

*National Society of Pediatric Surgery of the Republic of Moldova
PHI Institute of Mother and Child,
Natalia Gheorghiu National Scientific and Practical Center
of Pediatric Surgery*

Moldavian Journal of Pediatric Surgery

A scientific practical journal

No. 3

*Formal publication of the National Society of
Pediatric Surgery of the Republic of Moldova
&
Natalia Gheorghiu National Scientific and
Practical Center of Pediatric Surgery*



Chișinău - 2018

EDITORIAL BOARD

HONORARY CHAIRMAN of the EDITORIAL BOARD:

Eva Gudumac academic of Academy of Science of
Republic Moldova, university professor

EDITOR-IN-CHIEF:

Babuci Stanislav

Coordinating editor:

Jalbă Alexandru

Editorial Secretaries:

Negru Ion
Dogotari Nicolai
Eremia Victor

Assistant editor for digital media:

Ambros Igor

International editorial consultants:

Bataev Saidhassan (*Moscow, Russia*)
Ignatiev Roman (*Moscow, Russia*)
Tica Constantin (*Constanta, Romania*)

ASSOCIATE EDITORS:

Anghelici Gh. (Chişinău, Moldova), Ardeleanu M.-A. (Salsburg, Austria), Bairov V.G. (S.-Peterburg, Russia), Bodnar O.B. (Chernivtsy, Ukraine), Boemers T. (Koln, Germany), Burnei Gh. (Bucharest, Romania), Catereniuc I. (Chişinău, Moldova), Cazacov V. (Chişinău, Moldova), Cebotari A. (Chişinău, Moldova), Curajos B. (Chişinău, Moldova), Danci A. (Chisinau, Moldova), Hotineanu A. (Chişinău, Moldova), Hotineanu V. (Chişinău, Moldova), Gladun N. (Chişinău, Moldova), Gladun S. (Chişinău, Moldova), Gorbatiuc O.M. (Kiev, Ukraine), Gupta Devendra (New Delhi, India), Guţu E. (Chişinău, Moldova), Korolkov O.I. (Kharkiv, Ukraine), Jianu M.M. (Bucharest, Romania), Ionescu S. (Bucharest, Romania), Kolesov C.B. (Moscow, Russia), Litovcenco A. (Chişinău, Moldova), Mesentsev A. (Kharkiv, Ukraine), Mishin A. (Chişinău, Moldova), Mishin I. (Chişinău, Moldova), Nacu V. (Chişinău, Moldova), Razumovskii A.Yu. (Moscow, Russia), Ryabykh S. (Kurgan, Russia), Sabetay C. (Craiova, Romania), Socolov Yu. Yu. (Moscow, Russia), Socolovskiy O.A. (Minsk, Belorusia), Shavga N.N. (Chişinău, Moldova), Shavga N.Gh. (Chişinău, Moldova), Shciuca S. (Chişinău, Moldova), Shchebenkov M. (S-Petersburg, Russia), Spataru R. (Bucharest, Romania), Ţurea V. (Chişinău, Moldova), Vetrila M. (Moscow, Russia)

EXECUTIVE EDITORIAL BOARD:

Bajurea A., Cojuşneanu N., Celac V., Feordohleb A., Iliadi A., Malanco S., Maliţev M., Nepaliuc Yu., Pasicovschi T., Petrovici V., Pisarenco A., Revenco I., Roller V., Siniţin L., Tomuz V., Vulpe V., Zaharia I.

Contents

Original Article

- Medical-social rehabilitation in a case of the metaepiphyseal osteomyelitis at the children**
Degtyar V.A., Lukianenko D.N., Baibakov V.M., Kaminskaya M.O., Hryhorenko L.V. 5
- Diagnosis errors in renal tumors in children**
Gudumac E., Bernic J., Petrovici V., Curajos B., Roller V. 12

Research Article

- Histopathological characteristic of atretic segments in esophageal atresia with distal traheoesophageal fistula**
Babuci S., Petrovici V., Negru I., Haidarlî D. 19

Clinical Studies

- The diagnostic significance of pulmonary scintigraphy in children with cystic fibrosis**
Balanetchi L., Selevestru R., Balan A., Krushelnitcaia E., Gudumac E., Sciuca S. 28
- Diagnostic and treatment of the acute pancreatitis in children**
Nepaliuc Iu., Mihalcean V., Gheras E. 31

Case Report

- Iatrogenic injury of the common bile duct during laparoscopic cholecystectomy in children – case report**
Danci A., Jalba A., Ambros I. 35

National Clinical Protocols

„Immortalis est ingenii memoria”

Seneca



Natalia Gheorghiu – Pioneer of Pediatric Surgery in Moldova

Medical-social rehabilitation in a case of the metaepiphyseal osteomyelitis at the children

Degtyar V.A.¹, Lukianenko D.N.¹, Baibakov V.M.², Kaminskaya M.O.¹,
Hryhorenko L.V.¹

*Dnepropetrovsk Medical Academy Ministry of Health of Ukraine¹,
Dnipro Medical Institute of Traditional and Non-Traditional Medicine²,
Department of Pediatric Surgery, Orthopedics and Traumatology (Dnipro, Ukraine)*

Abstract

Reabilitarea medico-socială în cazurile de osteomieliță metaepifizară la copii

Specialiștii în chirurgia și ortopedia pediatrică, preocupați de tratamentul și măsurile de reabilitare ale pacienților cu osteomieliță metaepifizară, nu acordă atenția cuvenită reabilitării socio-psiho-logice. Scopul cercetării constă în determinarea volumului metodelor de reabilitare a acestui grup de pacienți. Autorii au recurs la un sondaj sociologic, folosind chestionarul propriu. La întrebarea de bază a chestionarului - influențează boala realizarea planurilor de importanță vitală în viața pacientului, 8 (15,1%) respondenți au răspuns că osteomielița a distrus toate planurile din viața lor. Concluzia dată a fost primară în rândul bărbaților - 18,2%, comparativ cu femeile - doar 10% ($p > 0,05$). Volumul de reabilitare a fost combinat cu întrebări de abilitare - sistemul de măsuri terapeutice, care ar trebui să prevină și să elimine stările patologice la copiii cu osteomieliță metaepifizară. În articol sa demonstrat științific următoarele etape de reabilitare a copiilor cu osteomieliță metaepifizară: tratamentul osteomielitei metaepifizară în perioada acută și supravegherea clinică de către chirurg și ortoped până la 2 ani (reabilitare); recuperarea structurii și funcției segmentului afectat al membrului în timpul creșterii pacientului (observație clinică și corecție de către ortoped); corecția consecințelor osteomielitei metaepifizare.

Cuvinte cheie: copil, osteomieliță metaepifizară, reabilitare medico-socială, tratament, structura osoasă, regiunea metaepifizară

Abstract

Surgeons and orthopedists, which carried out medical and rehabilitative measures at the patients with metaepiphyseal osteomyelitis did not pay attention to the socio-psychological rehabilitation. Purpose of research is determination volume of methods for rehabilitation this group of patients. In our study we carried out sociological survey, using own questionnaire. On the basic question of the questionnaire – does the disease influence to the realization of vital important plans in a patient's life, 8 (15.1%) respondents had been answered, that osteomyelitis destroyed all plans in their life. The given conclusion was shown primary among male - patients – 18.2%, than among female – only 10% ($p > 0.05$). Volume of rehabilitation we combined with issues of abilitation – the system of therapeutic measures, which should prevent and eliminate pathological conditions at the children with metaepiphyseal osteomyelitis. In the article was scientifically proved the following stages of rehabilitation of children with metaepiphyseal osteomyelitis: treatment of metaepiphyseal osteomyelitis in the acute period and clinical supervision by the surgeon and orthopedist up to 2 years (rehabilitation); recovery of the structure and function of affected segment of a limb during growth of the patient (clinical observation and correction by orthopedist); correction consequences of the metaepiphyseal osteomyelitis.

Keywords: children, metaepiphyseal osteomyelitis, medical-social rehabilitation, abilitation, treatment, bone structure, metaphyseal region.

Correspondence to: e-mail: childsurgery@ukr.net; mob. + (050)9198547

Introduction

Review of the numerous studies [6, 8, 14, 15, 17, 18, 19, 17] demonstrated that acute clavicle osteomyelitis in children is representing in less < 3% of osteomyelitis cases. Acute clavicle osteomyelitis mainly affects older children and has generally good prognosis. Staphylococcus aureus is most commonly implicated and surgery may be needed [12, 24, 26].

Osteomyelitis is inflammation of bones located in the metaphysis and is more frequent in the lower limbs [25]. The diagnosis of osteomyelitis in childhood is usually straightforward and timely use of appropriate antimicrobial therapy has virtually eliminated mortality [13]. In 65-75% of cases the femur, tibia, or humerus is involved. Involvement of other long bones is less common and of bones such as clavicles, ribs, spine, and bones of the hands and feet is unusual; thus, at these sites, diagnostic problems may present [22]. Clavicle is involved in 1-3% [4].

A total of 89 articles were retrieved from literature search, which [2, 21, 29, 35] reported 16 cases of acute clavicle osteomyelitis in children and adolescents (ages ranging between 0 and 16 years) that were included in the analysis.

Infection after surgical treatment of fractures is a complication with significant morbidity and in rare cases even mortality [34]. Consequences of infections include delayed or non-union of the fracture [23]. Most research in this field focuses on peri-prosthetic infection, despite of the different treatment challenges in prosthetic surgery and osteosynthesis. Treatment algorithms have been developed, which dictate aggressive debridement, antibiotic treatment, and if necessary staged replacement of the prosthetic material [33].

Majority of articles is devoted to the bone and joint infections in children and acute hematogenous osteomyelitis [28]. Acute hematogenous osteomyelitis (AHO) is one of the commonest bone infections in childhood. The main clinical symptom and sign in AHO is pain and tenderness over the affected bone especially in the metaphyseal region [20].

The study [11] shows that acute osteomyelitis of the clavicle tends to affect older children, as in our case, in which the patient was a 12-year-old boy. Recurrence happened in 1/16 cases and persistence of symptoms happened in 2/16 cases.

Wang X. et all. (2017) considered, that chronic hematogenous osteomyelitis often results from the improper treatment of acute hematogenous osteomyelitis [32]. As a rule, the complications of chronic hematogenous tibia osteomyelitis treated with the induced membrane technique. A collective of authors [1] proved that acute clavicle osteomyelitis in children is rare representing <3% of osteomyelitis cases. Osteomyelitis was hematogenous in most cases,

with *S. aureus* being the most frequent cause, isolated from either blood or tissue. Acute clavicle osteomyelitis mainly affects older children and has generally good prognosis.

In the research of Morita M. et all. (2017) had been revealed various conditions, including bacterial infection, which can promote osteonecrosis: following invasive dental therapy with anti-bone resorptive agents, some patients develop osteonecrosis in the jaw; however, pathological mechanisms underlying these outcomes remain unknown [16].

Wagner JM. et all. (2017) study osteomyelitis as a frequent consequence of open fractures thus representing a common bone infection with subsequent alteration of bone regeneration. Impaired bone homeostasis provokes serious variations in the bone remodeling process, thereby involving multiple inflammatory cytokines to activate bone healing [31].

Tuck M. et all. (2016) described a patient with ALK-negative ALCL presenting with clinical and radiographic findings suggesting osteomyelitis 6 months after left rotator cuff repair surgery. ALCL should be considered in patients not responding to therapies for osteomyelitis [30].

In the case study [3], 66-year-old Caucasian female presented with insidious sciatic pain leading to an uncommon diagnosis of tuberculous (TB) osteomyelitis with unknown portal entry. Considering TB in the differential diagnosis of a 'bone abscess', it is of paramount importance to come to a correct diagnosis. At work [7] was study acute hematogenous osteomyelitis (AHO) in children as an ideal condition due to its representation of a wide spectrum of disorders that comprise pediatric musculoskeletal infection. Proper care for children with AHO is multidisciplinary and collaborative.

In the research [5] was demonstrated a case of a man aged 68 years presenting to the emergency department with a 3-day history of fever, low back, right hip and leg pain. It was diagnosed Staphylococcus aureus vertebral osteomyelitis complicated by recurrent epidural abscess and severe sepsis.

Hellebrekers P. et all. (2017) considered that infection after osteosynthesis is an important complication with significant morbidity and even mortality [9]. The authors analyzed the effect of such an aggressive standardized treatment regime with implant retention for acute, existing < 3 weeks, infection after osteosynthesis. Hudson JW. et all. (2017) research the response of mandibular osteomyelitis treated by surgical decortication with disruption of the affected adjacent periosteum in concert with long-term targeted antibiotic therapy [10]. The hypothesis is that, by removing the buccal cortical plate and disrupting the hypertrophically inflamed adjacent periosteum, the

medullary bone will be brought in contact with bleeding tissue and circulating immunologic factors and antibiotics, which will promote definitive resolution.

In Ukraine surgeons and orthopedists carried out medical and rehabilitative measures at the patients with metaepiphyseal osteomyelitis (MEO) with the purpose of physical recovery. At the same time, the given patients need firstly the social and psychological rehabilitation. Solution of these problems has a great medico-social significance.

Novelty. Problems of diagnosis and treatment of metaepiphyseal osteomyelitis are vital important in the territory of Ukraine. Firstly in Ukraine were proposed methods of medical-social rehabilitation of children with metaepiphyseal osteomyelitis: treatment of metaepiphyseal osteomyelitis in the acute period and clinical supervision by the surgeon and orthopedist up to 2 years (rehabilitation); recovery of the structure and function of affected segment of a limb during growth of the patient (clinical observation and correction by orthopedist); correction consequences of the metaepiphyseal osteomyelitis.

Purpose of research is to determine volume of methods for medical rehabilitation of the patients with MEO.

Objectives of research:

1. To study socio-psychological and physical condition of the patients with MEO.
2. To compare effectiveness of different methods of treatment and rehabilitation of children – in the

polyclinic, in the hospital, sanatorium-and -resort treatment (by the results of sociological survey).

3. To propose scientifically proved scheme of medical-social rehabilitation of the children with MEO.

Materials and methods of research

Research was conducted with using sociological survey by a specially designed questionnaire. Questionnaire included questions, which were focused on the socio-psychological and physical condition of the patients with MEO. We investigated contingent of persons (53 respondents), who were treated in the clinic 20 years ago with severe complications and consequences of MEO.

