requiring a preoperative laryngoscopy [66].

VCD is usually transient in most cases. The main concern in case of VCD is to ensure airway permeability. The multidisciplinary approach with the involvement of the otorhinolaryngologist is extremely important for the proper management of children with this complication, being available several treatment options, including: temporary intubation pending recovery of laryngeal nerve function, various laryngoplasty and renervation and tracheostomy. [47, 88]. Given that the most common manifestation of VCD is aspiration, these patients require some changes in diet, including thickening of the diet or the use of feeding tubes [35].

Postoperative dysmotility. Esophageal dysfunction is considered a common finding in children diagnosed and treated surgically for various forms of esophageal atresia, motility disorders being detected in 75-10 %% cases [105], their etiology remaining controversial [12, 21].

PD of the esophagus in children with esophageal atresia and eso-tracheal fistula are widely described in the literature, there are some controversies about their secondary multifactorial origin, caused by: abnormal development of vagus nerve and Auerbach plexus, vaginal nerve trauma, surgical mobilization and tauma, ischemia or major traction on the lower end of the esophagus during surgery or due to congenital architectural abnormalities [1, 90].

The dysfunction of the motor activity of the distal esophagus by anastomosis in patients with esophageal atresia with tracheoesophageal fistula was first described in 1957 by Haight, and several etiological factors were discussed, including: the presence of abnormal ganglion cells in the Auerbach plexus of muscles in the fistulous segment, the presence of tracheobronchial cartilaginous reminiscences [30], these changes being documented by us [8]. We note that impaired esophageal motility has also been found in cases of congenital esophageal stenosis

[46]. In the 70s and 90s of the twentieth century, some experimental studies have shown that esophageal peristalsis is a complex process involving both extrinsic and intrinsic innervation, experimentally demonstrating that the myogenic control system of the esophagus is able to produce contractions with a speed of propagation similar to normal esophageal peristalsis independently. This system can be modulated by extrinsic and intrinsic nerves [67, 85]. Thus, the myogenic mechanism that activates in accordance with the neural mechanisms would represent an additional level of control of the esophageal motor [77].

Esophageal motility disorders are classified into primary, secondary and tertiary. The primary motor disorders characteristic of esophageal atresia are the main cause of abnormal development of the muscular and nervous system (intrinsic and extrinsic innervation) of the esophagus, these statements being partially supported by several histopathological studies [33]. Some authors believe that traumatic surgery may contribute to esophageal dysmotility in cases of esophageal atresia due to a neurological defect caused by partial esophageal denervation [6], while several studies have found that abnormal innervation and neuromuscular defect of the esophagus are present until surgery [114]. Several authors have found the association of esophageal atresia with tracheoesophageal fistula with neural crest developmental malformations, hence the origin and innervation of the esophagus [75]. Some experimental studies have shown significant changes in the intramural nerve components of the esophagus in laboratory animals with esophageal atresia and tracheoesophageal fistula [78]. Be an important factor contributing to esophageal dysmotility observed in esophageal atresia with tracheoesophageal fistula [12, 21]. There are also clinical studies that have concluded that the significantly low density of Cajal interstitial cells in esophageal atresia is an important factor in favor of the pathogenesis of esophageal dysmotility observed in these patients [64]. However, there is little information available that would reflect the particularities of the intramural nerve components of the human esophagus in cases of esophageal atresia with lower tracheoesophageal fistula [12].

Some authors believe that pathological changes found in the arthritic segments in case of esophageal atresia with eso-tracheal fistula, including muscle distortion by fibrosis, glandular and neuronal pathological changes, the presence of tracheobronchial cartilaginous reminiscences may contribute to dysmotility and surgery after surgery. The eso-tracheal fistula should be sectioned 3 mm distally from its origin in the trachea, the morphological changes in this area being suitable for primary anastomosis [1, 30]. In children, the heterotopic gastric mucosa in the normal esophagus can often be seen on endoscopic examination (up to 5.9%), presenting as a patch with sizes ranging from a few millimeters to a few centimeters, usually single or rarely ring-shaped, asymptomatic or causing dysphagia, odynophagia, esophageal strictures, bleeding and respiratory symptoms. The association of heterotopic gastric mucosa with esophageal atresia with eso-tracheal fistula is rarely described, most cases being found endoscopically after malformation repair [40, 98]. There are studies describing the presence of gastric epithelium in both the mucosa of the proximal esophageal and distal segments [31]. Some complex studies have found that the prevalence of Barrett's esophagus is 4 times higher in young adults treated with esophageal atresia, and the prevalence of esophageal carcinoma is 108 times higher than in the general population, these findings requiring an endoscopic follow-up evaluation. of life [102].

Esophageal dysmotility in children with esophageal atresia causes the development of gastroesophageal reflux, dysphagia, eating disorders, aspiration, these symptoms persisting into adulthood, negatively influencing the quality of life. Chronic exposure of the esophageal mucosa to the action of the acid environment can lead to Barrett's esophagus and esophageal carcinoma [33, 37, 59, 89, 102].

Anastomotic strictures (AS) of the esophagus are one of the major complications, affecting 9% -79% of children undergoing surgery for esophageal atresia [84]. Among the factors involved in the pathogenesis of this complication are: suturing technique and suturing material, anastomosis dehiscences, degree of tension of the anastomosis area, gastroesophageal reflux [57, 72, 92]. There is currently no consensus on the definition of AS in children, reducing the diameter of the lumen requiring a comparison with the lumen of a normal esophagus depending on age and weight [13]. Several studies have indicated that the long-term prophylactic use of H2 blockers can prevent anastomotic stricture after surgical treatment of esophageal atresia [68]. At the same time, some authors have a reserved attitude towards the efficacy of proton pump inhibitors in SE prophylaxis [25, 28]. Clinical symptoms of anastomotic strictures include difficulty eating and swallowing, regurgitation and vomiting, insignificant addition to body mass, respiratory symptoms (cough, aspiration, recurrent respiratory infections, oxygen desaturation during feeding) [94] .

The diagnosis of anastomotic strictures includes contrast radiography of the esophagus and endoscopic examination. Radiological images allow highlighting the morphology of the esophagus and the detection of associated abnormalities, lung diseases, while endoscopy allows a proper diagnosis and combined treatment [94]. In order to quantify the severity of the stricture and monitor the effectiveness of the treatment, the anastomotic stricture index was described. Some authors have proposed that this index (SI) be calculated according to the formula:

SI = (D - d) / D x100, where D - is the diameter of the esophagus below the stricture, and d - the diameter of the stricture. Usually, patients became symptomatic in cases when SI> 50% before the onset of dilatations [9, 83]. The symptomatic structure may respond to a single dilation or may become refractory or recurrent. Anastomotic stricture is considered refractory in cases when SI> 10% after 5 sessions, recurrent stricture being considered in cases of recurrence of symptoms or SI> 50% after 4 weeks after obtaining an SI <10% [9].

It has been proposed that the esophageal anastomotic stricture index (EASI) be used as a predictor of the development and severity of anastomotic stricture after repair of esophageal atresia, this index being generated after radiological evaluation of the upper gastrointestinal tract in the early postoperative period (5- 10 days postoperatively) and represents a ratio between the diameter of the stricture and the diameter of the upper segment (U-EASI) and lower (L-EASI): EASI = (lateral d / D + d / D anteroposterior) / 2, where D is the diameter of the esophageal segment upper or lower and d is the diameter of the stricture [93].

Currently, the treatment of choice in SE is the endoscopic one, which includes several methods, the main point being the exercise of an expandable force in the lumen of the stricture and obtaining the increase of the diameter of the esophageal lumen. For this purpose, the basic methods used are expansion with spark plug or balloon catheter with radial expansion, the success rate being 58% -96% [25, 55, 87]. To improve dysphagia and maintain adequate oral nutrition in cases of SE, between 1 and 15 dilations are required [55], the frequency of dilation procedures after reconstructive operations being higher in the first 2 years of life [92]. Endoscopic evaluation is recommended after each dilation, with the aim of guiding decision making [25]. The perforation rate in case of SE endoscopic dilatations is 0.9% -8% [94, 97]. Some studies indicate that the use of balloon expansion is more effective, has fewer technical failures, and requires fewer expansion procedures compared to Savary-Gilliard-type expansion [36].

In refractory or recurrent forms of SE, it is preferable to resort to a conservative approach, before resorting to surgery, different adjuvant methods being proposed [63]. There is currently a growing interest in the use of intralesional corticosteroid injection [2, 95], a method proposed in the 1970s [4]. More frequently intralesional triamcinolone acetate, acetonides, betamethasone and dexamethasone are used [48, 109].

Some authors recommend using systemic corticosteroid therapy concomitantly with dilation procedures [41, 106].

The use of Mitomycin C, which is an antitumor antibiotic produced by *Streptomyces caespitosus* and isolated in 1958 [55], is based on the properties of inhibiting wound healing by regulating gene expression of extracellular matrix proteins, acting as an agent antiproliferative by decreasing fibroblast activity, collagen synthesis and scar formation [9]. Topical use or intralesional injection of this preparation concomitantly with SE dilation has been shown to be quite beneficial in the treatment of recurrent or refractory strictures [10, 19, 52, 58, 79]. Mitomycin C concentrations recommended in the treatment of SE range from 0.1 mg/ml to 1 mg / ml [25]. Several authors point to the usefulness of endoscopic electrocautery in the treatment of esophageal stenoses in adults [15]. Despite numerous reports of the use of this method in children, there is currently insufficient evidence to support endoscopic cauterization as an effective treatment in SE after esophageal atresia [9, 60]. In patients with strict dilatation-refractory, the temporary placement of a recoverable stent may be considered [3]. Some authors propose as an alternative the placement of the biliary stent as an effective, accessible and minimally invasive method in the treatment of refractory esophageal strictures after primary anastomosis applied in cases of esophageal atresia [36].

The inefficiency of conservative treatment in resolving refractory or recurrent esophageal stricture is found in 3% -7% of patients [9, 49]. Strict resection with esophageal reanastomosis is the most common surgical procedure performed in cases of refractory SE, segmental or total esophageal substitution being rarely used [94]. Most patients undergoing reanastomosis require postoperative dilation again, and some complications are observed, including: pseudodiverticula formation, anastomotic dehiscence, recurrent strictures [9].

REFERENCES

1. Al-Shraim M.M., Ibrahim A.H.M., Malki T.A., Morad N.A. Histopathologic profile of esophageal atresia and tracheoesophageal fistula. Ann. Pediatr. Surg. 2014. 10:1-6.
2. Altintas E., Kacar S., Tunc B. et al. Intralesional steroid injection in benign esophageal strictures resistant to bougie dilation. J. Gastroenterol. Hepatol. 2004. 19(12):1388-91.

3. Antoniou D., Soutis M., Christopoulos-Geroulanos G. Anastomotic strictures following wsophageal atresia repair: A 20-year experience with endoscopic balloon dilatation. J. Pediatr. Gastroenterol. Nutr. 2010. 51:464-7.
4. Ashcraft K.W., Holder T.M. The expeimental treatment of esophageal stric-tures by intralesional steroid injections. J. Thorac. Cardiovasc. Surg. 1969. 58:685-91.
5. Askarpour S., Peyvasteh M., Javaherizadeh H., Askari N. Evaluation of risk factors affecting anastomotic leakage after repair of esophageal atresia. ABCD Arq. Bras. Cir. Dig. 2015. 28(3):161-2.
6. Aspiro A., Faure C. Esophageal dysmotility: characterization and pathophysiology. Dis. Esophagus. 2013. 26(4)405-9.
7. Aworanti O., Awadalla S. Management of recurrent tracheoesophageal fistulas: a systematic review. Eur. J. Pediatr. Surg. 2014. 24(05):365-75.
8. Babuci S., Petrovici V., Negru I., Haidarlă D. Histopathological characteristic of atretic segments in esophageal atresia with distal eso-traheal fistula. Mold. J. Pediatr. Surg. 2018. 3:19-27.
9. Baird R., Laberge J.M., Lévesque D. Anastomotic stricture after esophageal atresia repair: A critical review of recent literature. Eur. J. Pediatr. Surg. 2013. 23:204-13.
10. Berger M., Ure B., Lacher M. Mitomycin C in the therapy of recurrent esophageal strictures: hype or hope? Eur. J. Pediatr. Surg. 2012; 22(2):109-16.
11. Bogs T., Zwink N., Chonitzki V., Holscher A., Boemers T.M. et al. Esophageal atresia with or without Tracheoesophageal Fistula (EA/TEF): Association of different EA/TEF subtypes with specific cooccurring congenital anomalies and implications for diagnostic workup. Eur. J. Pediatr. Surg. 2018. 28:176-82.
12. Boleken M., Demirbilek S., Kirimiloglu H., Kanmaz T. Yucesan S. et al. Reduced neuronal innervations in the distal end o the proximal esophageal atretic segment in cases of esophageal atresia with distal tracheoesophageal fistula. World J. Surg. 2007. 31(7):1512-7.
13. Bott T.S., von Kalle T., Schilling A., Diez O.H., Besch S. et al. Esophageal diameters in children correlated to body weight. Eur. J. Pediatr. Surg. 2019. 29:528-32.
14. Boybeyi Ture O., Tanyel F.C., Soyer T. Acquired tracheoesophageal fistula after esophageal atresia repair. Balkan Med, J, 2019. 37(1):47-9.
15. Brandimarte G., Tursi A. Endoscopic treatment of benign anastomotic esophageal stenosis with electrocautery. Endoscopy. 2002. 34(5):399-401.
16. Bruch S.W., Hirschl R.B., Coran A.G. The diagnosis and management of recurrent tracheoesophageal fistulas. J. Pediatr. Surg. 2010. 45(2):337-40.
17. Bruns N.E., Glenn I.C., Ponsky T.A. Esophageal atresia: state of the art in translating experimental research to the bedside. Eur. J. Pediatr. Surg. 2019. 29:328-35.
18. Chang E.Y., Chang H.K., Han S.J., Choi S.H., Hwang E.H., Oh J.T. Clinical characteristics and treatment of esophageal atresia: a single institutional experience. J. Korean Surg. Soc. 2012. 83:43-9.
19. Chapuy L., Pomerleau M., Faure C. Topical mitomycin-C application in recurrent esophageal strictures after surgical repair of esophageal atresia. J. Pediatr. Gastroenterol. Nutr. 2014. 59(5):608-11.
20. Cheng W., Bisho A.E., Spitz L., Polak J.M. Abnprmal enteric nerve morphology in atretic esophagus of fetal rats with adriamycin-induced esophageal atresia. Pediatr. Surg. Int. 1999. 15(1):8-10.
21. Cheng W., Poon K.H., Lui V.C.H., Yong J.L., Law S. et al. Esophageal atresia and achalasialike esophageal dysmotility. J. Pediatr. Surg. 2004. 39:1581-3.
22. Chick J.F.B., Gemmete J.J., Cline M., Srinivasa R.N. Successful thoracic duct embolization for treatment of an iatrogenic left chylothorax in a neonate after repair of a tracheoesophageal fistula and esophageal atresia. J. Vasc. Interv. Radiol. 2017. 28(09):1325-7.
23. Ciornei M., Savu B., Hanganu E., Popa D.E., Burlea M. Factori prognostici în evoluția postoperatorie a atrezieiesofagiene: experiența unui centruterțiar într-un interval de 5 ani. Rev. Română de Ped. 2015. 3:322-5.
24. Coran A.G. Redo esophageal surgery: the diagnosis and management of recurrent tracheoesophageal fistula. Pediatr. Surg. Int. 2013. 29(10):995-9.
25. Dall'Oglio L., Caldaro T., Foschia F., Faraci S., Federici di Abriola G. et al. Endoscopic management of esophageal stenosis in children: New and traditional treatments. World J. Gastrointest. Endosc. 2016. 8(4):212-9.
26. Dhua A.K., Ratan S.K., Aggarwal S.K. Chylothorax after primary repair of esophageal atresia with tracheo-esophageal fistula: successful management by biological fibrin glue. APSP J. Case Rep. 2012. 3(3):16.
27. Di Pace M.R., Caruso A.M., Catalano P., Casuccio A., Cimador M., De Grazia E. Evaluation of esophageal motility and reflux in children treated for esophageal atresia with the use of combined multichannel intraluminal impedance and pH monitoring. J. Pediatr. Surg. 2011. 46:443-51.
28. Donoso F., Lilja H.E. Risk factors for anastomotic strictures after esophageal atresia repair: prophylactic proton pump inhibitors do not reduce the incidence of strictures. Eur. J. Pediatr. Surg. 2017. 27(1):50-5.
29. Du J., Huang J., Li Y., Chen Y., Guo W., Hou D. The repair of esophageal atresia and major complications - a systematic review and our experience in dealing with the tracheoesophageal fistula. Ann. Laparosc. Endosc. Surg. 2019. 4:90. http://dx.doi.org/10.21037/ales.2019.06.07.
30. Dutta H.K., Mathur M., Bhatnagar V. A histopathological study of esophageal atresia and tracheoesophageal fistula. Pediatr. Surg. 2000. 35:438-41.
31. Emery J.L., Haddadin A.J. Gastric-type epithelium in the upper esophageal pouch in children with tracheoesophageal fistula. J. Pediatr. Surg. 1971. 6:449-53.