Results. The conducted rehabilitation in childhood age and in the long terms after diseases, respondents estimated as not in the full volume (tab. 1). Among these respondents, 28 (52.8%) patients were not received any treatment after discharge from the hospital and in the polyclinic. Treatment in the hospital received only 11 (20.8 %) respondents, sanatorium and resort treatment received 13 (24.5 %) of patients with MEO. To the main question of the questionnaire – does the disease influence on the implementation of life plans 8 (15.1%) of respondents reported, that osteomyelitis has crossed out all their plans for life (tab. 2). This conclusion often had done the male patients 18.2% against 10% of female ($p>0.05$). The given results were presented in (fig. 1).

Table 1. Rehabilitation of a primary disease among the respondents

Frequency of supervision and treatment	In the polyclinic		In the hospital		Sanatorium-and -resort treatment	
	absolute	%	absolute	%	absolute	%
1-2 times a year	9	17.0	2	3.8	4	7.6
2-3 times a year	5	9.4	1	1.9	–	–
3-4 times a year	2	3.8	–	–	–	–
Once in a few years	3	5.7	–	–	4	7.6
Unable to specify a term	6	11.3	8	15.1	5	9.4
Not treated	28	52.8	42	79.2	40	75.5
Generally	53	100	53	100	53	100

Discussions. Taking into account results of our research, rehabilitation of patients should begin in the acute period, during treatment of the complications, correction of the consequences. Psychological adaptation is necessary at the presence of a long-term corrected state of discomfort. Results of research have

been shown that all children, coming to the clinic with the diagnosis of metaepiphyseal osteomyelitis, should carry out a complex treatment, which allowed 93% of patients to decrease an inflammatory process (tab. 2).

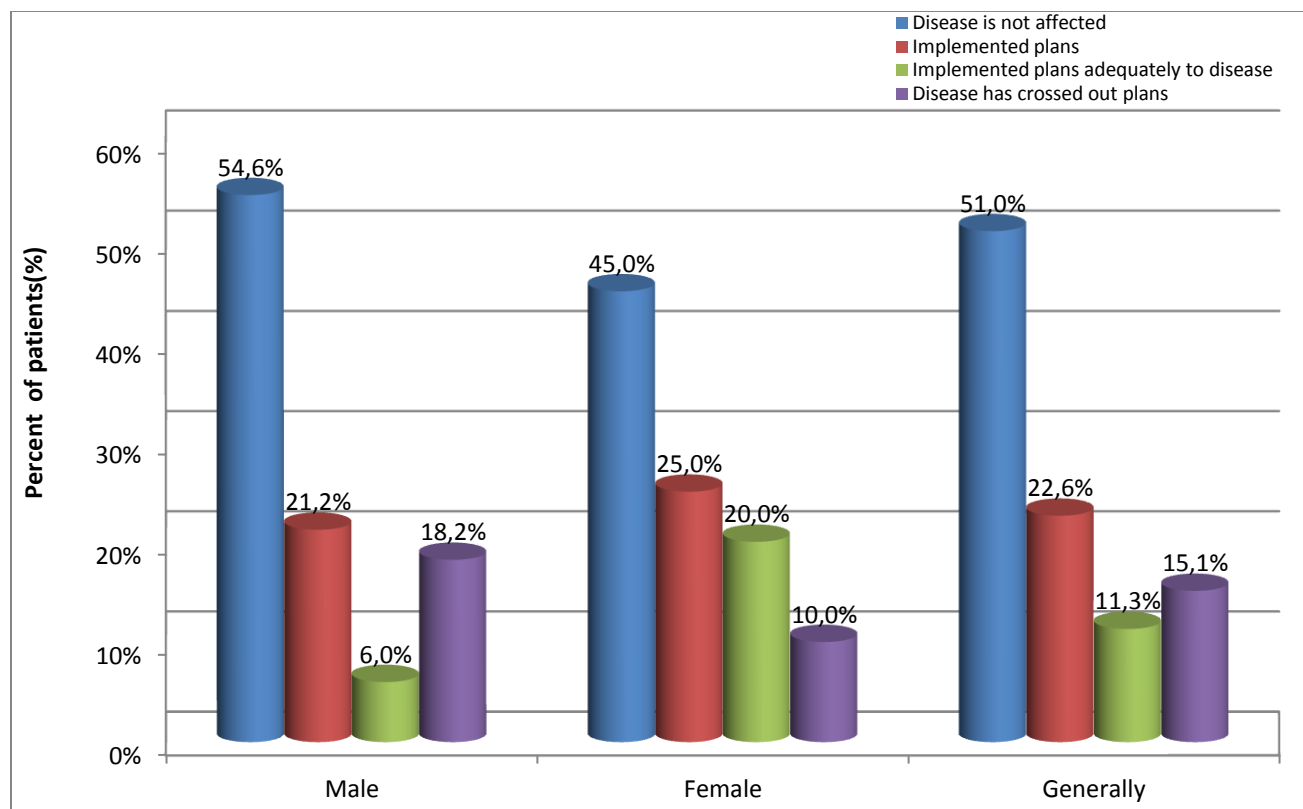


Fig. 1. Graphical presentation of realization plans for life for patients with MEO.

Table 2. Distribution of the respondents' answers, depending on the gender and realization of life plans

Implementation of life plans	Gender				Generally	
	male		female		absolute	%
	absolute	%	absolute	%		
Disease is not affected	18	54.6	9	45.0	27	51.0
Implemented plans	7	21.2	5	25.0	12	22.6
Implemented plans adequately to the disease	2	6.0	4	20.0	6	11.3
Disease has crossed out plans	6	18.2	2	10.0	8	15.1
Generally	33	100	20	100	53	100

Note. Difference between the distribution of respondents' answers by gender was not statistically significance ($p=0.393$, $\chi^2=2.99$).

The patient undergoes an inpatient treatment for 10-14 days, after that in the polyclinic conditions the restorative therapy and dynamic supervision till 2 months should be performing. Hereafter, a pathological process in the bone was estimated in the clinic, correction of the immobilization is carried out, if necessary – treatment of the disease recurrence.

After 4-6 months of the acute process relief or later, almost all children, depending on the age (after 3 years), were recommended treatment of bone in the sanatorium, which have to specialized on the bone and joint system. The basic indications for sanatorium-resort treatment, should be violations of the bone structure, which leads to the orthopedic complications and consequences, i.e. disability. During 2 years the child should be under the supervision of the pediatric surgeon and orthopedist in the polyclinic. Recovery of the patient is evaluated not only on the form and function of the extremities restoration, but primary – on the restoration of the bone structure. Observation of the patient, treatment of probable consequences of the disease should be carried out by orthopedists - traumatologist.

Since 2005 all children, suffering from MEO, coming to the polyclinic of the Dnipropetrovsk Regional Children Clinical Hospital in Dnipro city should be covered with the consultation of psychologist. The psychologist's work is carried out with children, who have orthopedic consequences of MEO, which allows to prepare children for the life and work, taking accounts these consequences.

Scientifically proved a scheme of rehabilitation patients with MEO, because MEO – is acute disease, which requires the immediate medical and surgical intervention as well as in a case of acute appendicitis. Firstly, all this facts determines that the doctor's tactics should be focused on a source of infection, elimination causative agent of inflammation, prevention of the bones' structures destruction and damage of the cartilage surfaces of the joints. Therefore, volume of rehabilitation we combine with modern issues of abilitation, which means system of medical measures, which should prevent and eliminate pathological state at the children of early age, patients with MEO.

There are several theories, which covered pathogenesis of acute hematogenous osteomyelitis: vascular (thromboembolic), allergic, neuro-reflex, etc. A numerous of them indicates that the issue is not fully understood.

Vascular (thromboembolic) theory, developed by L.A. Bobrov (1888) and Lexer (1894), was based on the peculiarities of blood supply of long tubular bones in the children, slowing of blood flow in metaphyses and formation of bacterial embolus,

which causes circulatory disorders, inflammation and necrosis of a bone. This theory is one of the leading in the pathogenesis of given disease.

Allergic theory was proposed by S.M. Derizhanov (1937). According to this theory, osteomyelitis can occur only in a sensitized organism, if "dormant" infection and nonspecific irritation have been shown (trauma, hypothermia, etc.).

Neuro-reflex theory (N.N. Elanskyi, 1954; V.A. Bashinskaya, 1954, 1959) explains the appearance of osteomyelitis by a long reflex spasm of blood vessels in the bone tissue. Environmental factors could provoke a vasospasm. The role of sensitization and presence of the latent infection are not denied. In the pathogenesis of this disease a great importance have autogenous foci of infection — caries, inflammation of the tonsils, adenoids, suppuration of the skin, infectious diseases, etc.

It occurs on a background of deficiency T-lymphocytes and increasing the number of B-lymphocytes. Improvement of the patients' state is accompanied by growth of nonspecific resistance of organism and increased number of T-lymphocytes, reducing amount of B and 0-lymphocytes. High rates of 0- and B-lymphocytes, especially in a case of increased level of antibodies IgG, indicates the development of purulent-septic process (Krivoruchenko V.I., 1980).

Mechanism of development this disease is complex, not fully understood. Classic modern concepts are focused on the connection of inflammation with microcirculation and an immune response of the body. Scheme of the proposed methods of medical-social rehabilitation is presented in the graphical structure (fig. 2).

Conclusions. In the article was scientifically proved the following stages of rehabilitation of children with metaepiphyseal osteomyelitis: treatment of metaepiphyseal osteomyelitis in the acute period and clinical supervision by the surgeon and orthopedist up to 2 years (rehabilitation); recovery of the structure and function of affected segment of a limb during growth of the patient (clinical observation and correction by orthopedist); correction consequences of the metaepiphyseal osteomyelitis. Firstly, metaepiphyseal osteomyelitis is the result of severe defects closely connected with correction of the psychological state, which allowed patients to create adaptation to the society (during whole period of life in the orthopedist and psychologist). The basic conclusion of the given research is inadequate and unsystematic medical rehabilitation, which was determined during investigation of the patients' outpatient records.

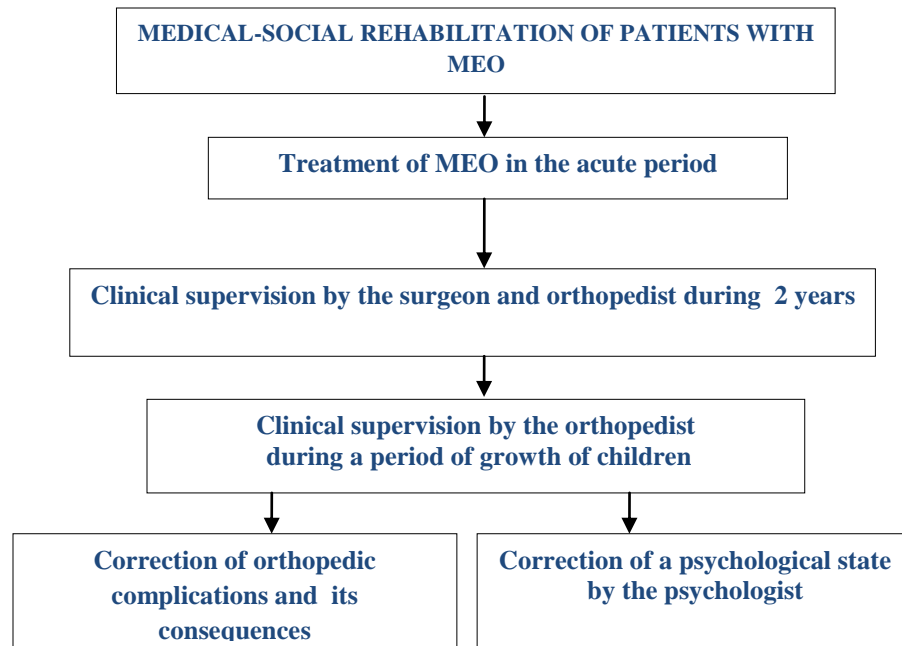


Fig. 2. Scheme of medical-social rehabilitation of patients with metaepiphyseal osteomyelitis.

REFERENCES

1. Chrysochoou E.A., Antachopoulos C., Badekas K., Roilides E. A rare case of clavicle osteomyelitis in a child and literature review. *Case Rep. Pediatr.* 2016; 82(52): 38.
2. Darouiche R.O. Treatment of infections associated with surgical implants. *N. Eng. J. Med.* 2004; 350:1422-9.
3. De Mulder P., Harth C., Ide L., Vallaey J., Baelde N., De Bo T. An uncommon cause of sciatic pain: tuberculous osteomyelitis of the ischial tuberosity. *Acta Clin. Belg.* 2017; 11:1-4. doi: 10.1080/17843286.2016.1271499.
4. Donovan R.M., Shah K.J. Unusual sites of acute osteomyelitis in childhood. *Clin. Radiol.* 1982; 33(2):222-30.
5. Dunphy L., Iyer S., Brown C. Rare cause of back pain: Staphylococcus aureus vertebral osteomyelitis complicated by recurrent epidural abscess and severe sepsis. *BMJ Case Rep.* 2016; doi: 10.1136/bcr-2016-217111.
6. Franklin J.L., Parker J.C., King H.A. Nontraumatic clavicle lesions in children. *J. Pediatr. Orthopaed.* 1987; 7(5):575-8.
7. Funk S.S., Copley L.A. Acute hematogenous osteomyelitis in children: pathogenesis, diagnosis, and treatment. *Orthop. Clin. N. Am.* 2017; 48(2):199-208.
8. Gerscovich E.O., Greenspan A. Osteomyelitis of the clavicle: clinical, radiologic, and bacteriologic findings in ten patients. *Skeletal Radiol.* 1994; 23(3):205-10.
9. Hellebrekers P., Leenen L.P., Hoekstra M., Hietbrink F. Effect of a standardized treatment regime for infection after osteosynthesis. *J Orthop Surg Res.* 2017; 12(1):41. doi: 10.1186/s13018-017-0535-x.
10. Hudson J.W., Daly A.P., Foster M. Treatment of osteomyelitis: A case for disruption of the affected adjacent periosteum. *J. Oral Maxillofac. Surg.* 2017; doi: 10.1016/j.joms.2017.03.008.
11. Kiedrowski M.R., Horswill A.R. New approaches for treating staphylococcal biofilm infections. *Ann. N. Y. Acad. Sci.* 2011; 1241:104-21.
12. Kocher M.S., Lee B., Dolan M., Weinberg J., Shulman S.T. Pediatric orthopedic infections: early detection and treatment. *Pediatr. Ann.* 2006; 35(2):112-22.
13. Lew P.D.P., Waldvogel P.F.A. Osteomyelitis. *Lancet.* 2004; 364(9431):369-79.
14. Lowden C.M., Walsh S.J. Acute staphylococcal osteomyelitis of the clavicle. *J. Ped. Orthopaed.* 1997; 17(4):467-9.
15. McGraw M.A., Mehlman C.T., Lindsell C.J., Kirby C.L. Postnatal growth of the clavicle: birth to 18 years of age. *J. Ped. Orthopaed.* 2009; 29(8):937-43.
16. Morita M., Iwasaki R., Sato Y. et al. Elevation of pro-inflammatory cytokine levels following anti-resorptive drug treatment is required for osteonecrosis development in infectious osteomyelitis. *Sci. Rep.* 2017; 7:46322.

17. Morrey B.F., Bianco A.J., Jr. Hematogenous osteomyelitis of the clavicle in children. *Clin. Orthopaed. and Relat. Res.* 1977; 125:24-8.
18. Moseley H.F. The clavicle: its anatomy and function. *Clin. Orthopaedics and Related Res.* 1968; 58:17-27.
19. Ogden J.A., Conlogue G.J., Bronson M.L. Radiology of postnatal skeletal development. III. The clavicle. *Skeletal Radiol.* 1979; 4(4):196-203.
20. Osmon D.R., Berbari E.F., Berendt A.R., Lew D., Zimmerli W., Steckelberg J.M., et al. Diagnosis and management of prosthetic joint infection: clinical practice guidelines by the infectious diseases society of America. *Clin. Infect. Dis.* 2013; 56(1):e1-25.
21. Parvizi J., Adeli B., Zimistowski B., Restepo C., Greenwald A.S. Management of periprosthetic joint infection: current knowledge: AAOS exhibit selection. *J. Bone Joint Surg.* 2012; 94:104.
22. Peltola H., Pääkkönen M. Acute osteomyelitis in children. *New Engl. J. Med.* 2014; 370(4):352-60.
23. Perren S.M. Physical and biological aspects of fracture healing with special reference to internal fixation. *Clin. Orthop. Relat. Res.* 1979; 138:175-96.
24. Pineda C., Vargas A., Rodríguez A.V. Imaging of osteomyelitis: current concepts. *Inf. Dis. Clin. N. Am.* 2006; 20(4):789-825.
25. Robben S. G. Ultrasonography of musculoskeletal infections in children. *Eur. Radiol., Suppl.* 2004; 14(4): 65-77.
26. Schuppen J., van Doorn M.M.A.C., van Rijn R.R. Childhood osteomyelitis: imaging characteristics. *Insights into Imaging.* 2012; 3(5):519-33.
27. Srivastava K. K., Garg L. D., Kochhar V. L. Osteomyelitis of the clavicle. *Acta Orthopaed. Scandinav.* 1974; 45(5):662-7.
28. Stojicic S., Shen Y., Haapasalo M. Effect of the source of biofilm bacteria, level of biofilm, maturation, and type of disinfecting agent on the susceptibility of biofilm bacteria to antibacterial agents. *J. Endo.* 2013; 39(4):473-7.
29. Trampuz A., Widmer A.F. Infections associated with orthopedic implants. *Curr. Opin. Infect. Dis.* 2006; 19:349-56.
30. Tuck M., Lim J. et al. Anaplastic large cell lymphoma masquerading as osteomyelitis of the shoulder: an uncommon presentation. *BMJ Case Rep.* 2016; doi: 10.1136/bcr-2016-217317.
31. Wagner J.M., Jaurich H., Wallner C., et al. Diminished bone regeneration after debridement of posttraumatic osteomyelitis is accompanied by altered cytokine levels, elevated B cell activity, and increased osteoclast activity. *J. Orthop. Res.* 2017; doi: 10.1002/jor.23555.
32. Wang X., Wang Z., Fu J. Induced membrane technique for the treatment of chronic hematogenous tibia osteomyelitis. *BMC Musculoskelet. Disord.* 2017; 18(1): 33.
33. Wehrli W. Rifampin: mechanisms of action and resistance. *Rev. Infect. Dis.* 1983; 5(Suppl 3): S407-11.
34. Worlock P., Slack R., Harvey L., Mawhinney R. The prevention of infection in open fractures: an experimental study of the effect of fracture stability. *Injury.* 1994; 25(1):31-8.
35. Zimmerli W., Trampuz A., Oschner P.E. Prosthetic-joint infections. *N. Engl. J. Med.* 2004; 351:1645-54.

Diagnosis errors in renal tumors in children

Gudumac E.^{1,2,3}, Bernic J.^{1,3}, Petrovici V.⁴, Curajos B.^{1,3}, Roller V.^{2,3}

*Nicolae Testemitanu SUMPh, Department of Surgery, Orthopedics and Pediatric Anesthesia¹,
Laboratory of Surgical Infections in Children²,
PHI Institute of Mother and Child, Academician Natalia Gheorghiu National Scientific
and Practical Center for Pediatric Surgery³,
Department of Morphopathology⁴*

Abstract

Erori de diagnostic în tumorile renale la copii

Diagnosticul, tratamentul și profilaxia patologiei canceroase, în special la copii rămâne o problemă de sănătate publică majoră atât la nivel global, regional, cât și național, inclusiv în Republica Moldova. Tumorile retroperitoneale, în special renale la copii frecvent atestă un patern malign rămân în continuare discuție privind diagnosticarea clinico-paraclinică în timp oportuni. Revizuirea activității diagnostice a unui eșantion de 62 pacienți într-o perioadă de 10 ani a stabilit frecvența și structura tumorilor renale la copii, în 15% din cazuri sa atestat persistarea unui diagnostic întârziat, cauzat de diverse erori atestate la diverse nivele ale asistenței medicale, determinând spitalizarea întârziată în subdiviziunile medicale specializate. În rezultatul studiului și a cauzelor atestate în prevenirea unor erori, în baza protocoalelor NWIS și SIOP sa elaborat o nouă conduită prevăzând și particularitățile diagnosticului histopatologic după noua clasificare privind paternul histopatologic al tumorii care va reduce posibilele deficiențe diagnostice spre un management diagnostic și medico-chirurgical oportun.

Cuvinte cheie: tumorile renale, diagnostic, tratament, profilaxie, copii

Abstract

The diagnosis, treatment and prophylaxis of cancer pathology, especially in children, remains a major public health issue on the global, regional and national level, including in the Republic of Moldova. Retroperitoneal tumors, especially those renal in children, frequently attest to a malignant pattern and there remains a discussion of clinical-paraclinical diagnosis over time. The review of the diagnostic activity of a sample of 62 patients over a period of 10 years determined the frequency and structure of kidney tumors in children, in 15% of cases the persistence of a delayed diagnosis, caused by various errors at different levels of health care, delayed in specialized medical subdivisions, was attested. As a result of the study and of the proven cases in the prevention of errors, based on the NWIS and SIOP protocols, a new behavior was developed, including the histopathological diagnosis features after the new histopathological pathology classification of the tumor, which will reduce the possible diagnostic deficits towards a timely diagnostic and medical-surgical management.

Keywords: renal tumors, diagnosis, treatment, prophylaxis, children

Correspondence to: e-mail: victorroller.vr@gmail.com; mob.: +37369354951

Introduction

Tumors of the renal-ureteral and neurogenic system in children are the most frequent tumors of the retroperitoneal space, characterized by various expansions to or in the abdominal cavity, mimicking gastro-duodenal, mesenteric, colon. Both retroperitoneal or intraabdominal locations frequently have a common general symptom. At the same time, retroperitoneal tumors in children, especially reno-ureteral, are much more common compared to mesenteric, colonial or gastro-duodenal. Tumors with renal localization in childhood ontogenesis account for about 5-11% of the total attested tumors at this age [10]. According to the literature, Wilms tumor (nefroblastoma) is the most common kidney tumor in childhood in over 90% of cases of kidney tumor [5]. The annual incidence is 8.1 to one million children, resulting in 600-700 new cases each year in the North America. Symptomatic manifestations of the tumor more frequently occur at the age of 1-4 years, the mean age at diagnosis of children with Wilms tumor of 3 years, being relatively unusual in the first 6 months and in children aged 6-10 years [3, 4]. A large number of children diagnosed with kidney tumor consult a physician with various symptoms, which depending on location, age and level of healthcare are initially treated as manifestations of other abdominal processes, which induces late diagnosis of renal tumor. According to statistical data, about 60,000 people with kidney tumor, including malignant, are diagnosed lately, often in late stages, and are confused with other conditions, including kidney malformations [6, 11]. Causes that can lead to diagnostic errors are multiple, including limited time spent on a consultation, incomplete examination, incorrect interpretation of imaging data, vasography, etc. The medical practice demonstrates that there is currently no evidence of clinical and paraclinical moments in making the delayed, erroneous or inappropriate diagnosis of tumor pathology in children, which justified the retrospective analysis of the problem.

The aim of the study was to evaluate the diagnostic activity, the morphology and morphopathology aspects of the renal tumors, to determine and avoid delayed diagnostic or diagnosis errors, to optimize the medical and surgical diagnosis of kidney tumors in children.

Material and methods

The data provided from the observation sheets, the children's development card, the previous exit tickets, the anamnesis, the personal evaluation, the diagnosis and the treatment, all processed statistically, served as materials for the study. The study was conducted within the Urology Department of PHI Academician Natalia Gheorghiu National Scientific and Practical Center for Pediatric Surgery on a sample of 62 children aged between 2 weeks and 18 years who were

diagnosed with renal tumors during 2007-2017. As a significant objective, this study included the elucidation of some risk factors in the development of renal tumors from the study group, the development of an appropriate correlation of diagnostic methods, treatment in the assessment of prognosis in kidney tumors in the child.

Results and discussions

As a result of the examination, the prevalence of male renal tumors predominantly constituted 54.8% (34 boys) compared to 45.3% (28 girls). 32.3% (20) of cases predominated between the age of 5 and 7 months, and 45.2% of children aged 3 to 5 years (28 cases). A frequency with statistical significance was renal tumor diagnosed in 22.6% (14 cases) in the infant's age from 2 weeks to 4 months. According to the data indicated in 87.1% (54) of medical records, 79.9% (41) of the children were born at term of 39-40 weeks, 18.5% (10) at term of 37-38 weeks and 5.6% (3) children were born at the 35-37 week limit.

Depending on the location of the tumor with a frequency of 62.3% (38 cases), the renal tumor affected the left kidney compared to the right kidney - 35.5% (22) of the cases. A case in our observations and medical diagnosis was the detection in 2 (3.3%) of cases of bilateral tumor localization.

In 35.5% (22) of primary diagnosed children, renal tumors were primarily surgically resolved, and in 64.5% (40) of cases due to delayed and difficult diagnosis, some complications were caused by the tumor and other circumstances. The children initially had a chemotherapy treatment, which led to a prognosis reserved for this category of children, as well as some difficulties in the correct treatment, including establishing the histopathological specific pattern.

Depending on the duration of the premorbid and morbid status in 32.3% (20) of cases, the presence of the renal tumor was suspected and / or diagnosed by the pediatrician or the family doctor to whom the parents addressed for various reasons. In 30.6% (19) of cases, the development or presence of a bulky expansion process and abdominal asymmetry were primarily reported by parents and later diagnosed by the doctor as renal tumor at different periods from the onset of manifestations observed by the parents. Another partiality of diagnosis in 35.5% (22) cases was the occasional diagnosis of renal tumors in the routine ultrasound of internal organs, and retrospectively referred to by parents as a general unstable symptomatology. In one case, 1.6% of the kidney disease was suggestively suspected as a malformation still at the USG in the perinatal period, and subsequently in the first year of life being confirmed as a renal tumor.

According to anamnesis and in-patient assessment, clinical symptomatology in the study group had a varied

and non-specific onset. In 48.4% (30) of cases, children showed a general symptom characterized by the persistence of a abdominal algic syndrome, apathy, subfebrility, fatigue, observed in the last 1-4 months. In 30.6% (19) of cases in parallel there were more obvious digestive disorders - dyspepsia and vomiting during 1-3 months. At a rate of 8.1% (5 cases), renal tumor evolution evolved hidden under the acute abdomen and 3.2% (2) cases of abdominal trauma in connection with what was urgently hospitalized in the Mother and Child Institute. In 6.5% (4 cases), the evolution indicated the presence of a renal tumor, which was occasionally detected in ultrasound examinations (USG) in the absence of premorbid status.

According to the morphological imaging data (fig. 1, 2) and morphopathological retrospectives in 50.0% of the children, the renal dimensional tumor varied within the limits of 4x5cm, with 37.1% within the limits of 8x7cm. 12.9% of children were confirmed with major and impressive tumors, of which 8.1% were 14x10cm and in 4.8% of cases in the limits of 11.5x7.5cm.

Another feature attestable at the time of tumor diagnosis was the presence of a significant correlation between the tumor dimensions and the parenchyma of the kidney, which recorded 72.6% (45) of cases a tumor cortex between 35-60% of the renal area and in a frequency of 27.4% (17) of children with a larger area of 60-70% compared to renal parenchyma, of which in 3 cases the tumor occupied about 90% of the renal mass with a weight of 370.0g and 420.0g

We note that in 2 children (3.2%) aged 1 to 3 months the presence of the renal tumor was diagnosed with delay, the diagnosis being difficult only for the USG method, therefore, computerized tomography (CT) with vascography was used. Surgical interventions in all cases were performed in accordance with the morbid tumor status of children, the anatomic features of the deformed tumor kidney according to the procedures provided by the national and international protocols (fig. 3, 4). According to the morphopathological pattern of kidney tumors, there were determined nephroblastic tumors - 48.4%, 19.6% - mesenchymal tumors, 18.3% - mesenchymal epithelial tumor, 13.8% - mixed tumors. Focal hemorrhagic necrosis, necrotic ischemic processes, and some inflammatory associations of the tumor and renal parenchyma were confirmed in 59.2% of tumor cases (fig. 3). In 23.6% of cases, very rare variations were observed, such as mesenchymal blast-epithelial mixed nephroblastoma, stromal epithelial nephritis, cystic multilocular nephroma, blastic neprorblastoma associated with fibroadenoma (fig. 4-6). In our case, on the diagnosis of kidney tumors in children, there was also the diagnosis of kidney tumor in 2 children of the same family (both girls) - the first underwent a surgery of a primary diagnosed kidney tumor, and in the second girl the tumor was determined after examination at the doctor's indication far more late, being diagnosed the presence of bilateral renal tumor, the child was hospitalized for evidence and solving at the Institute of Oncology.