32. Farra J., Zhuge Y., Neville H.L., Thompson W.R., Sola J.E. Submucosal fibrin glue injection for closure of recurrent tracheoesophageal fistula. Pediatr. Surg. Int. 2010. 26(2):237-40.
33. Faure C., Grunder F.R. Dysmotility in esophageal atresia: pathophysiology, characterization, and treatment. Front. Pediatr. 2017. 5:130. doi: 10.3389/fped.2017.00130
34. Friedmacher F., Kroneis B., Huber-Zeyringer A., Schober P., Till H., Sauer H., Hollwarth M.E. Postoperative complications and functional outcome after esophageal atresia repair: results from longitudinal single-center follow-up. J. Gastrointest. Surg. 2017. 21(06):927-35.
35. Fung S.W., Lapidus-Krol E., Chiang M., Fallon E.M., Haliburton B., Propst E.J., Chiu P.P. Vocal cord dysfunction following esophageal atresia and tracheoesophageal fistula (EA/TEF) repair. J. Pediatr. Surg. 2019. 54(8):1551-6.
36. Gerrish A.W., Kalmar Ch.L., Yeaton P., Safford S.D. Endoscopic biliary stent placement for anastomotic stricture following esophageal atresia repair in infant. J. Pediatr. Surg. Case Rep. 2018. 34:45-8.
37. Gottrand M., Michaud L., Sfeir R., Gottrand F. Motility, digestive and nutritional problems in esophageal atresia. Paediatr. Resp. Rev. 2016. 19:28-33.
38. Gupta M., Agnihotri L., Virdi V.J.S., Mandial V. Esophageal Atresia and tracheoesophageal fistula: Study of various factors affecting leak rate. Int J Sci Stud 2016. 3(12):23-6.
39. Gutiérrez San Román C., Barrios J.E., Lluna J. et al. Long-term assessment of the treatment of recurrent tracheoesophageal fistula with fibrin glue associated with diathermy. J. Pediatr. Surg. 2006. 41(11):1870-3.
40. Harrison L.J.R., Kenwright D., Stringer M.D. Esophageal heterotopic mucosa in esophageal atresia. J. Pediatr. Surg. 2018. 32:23-6.
41. Hishiki T., Kouchi K., Saito T., Terui K., Sato Y. et al. Successful treatment of severe refractory anastomotic stricture in an infant after esophageal atresia repair by endoscopic balloon dilation combined with systemic administration of dexamethasone. Pediatr. Surg.Int. 2009. 25:531-3.
42. Holland A.J.A., Fitzgerald D.A. Oesophageal atresia and tracheo-oesophageal fistula: current management strategies and complications. Pediatr. Resp. Rev. 2010. 11:100-7.
43. Ioannides A.S., Copp A.J. Embryology of oesophageal atresia. Semin. Pediatr. Surg. 2009. 18:2-11.
44. Jain P., Debnath P.R., Jain V., Chadha R., Choudhury S.R., Puri A. Multiple anastomotic complications following repair of oesophageal atresia with tracheoesophageal fistula: A report of two cases. Afr. J. Paediatr. Surg. 2011. 8:244-8.
45. Kawagara H., Kubota A., Hasegawa T., Okuyama H., Ueno T. et al. Lack of distal esophageal contractions is a key determinant of gastroesophageal reflux disease after repair of esophageal atresia. J. Pediatr. Surg. 2017. 42:2017-21.
46. Kawahara H., Oue T., Okuyama H. Esophageal motor function in congenital esophageal stenosis. J. Pediatr. Surg. 2003. 38:1716-9.
47. King E.F., Blumin J.H. Vocal cord paralysis in children. Curr. Opin. Otolaryngol. Head Neck Surg. 2009. 17(06):483-7.
48. Kochhar R., Poornachandra K.S. Intralesional steroid injection therapy in the management of resistant gastrointestinal strictures. World J. Gastrointest. Endosc. 2010. 2:61-8.
49. Koivusalo A.I., Pakarinen M.P., Lindahl H.G., Rintala R.J. Revisional surgery for recurrent tracheoesophageal fistula and anastomotic complications after repair of esophageal atresia in 258 infants. J. Pediatr. Surg. 2015. 50:250-4.
50. Kovesi T., Porcaro F., Petreschi F., Trozzi M., Bottero S., Cutrer R. Vocal cord paralysis appears to be an acquired lesion in children with repaired esophageal atresia/tracheoesophageal fistula. Int. J. Pediatr. Otorhinolaryngol. 2018. 112:45-7.
51. Kovesi T., Rubin S. Long-term complications of congenital esophageal atresia and/or tracheoesophageal fistula. Chest. 2004. 126(3):915-25.
52. Lakoma A., Fallon S.C., Mathur S., Kim E.S. Use of Mitomycin C for refractory esophageal stricture following tracheoesophageal fistula repair. Eur. J. Pediatr. Surg. Rep. 2013. 1(1):24-6.
53. Lal D.R., Gadepalli S.K., Downard C.D., Ostilie D.J., Minneci P.C. et al. Perioperative management and outcomes of esophageal atresia and tracheoesophageal fistula. J. Pediatr. Surg. 2017. 52:1245-51.
54. Lelonge Y., Varlet F., Varela P., Fourcade L., Gutierrez R. et al. Chemocauterization with trichloroacetic acid in congenital and recurrent tracheoesophageal fistula: a minimally invasive treatment. Surg. Endosc. 2016. 30(4):1662-6.
55. Lévesque D., Baird R., Laberge J.-M. Refractory strictures post-esophageal atresia repair: what are the alternatives? Dis. Esoph. 2013. 26:382-7.
56. Liyang Y., Zhan G., Zewei Z., Jianchuan Q., Wei W., Xiwang L. Use of pericardium to repair anastomotic leak after esophageal atresia surgery; experience with one case. Turk Pediatr. Ars. 2017. 52(1):43-5.
57. Macchini F., Parente G., Morandi A., Farris G., Gentilion V., Leva E. Classification of esophageal strictures following esophageal atresia repair. Eur. J. Pediatr. Surg. 2018. 28:243-9.
58. Madadi-Sanjani O., Zimmer J., Gosemann J.H., Ure B.M., Lacher M., Boehm R. Topical Mitomycin C application in pediatric patients with recurrent esophageal strictures - report on unfavorable results. Eur. J. Pediatr. Surg. 2018. 28(6):539-46.
59. Mahoney L., Rosen R. Feeding difficulties in children with esophageal atresia. Paediatr. Resp. Rev. 2016. 19:21-7.
60. Manfredi M.A., Clark S.J., Medford S., Staffa S.J., Ngo P.D. et al. Endoscopic electrocautery incisional therapy as a treatment for refractory benign pediatric esophageal strictures. J. Pediatr. Gastroenterol. Nutr. 2018. 67(4):464-8.
61. Mathur S., Vasudevan S.A., Patterson D.M., Hassan S.F., Kim E.S. Novel use of glycopyrrolate (Robinul) in the treatment of anastomotic leak after repair of esophageal atresia and tracheoesophageal fistula. J. Pediatr. Surg. 2011. 46:E29-E32.
62. Mazurak M., Patkowski D. The visionaries, the virtuosos, and the history of congenital esophageal atresia surgery. Ann. Thorac. Surg. 2018. 106:305-8.

63. Michaud L., Gottrand F. Anastomotic strictures: conservative treatment. J. Pediatr. Gastroenterol. Nutr. 2011. 52(Suppl 1):S18-9.
64. Midrio P., Alaggio R., Strojna A., Gamba P., Giacomelli L. et al. Reduction of interstitial cells of Cajal in esophageal atresia. J. Pediatr. Gastroenterol. Nutr. 2010. 51(5):610-7.
65. Morini F., Conforti A., Bogolan P. Perioerative complications of esophageal atresia. Eur. J. Pediatr. Surg. 2018. 28:133-40.
66. Mortellaro V.E., Pettiford J.N., St. Peter S.D., Fraser J.D., Ho B., Wei J. Incidence, diagnosis, and outcomes of vocal fold immobility after esophageal atresia (EA) and/or tracheoesophageal fistula (TEF) repair. Eur. J. Pediatr. Surg. 2011. 21:386-8.
67. Mukhopadhyay A.K., Weisbodt N.W. Neural organization of esophageal peristalsis: role of vagus nerve. Gastroenterol. 1975. 68(3):444-7.
68. Murase N., Uchida H., Kaneko K., Ono Y., Makita S., Yokota K. Propylactic effect of H2 blocker for anastomotic stricture after esophageal atresia repair. Pediatrics Int. 2015. 57:461-4.
69. Nazir Z., Khan M.A.M., Qamar J. Recurrent and acquired tracheoesophageal fistula (TEF) – minimally invasive management. J.Pediatr. Surg. 2017. 52(10):1688-90.
70. Oestreicher-Kedem Y., DeRowe A., Nagar H., Fishman G., Ben-Ari J. Vocal fold paralysis in infants with tracheoesophageal fistula. Ann. Otol. Rhinol. Laryngol. 2008. 117(12):896-901.
71. Okata Y., Maeda K., Bitoh Y., Mishima Y., Tamaki A. et al. Evaluation of the intraoperative risk factors for esophageal anastomotic complications after primary repair of esophageal atresia with tracheoesophageal fistula. Pediatr. Surg. Int. 2016. 32(9):869-73.
72. Parolini F., Leva E., Morandi A., Macchini F., Gentilino V., Di Cesare A., Torricelli M. Anastomotic strictures and endoscopic dilatations following esophageal atresia repair. Pediatr. Surg. Int. 2013. 29:601-5.
73. Pathak M., Saxena R., Gupta N., Sinha A. Chylothorax mimicking as anastomotic leak in a case of esophageal atresia. J. Clin. Neonatol. 2018. 7:279-81.
74. Patria M.F., Ghislanzoni S., Macchini F., Lelli M., Mori A. et al. Respiratory morbidity in children with repaired congenital esophageal atresia with or without tracheoesophageal fistula. Int. J. Environ. Res. Public Health. 2017. 14:1136. Doi:10.3390/ijerph14101136.
75. Pederiva F., Burgos E., Francica I., Zuccarello B., Martinez L., Tovar J.A. Intrinsic esophageal innervations in esophageal atresia without fistula. Pediatr. Surg. Int. 2008. 24(1):95-100.
76. Petit L.M., Righini-Grunder F., Ezri J., Jantchou P., Aspirot A., Soglio D.D., Faure C. Prevalence and predictive factors of histopathological complications in children with esophageal atresia. Eur. J. Pediatr. Surg. 2019. 29:510-5.
77. Preiksaitis H.G., Diamant N.E. Myogenic mechanism for peristalsis in the cat. Am. J. Physiol. 1999. 277(2):G306-13.
78. Qi B.Q., Uemura S., Farmer P., Myers N.A., Hutson J.M. Intrinsic innervations of the oesophagus in fetal rats with oesophageal atresia. Pediatr. Surg. Int. 1999. 15(1):2-7.
79. Rashed Y.K., El-Guindi M. Endoscopic postdilatation application of Mitomycin C. in children with resistant esophageal strictures. Korean J. Pediatr. 2019. 62(10):395-9.
80. Rayyan M., Allegaert K., Omari T., Rommel N. Dysphagia in children with esophageal atresia: current diagnostic options. Eur. J. Pediatr. Surg. 2015. 25(4):326-32.
81. Rintala R.J., Sistonen S., Pakarinen M.P. Outcome of esophageal atresia beyond childhood. Semin. Pediatr. Surg. 2009. 18:50-6.
82. Rozensztrauch A., Smigiel R., Patkowski D. Congenital esophageal atresia – surgical treatment results in the context of quality of life. Eur. J. Pediatr. Surg. 2019. 29:266-70.
83. Said M., Mekki M., Golli M., Memmi F., Hafsa C. et al. Balloon dilatation of anastomotic strictures secondary to surgical repair of oesophageal atresia. Br. J. Radiol. 2003. 76:26-31.
84. Salo M., Stenstrom P., Anderberg M., Arnbjornsson E. Anastomotic strictures after esophageal atresia repair: timing of dilatation during the first two postoperative years. Surg. J. 2018. 4:e62-e65.
85. Sarna S.K., Daniel E.E., Waterfall W.E. Myogenic and neural control systems for esophageal motility. Gastroenterology. 1977. 73:1345-52.
86. Scottoni F., Fusaro F., Conforti A., Morini F., Bagolan P. Pleurodesis with povidone-iodine for refractory chylotorax in newborns: personal experience and literature review. J. Pediatr. Surg. 2015. 50(10):1722-5.
87. Serhal L., Gottrand F., Sfeir R., Guimber D., Devos P. et al. Anastomotic stricture after surgical repair of esophageal atresia: frequency, risk factors, and efficacy of esophageal bougie dilatations. J. Pediat. Surg. 2010. 45:1459-62.
88. Sipp J.A., Kerschner J.E., Braune N., Hartnick C.J. Vocal fold medialization in children: injection laryngoplasty, thyroplasty, or nerve reinnervation? Arch. Otolaryngol. Head Neck Surg. 2007. 133(8):767-71.
89. Sistonen S.J., Koivusalo A. , Lindahl H., Pukkala E., Rintala R.J., Pakarinen M.P. Cancer after repair of esophageal atresia: population-based long-term follow-up. J. Pediatr. Surg. 2008. 43:602-5.
90. Smith N. Oesophageal atresia and trachea-oesophageal fistula. Early Human Develop. 2014. 90:947-50.
91. Smithers C.J., Hamilton T.E., Manfredi M.A., Rhein L., Gallagher D., Foker J.E., Jennings R.W. Categorization and repair of recurrent and acquired tracheoesophageal fistulae occurring after esophageal atresia repair. J.Pediatr. Surg. 2017. 52(3):424-30.
92. Stenstrom P., Anderberg M., Borjesson A., Arnbjornsson E. Dilation of anastomotic strictures over time after repair of esophageal atresia. Pediatr. Surg. Int. 2017. 33:191-5.