Fig. 1. Renal ultrasonography. Patient S. Renal tumor on the right without signs of vessel thrombosis

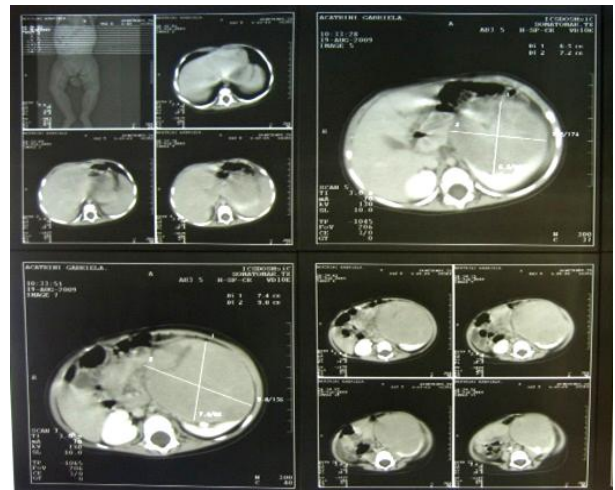


Fig. 2. CT. Patient A. CT aspect of right kidney tumor



Fig. 3. Patient N. 1 year old (no. 43/278). Mesoblastic nephrom of the left kidney with thrombosis and haemorrhage



Fig. 4. Patient S., 5 years old (no.4087 / 19250). Blast-epithelial mixed nephroblastoma with mesenchymal component. After 2 chemotherapy treatments

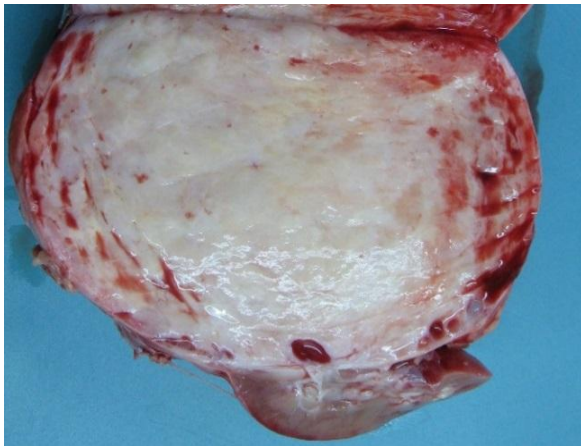


Fig. 5. Patient C, 2 years old (no.1294/6486). Mezenchimal-epithelial nephrom of the left cystic focal kidney.



Fig. 6. Patient M., 3 years old (No. 846/5467), cystic formation. The tumor is polycystic and is separated from renal parenchyma by a fibrous capsule

However, we note that 6-7 decades ago, kidney tumor mortality varied between 70-75%, currently due to protocols developed by the Wilms National Research Group (NWIS) used in the United States of America, Canada and those developed by the International Society for Pediatric Oncology (SIOP) used in European countries, mortality has significantly decreased, in 80% of cases, patients are treated with initial chemotherapy. Survival is similar in some of the protocols, currently being 900 / o.m [2, 7, 8]. The NWIS protocol is directed to performing nephrectomy and establishing the morphopathologic diagnosis in optimal time, the one proposed by SIOP provides for initial treatment with adjuvant chemotherapy [8].

Morphopathological diagnosis is based on the absence or presence of blastem-epithelial elements or anaplasia, depending on which tumors are divided into tumors with favorable and unfavorable histology [9]. According to some studies, cellular anaplasia occurs with a frequency of 11% of cases of Wilms tumor. According to the SIOP protocols, patients with Wilms tumors with a favorable histological pattern, ie characterized by a low epithelial-blastomatoid component, or the predominance of epithelial-stromal cells only after preoperative chemotherapy have a better prognosis than those with large amounts of cellular blast in tumors [1]. In the evaluation of 15% (9) of the cases, some discrepancies, regarding the operational

management and the diagnostic opportunity, including in the cases of abdominal trauma, were found (2 cases fig. 3-5).

Clinical case reporting: The female patient, S.A, aged 1 year and 5 months, (fig. 7), was hospitalized urgently after 10 days of having occasionally sustained a lumbar traumatism injury on the right of the table horn (according to the parents). The child was evaluated by the family doctor. Ultrasound of the urinary system was performed - without any obvious pathological changes, being left in out-patient conditions. Upon admission to the Mother and Child Institute, the general condition is confirmed, it is severe, periodically subfebrile, pale skin and mucous membranes. Heavy breathing in the lungs. The cord - no stealthy noises. The asymmetric abdomen, enlarged in dimensions in the hippocampus and the right flank, the pronounced vascular drawing with venous stasis, the abdominal wall in the precordial area (fig.7). Palpation of the abdomen detects a tough, irregular, sensitive tumor, located in the abdomen on the right. Electrocardiogram at admission - no changes, sinus rhythm.

Biological status examinations: Anemia, increased VHS (Hb.-98 g / l; Er.- 2.3×10^{12} / l; L. 7.4×10^9 / l, non-

segm. -7.0, segm. - 8, VSH - 15mm / h, total protein - 64 g / l, serum urate - 4.3, serum creatinine - 0.057 mmol / l, bilirubin - 9.4 mcmol, transaminase - 1, Na - 141 mmol / l). The imaging examinations revealed: Doppler ultrasound - the formation as intense vascularized arterial and venous without signs of thrombosis in the renal vein; CT - kidney tumor of the right kidney of major size 14x10 cm. General urine test: color - yellow, transparent, reaction - acid, protein - negative, flat epithelium - unique in the field of view, leukocytes - 2-4 in the field of view. Taking into account the generally appreciated serious condition, the major dimensions of the tumor, the previous trauma, the consultation of the pediatrician, chemotherapy was done in the Department of Pediatric Oncology of the Institute of Oncology. After three chemotherapy treatments (vincristine - 0.75 mg on the 1st, 8th, 5th days and adriamycin- 20 mg on the 15th day), surgical treatment followed by transabdominal approach on the right (fig. 8-10). On the day of surgery, the asymmetric and enlarged in size abdomen persists in the hippocampus and the right flank, palpating the same tumor-specific features (fig.7).



Fig. 7. Patient S. On the day of surgery. Abdominal expansion on the right

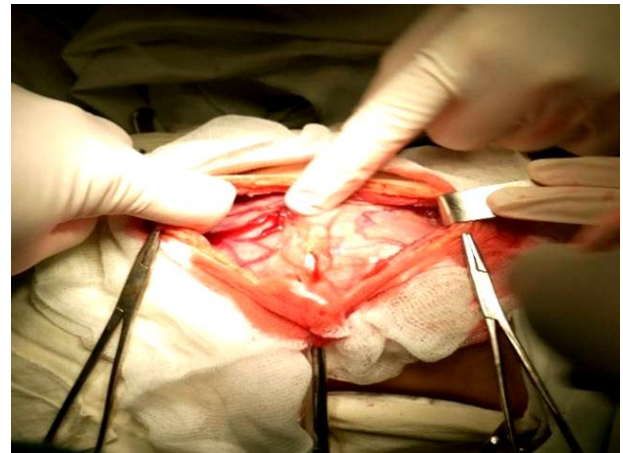


Fig. 8. Intraoperative aspect of the renal tumor in the incision

The post-operative period evolved without any local or general complications, 8 days after the surgery, the patient was transferred to the Oncology Department of the PHI Oncology Institute to continue the chemotherapy treatment and to rigorously check the renal function along the way.

Therefore, the case at first glance, presents a difficult and delayed diagnostic management in a child with Wilms tumor (mesoblastic nephroblastoma), retrospectively made. These cases in medical diagnosis

are frequently treated as diagnostic errors. Currently, according to the specialty literature, the majority opinion considers that the wrong diagnosis should be replaced by the medical error because the diagnosis is based on the signs and symptoms identified when the patient is present at the doctor, as well as by the communicable aspect of the parents. On this subject Mr. Prof. Vasile Astarastoaeie, the president of the Romanian College of Physicians, states that "The systemic approach to the disease is totally lacking" [6].

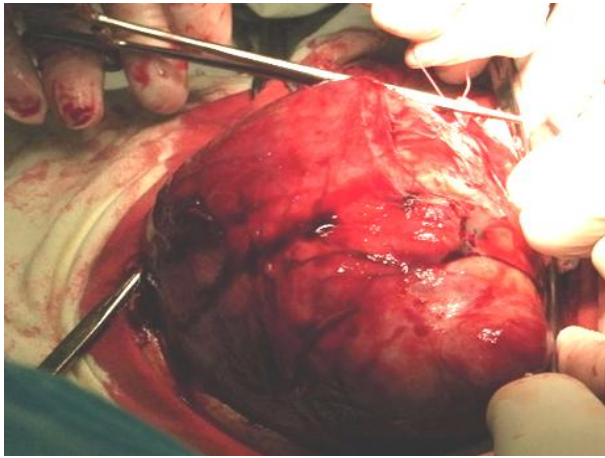


Fig. 9. Ablăție a vaselor, legătura piciorușului vascular renotumoral

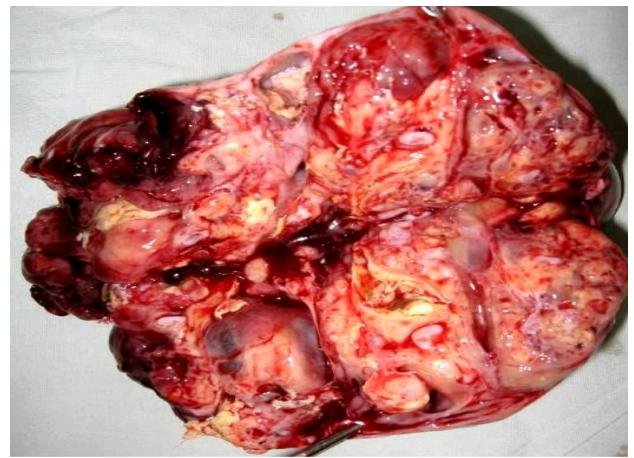


Fig. 10. Piesa anatomico-chirurgicală a tumorii în secțiune

However, we mention that early diagnosis of a kidney tumor, especially Wilms' Tumor, including its variations, is very important because it will have a better prognosis and a more favorable post-procedural or post-interventional evolution. At the same time, despite the fact that many patients show statistically favorable post-procedural or post-interventional evolution, but the medium and long-term prognosis seems to be unfavorable in most cases.

The Wilms tumor, defined by Beekwith (1975) as a renal tumor, is composed of metanephrogen blast and its stromal and epithelial derivatives, at different stages of differentiation, which give it a histopathological pattern in different variations, attested in our practice as well. It is known that environmental factors do not play an important role in tumor development or histopathological changes. Currently, it is indicated in a genetic predisposition with a determined role in tumor development.

Research on histological classification, staging schemes, early diagnosis, initial stages (TNoMo, T2 NoMo) have a fatal histology and an unfavorable prognosis. The favorable progression may be in the case of small areas of neoplasms, cellular aplasia and small focal areas of penetration of the capsule. Thus, the prognosis is unaffected first, depending on the size of the tumor and its weight. The most unfavorable factors are: the age of the child in the tumor, the advanced stage of the tumor and the unfavorable histopathological pattern.

Therefore, the results we have obtained in our study and our clinic experience together with literature data, taking into account the international protocols recommended by NWIS of the US and the European SIOPs, make us recommend a more cautious assessment of children who have abdominal pain, haematuria, constipation, urinary tract infection, diarrhea, presence of trauma in anamnesis expansion or palpation of a formation in the abdomen, etc. Therefore,

the medical-surgical tactic in cases with the aforementioned symptomatology is suggestive of the tumor or in those occasionally detected or suspected will include the following:

- Anamnesis (perinatal development, presence of tumors or anomalies in family members, relatives, evolution of symptomatic morbid status, etc.);
- Anthropometric, weight, functional cardio-respiratory examinations etc.;
- Laboratory blood counts, urine summary exam, coagulogram, creatinine, etc.;
- USG imaging investigations of abdominal cavity and retro-peritoneal space;
- Computerized (CT) CT scan with contrast, chest CT in difficult or complicated cases, including MRT (on indication), Kidney Renoscintigraphy;
- Puncture-biopsy of the tumor formation under ultrasound guidance, with a 2-3 point score to establish the tumor parenchymal pathway (favorable, standard, unfavorable according to NWIS and SIOP), except in cases of cystic tumor.

Conducting in such order and urgently will allow the assessment of the general condition of the patient, the location of the tumor and the degree of spread, the morphopathological confirmation of the tumor pattern, on which the medical-surgical tactic and prognosis of the disease will depend.

The medical-surgical treatment tactic, after making the diagnosis, will be performed according to the complex program: surgery, chemotherapy, radiotherapy.

Conclusions. The study concluded, that during the last 10 years in the Republic of Moldova, as well as in many countries of the world, there is an increase in the number of kidney tumors, especially of nefroblastoma in different morphopathological variations at different ages. The widespread use of

imaging methods has led to an increase in the diagnosis rate of renal tumors in incipient stages and in children aged 0-1 year, yet an impressive number of tumors are diagnosed late and are a pressing problem of medical diagnosis. As a result of the study, according to NWIS and SIOP, a follow-up of the work of pediatricians,

family doctors, and special care physicians, was carefully quantified for the careful consideration of children, in order to determine, as early as possible, the features of retroperitoneal kidney tumors in children, in order to prevent diagnostic errors and possible complications.