93. Sun L.Y.C., Laberge J.M., Yousef Y., Baird R. The Esophageal Anastomotic Stricture Index (EASI) for the management of esophageal atresia. J. Pediatr. Surg. 2017. 50:107-10.
94. Tambucci R., Angelino G., De Angelis P., Torroni F., Caldaro T. et al. Anastomotic strictures after esophageal atresia repair: incidence, investigations, and management, including treatment of refractory and recurrent strictures. Front. Pediatr. 2017. 5:120. doi: 10.3389/fped.2017.00120.
95. ten Kate C.A., Vlot J., IJsselstijn H., Allegaert K., Spaander M.C.W. et al. Intralesional steroid injections to prevent refractory strictures in patients with oesophageal atresia: study protocol for an international, multicentre randomised controlled trial (STEPS-EA trial). BMJ Open. 2019. 9:e033030. doi:10.1136/ bmjopen-2019-033030.
96. Thakkar H.S., Hewitt R., Cross K., Hannon E., De Bie F. et al. The multi-disciplinary management of complex congenital and acquired tracheo-oesophageal fistulae. Pediatr. Surg. Int. 2019. 35:97-105.
97. Thyoka M., Timmis A., Mhango T., Roebuck D.J. Balloon dilatation of anastomotic strictures secondary to surgical repair of esophageal atresia: a systemic review. Pediatr. Radiol. 2013. 43:898-901.
98. Tran S., Misra S., Bittner J.G., Pipkin W., Harley R., Howell C.G. Heterotopic gastric mucosa of the upper esophagus following repair of esophageal atresia with tracheoesophageal fistula. J. Pediatr. Surg. 2011. 46(1):e37-9.
99. Uchida K., Inoue M., Otake K., Okita Y., Morimoto Y. et al. Efficacy of postoperative elective ventilatory support for leakage protection in primary anastomosis of congenital esophageal atresia. Pediatr. Surg. Int. 2006. 22:496-9.
100. Vaghela M.M., Mahajan J.K., Sundram J., Bhardwaj N., Rao K.L.N. Role of glycopyrrolate in healing of anastomotic dehiscence after primary repair of esophageal atresia in a low resource setting – a randomized controlled study.J. Pediatr. Surg. 2017. 52:420-3.
101. van der Zee D.C., Tytgat S.H.A., Herwaarden M.Y.A. Esophageal atresia and tracheo-esophageal fistula. Semin. Pediatr. Surg. 2017. 26: 67-71.
102. Vergouwe F.W.T., Jsselstijn H.I., Biermann K., Erler N.S., Wijnen R.M.H. et al. High prevalence of Barrett s esophagus and esophageal squamous cell carcinoma after repair of esophageal atresia. Clin. Gastroenterol. Hepatol. 2018. 16:513-21.
103. Wang B., Tashiro J., Allan B.J., et al. A nationwide analysis of clinical outcomes among newborns with esophageal atresia and tracheoesophageal fistulas in the United States. J Surg Res 2014. 190(02):604-12.
104. Woo S., Lau S., Yoo E., Shaul D., Sydorak R. Thoracoscopic versus open repair of tracheoesophageal fistulas and rates of vocal cord paresis. J. Pediatr. Surg. 2015. 50:2016-8.
105. Yalcin S., Demir N., Serel S., Soyer T., Cahit Tanyel F. The evaluation of deglutition with videofluoroscopy after repair of esophageal atresia and/or tracheoesophageal fistula. J. Pediatr. Surg. 2015. 50:1823-7.
106. Yan X., Nie D., Zhang Y., Chang H., Huang Y. Effectiveness of an orally administered steroid gel at preventing restenosis after endoscopic balloon dilation of benign esophageal stricture. Medicine (Baltimore). 2019. 98(8):e14565.
107. Yoon J.H., Lee H.L., Lee O.Y. et al. Endoscopic treatment of recurrent congenital tracheoesophageal fistula with Histoacryl glue via the esophagus. Gastrointest. Endosc. 2009. 69(7):1394-6.
108. Zani A., Jamal L., Cobellis G., et al. Long-termoutcomes following H type tracheoesophageal fistula repair in infants. Pediatr Surg Int 2017. 33(02):187-90.
109. Zhang Y.W., Wei F.X., Qi X.P., Liu Z., Xu X.D. et al. Efficacy and safety of endoscopic intralesional triamcinolone injection for benign esophageal strictures. Hindawi Gastroenterol. Res. Pract. Vol. 2018. Art. ID 7619298, 7 p. https://doi.org/10.1155/2018/7619298.
110. Zhao R., Li K., Shen C., Zheng S. The outcome of conservative treatment for anastomotic leakage after surgical repair of esophageal atresia. J. Pediatr. Surg. 2011. 46(12):2274-8.
111. Zhu H., Shen C., Xiao X., Dong K., Zheng S. Reoperation for anastomotic complications of esophageal atresia and tracheoesophageal fistula. J. Pediat. Surg. 2015. 50:2012-5.
112. Zhu H., Wang Ma Zheng S., Dong K., Xiao X., Xhen C. Diagnosis and management of post-operative complications in esophageal atresia patients in China: a retrospective analysis from a single institution. Int. J. Clin. Exp. Med. 2018. 11(1):254-61.
113. Zimmer J., Eaton S., Murchison L.E., Ure B.M., Dingemann C. State of play: eight decades of surgery for esophageal atresia. Eur. J. Pediatr. Surg. 2019. 29(1):39-48.
114. Zuccarello B., Spada A., Turiaco N., Villari D., Parisi S. et al. Intramural ganglion structures in esophageal atresia: A morphologic and immunohistochemical study. HPC. Int. J. Pediatr. Vol. 2009. Article ID 695837. 7 pag. doi:10.1155/2009/695837.

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THE PANTHEON OF HONOR

Ion Fuior: the personality who have made history in surgical pediatric pathology

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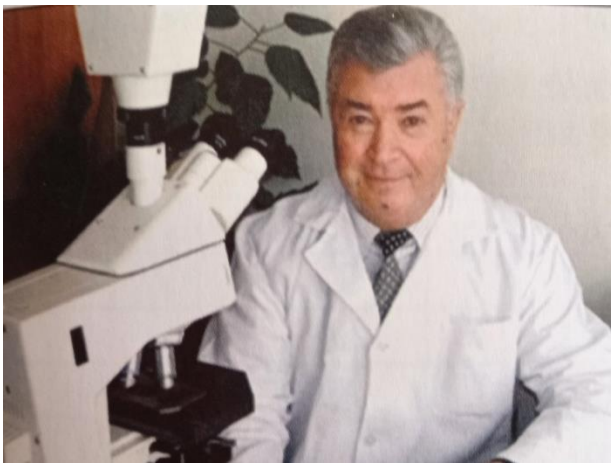

I o n F u i o r (19.02.1944 - 08.04.2008) – habilitated doctor in medical sciences, university professor of SUMPh "Nicolae Testemitanu", founder and coordinator of the Scientific Laboratory of Morphopathology (SLM) and of the Scientific-Consultative and Organizational-Methodical Republican Center (SCOM RC) of Pediatric profile, main specialist of the Ministry of Health of Republic of Moldova, in Pediatric, Obstetrics and Gynecology Morphology, "Emeritus of Health Care" - landmarks of a devotion and responsibility towards the field of medical science and an exemplary professional activity.

The history of university medicine, curative-diagnostic practices and of the local morphopathology lists the activity of great professional value and the fruitful contribution brought by the late Hab. Dr. in medicine Ion Fuior, being the first university professor in Pediatric Morphopathology. Moreover, it is an honor and an obligation to know the activity and merits of this Honorable Man which place him in the Memorial Pantheon of the famous in the field of medicine and our specialty.

It is complicated and painful to laconically relate the professionalism accumulated in the field, loyalty and respect for collaborators, the significance of valuable scientific researches conducted and brought into local science by university professor Ion Fuior. Tthe team he formed and guided in the specialty lost him with regret 13 years ago, on 08.04.2008, when he passed away.

Curiiculum vitae provides us with important data about the training, professional achievements, research field, interdisciplinary collaborations, scientific events,

supplementary administrative functions and distinctions of Mr. Hab. Dr. in medicine, Ion Fuior during 64 years of life.

Ion Fuior began his history of personality on February 19, 1944, when he was born in the northern region of Moldova, Alexandreni village, Edinet district. Later in 1961 he graduated with promising successes from middle school no. 1 in the town. Edineți. The next steps in continuity were the studies in the town Chisinau, at the Faculty of General Medicine of the State Institute of Medicine in Chisinau (SIMC), currently State University of Medicine and Pharmacy ”Nicolae Testemitsanu” (SUMPH) - "Nicolae Testemitanu".

After graduating with eminence in 1967 from the Faculty of General Medicine of SIMC he continued with a post-graduate course of study, specialty Pathological Anatomy (a.1967-1970) - Department of Pathological Anatomy, where he works as a university assistant. At the same time, he is working on the topic of PhD thesis, under the direction of his thesis supervisor, Hab. dr. in medicine, university professor, Academician of the Republic of Moldova Vasile Anestiade, and in 1972 he successfully defended his doctoral thesis in medicine with the topic "Characteristics of amino acids of the aortic wall in case of atherosclerosis”.

During 1975-1988, Mr. I. Fuior continues his activity as a university assistant, senior scientific collaborator in the Scientific Laboratory "CSRL" of SIMC. During this period, with the organization by the Ministry of Health of Republic of Moldova in 1970 of the Republican Service of Pediatric Profile Morphopathology at the Department of Pathological Anatomy of the Republican Children's Clinical Hospital (CRHC), currently CRHC "Emilian Coțaga", to coordinate the problems of profile diagnosis in Pediatrics, since February 1975, Mr. I. Fuior is appointed as Chief Non-Titular Specialist of the Republic of Moldova in Pathological Anatomy of Pediatric profile. In the same year, by the order of Mr. V. Revenco, PhD in medical sciences, I. Fuior is employed and appointed as a Consultant in the Municipal Service of Pediatric Morphopathology (MSPM), based at that time in the Department of Pathological Anatomy at the Municipal Clinical Hospital for Infectious Diseases of Children (MCHIDC), currently CMAP, being deployed within the Morphopathology Service at the base of “Gheorghe Paladi” hospital.

The professional evolution of Mr. Ion Fuior in terms of the development and history of the local Pathological Anatomy of pediatric, obstetric and gynecological profile has a pioneer character. Since 1976, Dr. Ion Fuior, through collaborations with university and institutional scientific research collectives abroad in the field of Pathological Anatomy of Pediatric profile, participates in the modules of refinement in the internationally renowned institutions of the Russian Federation (Moscow, Leningrad, Tver, Saratov, Rostov-on-Don, Ivanovo), of the Republics: Ukraine (Kiev, Kharkov), Lithuania (Riga), Uzbekistan (Tashkent) and Georgia (Tbilisi), while applying efforts in the development of pathological Anatomy of Pediatric and Obstetrical profile.

Through his colaboration with the interdisciplinary medical and local morphopathology staff, in 1976, Mr Ion Fuior together with the head of Pathological Anatomy Pediatric Profile Department, Hab. dr. In medical sciences, univ. prof. A. V. Ținzerling, The Institute of Pediatrics of Russian Federation, organizes within SIMC the first module of improvement of doctors with the topic "Patomorphology of pathologies commonly found in children".

As the Senior specialist of Health Ministry of Republic of Moldova, He interested and organized abroad trainigs for morphopathologists from the CRHC ”E. Coțaga” profile sections: Mrs. Nina Salita in the Institutions from Kiev, Leningrad, Saratov and from MCHIDC: Mr. V. Cardaniuc in Moscova with refinement in histopathological diagnosis by biopsy of human pathologies.

With the founding of the Republican Center for the Protection of Mother and Child Health (RC PMCH), during 1983-1984, with subdivisions specialized in Somatic and Surgical Pediatrics, Obstetrics and Gynecology, profile Morphopathology, Mr. Ion Fuior brings a fruitful contribution to the organization of the activity of the subdivision as Centralized Section of Pathological Anatomy (CSPA). In the same time with the organization of Pediatric profile, He starts the study and diagnosis of obstetric and gynecological pathologies, organizes the team of pathomorphologists, lab technicians which would be trained in histology and updates the methodologies of morphopathological diagnosis, the head of CSPA being called the specialist doctor in Pathological Anatomy - Mrs. Nina Salita.

In 1985, together with the staff of the Department of Pathological Anatomy, Mr. Ion Fuior as the main specialist organizes the training and improvement of doctors, residents in pathology of profile, later CSPA becoming the clinical basis of SUMPH "N. Testemitanu".

In 1988, with the founding of the Institute of Scientific Research in the field of Mother and Child Health Protection (ISRMCHP), director being hab. dr. in medical sciences, the university professor of SAM of Republic of Moldova Eugen Gladun organized the Scientific Laboratory of Morphopathology located in the CSPA block, as head of the Laboratory being chosen by competition Mr. Ion Fuior. At that time, under the coordination of Mr. Ion Fuior, the Laboratory was provided with equipment for electron microscopy, fluoriscent microscopy and photonical microscopy; through the competition were employed recognized in the country and abroad specialists in electron and fluoriscent microscopy as Dr. in medical sciences Vasile Rusu and

Victor Macari. The main scientific research directions of the Laboratory were aimed at solving the pressing problems addressed by the Ministry of Health in order to improve the health of the mother and child. A number of new methods of histological and histochemical investigations are implemented. In 1990 in the compartment of Clinical Morphopathology of CSPA is implemented diagnosis with the application of cryotomy, widely used in scientific research, intraoperative diagnosis of tumors and placental pathology in the early postpartum period.

The entire professional activity of Mr. Ion Fuior during 1975-2008 was carried out as an organizer, scientific researcher, consultant and practicing physician in the field of Pediatric, Obestestrical and Gynecological Morphopathology. The main objectives of the scientific research activity were dedicated to the research of pathological processes and diseases installed in the ontogenesis of the human body - periods of formation, development, growth and maturation of the child, which was an important step in the development of the Service of Morphopathology and local Cytopathology of profile, training and perfection of young medical professionals.

New research directions were established in the scientific field with the abortion of the topics for habilitated doctor thesis: Ion Fuior – The role of intrauterine infection in perinatal pathology; Vasile Rusu - Problems of the scar uterus; Victor Macari - Ultrastructural changes in congenital vices of the large intestine.

In 1995 Dr. Ion Fuior defends the thesis of habilitated doctor in medicine in specilities: 14.00.15 - Pathological anatomy and 14.00.09 – Pediatrics with the topic "Intrauterine infection in perinalai pathology (contemporary morphophysiopathological conceptions of pathogenesis and treatment bases)", scientific consultants Vasile Anestiadi, academician of SA, laureate of the State Prize., hab. dr. in medical sciences, univ. prof. and Eugen Gladun, academician of SA., hab. dr. in medical sciences, univ. prof.

The results of the carried out researches, the vision in the fields of speciality, the vast knowledge in the researched directions allowed Mr. Ion Fuior to develop a series of concepts and gain valuable data, not only for practical morphopathology, but also for theoretical medicine at the confluence of several disciplines.

In pictures - Hab. Dr. in Medical Sciences, Professor Ion Fuior and his disciples

Since 1989-1990 Mr. Ion Fuior, at the same time with scientific activity initiates the formation and training of a team of young doctors with abroad trainings and participations at different courses, internships, scientific conferences: Ucraina (Odesa), Belarusi (Minsc). In 1989, together with Ministry of Health of Republic of Moldova and professors Н. Суркова, А. Еремеева from the Department of pathological anatomy from ЦОЛИУВ, Moscow, Mr. Ion Fuior organizes the second training module in Pediatric Morphopathology called ” Pathological anatomy of diseases of the perinatal and infantile period". During the period 1992-1997 in the Scientific Laboratory, young scientific researchers were hired through competition.

Based on the rich experience of his own scientific researches and deep analysis of the literature, Mr. I. Fuior revealed new ideas in a series of original scientific articles in country and abroad, revealed new morphological aspects of intrauterine infection ethiopathogeny, pneumopathy, intrauterine DIC syndrome, VAP effect, etc.. IN 1999 SUMPH ”Nicolae Testemițanu” entitled Mr. Ion Fuior as university professor. Under the leadership of Mr. Ion Fuior, at the same time, the themes of the doctor in medical sciences are initiated and approved: "Structure of congenital vices in children in the Republic of Moldova" - Stefan Samciuc; "Morphogenesis of congenital immunodeficiencies" - Lilia Sinita; "Particularities of the foetal and newborn damage in intrauterine infection" -

Valeriu David; "Parasitic pathology of the digestive tract in children" - Vergil Petrovici.

During 1988-1994 Mr. I. Fuior and the staff of the Scientific Laboratory participated with reports at a series of congresses, symposiums in Ukraine, the Republic of Georgia (Tbilisi), Romania (Bucharest, Cluj -Napoca, Oradia), later through SUMPH "Nicolae Testemițanu" organizes post graduate studies in 1992-1995 for young specialist Victor Rusu in Cluj-Napoca County Clinical Hospital, Romania. In 1998 at the base of the CSPA and the Scientific Laboratory of Morphopathology of Mother and Child by order of the Director, Professor Eugen Gladun organized the Scientific-Consultative and Organizational-Methodical Republican Center (SCOM RC) of Pediatric Profile, coordinated by the head of the Scientific Laboratory of Morphopathology - Ion Fuior (p.a.1998-2008), directed towards optimizing the morphopathological diagnosis of profile problems in the Republic. Subsequently, through the efforts of Mr. Ion Fuior, during 1996-1997, the Department of Pediatric Pathological Anatomy was founded within the CSPA, in Balti, coordinator of the compartment being prepared and appointed morphopathologist Arcadie Chilaru.

In 2004, by Mr Ion Fuior, in the international project „Diagnostic Techniques in Pediatric Renal Diseans", al Institutional Partnerships, Swiss National Science Foundation organized during 2000-2007 with the participation of professors Volker Nickeleit - Department of Pathology, University of North Carolina (USA), Ernst Leumann Children's University Hospital Zurich (Elveția) organized at the base of SCOM RC the practical seminar „Diagnostic Techniques in Pediatric Renal Pathology" with the training of the center's doctors and those invited from the districts of the republic directed to the particularities of the diagnosis in "Infectious Glomerulonephritis", "Nephrotic syndrome – congenital NS, amyloidosis, diabetic nephropathy". Through this foundation, in June 2004 Mr. Ion Fuior organizes the internship of doctors from SCOM RC in the field of diagnosis of renal pathology by puncture-biopsy in the Department of Pathology of the Institute of Surgical Pathology - Zurich, Switzerland, which subsequently resulted in the implementation of renal biopsy in IMSP ISRMCHP.

During the period of activity Mr. Ion Fuior through his modesty, the multiple principledity has done remarkable activity as a member of the presidium of the League of Physicians of the Republic of Moldova, has served as President of the Medical College and Chairman of the Bioethics Commission of ISRMCHP, member of the College of Editorial of the Scientific Journal"Buletin de Perinatologie" etc.

The collaborators of the Scientific Laboratory of Morphology, SCOM RC and the staff of other specialties in the subdivisions of the Institute have respected and considered him as a sincere, optimistic, devoted to specility man, as coordinator, for elegance, competence, deep lysted spirit and human qualities, collegiality, flexibility and freedom of opinion and understanding of human values, efforts made in the training of specialists in morphopathological diagnosis of profile. During 1988-2008, with the input of Mr. I. Fuior were trained and guided in the specialty 15 morphopathologists; many of them continue to work in country in the field of morphopathology at the base of ISRMCHP and SAPC in the municipalities and districts of the Republic, others abroad in Ukraine and the Russian Federation.

Professor I.Fuior together with professor V.Nickeleit (USA) and E. Leumann (Switzerland) and morphopathologists from the SCOM RC.

The remarkable merits and qualities of the scientist I. Fuior over the years have been appreciated at their fair value countless times either by the leadership of the state or the institution in which he worked, being decorated with numerous ministerial, governmental diplomas and the medal "Eminent doctor".

Handing to Mr. I. Fuior of the Honorary Diploma of the Government of Moldova, 2007.

During his work Mr. Ion Fuior manifested the most beautiful qualities of scholar, teacher, organizer and director. Under His guidance as a leader and consultant 7 theses of habilitated doctor and 10 theses of PhD in medical sciences in the disciplines of Pediatrics, Obstetrics and Gynecology were defended. He was the scientific adviser of 3 scientific works successfully done with the title of PhD in Medical Sciences in Pathological Anatomy.

The work carried out by the scientist Ion Fuior with the main directions of perinatal and infantile pathology is widely known. His scientific work was noted by his original work by hab. dr. in medical sciences, current to date and by multiple works on morphological and etiopathic peculiarities of infectious pathology, congenital malformations, congenital immunodeficiencies etc. He is the author of over 200 scientific works, patents, scientific innovations, methodical recommendations including the last recommendation – "The importance of the pathogenetic principle in clinical and anatomological diagnosis in pediatric practice" from 2007, which in assembly made it a beautiful and honorable reputation, both in the country and abroad.

All that he has achieved during the work as a Senior Specialist of Ministry of Health of Republic of Moldova, assistant professor, professional in Pediatric Morphopathology, organizer and scientific researcher of the Scientific Laboratory of Morphopathology and coordinator of SCOM RC, what he has left in our memory and conscience is the expression of a notorious personality serving the good benchmarks of a devotion and responsibility towards the field of medical sciences , a speciality and exemplary professional activity, being a role model for the young people and our next colleagues.

Every man has a future ahead of him and it's good if he doesn't wait for it to come, but he makes it through his daily work so that he can realize it and later open it to others...

Conflicts of interest: *authors have no conflict of interest to declare*

Brief Communication

Reconstructive operations of serious scoliotic deformation in children

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The differential election of treatment option in spine deformation management depends on the age of patient, extent of deformation, spine mobility and neurological impairment. Application of high technologies allows achieving good results in these patients [5, 6].

Irrespective of etiology, spine deformations in adolescents represent the cause that influences the main peculiarities of the spinal column: its safety and stability; initially it is manifesting by pains, static's infringements, and internals' dysfunction, subsequently it leads to severe decrease of quality of the life [1, 2, 3, 10]. The choice of surgical and therapeutic options in the management of spine deformations at children is still controversial. [4, 7, 9, 10].

In Clinic of Vertebrology, Orthopedics and Traumatology of the "N. Georgiu" Scientifically-Practical Center of Children's Surgery 58 children with scoliosis (*>70°*) of different etiology, for correction of deformation at which was used polysegmentary constructions, have been pre- and post-operatively examined with a follow-up of 1 to 5 years (2016 – 2020). The evaluation included collecting of anamnesis data, clinical examination, labs and imaging (standard radiography/ with functional tests, magnetic resonance). Children were aged between 5 and 17,5 years; they were predominantly girls – 61(56 %).

Patients were parted, on 3 categories: I category – 26 patients with complete growth (14-16 years) (medium – 14,8 years) and idiopathic mobile spine deformations, curvature angle to 70-85°, coefficient of Harrington >5; II category – 18 patients with complete growth (14-17 years) and idiopathic rigid forms of deformation (medium – 15,9 лет), curvature angle is more than 85-90° and coefficient of Harrington < 5; III category – 16 patients with juvenile idiopathic and congenital deformations (5-12 years).

The main goals of surgical interventions were: elimination of deformation and disbalance correction and spine stabilization. Surgery allowed obtaining the following results: reconstruction of forward and average spine columns, restoration of physiological spine profiles (frontal and sagittal); restoration of normal anatomy of the vertebral channel; stabilization of the spine-impellent segment.