REFERENCES

1. Breslow N.E., Palmer N.F., Hill L.R., et al. Wilms' tumor: prognostic factors for patients without metastases at diagnosis, results of the National Wilms' Tumor Study. *Cancer*. 1978; 41:1577-89.
2. Gadd S., Huff V., Huang C-C., et al. Clinically relevant subtypes identified by gene expression patterns support a revised ontogenic model of Wilms tumor: a Children's Oncology Group study. *Neoplasia*. 2012; 14: 742-56.
3. Hrabovsky E.E., Othersen H.B. Jr., deLorimier A., et al. Wilms' tumor in the neonate: a report from the National Wilms' Tumor Study. *J. Pediatr. Surg.* 1986; 21:385-7.
4. Nocol P.F., Rollins M.D., Muratore C.S. *Fundamentals of Pediatrics Surgery*, Springer International Publishing. 2017; p. 777-86.
5. Pastore G., Znaor A., Spreafico F., et al. Malignant renal tumours incidence and survival in European children (1978-1997): report from the Automated Childhood Cancer Information System Project. *Eur. J. Cancer*. 2006; 42:2103-14.
6. Programul Național de control al cancerului pentru anii 2016-2015. Hotărârea Guvernului nr. 1291 din 2 decembrie, 2016.
7. Shannon B.A., Cohen R.J., Segal A., et al. Clear cell renal cell carcinoma with smooth muscle stroma. *Hum. Pathol.* 2009; 40:425-9.
8. Sonn G., Shortliffe L.M.D. Management of Wilms tumor: current standard of care. *Nat. Clin. Pract. Urol.* 2008; 5 :551-60.
9. Verschuur A.C., Vujanici G.M., van Tinteren H., et al. Stromal and epithelial predominant Wilms tumours have an excellent outcome: the SIOP 93 01 experience. *Pediatr. Blood Cancer*. 2010; 55:233-8.
10. Ивановская Т.Е., Леонова Л.В. Патологическая анатомия болезни плода и ребенка. *М.: Медицина*. 1987; 256с.
11. Пытель Ю.А., Золотарев И.И. Ошибки и осложнения в рентгенологическом исследовании почек и мочевых путей. *М.: Медицина*. 1987; 256с.

Research Article

Histopathological characteristic of atretic segments in esophageal atresia with distal eso-traheal fistula

Babuci S.^{1,3}, Petrovici V.², Negru I.¹, Haidarli D.¹

PHI Institute of Mother and Child, Academician Natalia Gheorghiu National Scientific and Practical Center for Pediatric Surgery¹

Department of Morphopathology²

Laboratory of surgical infections in children of Nicolae Testemitanu SUMPh³

Abstract

Caracteristica histopatologică a segmentelor atretice în atrezia de esofag cu fistulă eso-traheală distală

Analiza rezultatelor studiului efectuat privind particularitățile macro- și microanatomice ale componentelor structurale și a celor morfologice ne demonstrează că în cadrul atreziei esofagiene cu fistulă eso-traheală inferioară concomitent cu aspectele macroscopice, histologic sunt prezente o serie de modificări cu importanță predictivă asupra perioadei postoperatorii, care pot fi clasate în două grupe: *primare* – caracterizate de tulburările histogenerezii la etapa embrionară (displazia fibro-musculară, ectopia cartilajului displazic la nivelul esofagian și a mucoasei gastrice, duplicaturile esofagului, membrana esofagiană incompletă, aganglioneza) și *secundare* – atrofico-hipertrofice evaluate pe parcursul etapei fetale de la 12-13 săptămâni gestație care variază după prezența lor și după localizare (hipetrofia și/sau atrofia fasciculilor musculare, ectaziile varicoase vasculare, procesele inflamatorii, dismaturia structurilor nervoase. Prezența insulițelor de mucoasă gastrică foveolară în segmentul distal cu fistulă eso-traheală poate servi un substrat morfologic favorabil de dezvoltare a esofagului Barrett la bolnavii cu atrezie de esofag sau malignizare, fapt ce impune necesitatea unei evaluări endoscopice de urmărire permanentă.

Cuvinte cheie: atrezia de esofag, displazie fibro-musculară, fistulă eso-traheală

Abstract

The analysis of the results of the study of the macro- and microanatomic peculiarities of the structural and morphological components shows that in the esophageal atresia with inferior eso-tracheal fistula concurrently with the macroscopic, histological aspects there are a number of changes with predictive importance on the postoperative period, can be classified into two groups: primary - characterized by histogenesis disorders at the embryonic stage (fibro-muscular dysplasia, ectopic dysplastic cartilage at esophageal and gastric mucosa, esophagus diets, incomplete esophageal membrane, aganglionosis) and secondary - atrophic-hypertrophic evolution during the fetal stage from 12-13 weeks gestation that varies according to their presence and location (muscle hypertrophy and / or muscle atrophy, vascular varicose ectasis, inflammatory processes, dismutation of nerve structures). The presence of the islets of foveolar gastric mucosa in the distal segment with eso-tracheal fistula may serve as a favorable morphological substrate for the development of the Barrett esophagus in patients with esophageal atresia or malignisation, which necessitates an endoscopic evaluation of permanent follow-up.

Key words: esophageal atresia, fibro-muscular dysplasia, eso-tracheal fistula

Correspondence to: e-mail: babuci@newmail.ru; mob.: +373 79574683

Introduction

Esophageal atresia with eso-tracheal fistula is a severe, relatively common congenital malformation (approximately 1 in 3,000 live births) found in the neonatal period, representing a challenge for the pediatric surgeon both in terms of surgical procedure and management of postoperative morbidity [11]. Although postoperative mortality in this malformation has decreased significantly, a higher incidence of postoperative morbidity is determined by both the anastomotic complications [27] and respiratory and gastrointestinal problems, some of which persist throughout life [7, 12]. Some studies have indicated that the incidence of postoperative complications ranges between 20% and 60% [28]. Fistulae and anastomotic strictures, dysphagia, gastroesophageal reflux, motility disorders, epithelial metaplasia, tracheomalacia represent changes frequently documented radiologically, scintigraphically and endoscopically [14, 18]. In this context, there is a need for complex prospective histopathological studies with the aim of describing more details in the pathogenesis of these postoperative consequences. In the literature there are few reports of histopathology of esophageal atresia with eso-tracheal fistula [1, 3, 12].

The aim of the study was to evaluate the spectrum of morphopathological changes detected in both atresiac segments of the esophagus in cases of esophageal atresia with lower eso-tracheal fistula.

Materials and methods

The histopathological study was performed on 21 patients, including autopsy materials on unoperated specimens from 8 newborn babies with the presence of esophagus atresia and inferior eso-tracheal fistula in 13 cases - from newborns operated. The evaluation of macro-microanatomic peculiarities in esophageal atresia with inferior esotracheal fistula was performed at 3 levels: the atresia upper segment, the esotracheal fistula and the inferior segment. Serial sections of both the proximal (flanking) segment of the esophagus and of the distal fistula segment were performed. The study material, after a preventive fixation in 10% formalin solution, was histologically processed according to the histological standard. The hematoxylin-eosin (H-E), van Gieson (VG) and orcein staining methods were used.

Results and discussions. In the cases of the study group, the presence of a diastase between the esophageal segments ranging from 0.3-0.5cm to 6.8cm (fig. 1A) was established. More frequently, in 14 cases (66.7%) was attested diastasis of 2-2.5 cm. The length of the upper segment oscillates between 2.3 and 4.5cm with a diameter of 2.0-2.7 cm. Macroscopically, the upper esophageal segment in most cases exhibited a marked hypertrophy of the wall, the thickness of which consisted of 0.3-0.4 cm, the mucosa with bulky longi-

tudinal pleats, frequently oriented chaotically zoned (fig. 1B). In 11 cases (52.4%), were found erosions or exulcerations in the mucosa. The lower esophageal segment was much hypoplastic (fig. 1A), having a diameter of 0.5-0.9 cm over 1-3cm, more commonly the level of tracheal communication being located at 1.0-1.5cm from the bifurcation (fig. 1C), in 16 cases - in the bifurcation region, and in 4 cases - in the main bronchus, including the left one - 3 cases and in the right one - 1 case. More frequently, in 15 cases (71.4%) the vagus nerve had a rectilinear tract, in 5 cases (23.8%) a slightly or moderately undulated or bilateral curve was observed, and in one case (4.8 %) - spiral positioning around the upper atrophied esophageal segment. The histological examinations performed at the level of the upper esophageal atresia segment allowed for a well differentiated structure in the upper and middle third of the esophageal wall in 12 cases (57.1%) (fig. 2A), in 9 cases (42.9%) , in the distal portions of this segment observing the predominance of lax fibrous tissue endowed with a blood and lymphatic vascular network with a decrease of the glandular elements. Closer to the esophageal end, were observed muscle hypertrophy and thickening of the submucosa, the latter being unevenly defined in the bundles by the presence of conjunctive tissue bridges. The muscular tunica of the esophageal wall at this level also marked the presence of hypertrophy (fig. 2B).

Glandular elements were dispersed, with acinar structure, atrophic or dilated acinus. At the same time, inflammatory focal or diffuse processes were observed (fig. 2C), being present in areas with exucérations or eroded. In some areas of the mucosa, could be observed areas with exucération or erosion. In some areas, its own muscular tunic was made up of atrophied striated muscle fibers. The internal muscle layer contained chaotically distributed muscle fibers, or their zonal deficiency, sometimes being completely substituted by conjunctive tissue (fig. 2D).

In the middle areas of the superior esophageal segment, in some cases, the submucosa was predominantly constituted of densely fibrillated connective tissue or with predominance of collagen fibers in abundance towards the apical atresiac segment with a much diminished vascular network. At this level, was documented the diminution of the autonomic and myenteric nerve network. Quite often, muscular fascicles of the esophageal muscles were completely replaced by mesenchymal and collagenous connective tissue, often in the appearance of steeply atrophied beams and monstrous hypertrophies. Such changes have been appreciated that the primary disorder, that fibro-muscular structural-tissulare dysmorphia. In 11 cases(52,4%), malformative modification of the fibro-muscular tissue during superior atresiac segment had focal and mosaic aspect.

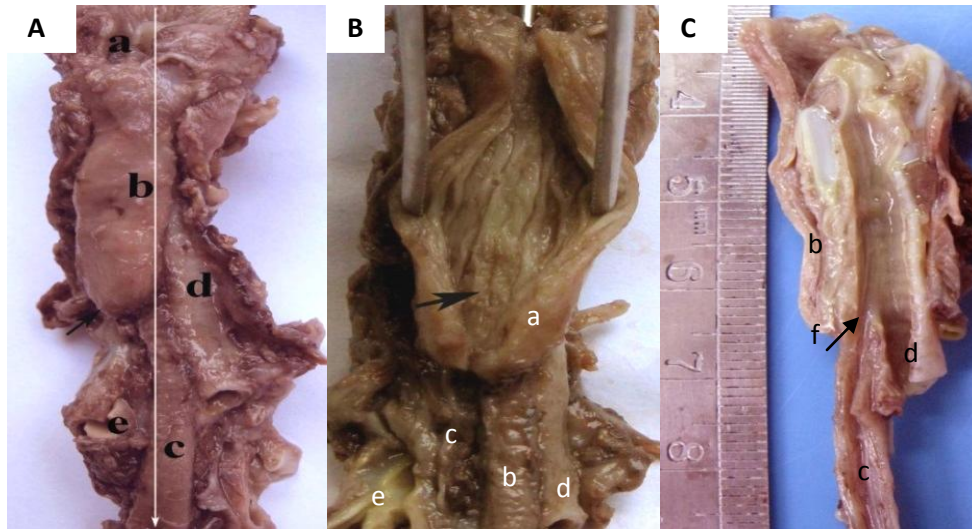


Fig. 1. Macroanatomic aspect of the esophageal tract with inferior tracheoesophageal fistula. **A)** a - Laryngean region; b - the proximal atresial segment of the esophagus; c - distal esophageal segment; d - trachea; e - cardiac vascular magistral device; **B)** sectional aspect of the proximally attracted segment: a - proximal segment with mucosal follicular hypertrophy (→); b - the distal segment, c - the corrugated vagus nerve (→); d - trachea; e - cardiac vascular magistral device; **C)** sectional aspect of the lower atresized segment: b - proximal proximal esophageal segment; c - distal esophageal segment; d - trachea; f - inferior eso-tracheal fistula (→);

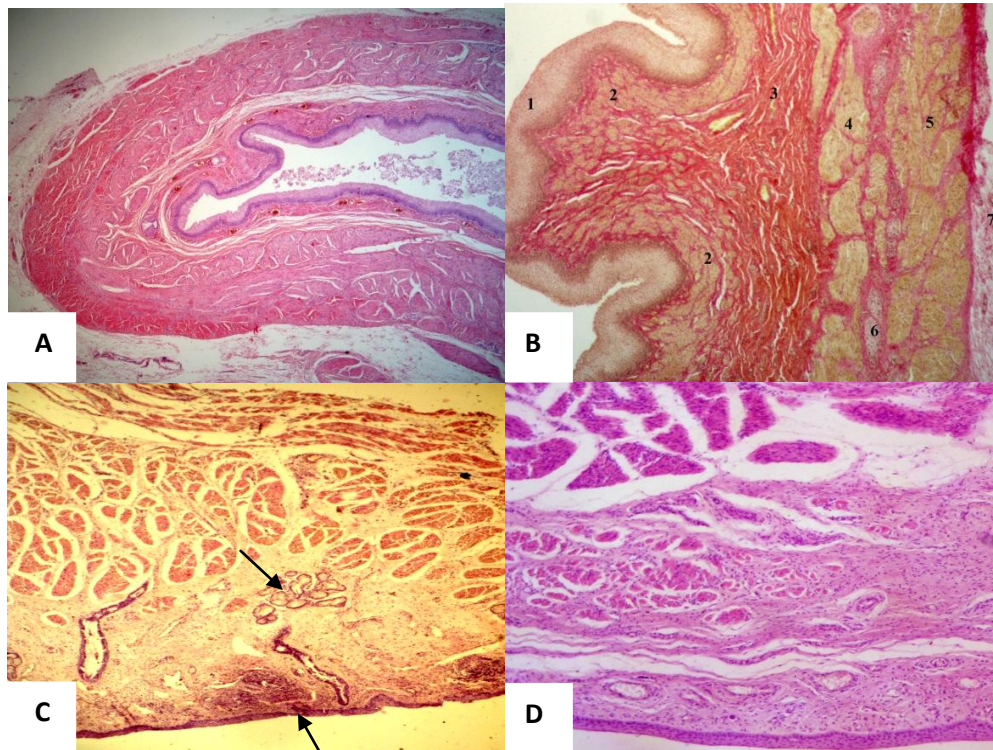


Fig. 2. Microanatomy of the proximal atretic segment: **A)** Hypertrophy of the tunic muscle in the middle portion of the proximal esophageal atretic segment by the fastening of the inner tunic by conjunctive tissue bridges. Color. H-E. x25; **B)** Structure of the proximal atresized segment: 1 - squamous epithelium; 2 - the mucous membrane tunic; 3 - submucosa; 4 - internal circular muscle layer; 5 - external longitudinal muscular layer; 6 - intermuscular nervous plexus; 7 - adventitia. Color. VG. x 25. **C)** Initial area of the proximal esophageal segment – 1) solitary glands with dilated ducts, 2) inflammatory processes at submucosa with epithelial atrophy. Color. H-E. x25; **D)** Abundance of conjunctive tissue with zonal substitution of internal muscle tunic. Color. H-E. x25.