Tactics of surgical interventions, depending on category was following: the I category – 26 patients with complete body growth (13-15 years) and idiopathic plentiful spine deformations was carry out one-stage dorsal correction (fig. 1)

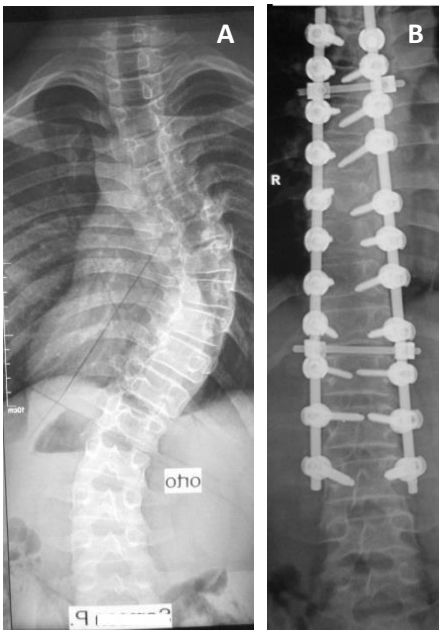

Fig. 1. A - Before operation the angle of deformation was 70°; B - After operation - 0 °, Correction of deformation is 100%

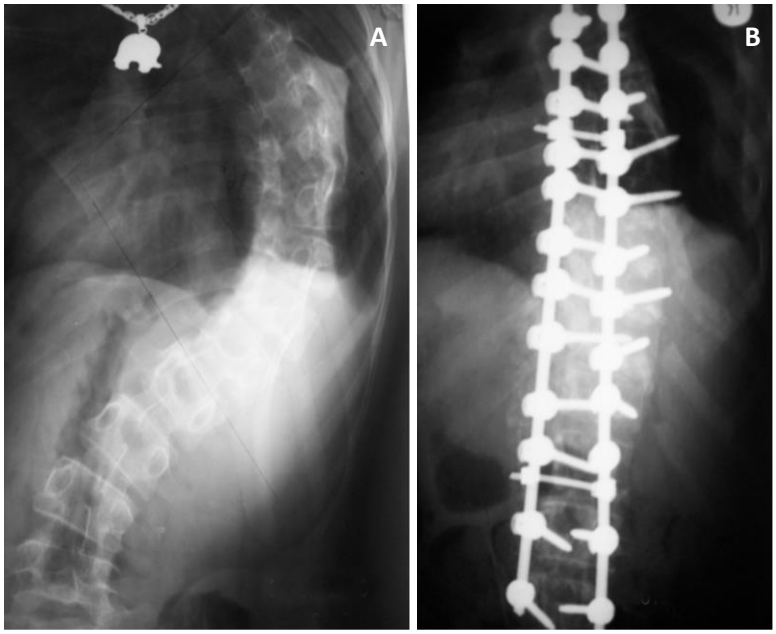

Fig. 2. A - Before operation the angle of deformation was 127 °; B - After operation - 29 °; Correction of deformation is 98 °

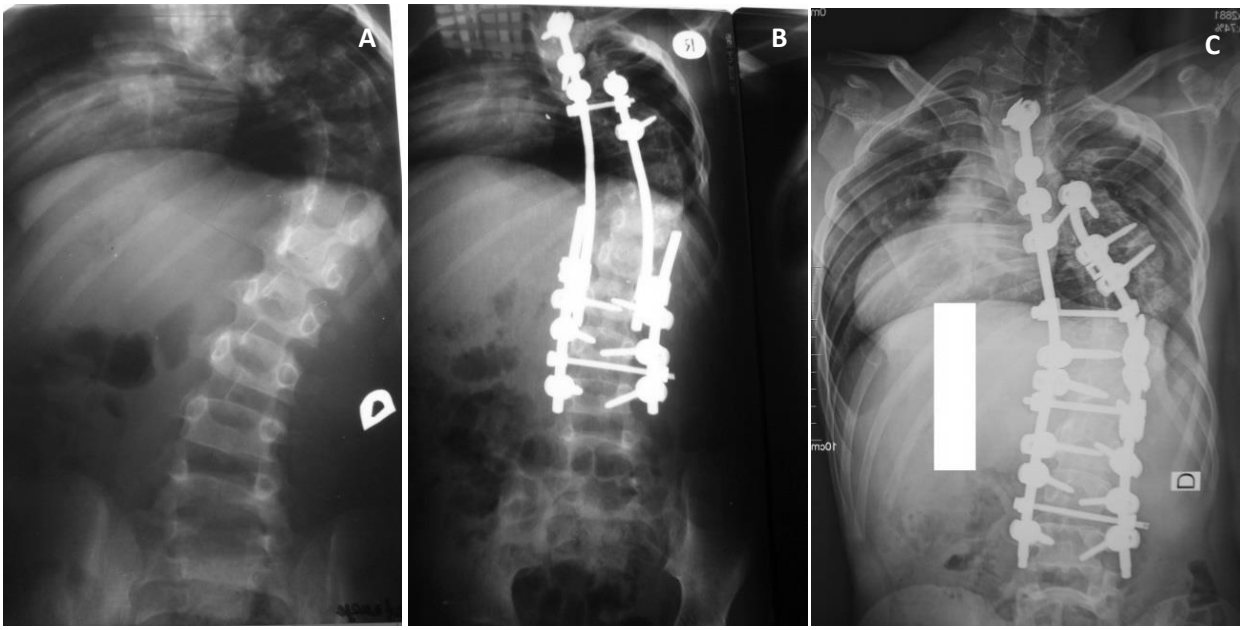

Fig. 3. A - Before operation; B - After operation of "blocking spondylosyndesis" at curvature top with the following dorsal correction by "a growing construction"; C - After

The II category – 18 patients with complete body growth (14,5-17,5 years) and idiopathic rigid forms of deformation by the first stage was executed forward spine mobilization (a multilevel discectomy), the second – dorsal correction of deformation by C-D system (fig. 2).

The III category–16 patients with juvenile idiopathic and congenital deformations (5,5-11 years) was carried out "blocking spondylosyndesis" at curvature top with the following dorsal correction by "a growing construction". In process of children growth through minimum invasive access the phased system's distraction is carried out. One step of a distraction equals 1-1,5 cm. Intervals of stage-by-stage correction depend on age growth activity and rates of deformation advance: from 6-8 months to 1,5-5 years (fig. 3).

The comparative analysis of the quality of the life of patients with severe spine deformations (according to a questionnaire „EQ-5D"), before and after surgical intervention, has shown that the quality of the life of patients in postoperative period essentially improved, in comparison with the preoperative period, from 12,7±0,3 points to 6,7±0,1. The distant results of surgical treatment were good: (correction > 55%) –39 (68, 4%), satisfactory (55%-40%) –12 (21,1%), and unsatisfactory (< 40%) –7 (12,3%). Complications took place in 9 (15,8%) cases.

At the present moment at scoliotic illness' treatment, surgical tactics remains discussed in the following aspects:

- At what age is it better to operate?
- What surgical technique will be more effective?
- Whether surgical intervention at the level of zones of growth and intervertebral disks will be expedient?

Data of epidemiological research, conducted Scientifically-Practical Center of Children's Surgery by randomization method, showed that in 2011 the frequency of scoliotic illness of RM reached on 7,8% at children and teenagers (till 18 years), from which 0,26% – the deformation angle was >70°. They make 5,2% in structure of diseases of a locomotorium apparatus [8, 11].

Conclusions.

1. The tactics of surgical treatment of spine deformations and further forecast depend on the type of neurological infringements and the character of bones' damages.
2. Optimum method of correction of difficult rigid scoliotic spine deformations were: forward spine release; dorsal correction and backbone fixation by a metal construction.
3. Surgical treatment of difficult juvenile scolioses began at 10-12 years old, and combined forward spine release with the following dorsal correction without posterior spine fusion execution.
4. In cases of congenital deformations primary operative defect's correction was carried out at children at the age of 3-7 years – "blocking spondylosyndesis" at curvature top with the following dorsal correction by "a growing construction" without posterior spine fusion execution.
5. Final correction of deformation, posterior spine spondylosyndesis and thoracoplasty are carried out on the end of spine growth.

REFERENCES

1. Antonescu D. Diformităţile coloanei vertebrale: scolioze-cifoze. Ann. Patol. Aparat. Locomot. 2008. 101:164-265.
2. Cotrel Y., Dubousset J., Guillaumat M. New universal instrumentation in spinal surgery. Clin. Orthopaed. Rel. Res. 1988. 227:10-29.
3. Jianu M. Scolioza pediatrică. Pro Editura şi Tipografie. Bucureşti. 2005. 141 p.
4. Jonge T., Dubousset J.F., Illes T. Sagittal plane correction in idiopathic scoliosis. Spine. 2002. 27(7):745-61.
5. Lenke L.G., Betz R.R., Haher T.R., Lapp M.A. et al. Multisurgeon assessment of surgical decision-making in adolescent idiopathic scoliosis. Spine. 2001. 26(9):2347-53.
6. Lenke L.G., Bridwell K.H., Baldus C. Cotrel-Dubousset instrumentation for adolescent idiopathic scoliosis. J. Bone Jt Surg. 1992. 74-A(7):1056-67.
7. Merola A., Haher T., Brkaric M., Panagopoulos G. et al. A multicenter study of the outcomes of the surgical treatment of idiopathic adolescent scoliosis using the SRS outcome instrument. Spine. 2002. 27(18): 2046-51.
8. Şavga N.N., Şavga N.G. Operaţii de reconstrucţie în diformităţile scoliotice la copii. Bul. Perinatol. 2013. 59(3):148-51.
9. Suk S., Kim W., Lee C. Indication of proximal thoracic curve fusion in thoracic adolescent idiopathic scoliosis. Spine. 2000. 25(18): 2342-9.
10. Ulrich E.V. Spinal abnormalities in children. Manual for SPb doctors. ELBI-SPb. 1995. 364 p.
11. Villemure I., Aubin C., Grimand G., Dansereau J., Labelle H. Progression of vertebral and spinal three-dimentional deformities in adolescent idiopathic scoliosis. A longitudinal study. Spine. 2001. 26(20): 2244-50.

Best Practice in Diagnosis and Treatment

The role of neuronal intestinal abnormalities in the genesis of colostasis in children operated for anorectal malformation

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Abstract

Rolul anomaliilor neuronale intestinale în geneza colostazei la copiii operați pentru malformații anorectale

În baza unui examen clinico-paraclinic multilatelateral s-a apreciat structura cauzală a colostazei postoperatorii la copiii operați pentru malformații anorectale. Studiul efectuat a relevat faptul că malformațiile neuronale intestinale sunt una din cele mai frecvente cauze ale colostazei postoperatorii, atingând rata de 60% din cazuri. O deosebită importanţă în acest studiu s-a acordat examenului histomorfologic a bioptatelor colorectale prin metoda colorației cu hematoxilin-euzină și van Gieson combinată cu testul histochimic la activitatea acetilcolinesterazei (AChE) și NADP. Combinarea acestor metode ne-a permis obiectivizarea modificărilor cantitative și calitative a inervației colonice și a influiențat tactica curativă ulterioară.

Cuvinte-cheie: anomalii neuronale intestinale, colostază, malformații anorectale, copii

Abstract

Based on a multilateral clinical-paraclinical examination was determined the causal structure of postoperative colostasis in children operated for anorectal malformations. The study revealed that intestinal neuronal malformations are one of the most common causes of postoperative colostasis, reaching the rate of 60% of cases. A special importance in this study was given to the histomorphological examination of colorectal bioptates by the method of staining with hematoxylin-eosin and van Gieson combined with the histochemical test on acetylcholinesterase (AChE) and NADP activity. The combination of these methods allowed us to objectify the quantitative and qualitative modifications of the colonic innervation and influenced the subsequent curative tactics.

Keywords: neuronal intestinal abnormalities, colostasis, anorectal malformations, children

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Introduction

At present, the frequency of chronic colostasis in children operated for anorectal malformation (ARM) remains high [3, 4]. The attempt to analyze this phenomenon by intraoperative trauma of the rectoanal neuro-vascular bundle and pelvic muscle structures was unsuccessful [1, 7]. Chronic constipation unresponsive to conservative treatment in postoperative period was registered in 35.0-72% of cases of ARM, including the low forms, where surgical manipulation had no traumatic attitude towards loco-regional perineal formations [2]. In this context, it is necessary to find other causes of chronic constipation in children operated for ARM [5, 6].

Aim: Assessment of the impact of adjacent rectal and perineal innervation in the origin of chronic constipation in children operated for ARM.

Methods

Were evaluated postoperatively 51 patient who had undergone surgery for ARM during the period 2015-2020 in the Scientific-Practical Center of Pediatric Surgery "Natalia Gheorghiu". 15 (29.4%) children had chronic constipation, which is the reason for specialized clinical-paraclinical examination. The nosological structure of ARM in patients with postoperative constipation was: anorectal atresia (ARA) without fistulas - 40.0%; ARA with fistulas - 60.0%. In most cases (73.3%)- children were operated in neonatal period, of which radical surgical treatment was performed for 5 (33.3%) children with low forms of anorectal atresia and for 6 (40.0%) children was applied protective colostomy to combat mechanical intestinal occlusion. The rest (26.7%) of patients with perineal, vaginal, vestibular fistulas that allowed a satisfactory intestinal transit were operated in the first 3-6 months of life. The reconstructive-plastic surgical procedures were selected individually adapted to the case. In the low forms of ARM were used: Pellerin's Y-V type of plasty; removal of the cutaneous membrane. Regarding the high and intermediate forms of anorectal malformations were used: the Pena procedure- posterior sagittal anorectoplasty (PSARP); abdomino-perineal PSARP.

It's obvious that the age at which the child was operated, the type of surgery, the concomitant malformations, the pathologies and the associated complications determined the intestinal transit, rectal evacuation and continence. Moreover, of course, we are aware that these children presented postoperatively a wide range of anatomical and functional deviations specific for ARM, we, however, will refer only to the objective and reasoned elucidation of the position of intestinal neuronal malformations of the colon in severe postoperative constipation.

Clinically, special attention is paid to interviewing parents and the patients, assessing the child's psycho-emotional status and the socio-economic climate in the family. The loco-regional examination (visual, instrumental) provided the respective information about the anal position (anal index), the dimensions of the anal orifice (dilatometry), the healing deformations, the prolapse of rectal mucosa, etc.

The clinical detection of severe constipation requires special paraclinical examination aimed to objectify and decipher the causal nature of disorder. For this we used: radiological examination (irigoscopy); anorectal manometry; electromyographic and electroneurographic examination of the external anal sphincter (EAS), puborectal sling (PRS).

The major importance in this study is the histomorphological examination of colorectal bioptate-(Swenson`s biopsy). The characteristic of histomorphological modifications in bioptate was performed by coloration with hematoxylin-eosin, combined with the histochemical test on acetylcholinesterase activity (AChE) and NADP.

The obtained data were processed as means, calculating the standard deviation based on the Student criterion.

Results

Based on the questioning the parents of the children in our study, it was found that colostasis began recently postoperatively. We note that a protective colostomy was applied to 40.0% of children recently postnatal, which until its liquidation ensured daily colonic evacuation.

The specialized loco-regional examination allowed us to detect anal stenosis in 13.3% of cases, which clarified colostasis as a result of organic infrarectal obstruction, some of which were resolved by conservative methods, others by surgical treatment (Diamond-shaped flapreconstructive anoplasty).

Electromanometry allowed the finding of the kinetic activity of the rectal ampulla and the anal sphincter based on the following parameters: rectal basal pressure; basal pressure of the internal anal sphincter; recto-anal reflex of inhibition; Valsalva reaction and triggering the nececity for empirical evacuation. We mention the absence of rectoanal inhibitory reflex in 3 (20%) cases with postoperative colostasis, who suspect congenital achalasy, post-traumatic dysfunction of the internal anal sphincter or aganglionosis zone. Subsequently, these children was obligatory examined by irigography and histomorphology. In 40.0% of cases, the viscoelasticity curve of the rectal ampulla reveals a decrease in the sensitivity of the excitability threshold, which means that, needed increased volume of rectal content to trigger the act of defecation. In most cases (84.8%) the profilometry of the anal canal showed its dimensional decrease and functional depletion of the sphincter apparatus. The data of manometric research do not argue with absolute credibility the causal genesis of severe constipation, presenting a rather valuable objective information about affecting the extrinsic neuromuscular integrity of the

newly formed colorectoanal segment, which involves the physiology of colonic evacuation.

Electromyography (EMG) and electroneurography (ENG) allowed to define the disorders of neuromuscular innervation not only at the level of the anal sphincter, but also at communication channels with the segmental and supra-segmental defecation center. In favor of chronic postoperative colostasis of extrinsic neurological genesis also speak the pathological changes detected in the bioelectrical activity of EAS and APR, in the terminal latency of the pudendal nerve, the delayed somato-sensor response on the spinal roots, cortical areas of interest, n. pudendal and at examination of the bulbous-cavernous reflex. Subsequently, the extrinsic dysfunctional neurological and neuromuscular etiopathogenic character was verified in 26.6% of the total number of children with colostasis after surgical correction of MAR.

Radiological examination was used for differential diagnosis in 13 (86.6%) chronically constipated children, operated for ARM in the neonatal period and the first year of life. Simple radiogical image of the lumbosacral area revealed congenital lumbosacral osteogenic deffects (spina bifida and sacrococcygeal agenesis) in 13.3% of cases. Osseous defects detected in this segment of the spine suggest for a possible anatomical and functional damage of the adjacent rectoanal and perineal neuromuscular apparatus with a possible dysfunctional influence that causes infrarectal obstruction. The irigoscopy was performed to define the organic colonic parameters. At 9 (60.0%) children was appreciate left side megadolicocolon, 3 of them had a radiological area suspected for aganglionic zone.

All children with organic changes of colon underwent for rectal biopsy (Swenson's procedure) with subsequent histomorphological examination.

The information obtained by hematoxylin-eosin and van Gieson staining of studied bioptate allowed a precise visualization of the pathological modifications of the colon, with different intensity and spread of every stratum of intestinal wall (fig. 1, 2).

At 3 (5.6%) children, the intestinal neurvous ganglions staining with hematoxylin-eosin did not visualize in the intermuscular and submucosal area, suspected for Hirschsprung's disease (fig. 3). For the confirmation of intramural innervation lesions in these children, we decide to define the AChE and NADP activity (fig. 4).

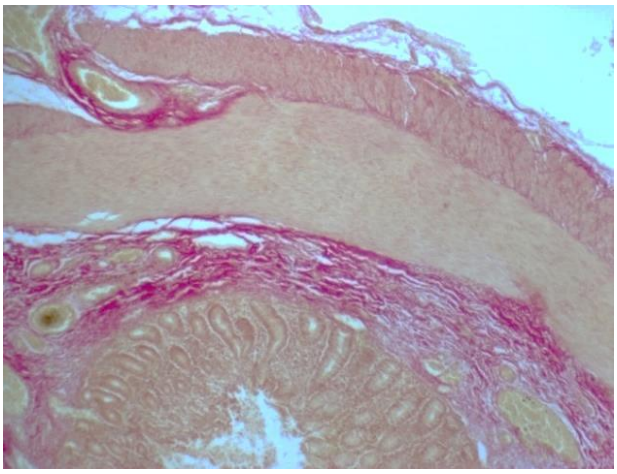

Fig. 1. Aganglionosis of the submucosa and muscular tunic of the rectocolonic area. Unevenly accentuated conjunctival network. Color. van Gieson. × 15

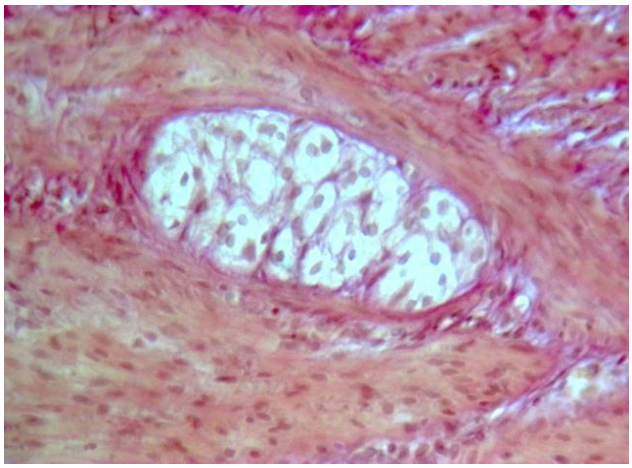

Fig. 2. Auerbach's myenteric plexus consists mostly of resected colonic glial cells. Color. van Gieson. × 40

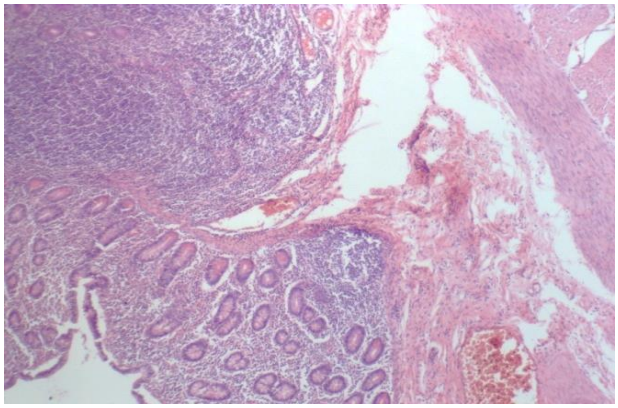

Fig. 3. Aganglionosis. Asymmetric reactive hyperplasia of the lymphoid follicles of the submucosal lamina. Accentuation of connective tissue. H&E coloring. × 15

For the confirmation of intramural innervation lesions in these children, we decide to define the AChE and NADP activity (fig. 4). In 3 cases, the data analysis revealed congenital aganglionosis, which was characterized by absence of nervous ganglion in both plexuses of the colon, on a limited rectal extension. At the same time, in the area without ganglia, were detected fascicles of nerve fibres, which was thickened and convuled, deformed and fragmented, situated in submucosal, intermuscular and intramuscular areas.

Intestinal colonic neuronal malformations were detected in 6 cases. For them was characteristic detection of large nerve ganglions with an increased number of neurocytes (up to 15-20); ganglions with a low number of neurons (1-2 neuronal cells); hypoganglionosis, which is characterized by a reduction in quantity of ganglion unit per view area; ectopy of nerve ganglions and neurons in the muscular stratum; hypertrophy of nerve fibers with their accretion in the muscular and submucosal stratum, etc.

So, the multimodal clinical and paraclinical examination of 15 children operated for ARM, who were chronically constipated postoperatively, shows that in 60.0% of cases the pathological retention of intestinal evacuation was caused by damage of the innervation integrity of the newly formed colorectoanal segment.

The study revealed that intestinal neuronal malformations are one of the most common causes of postoperative constipation in children operated for ARM. In this context, it is very important early detection of intestinal neuronal malformations, which would allow a solution in the beginning of the pathological process, ensuring the prophylaxis of secondary disorders of colonic. This is possible only on the base of complex histomorphological examination of bioptates taken intraoperatively at the first stage of treatment, in case than is applied colostomy or after rectal biopsy in children with persistent postoperative colostasis.

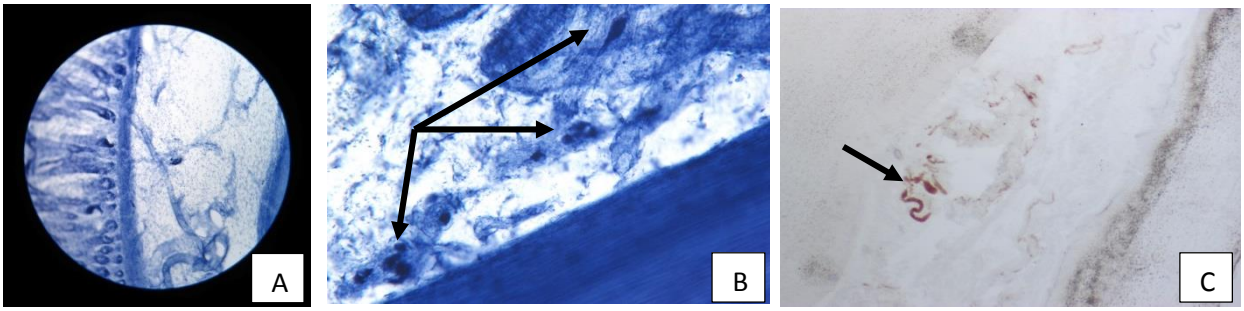

Fig. 4. A - Disorders of colonic innervation. Superficial submucosal solitar nerve ganglion Meissner (× 4). B - Deep, chaotic submucosal nerve plexus Henle, consisting of groups of neurons in adjacently of the inner stratum of muscular tunic (× 20). C - pathological nerve fibers in the neorect

In conclusion, we mention that lossing of the opportune moment for the early detection of IND and the overlapping of disorder of extrinsic innervationin the postoperative period conditioning major difficulties in differential diagnostic for identify the cause of constipation in ARM, the solution of which requires the involvement of a multimodal clinical-paraclinical examination.

REFERENCES

1. Bischoff A., Bealer J., Peña A. Controversies in anorectal malformations. Lancet Child Adolesc Health. 2017. 1:323-30.
2. Dewberry L., Peña A., Mirsky D. et al. Sacral agenesis and fecal incontinence: how to increase the index of suspicion. Pediatr. Surg. Int. 2019. 35:239-42.
3. Holschneider A.M., Hutson J.M. Anorectal malformations in children: embryology, diagnosis, surgical treatment, follow-up. Berlin: Springer; 2006.
4. Levitt M.A., Peña A. Anorectal malformations. Orphanet J. Rare Dis. 2007. 26(2):33-46.
5. Li L., Li Z., Huo H.S. et al. Sensory nerve endings in puborectalis and anal region: Normal findings in the newborn and changes in anorectal anomalies. J. Pediatr. Surg. 1990. 25:658-64.
6. Schalow G. Impulse patterns of single encoding sites of human secondary muscle spindle afferents. Electromyogr. Clin. Neurophysiol. 1993. 33:451-64.
7. Tsuda T., Iwai N., Kimura O., Kubota Y., Ono S., Sasaki Y. Bowel function after surgery for anorectal malformations in patients with tethered spinal cord. Pediatr. Surg. Int. 2007. 23(12):1171-4.

Miscellaneous

Clinical-morphological aspects in the cyst of branchial arc II in children

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Abstract

Aspecte clinico-morfologice în chistul de arc II branchial la copil

Cazul prezentat ilucidează principiile de diagnostic și tratament chirurgical în chistul de arc II branchial la copii, autorii descriind și modificările morfopatologice caracteristice în această formațiune malformativă.
Raritatea cazului prezentat are ca scop de a atenționa necesitatea unui indice de suspiciune sporit în cazurile unor formațiuni cervicale laterale pentru un diagnostic adecvat și un tratament corespunzător, examenul histologic al piesei de rezecție fiind obligator.

Cuvinte-cheie: arc branchial, cleft branchial, chist cervical lateral

Abstract

The case illustrates the principles of diagnosis and treatment of branchial second arch cyst in children, the authors also described the morphopathological changes found in this malformative formation. The rarity of the presented case aims to warn of the need for an increased index of suspicion in cases of lateral cervical formations for proper diagnosis and treatment, the histological examination of the resection piece being mandatory.

Keywords: branchial arch, branchial cleft, lateral cervical cyst

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Introduction

Branchial arch abnormalities are a heterogeneous group of rare benign malformations, located along the sides of the face and neck in the form of sinuses, fistulas, cysts or cartilaginous reminiscences, resulting from involuntary errors of the branchial apparatus during embryonic periods. [14, 23]. These malformations constitute about 17 - 30% of the congenital formations of the head and neck in children [19, 21, 28], of these the most frequent (90-95% of cases) being diagnosed with abnormalities derived from the second branchial arch. The lesions derived from the first branchial arch constitute about 1-8%, and the reminiscences from arches 3 and 4 are much less common [25, 28, 29]. Branchial abnormalities are usually diagnosed in children up to 5 years of age, but can also be seen in adolescents or adults, showing an increase in volume or signs of infection [15].

Abnormalities of the second branchial arch, first described by Bailey in 1929 [10], are more commonly present in the submandibular space, and are found anywhere along the second tract of the branchial arch, which extends from the skin covering the supraclavicular fossa, between the internal and external carotid arteries to enter the pharynx at the level of the amygdala fossa [1]. We present a case of cervical brachial cyst, which after localization corresponds to the origin of the second branchial arch.

Case description

Patient R.E., 14 years old, was sent by the family doctor for a cervical volume formation on the right, being presumed cervical lymphadenitis. The examination found the presence of a formation located below the earlobe, along the sterno-cleido-mastoid muscle, partially mobile, elastic consistency, tense, painful to the touch, hyperemic regional skin. At this age, the formation was not observed. In the last month, the volume formation has obviously increased in size, becoming painful and causing discomfort at swallowing.