In 16 cases (76,2%), in the apical area of the upper segment and in the area of the wall within 0.5 to 1.2 cm from the apex of the atresia have been registered areas of accentuated fibrosis processes. In this segment, muscular tunic was presented in part by fibers or myocytes chaotic arranged through conjunctive tissue. Frequently, muscle fascicle wer reduced, the present fascicles was disorganized, with different orientation, often in a cross-section with a steep appearance. In 8 cases(38,1%), in the area of the anterior wall of the distal areas of this esophageal segment internal muscular wall, was presented by single fiber or chaotic muscle fascicles, some hypertrophied and others are present only in like shadows, those changes are present and in the external mucular wall, where they could be viewed solitary fiber or hypertrophied fascicles (fig. 3A).

Concomitant with the changes described, in three cases, the wall structure of the upper esophageal segment has been detected the presence of tubular form of duplication of the esophagus with a length of 1.4; 2,0 and 2.1 cm communicating with the esophageal lumen, remaining unrecognized preoperative (fig. 3B,C). In one case, histologically has been detect the presence of a diverticulum in middle part of the upper segment of atresia which have a size of 1.2 x 0.8 cm and a wall thickness of 0.1 cm. Another case is characterized by the presence of a small diverticulum but associated with the membrane, some like fold of the fibromucosal wall, at a distance of 1.6 cm from the larynx which partially obstruct the esophageal lumen (fig. 3D).

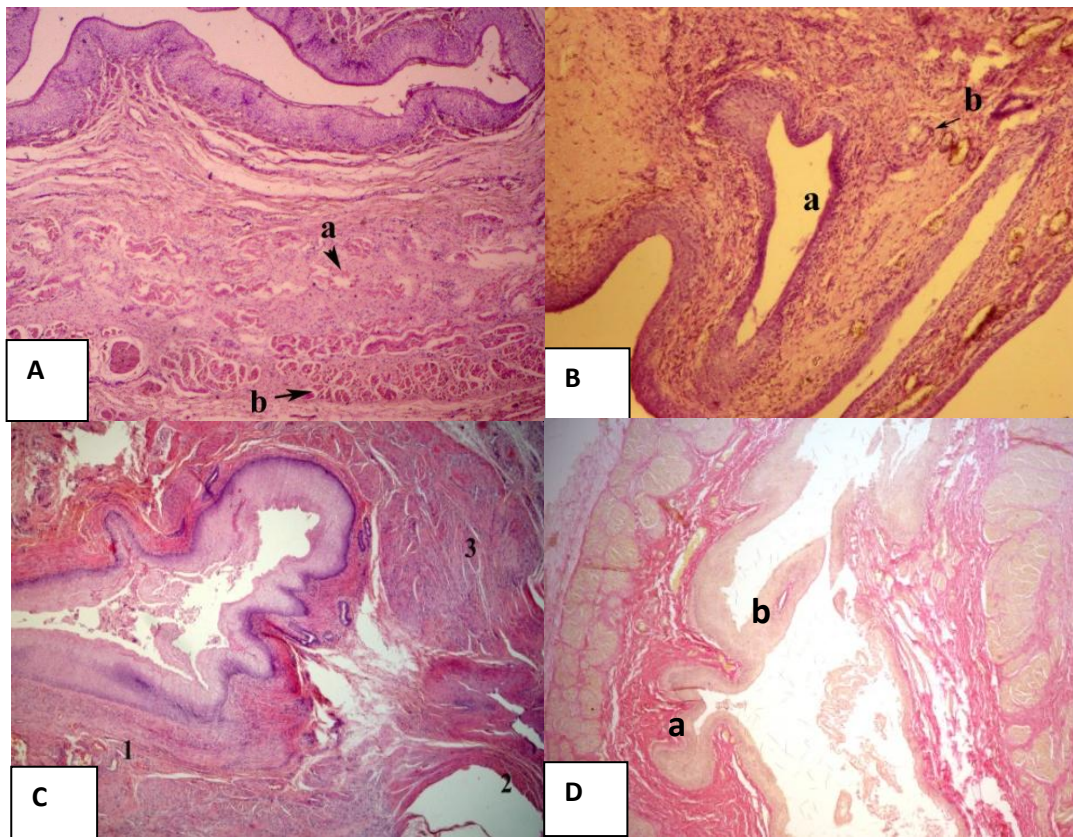


Fig. 4. Histological aspects of the upper esophageal segment. A) Abrasive fascicles and myocytosis chaotic oriented in to fibrous tissue, ganglioneurons with morphological dismutation x75. Color. H-E.B)Intramural tubular duplication of esophagus (a) with solitary glandular structures (b) × 25. Color. H-E. C) Intramural tubular duplication of the proximal segment to the anastomosis dehiscence. Microfoto. 1 - the anterior wall of the esophagus; 2 - suture level of anastomosis; 3 - preanastomotic hypertrophy of muscle tunics x 25. Color. H-E. D) Diverticol (a) associated with a fibro-epithelial transverse membrane.

In 19 cases (90,5%), the lower end compared of the upper esophageal segment, has been registered the volume hypoplasia of the esophageal tube a lengs 1-3 cm, with 0.5-0.9 cm in diameter. In 13 cases (61,9%), the wall thickness varied within 0.15-0.3 cm and in 38,1% of the cases(8 cases) that had a thickness of proximal end 0.3-0.4 cm. In two cases (9,5%) it was found lumen not like tube but fissured fistula. Throughout they, were not observed hypertrophic aspects of mucosal fibro-epithelial ply. Depending on the location of the fistula, in 15 cases (71,4%) the prevalence was found form when eso-tracheal fistula it opening at 1.0-1.5 cm superior to the tracheal bifurcation predominantly on the side wall, in 5 cases (23,8%) - at the level of the bifurcation and in one case (4,8%), fistula in the right bronchus at 0.3 cm from the bifurcation.

The histological examination of the distal segment with fistula (fig. 4), allowed to document the presence of dysplastic changes in microstructure, propensity primary origin, more pronounced than the changes detected in the proximal atresic segment. In 7 cases (33,3%), over a lengt of 0.3 to 0.5 cm in mosaical aspect or totally was found reduction or lack of muscle layers, the wall is presented by a fibro-epithelial-conjunctive plate, the conjunctive part being

sclerogenic in varying intensity. The vascular network being diminished and/or with varicosities of the venous component. Glandular structures were cystic or adenomatous. At the tracheo-esophageal junction and adjacent or found the presence of fibrous-cartilaginous dysplasia manifested by immature cartilaginous tissue with glandular structures in various ratios with dilated acinar segments (fig. 4A), those having esophageal and / or tracheal origin. On the tract of the distal segment, towards the stomach the esophageal fistulated tube, gradually in the mosaic aspect took over a normal microanatomic structure. In 14 cases (66.7%), the muscular layers, more frequently in the outbreak, contained muscle fibers or fascicles atrophic, while were observed few hypertrophic muscles, which were frecrently repartisated chaotically in a connective tissue mass (fig. 4B).

At 1-2.5 cm from the eso-tracheal junction of the fistula, were found dysplastic fibrosis processes under sclero-cicatricial aspects with the disordonation of the muscular coats (fig. 4C), which consequently passed into a large or less normal structure of the esophagus but with a hypertrophy of the his own coats of the submucosa (fig. 4D) showing a narrowing of the esophageal lumen.

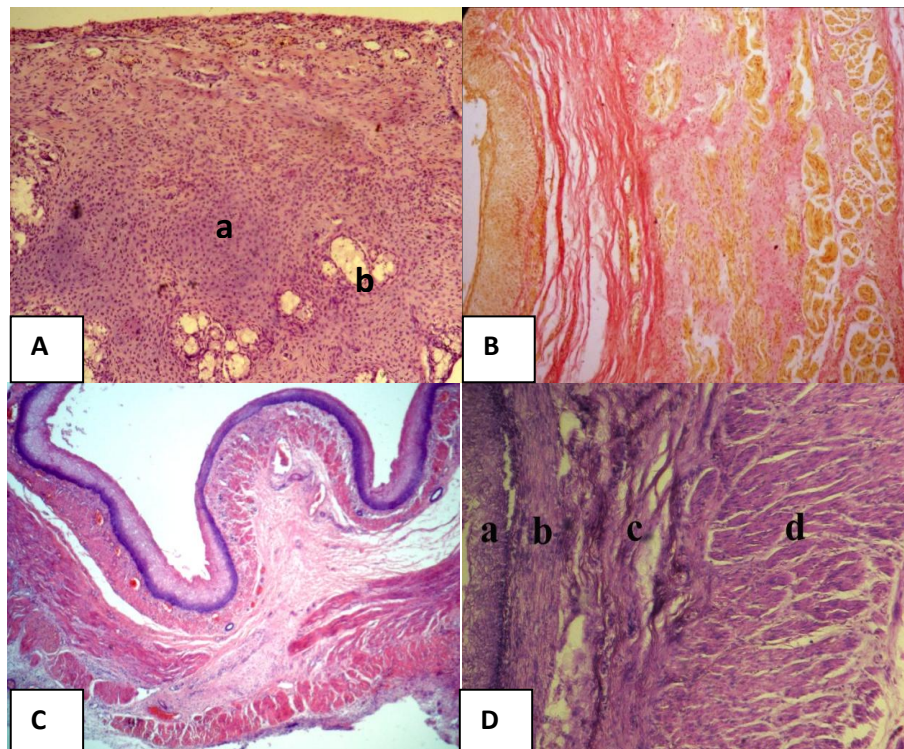


Fig. 4 The proximal segment within 2.0 cm of the fistula. A) immature cartilaginous dysplastic tissue (a) with glandular structures (b) in the fistula x25 area. Color. H-E; B) Fibromuscular dysplasia of the distal segment within 1.8 cm of the fistula x200. Color. VG; C) Submucosal cicatricial tissue at the level of a fold x200. Color. H-E; D) Microscopic structure of the distal segment at 2.5 cm from the fistula: a - the epithelial layer, b - the muscular tunic of the mucosal, c - the submucosa, d - the inner muscular tunic. Color. H-E. x 25

In 2 cases(9,5%), it has been observed the presence of tubular esophageal duplication of distal esophageal segment, communicating with the lumen of esophagus (fig. 5).

At the distal esophageal tube, in 3 cases (14,3%), it was observed the presence the inslets of gastric mucosa in sizes from 11 to 15 μ to 0.8-1.2 cm (fig. 6). The vascular network of the distal esophageal segment, especially in the submucosa, was manifested by a much more congestive and microvascular aspect, in which case varicose ectasis and musculature were observed (fig. 6B). The ectopic of gastric mucosa was certified from a distance of 2 cm from the cardiac region to 5-6 cm on the distal esophageal tube.

Examination of the trunk and ganglion-neuronal component of the nerve network at both the proximal atresia segment and the distal segment allowed to cause significant alterations. At the upper and middle third level, the esophageal segment attracted higher structural changes in the trunk and gentle nerve mesenteric nerve network had aspects within the limits of the conventional norm. In the lower third and especially at the apical parts of the atresized segment, including in

the areas with a more pronounced fibrous, the mesenteric network appeared to be present in the chaotic aspect, being predominantly attested in the outer layers with a varied morphology of the ganglio-neural structures, which had a polymorphic cell component containing mature neurons, as well as the glia cell component reflecting a dismutation (fig. 7). Nervous plexes at this level were present through thin nerve trunks, more commonly seen in the outside of the tunic. At this level, the nerve plexuses were better evidenced, including in the intramuscular area where they were presented by nerve fascicles in the absence of ganglionuclear cells (fig. 7A). In some sectors, the external muscular tunic could be presented with hypotrophic fibers or bundles compared to the inner tunic, which was conjunctively substituted. Concomitant with these changes, the presence of nerve plexes with fine neuronal cells was found (fig. 7B, C). We note that in the areas with fibromuscular dysplasia, some pathological changes of the mezenteric nerve network and of the ganglioneuronal structures, manifested by granular and vacuolar dystrophy (fig. 7D), were noted. Analogical modification were attested and in the distal segment.

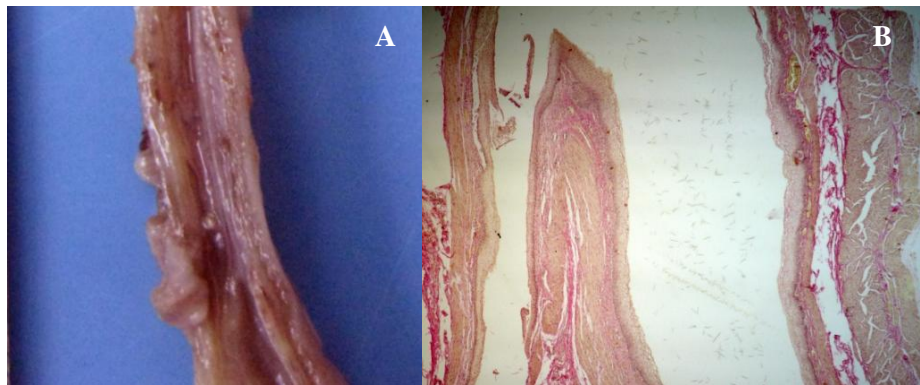


Fig. 5. The macroscopic appearance (A) and microscopic (B) of the communicating

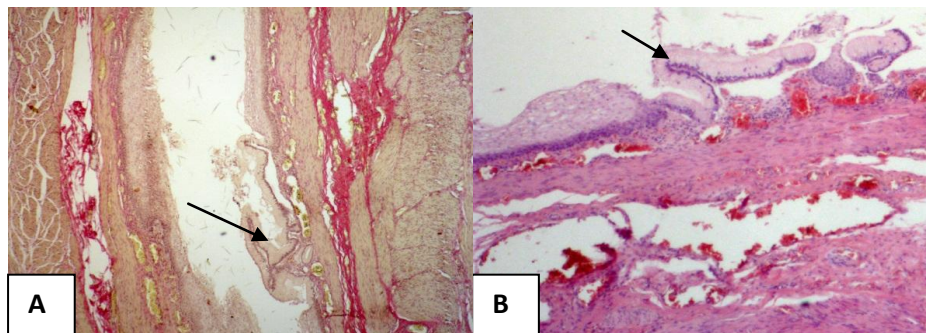


Fig. 6. Histological aspects of the distal segment. A) ectopic gastric mucosa at a distance of 1.5cm from cardia (\rightarrow). X75. Color. H-E; B) Segmental ectopie of gastric mucosal (\rightarrow) 4.5 cm from the cardiac region, varicose ectasis of the submucosal and intramural vascular network. x25. Color. H-E.