The data of the laboratory examination did not show any pathological deviations.

The ultrasound examination of the cervical region found the presence of a clear contour formation with dimensions 56x29 mm, with liquid and solid content.

Angiographic computed tomography revealed an ovoid, encapsulated, clearly contoured cystic formation, with protein liquid content (average density + 29UH), with dimensions (vert. X transv. X anterior) - 5.4cm x 3.1cm x 4.6cm. Post-contrast - moderate amplification at the level of the capsule up to + 100UH, without pathological amplification of the internal content, without intrastromal septa. Mass effect exerted by compression and cranial displacement of the left submendibular gland. Relationships with other anatomical structures: anterior and medial - platysma, subcutaneous and cutaneous tissue, medial - laryngeal cartilage, posterior - carotid space (including neurovascular bundle) and sternocleidomastoid muscle, superior - submendibular gland. Conclusion: CT imaging data suggestive for cystic formation of the soft tissue region of the right neck, possibly infected type 2 gill cyst (fig. 1).

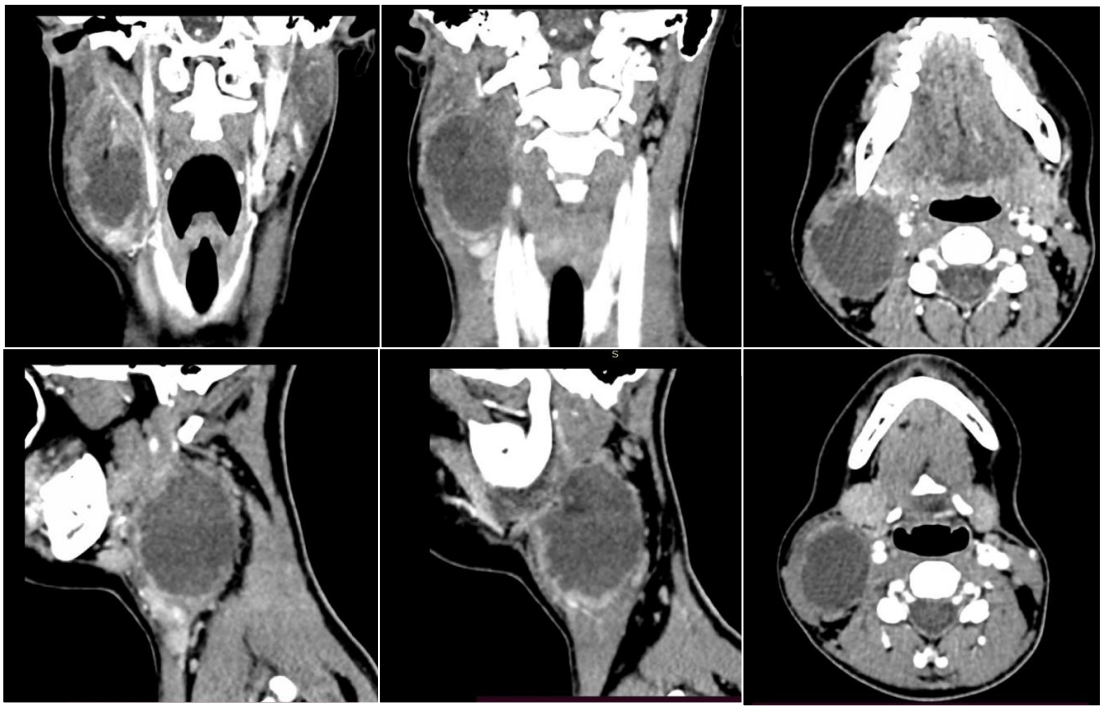

Fig. 1. Patient R.E., 14 years old. Preoperative CT: imaging data suggestive of a cystic formation of the soft tissues of the neck, possibly an infected type 2 gill cyst (explanations in the text).

Under general anesthesia with oro-tracheal intubation, surgery was performed, using the incision approach along the anterior edge of the sternocleidomastoid muscle, taking into account the large size of the formation. After incision of the skin and the superficial cervical fascia, plateau dissection, fascia colli propria dissection and lateral displacement of the sternocleidomastoid muscle with subsequent mobilization of the cystic formation were used, and its careful detachment from the adjacent neuro-vascular package was necessary. these anatomical structures, achieving complete excision of the cyst (fig. 2). We mention that intraoperatively a thin sinus tract was observed, which had a deep path that crossed the upper part of the carotid artery bifurcation to the pharynx, which, after mobilization, was ligated and excised. The operation ended with the restoration of the anatomical layers and the application of a drain. When the cyst was opened, gray liquid content was removed. On microbiological test of liquid content there was not detected the microbial flora, but the test from nasopharynx revealed streptococus oralis. The postoperative period was without events.

Histological examination revealed that the cystic formation was presented from fibrotic connective tissue, endowed with vascular network, lined with untradified multilayered squamous epithelium at 90% of the surface (fig. 3A). The subepithelial area was frequently presented by the presence of the dispersed lymphocyte cell component or of various intensity, in some areas, the cyst wall being presented by the parenchyma of the lymph node, characterized by the cortical area with follicular structures and small centers with insignificant reactive aspects. with lymphocyte content. The area of the ganglion hilum was represented as an integral part of the cystic wall, the respective area being designated adjacent to the epithelial envelope by the presence of a network of small-caliber lymphatic sinusoidal-tubular vessels lined with lymphocytes. Outside, the presence of the conjunctival capsule of the ganglion could be observed (fig. 3C). More frequently, the lymphatic tissue is attested in stratified strips in the capsule area (fig. 3B) or in the subepithelial area where the follicular structures were missing. In some areas, the lymphatic tissue was much thinner in the subepithelial area, with predilection in areas with a lower thickness of the cystic wall (fig. 3A, B). The ganglion, intimately attached to the cystic wall, presented the cortical area where there was an insignificant hyperplasia due to the germinal centers (fig. 3D).

In the samples taken from the adjacent area at the level of the sinus tract, which represents a tubular cord, the presence of the squamous-cellular epithelial covering, frequently detached, was attested. The lymphatic tissue had a dispersed or micro-nodular cellular manifestation associated with plasma cells and fibrillar-conjunctive reaction with sclerogenic changes (fig. 4A). Analogous changes were also found in the distal areas of the sinus tract with aspects of desquamation and partial detachment (fig. 4B).

We note that the tissue and ganglion structures involved in the structure of the cystic wall as well as the adherent ganglion were made of matured tissue, without atypia or proliferation, including the lack of metastatic neoplasms. Also, no active polymorphic-cellular inflammatory processes or the presence of PMN granulocytes were detected. No other types of tissue were found.

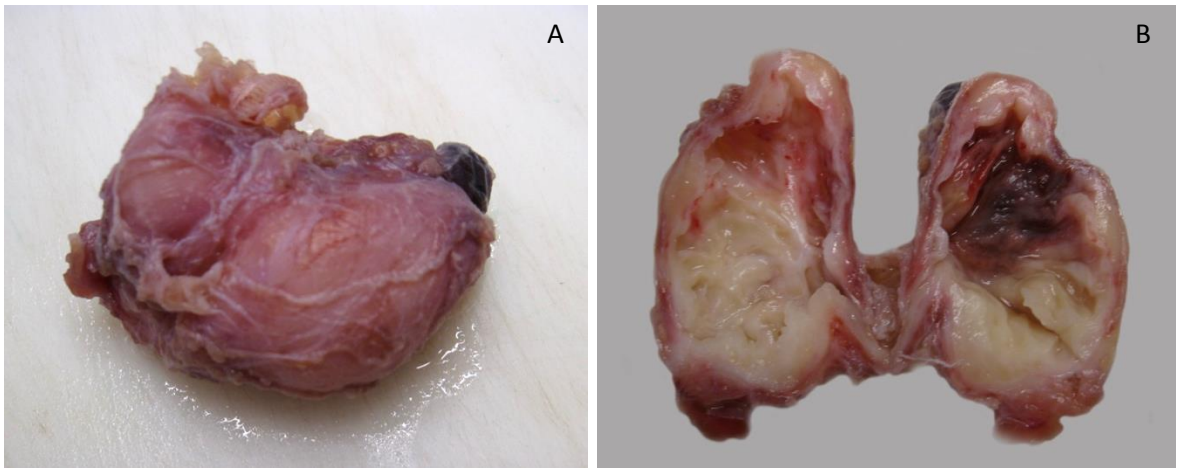

Fig. 2. External appearance of the cystic formation (A) to which a lymph node adheres and in section (B) where the internal folded-lacunar surface of the cyst is observed and communication with the sinus tract (arrow)

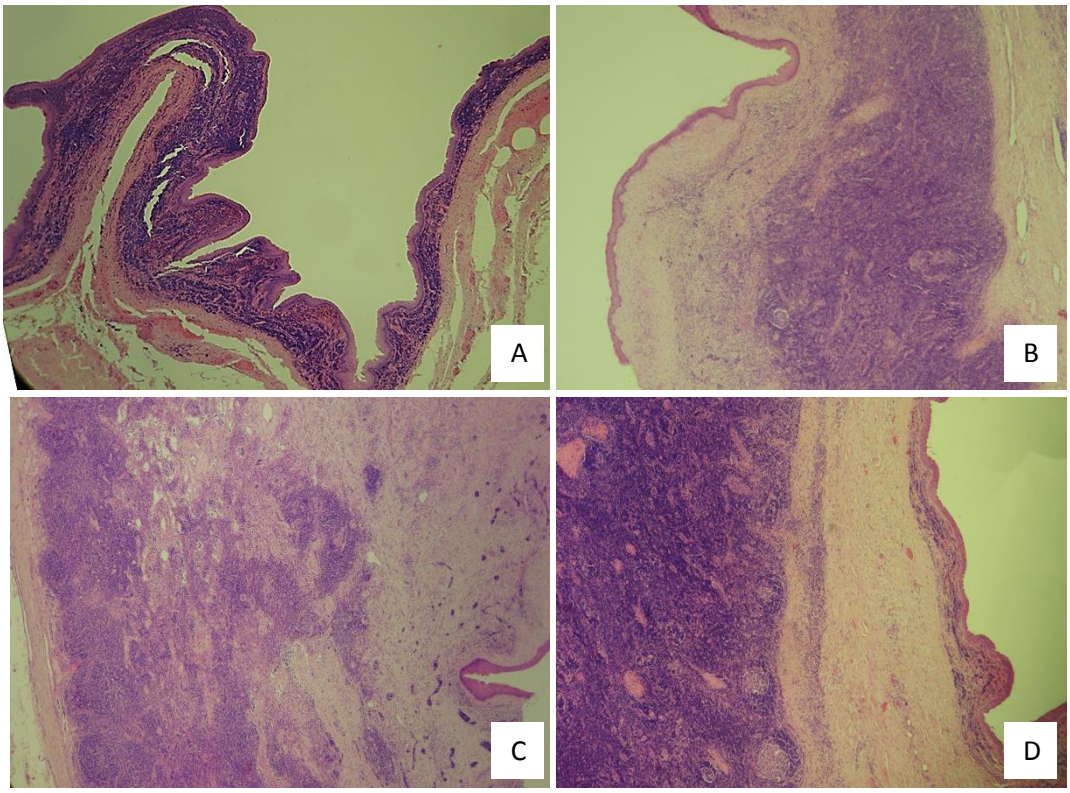

Fig. 3. Cystic wall structure: A - Folded appearance of the inner surface with strips of dense lymphatic tissue in the subepithelial area; B - Strips of lymphatic tissue in the area of the cystic wall; C - Lymph node integrated part of the cystic wall; D - Lymph node closely adhering to the cystic wall, follicular hyperplasia of the cortical follicles.

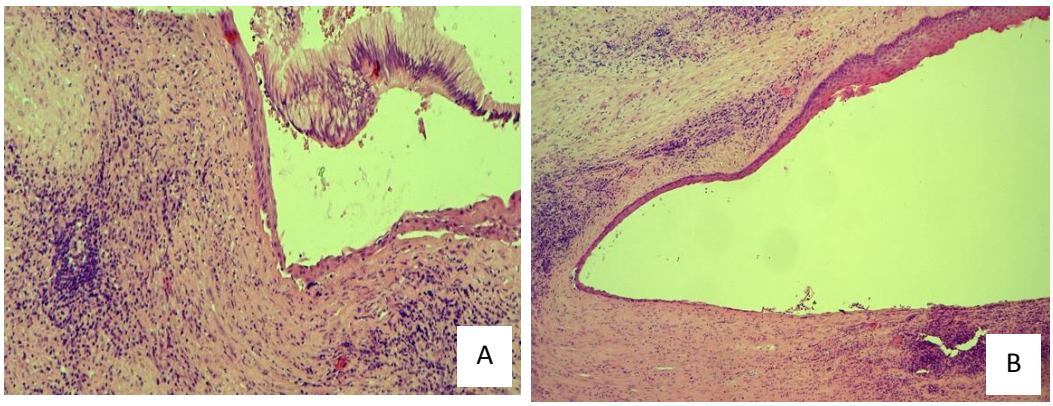

Fig. 4. The structure of the wall at the level of the tubular cord in the communication area. A - Fragments of multilayered prismatic epithelium; B - The blind area of the tubular cord partially lined with squamous cell epithelium with desquamation and detachment aspects..

Discussions

The first description of the branchial apparatus was attributed to Von Baer (1827). In 1828, Rathke described the development of pharyngeal arches in the human fetus, and in 1832, Acherson first described branchial fistula and proposed the notion of branchial cyst (Prasad S.C. et al., 2014).

The appearance of the branchial apparatus can be seen starting with the 4th week of embryonic development, being made up of six pairs of mesodermal arches separated inside the endoderm, which form the four pharyngeal sacs and outside ectoderm, which form the four branchial clefts (splits) .

The first two arcades proliferate, and the last two become rudimentary [3, 6]. Mesodermal tissue contains the artery, nerve, cartilage, and muscle for each branchial arch [12, 22].

The origin of branchial anomalies is a contested one, being proposed various theories:

- Congenital theory, which claims that branchial cysts develop from remnants of the embryonic branchial apparatus;
- Lymph node theories, according to which King (1949) concluded that the cyst comes from cystic changes of the parotid epithelium that are trapped in the upper cervical lymph nodes during the embryonic period;
- Branchial theory.

Bailey H. (1929) classified the anomalies of the second branchial cleft into four subtypes, taking into account the topography [1, 25, 27]:

Type I - the most superficial (located at the level of the superficial fascia), it is located along the anterior surface of the sternocleidomastoid muscle deep to platys, but has no contact with the carotid sheath;

Type II - the most common subtype in which the branchial cyst (located at the level of the deep fascia of the neck, in relation to the large vessels), is located anteriorly by the sternocleidomastoid muscle, posteriorly by the submandibular gland, adjacent and laterally by the carotid thorax;

Type III - branchial cyst (developed in the lodge of large cervical vessels) extends medially between the bifurcation of internal and external carotid arteries, lateral to the pharyngeal wall;

Type IV - the small cystic formation, which is located deep in the carotid sheath in the space of the pharyngeal mucosa and opens into the pharynx.

Some authors refer to the classification proposed by Proctor B. (1955) [26].

Clinically, cysts derived from the second branchial arch are manifested by the presence of a painless swelling located anterior to the sternocleidomastoid muscle between the mandibular angle and the clavicle. During an infection of the upper respiratory tract, an acute increase in size can be observed. Depending on the size, they can be manifested by compressive symptoms with dyspnea, stridor, dysphagia or dyssonia. Bilateral localization of these formations has been reported, and in some cases their presence is part of the branchio-oto-renal syndrome, an autosomal dominant disorder [16, 17].

Branchial abnormalities should be suspected in cases of unexplained recurrent throat infections or cervical volume formations and drainage in the area of the anterior edge of the sternocleidomastoid muscle. Although the complete anamnesis and objective examination may be adequate for diagnosis, preoperative imaging examination (fistulography, ultrasonography, computed tomography, and contrast magnetic resonance imaging) is helpful in confirming the clinical diagnosis [25].

Preoperative differential diagnosis includes thyroglossal duct cyst, cervical lymphadenitis, cervical abscess, toxoplasmosis, tuberculosis, dermoid cyst, dermal inclusion cyst, hydatid cyst, lymphangioma and malignant neoplasm [19].

From a histological point of view, branchial cysts are lined with stratified squamous epithelium (90% of cases), noting that in some cases pseudostratified columnar epithelium can be detected (8%), and in 2% their combination is found. Abundant lymphoid tissue is present in the connective tissue pears, which have germination centers separate from the epithelial cells of a thin basement membrane [2, 16, 30]. Some authors consider that branchial cysts are more frequently lined with squamous epithelium, while sinuses and fistulas tend to be lined with ciliated, columnar epithelium [7]. The increase in size of branchial cysts in short periods of time may be due to reactive hyperplasia of the lymphoid tissue [31]. Similar changes have been described by us. Cases describe cases of carcinoma that developed from the branchial cyst [18].

The microbiological profile of infected branchial abnormalities is not related to age and is different from that of throat infections, with monobacterial infections predominating. Empirical antibiotic treatment should cover Streptococcus species, including penicillin-resistant species, as well as clindamycin-resistant anaerobes. Possible empirical options are second- or third-generation cephalosporins (cefuroxime, ceftriaxone) with the addition of metronidazole against b-lactam-resistant anaerobes [9].

The treatment of choice for branchial abnormalities is radical surgical excision, the timing of surgery being controversial [5, 13]. In order to facilitate radical resection, some authors propose the intraoperative injection of fistulas and branchial cysts with a mixture of fibrin adhesive and methylene blue [20]. Some studies have demonstrated the efficacy and safety of ethanol ablation or sclerotherapy with dilute doxycycline or OK-432 as alternative treatment methods for patients with branchial abnormalities who refuse or are eligible for

surgical treatment [4, 8, 11]. In the specialty literature, a postoperative recurrence rate is reported that varies between 3% and 22%, the causes of recurrences being attributed to preoperative infection and incomplete excision [24].

Therefore, the case presented that branchial cysts in children may remain asymptomatic for long periods of time, but may reach large sizes in short periods of time, causing pain and compression of adjacent tissues. The rarity of the presented case aims to warn of the need for an increased index of suspicion in cases of lateral cervical formations for proper diagnosis and treatment, the histological examination of the resection piece being mandatory

REFERENCES

1. Adams A., Mankad K., Offiah C., Childs L. Branchial cleft anomalies: a pictorial review of embriological development and spectrum of imaging findings. Insights Imaging. 2016. 7:69-76.
2. Arshad M., Ashafaq U., Aslam M. Branchial cleft cyst; second branchial cleft cyst and sinus, diagnosis and management. Professional Med. J. 2019. 26(3):523-7.
3. Bajaj Y., Ifeacho S., Tweedie D., Jephson C.G., Albert D.M. et al. Branchial anomalies in children. Int. J. Pediatr. Otorhinolaryngol. 2011. 75:1020-3.
4. Begley K.A., Murakam J.W. Sclerotherapy as treatment of a branchial cleft fistula in a pediatric patient. Otolaryngol. Case Rep. 2021. 19:100279. Doi:10.1016/j.xocr.2021.100279.
5. Erikci V.S. Pediatric congenital neck masses: A review article. Clin. Surg. 2017. 2:1791.
6. Fanous A., Morcrette G., Fabre M., Couloigner V., Galmiche-Rolland L. Diagnostic approach to congenital cystic masses of the neck from clinical and pathological perspective. Dermatophol. 2021. 8:342-58.
7. Grohman N.G., Herrington H.C. Second branchial cleft anomalies. Operative Techn. Otolaryngol. Head Neck Surg. 2017. 28(3):156-60.
8. Ha E.J., Baek S.M., Baek J.H., Shin S.Y., Han M., Kim C.H. Efficacy and safety of ethanol ablation for branchial cleft cysts. Am. J. Neuroradiol. 2017. 38(12):2351-6.
9. Hirshoren N., Fried N., Weinberger J.M., Eliashar R., Korem M. The microbiology characteristics of infected branchial cleft anomalies. OTO Open. 2019. Doi:10.1177/2473974X19861065.
10. Jain N., Dham R., Shishodia S., Mahajan N. Anomalies of the branchial arch apparatus in children: case series and review of literature. Int. J. Otorhinolaryngol.Head Neck Surg. 2018. 4(6):1517-23.
11. Kim M.G., Lee N.H., Ban J.H., Lee K.C., Jin S.M., Lee S.H. Sclerotherapy of branchial cleft cysts using OK-432. Otolaryngol. Head Neck Surg. 2009. 141(3):329-34.
12. LaRiviere C.A., Waldhausen J.H.T. Congenital cervical cysts, sinuses, and fistulae in pediatric surgery. Surg. Clin. N. Am. 2012. 92:583-97.
13. Lee D.H., Yoon T.M., Lee J.K., Lim S.C, Clinical study of second branchial cleft anomalies. J. Ctaniofacial Sug. 2018. 29(6):e557-e560.
14. Magdy E.A., Hamza A., Youssef A., Yoneis A. Second branchial cleft fistula/sinus tract endoscopy: a novel intraoperative technique assisting complete surgical resection. Eur. Arch. Othorhinolaryngol. 2021. 278(3):833-8.
15. Mattioni J., Azari S., Hoover T., Weaver D., Chennupati S.K. A cross-sectional evaluation of outcomes of pediatric branchial cleft cyst excision. Int. J. Pediatr. Otolaryngol. 2019. 119:171-6.
16. Muller S., Aiken A., Magliocca K., Chen A.Y. Second branchial cleft cyst. Head and Neck Pathol. 2015. 9:379-83.
17. Nahata V. Branchial cleft cyst. Indian J. Dermatol. 2016. 61:70.
18. Nakano A., Mishima K., Katase N., Ueyama Y. A case of scquamosus cell carcinoma arising from branchial cleft cyst. J. Oral Maxillofac. Surg. 2015. 73:781-5.
19. Pacheco-Ojeda L., Ayala-Ochoa A., Salvador K. Branchial cysts in Quito, Ecuador. Int. Arch. Othorhinolaryngol. 2020. 24(3):347-50.
20. Piccioni M., Bottazzoli M., Nassif N., Stefini S., Nicolai P. Intraoperative use fibrin glue dyed with methilene blue in surgery for branchial cleft anomalies. Laryngoscope. 2016. 126(9):2147-50.
21. Prasad S.C., Azeez A., Thada N.D., Rao P., Bacciu A., Prasad K.C. Branchial anomalies: diagnosis and management. Int. J. Otolaryngol. 2014. 237015. doi: 10.1155/2014/237015.
22. Prosser J.D., Myer C.M. Branchial cleft anomalies and thymic cysts. Otolaryngol. Clin. N. Am. 2015. 48(1):1-14.
23. Pupic-Bakrac J., Skitarelic N., Pupic-Bakra A., Baraka I., Srzentic M., Novakovic J., Terkes V. Branchial cleft anomalies: hybrid „Branchial inclusion" theory. Eur. Arch. Othorhinolaryngol. 2021. 278:2593-2601.
24. Reddy A., Valika T., Maddalozzo J. Definitive surgical management for seond branchial cleft fistula: a case series. J. Otolaryngol. Head and Neck Surg. 2020. 49:55. https://doi.org/10.1186/s40463-020-00453-2.
25. Shen L.F., Zhou S.H., Chen Q., Yu Q. Second branchial cleft anomalies în children: a literature review. Pediatr. Surg. Int. 2018. 34(12):1251-6.

26. Spinelli C., Rossi L., Strambi S., Piscioneri J., Natale G., Bertocchini A., Messineo A. Branchial cleft and pouch anomalies in childhood: a report of 50 surgical cases. J. Endocrinol. Invest. 2016. 39(5):529-35.
27. Vlad N., Moldovanu R., Filip V., Preda C., Crumpei F., Prepeliță G. Chistul branchial cervical lateral – un diagnostic diferențial uitat pentru gușa nodulară. J. Chirurgie (Iași). 2008. 4(1):39-44.
28. Waldhausen J.H.T. Branchial cleft and arch anomalies in children. Semin. Pediatr. Surg. 2006. 15:64-9.
29. Xing M.H., Mundi N., Govindan A., Khorsandi A., Urken M.L. Unusual location of a second branchial cleft cyst presenting in the suprasternal notch. Head & Neck. 2021. 43:E27-E29.
30. Zaifullah S., Yunus M.R., See G.B. Diagnosis and treatment of branchial cleft anomalies in UKMMC: A 10-year retrospective study. Eur. Arch. Otorhinolaryngol. 2013. 270:1501-6.
31. Иванова С.В. Клинико-морфологическая характеристика срединных, боковых кист и свищей шеи. Автореф. Дисс. 2005. 161 с.

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Images in Pediatric Surgery

Complicated pulmonary hydatid cyst with endobronchial eruption

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Keywords: complicated hydatid cyst, endobronchial eruption, computed tomography

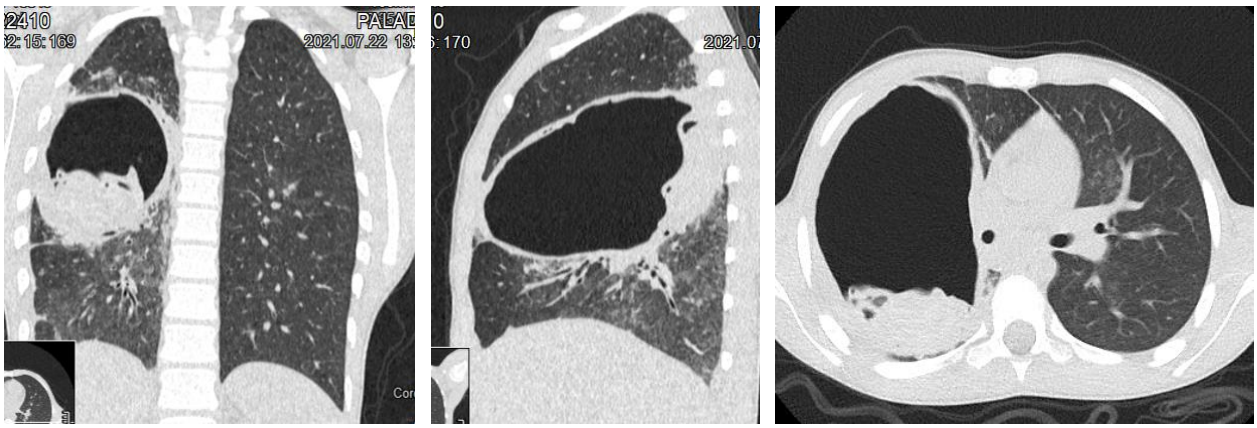

Figure 1: Patient P.A., 11 years old. Preoperatory CT: hidatid pulmonary cyst with endobrochial eruption situated in middle lob of right lung. The floating membrane sign is displayed.

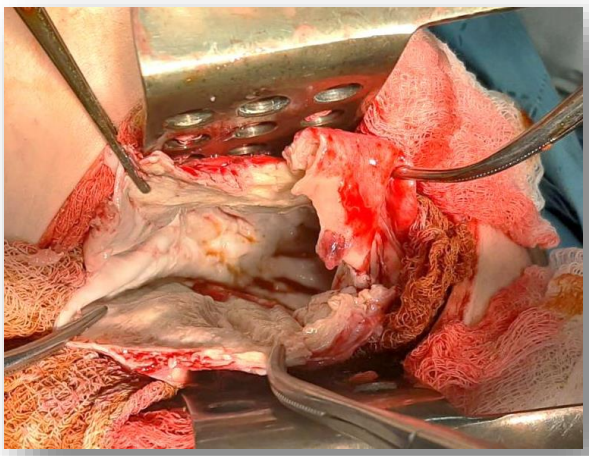

Figure 2: Patient P.A., 11 years old. Intraoperative appearance of the remaining cavity after removal of the hydatid cyst larva and excision of the walls to the lung tissue