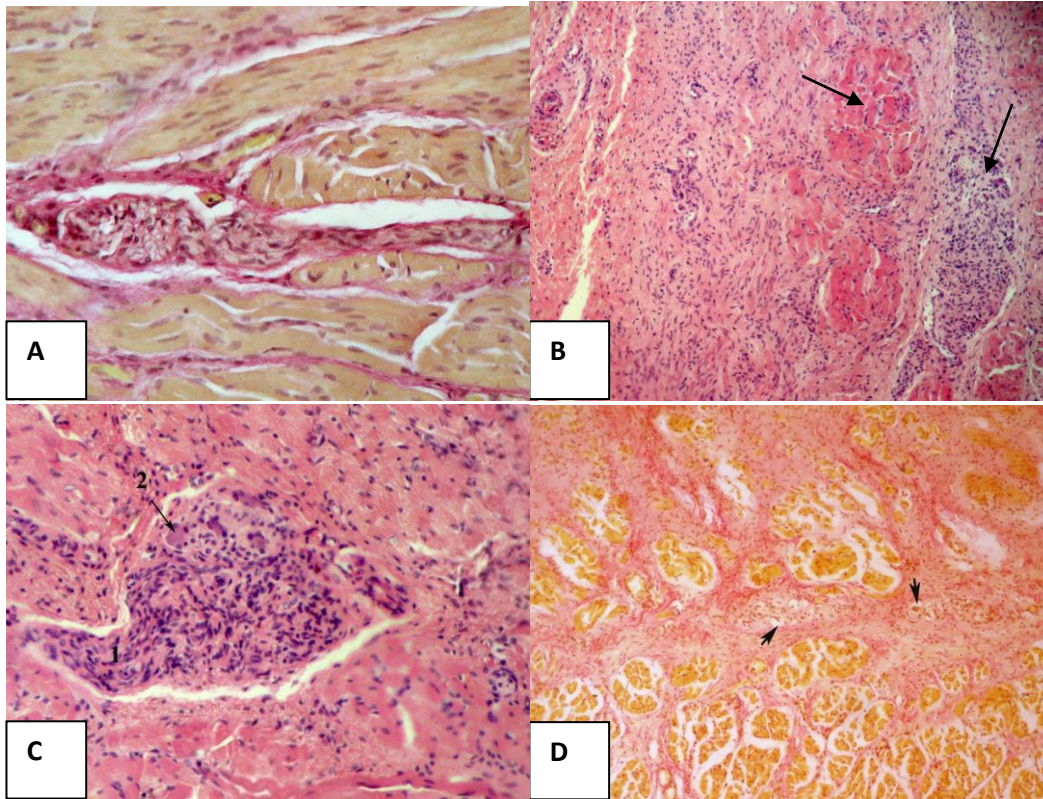


Fig. 7. Microanatomy of the nerve component A) Intramuscular ganglionar aneuronal nerve plexus x200. Color. VG; B) Steep fascicles and fibres - chaotic oriented myocytes in connective fibrous tissue x75. Color. H-E; C) Ganglioneurons of the intermuscular plexus: 1 - nerve fascicles, neural ganglion; 2- neurons x200. Color. H-E. D) Myenteric nerve ganglia with vacuolar dystrophy. Color. VG. x100.

Discussions. Notwithstanding the remarkable results obtained in surgical treatment of esophageal atresia, the incidence of postoperative morbidity remains high, with several factors influencing the prognosis of these patients were identified [27]. According to some studies, most frequently were registered respiratory problems (about 37%), anastomotic stenosis (22% - 40%), dysphagia (15% - 100%), gastroesophageal reflux requiring antireflux surgery (12%), recurrent fistulas 4% - 17%) etc. [2, 9, 14, 17].

Postoperative esophageal dysmotility in children with esophageal atresia and esophageal fistula are described extensively in the literature, with some controversy over their secondary multifactorial origin due to: abnormal development of the vagus nerve and Auerbach plexus, vagal nerve trauma, surgical mobilization and trauma, ischemia or major traction on the lower end of the esophagus during surgery or due to congenital architectural anomalies [1, 21]. Some authors believe that the pathological changes found in atretic segments in the case of esophageal atresia with esophageal fistula, including muscular distortion

through fibrosis, glandular and neural pathological changes, the presence of tracheobronchial cartilaginous reminiscences may contribute to discomfort and esophageal stricture after surgery. The esophageal fistula should be sectioned 3 mm distal from its origin in the trachea, morphological changes in this area being appropriate for primary anastomosis [1, 3].

In children, heterotopic gastric mucosa in the normal esophagus can often be seen in the endoscopic examination (up to 5.9%) in the form of a patch that ranges from a few millimeters to a few centimeters, usually unique or rarely in the form of circumferential ring, asymptomatic or causing dysphagia, odinophagia, esophageal strictures, bleeding and respiratory symptoms. The association of heterotopic gastric mucosa with esophageal atresia with esophageal fistula is rarely described, most of the cases being endoscopically diagnosed after surgical correction of the malformation [8, 23]. There are studies that describe the presence of gastric epithelium in both the proximal esophageal and distal segment [1, 5]. Some complex studies have found that the Barrett esophagus prevalence 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, and these findings require the need for an endoscopic follow-up all life [25].

The term "esophageal duplication" includes three morphological variants:

- 1) cystic (communicating or noncommunicating),
- 2) tubular and
- 3) diverticular, developing as a consequence of abnormal tracheoesophageal separation [4, 19]. The association of esophageal atresia with esophageal duplication is quite rare [10, 24]. There are few reports that have detected oesophageal duplications in the muscular tunic of the esophageal wall [20], this type being called segmental intramural duplication of the esophagus [15]. Unique cases have been presented over the years [6, 16, 24, 26]. Usually, non-communicating intramural duplications of the proximal segment remain undiagnosed preoperatively and during surgery, resulting in significant potential for postoperative complications [20], including the failure of anastomosis [24], found by us in 2 cases. Cases of coexistence of esophagus atresia with esophageal fistula and cystic duplication are exceptionally rare, most of them being diagnosed at a later age due to symptoms or complications. The authors argue that it is preferable to resolve both malformations in neonatal surgery at one stage, thus reducing the possibility of developing postoperative complications [13,,22].

Thus, the analysis of the results of the study on the macro- and microanatomic peculiarities of structural and morphological components shows that in the esophageal atresia with inferior eso-tracheal fistula, concurrently with the macroscopic, histological aspects there are a series of changes with predictive importance on postoperative period, which can be classified into two groups: primary - characterized by

histogenesis disorders at the embryonic stage (fibromuscular dysplasia, esophageal dysplastic cartilage ectopia and gastric mucosa, esophagus dysplasias, incomplete esophageal membrane, aganglionosis) and secondary - atrofico-hipertrophy evolved during the fetal stage from 12-13 weeks gestation that varies according to their presence and location (muscle hypertrophy and / or atrophy of the muscles, vascular varicose ectasis, inflammatory processes, dismutation of neuronal structure.

Conclusions.

1. The results of this study allowed to confirm the presence of advanced structural morphopathological changes, which can significantly influence the regenerative-reparative processes of the esophagus after reconstructive operations in cases of esophagus atresia with distal tracheoesophageal fistula.

2. Concurrent fibro-muscular dysplasia changes with morphopathological changes of ganglioneuronal structures are responsible for esophageal motility disorders after reconstructive surgery in cases of esophageal atresia with distal eso-tracheal fistula.

3. In cases of esophageal atresia with distal eso-tracheal fistula, there may be some concomitant structural malformations (intramural communicating duplication of the atresial esophageal segments, diverticulum), which remain undiagnosed preoperatively and during surgery, determining a significant potential for postoperative complications, including the failure of anastomosis.

4. The presence of foveolar gastric mucosa in the distal segment of the eso-tracheal fistula may serve as a favorable morphological substrate for the development of the Barrett esophagus in patients with esophageal atresia or malignancy, which necessitates the need for an permanent endoscopic evaluation.

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. 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.
3. Dutta H.K., Bhatnar V. A histopathological study of esophageal atresia and tracheoesophageal fistula. *Pediatr. Surg.* 2000; 35:438-41.
4. El-Gohary Y., Gittes G.K., Tovar J.A. Congenital anomalies of the esophagus. *Semin. Pediatr. Surg.* 2010; 19:186-93.
5. 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.
6. Frank R. C., Paul L.W. Congenital Reduplication of the Esophagus. *Radiology.* 1949; 53:417.

7. Gottrand M., Michaud L., Sfeir R., Gottrand F. Motility, digestive and nutritional problems in esophageal atresia. *Paediatr. Resp. Rev.* 2016; 19:28-33.
8. Harrison L.J.R., Kenwright D., Stringer M.D. Esophageal heterotopic mucosa in esophageal atresia. *J. Pediatr. Surg.* 2018; 32:23-6.
9. 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.
10. Inan M., Basaran U.N., Aksu B., Dereli M., Dortogan Z. Esophageal duplication associated with esophageal atresia and tracheoesophageal fistula in a child. *Int. J. Pediatr. Otorhinolaryngol. Extra.* 2007; 2:202-5.
11. Ioannides A.S., Copp A.J. Embryology of oesophageal atresia. *Semin. Pediatr. Surg.* 2009; 18:2-11.
12. 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.
13. Knod J.L., Garrison A.P., Frischer J.S., Dickie B. Foregut duplication cyst associated with esophageal atresia and tracheoesophageal fistula: A case report and literature review. *J. Pediatr. Surg.* 2013; 48:E5-E7.
14. Kovesi T., Rubin S. Long-term complications of congenital esophageal atresia and/or tracheoesophageal fistula. *Chest.* 2004; 126(3):915-25.
15. Maier H.C. Intramural Duplication of the Esophagus. *Ann. Surg.* 1957; 145:395.
16. Minnis J.F., Burko H., Breverri G. Segmental duplication of the esophagus associated with esophageal atresia and tracheoesophageal fistula. *Ann. Surg.* 1962; 156(2):271-5.
17. 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.
18. Rintala R.J., Sistonen S., Pakarinen M.P. Outcome of esophageal atresia beyond childhood. *Semin. Pediatr. Surg.* 2009; 18:50-6.
19. Saha A.K., Kundu A.K. Tubular duplication of the oesophagus presenting with dysphagia. *Singapore Med. J.* 2014; 55(6):e90-e92.
20. Snyder C.L., Bickler S.W., Gittes G.K. et al. Esophageal duplication cyst with esophageal web and tracheoesophageal fistula. *J. Pediatr. Surg.* 1996; 31(7):968-9.
21. Smith N. Oesophageal atresia and trachea-oesophageal fistula. *Early Human Develop.* 2014; 90:947-50.
22. Spataru R.I., Popoiu M.C., Ivanov M. Foregut duplication cyst associated with esophageal atresia - one-stage neonatal surgical repair. *Indian J. Surg.* 2015; 77(Suppl 1):S52-S55.
23. 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.
24. Trobs R.B., Barenberg K., Reza Vahdad M., Tannapf A. Noncommunicating tubular duplication of the upper puch in esophageal atresia without fistula. *J. Pediatr. Surg.* 2009; 44:1646-8.
25. 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.
26. Wiersema J. S. Partial Reduplication of the Oesophagus with Oesophageal Atresia and Oesophago-tracheal Fistula. *Arch. Chir. Neerl.* 1956; 8:97.
27. Zhu H., Shen C., Xiao X., Dong K., Zheng S. Reoperation for anastomotic complications of esophageal atresia and tracheoesophageal fistula. *J. Pediatr. Surg.* 2015; 50:2012-5.
28. 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.

Clinical Studies

The diagnostic significance of pulmonary scintigraphy in children with cystic fibrosis

Balanetschi L.^{1,4}, Selevestru R.¹, Balan A.¹, Krushelnitscaia E.³
Gudumac E.², Sciuca S.¹

*Nicolae Testemitanu SUMPh, Clinic of Pneumology, Department of Pediatrics¹
Department of Pediatric Surgery, Orthopedics and Anesthesiology²
PHI Institute of Mother and Child, Radiology and Imaging Section,
Chisinau, Republic of Moldova³
Children Emergency Hospital, Department of Pediatric Surgery and Orthopedics,
Cluj Napoca, Romania⁴*

Abstract

Semnificația diagnostică a scintigrafiei pulmonare la copii cu fibroză chistică

Scopul acestui studiu constă în caracteristica perfuziei pulmonare prin metoda scintigrafică cu Tc-99 la 17 copii cu fibroză chistică. Examenul scintigrafic a arătat prezența tulburărilor de perfuzie la majoritatea copiilor cu diferite grade de severitate a bolii. Reducerea perfuziei (în unele cazuri, absența perfuziei) a fost observată în toate zonele pulmonare afectate, mai frecvent localizate în plămânul drept (lobii superior și mediu), o incidență mai rară fiind constatată la nivelul plămânului stâng (zonele superioare și inferioare). Tulburarea severă de perfuzie la copiii cu fibroză chistică este un indice indirect, care arată gradul de intensitate și extensie a proceselor fibroase.

Cuvinte cheie: fibroză chistică, scintigrafie pulmonară, copii

Abstract

The aim of this study consists in the characteristic of the pulmonary perfusion by scintigraphic method with Tc-99 in 17 children with cystic fibrosis. Scintigraphic exam showed the presence of perfusion disturbances in the most of the children with the different severity grade. The perfusion reducing (in some cases absence of the perfusion) was observed in the all pulmonary areas with more often location in the right lung (upper and middle lobes) and more rare incidence in the left lung (upper and lower zones). The severe perfusion disorder in children with cystic fibrosis is an indirect index, which shows intensity grade and extensity of fibrous processes.

Keywords: cystic fibrosis, pulmonary scintigraphy, children

Correspondence: svetlana.sciuca@usmf.md; mob. +373 79471374

Introduction

Cystic fibrosis (CF) is an acquired abnormality with the autosom-recessive type of transmission, which is determined by the CFTR (conductor of the Cystic Fibrosis transmembrane regulator) gene change (mutation) that causes cystic fibrosis. This is a progressive, chronic disease, in which the mucus becomes dry, adherent and viscous. Mucus builds up and blocks the passages from various organs, especially in the lung and pancreas. At the lung, the mucus can cause severe respiratory problems and lung disease emergence. At the pancreas, mucus causing digestive impairment and malnutrition, which may result in impaired growth and normal development [3, 6, 7].

Congenital mutations of the CFTR gene cause changes of the protein, which is responsible for the transport of ions through the cell membrane. It causes the secretion of exocrine gland disturbances (these glands secrete the level areas covered by epithelium, and not in the bloodstream) especially at the respiratory system and gastrointestinal tract [5, 7].

Only a small percentage of patients with cystic fibrosis live more than 40 years. The incidence in Moldova constitute 1:2000-1:3000 of newborns, and this percentage is growing. The severity determines the progress of the disease and requires confirmation of medical technique that will appreciate the structural changes of the lungs [1, 5, 6].

Pulmonary scintigraphy, imaging method, is being used for the evaluation of pulmonary perfusion [2, 4]. This diagnostic imaging technique is based on the principle of detecting gamma radiation emitted as a result of the injection of a radioactive isotope with a particular tropism for organ, or lesion and converting photons emitted into electrical signals, which are viewed at the oscilloscope, in the form of scintigraphic image. This method has an important role in the early identification of pulmonary vascular defects, especially in cystic fibrosis and other fibrosing chronic lung disease [3, 4]. Repeat scintigraphy can provide data about pulmonary revascularization in affected areas.

Aim. Assessment of pulmonary perfusion in children with cystic fibrosis to evaluate the intensity of the fibrosis process and spread of bronchiectasis.

Materials and methods

The team of researchers from the Pneumology clinic, Mother and Child Institute, were investigated 18 children with cystic fibrosis, in ages between 2 and 18 years old, among whom 4 girls and 14 boys. Most of them has a mixed form of the disease (pulmonary and intestinal). The children were examined in detail to confirm the diagnosis of cystic fibrosis. All children had the increased values of sweat test (>60 mEq/L, Macroduct, USA). $\Delta F508$ mutation has been con-

firmed in 9 children, 1 child with mutation R334W and 1 child – L551D.

Lung perfusion in children with cystic fibrosis has been studied through pulmonary scintigraphy using Gamma-camera (Siemens, Germany) with the Tc-99 MAA. The imaging examination included ultrasound results, pulmonary radiography, thoracic HRCT.

Results. Most children with cystic fibrosis have had severe disease evolution (12 children), 5 children had moderate degree. The colonization of a chronic bronchial tree with *Staphylococcus aureus* was present at 10 children with cystic fibrosis, *Haemophilus influenzae* – 9 children, *Pseudomonas aeruginosa* – in 5 cases. In some cases it is found microbial agents association. Clinical manifestations were dominated by severe pulmonary disease with pulmonary fibrosis to 8 children, bronchiectasis (5 cases), fibrous atelectasis (2 cases), chronic bronchitis (11 children). The severity of respiratory manifestations in children with cystic fibrosis was confirmed by respiratory failure with restrictive and obstructive pulmonary disorder II-III degree (10 children). In 2/3 cases were present growth disorders.

Scintigraphic examination identified pulmonary perfusion disturbances in 17 children with different characteristics and the degrees of severity. Moderate reduction in pulmonary perfusion of the right lung in the upper sectors (fig. 1) was detected in 76.5% of cases, the medium sectors have pulmonary perfusion disorders at 47.1% of children, involving lower lung zones with the focal character were revealed in 35.3%. In accordance with data from the literature on the right upper lobe impairment is an important criterion for imaging diagnosis of pulmonary manifestations in cystic fibrosis. In the left lung the severity of perfusion disorders were less expressed, but in 35.3% of the cases have been observed serious changes in the upper segments, in 41.2% - lower lung area, less pronounced in the medium sectors – 29.4%.

The perfusion was absent in pulmonary sectors of the lung (fig. 2) in 3 children. Severe problems with the total absence of perfusion was reflected in the right lung: upper lobe – 4 children, medium lobe – 3 children, lower lobe – 1 case. The left lung was affected in unique cases with upper lobe involvement (1 child) and medium sectors (1 child). Only in a child with cystic fibrosis lung perfusion has not suffered pathological changes. Contrasting the results of pulmonary radiography obtained by radiographic methods (chest radiography, pulmonary computed tomography) with scintigraphic exploratory data revealed a correlation of these diagnostic procedures for the identification of the pulmonary fibrosis, bronchiectasis.

Infusion disorders caused in children with cystic fibrosis is an indirect index that can show the intensity and spread of pulmonary fibrosis.

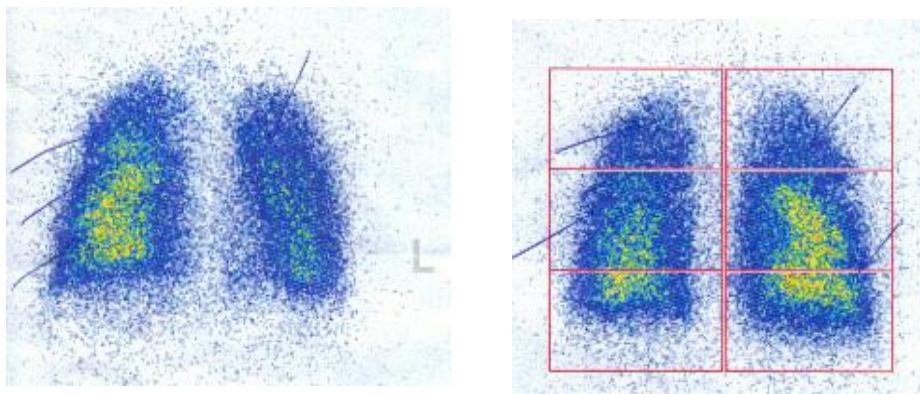


Fig. 1. Pulmonary scintigraphy in children with cystic fibrosis. Moderate reduction in pulmonary perfusion of the right lung

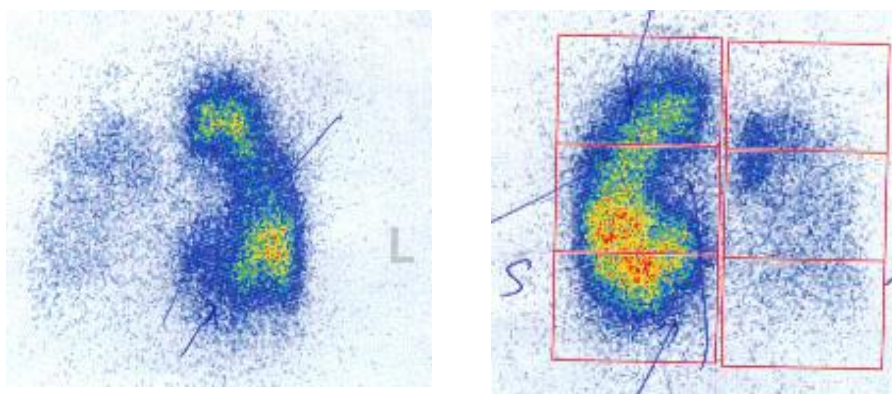


Fig. 2. Pulmonary scintigraphy in children with cystic fibrosis. Absent perfusion in pulmonary sectors of the lung

Conclusion. Pulmonary perfusion in children with cystic fibrosis is reduced in all areas with diffuse lung disorders, the most severe in the right upper lobe.

Pulmonary scintigraphy can be recommended as a screening test for the evaluation of intensity of lung fibrosis in children with cystic.

REFERENCES

1. Cystic Fibrosis Foundation Patient Registry. *Annual data report 2016*. <https://www.cff.org/Research/Researcher-Resources/Patient-Registry/2016-Patient-Registry-Annual-Data-Report.pdf>
2. Goudard E., Fauveau-Robine G., Grimfeld A. Interest of lung scintigraphy in the follow – up of cystic fibrosis (CF) and other chronic obstructive pulmonary disease (COPD). Two case reports in children. *Arch. Pediatr.* 2005; 12(10):1487-91. Margaret Rosenfeld, Philip M. Farrell, Margaret Kloster, et al.: Association of Lung Function, Chest Radiographs and Clinical Features in Infants with Cystic Fibrosis. *Eur Respir J.* Author manuscript; available in PMC 2014 March 01
3. Piepsz A., Wetzburger C., Spehl M., Machin D., Dab I., Ham H.R., Vandevivere J., Baran D. Critical evaluation of lung scintigraphy in cystic fibrosis: study of 113 patients. *J. Nucl. Med.* 1980; 21(10):909-13.
4. Paranjape Shruti M., Mogayzel Peter J. Cystic fibrosis. *Pediatr. Rev.* 2014; 35(5):195-205.
5. Stephenson A. Canadian cystic fibrosis registry. 2016 Annual Data Report. <https://www.cysticfibrosis.ca/uploads/2016-Registry-Annual-Data-Report.pdf>
6. Капранов Н.И., Шабалова Л.А., Каширская Н.Ю. и др. Муковисцидоз (Современные достижения и проблемы). *Метод. Рекоменд. М. Медпрактика.* 2001; 76 с.

Diagnostic and treatment of the acute pancreatitis in children

Nepaliuc Iu.^{1,2}, Mihalcean V.², Gheras E.²

Nicolae Testemitanu SUMPh¹

Children's Municipal Clinical Hospital "V. Ignatenco", Chisinau, Republic of Moldova²

Abstract

Diagnosticul și tratamentul pancreatitei acute la copii

Acest studiu reprezintă o analiză retrospectivă a rezultatelor obținute în diagnosticul și tratamentul a 36 de pacienți cu pancreatită acută, inclusiv 12 cazuri (25%) cu forme distructive și 24 (75%) - cu forme hemoragice. Cele mai frecvente cauze ale formelor grave de pancreatită distructivă la copii au fost determinate de traumatismele abdominale (54%), factorii alimentari și diverse medicamente (40%).

Toți copiii cu pancreatită acută au fost evaluați clinic, efectuându-se analiza generală de sânge și analiza urinei, indicii amilazei, lipazei și datele imagistice (USG și CT abdominal). Managementul pacienților a inclus o abordare diferențiată conservativă, cât și tratament chirurgical, în funcție de forma clinică a maladiei și evoluția bolii.

Opt pacienți cu pancreatită distructivă severă din grupul de studiu au necesitat intervenție chirurgicală de urgență, având ca indicație manifestarea clinică de abdomen chirurgical acut. Cinci pacienți au fost supuși intervenției laparoscopice, iar 3 pacienți - laparotomiei mediane cu drenajul burselor omentale și a cavității abdominal cu rezultate bune la distanță.

Cuvinte cheie: pancreas, traumă, copii, protocol, chirurgie, opțiuni conservative

Abstract

This study conducted a retrospective analysis of the diagnosis and treatment results of 36 patients with acute pancreatitis including 12 cases (25%) of destructive and 24 (75%) of hemorrhagic forms of pancreatitis. The most common causes of severe destructive pancreatitis in children include abdominal traumas (54%), dietary factors and certain medications (40%).

All children with acute pancreatitis were assessed in the context of clinical data, CBC (Complete Blood Count) and urinalysis, amylase and lipase and imaging data (USG and abdominal CT). The management of patients required both a differential conservative and a surgical approach depending on the clinical form of destructive pancreatitis and disease evolution.

Eight patients with severe destructive pancreatitis from the study group required an emergency surgical intervention, based on a clear clinical manifestation of surgical acute abdomen. Five patients underwent a laparoscopic procedure and 3 patients were subjected to median laparotomy with drainage of the omental bursae and abdominal cavity, showing good follow-up results at distance.

Key words: Pancreas, Trauma, Pediatric, Guidelines, Surgery, Conservative

Correspondence to: [e-mail: docentiuri@gmail.com](mailto:docentiuri@gmail.com); mob.: +37369244341

Introduction

Acute pancreatitis is relatively rare in children and makes up about 0.5% - 1.5% of the total number of

children admitted in the surgical wards [2, 10]. An increase in the number of cases of pancreatitis in children has been reported over the last decades. The incidence of interstitial forms makes up 70-80% of cas-

es. Destructive forms account for 25-30% of total cases of pancreatitis [2, 3].

The most common causes of destructive pancreatitis in children include abdominal traumas, dietary factors, and certain medication. Yet, the cause has not been identified in about 25% [5, 9]. Actually, the severe destructive pancreatitis is one of the most acute problems of pediatric surgery [1, 7].

Severe destructive pancreatitis shows a fulminant evolution leading to complications and even death of the patient. The mortality rate of acute pancreatitis is estimated at 2.1% [4, 10].

Perhaps, one of the most effective way to reduce the mortality rate in pancreonecrosis is the timely diagnosis and prognosis of the severity of the disease, since an appropriate treatment can reduce the pathological process and thus lead to a favorable disease outcome [4, 6]. So far, the early diagnosis and prognosis of destructive forms of acute pancreatitis remain an unsolved issue for emergency surgery [1, 5].

The diagnosis and treatment of acute pancreatitis in children often turns to be a difficult problem. The assessment of specific biochemical tests and imaging methods as abdominal ultrasound scanning, computed tomography, and MRI [6, 8] are important for diagnostic purposes. It is crucial to initiate a timely treatment approach, as well as to assess both indications and volume of surgical treatment [1, 7].

To analyze the contemporary methods used in the diagnosis of acute pancreatitis. Demonstration of the results of medical surgeries in acute destructive pancreatitis in children.

Material and methods

The retrospective analysis of patients hospitalized and treated in the "V. Ignatenko" Clinical Hospital in the last 3 years included 36 patients with acute pancreatitis aged 3 to 17 years. Edematous haemorrhagic forms of pancreatitis were found in 24 cases of all cases.



Fig. 1. The presence of free liquid in the omental bursa

Destructive forms were diagnosed in 12 children. 4 cases reported haemorrhagic pancreonecrosis, 4 cases showed necrotizing pancreatitis with external cysts and fistulas, and 4 cases were complicated by pancreatogenic peritonitis.

The most common causes of destructive pancreatitis in children are the abdominal traumas (54%), dietary factors, and certain medications (40%).

All children with acute pancreatitis were assessed in the context of clinical data, CBC and urinalysis, amylase and lipase and imaging data (USG and abdominal CT).

The analysis of medical records of patients with destructive pancreatitis revealed the following complaints: abdominal pain, vomiting and fever. The most commonly used diagnostic procedure is the determination of serum amylase concentration, which is 3 times higher in destructive pancreatitis, however, the lipase level assay is much more informative. The lipase concentration ranged from 80 to 900 u / l (the reference range is of 5.6 - 51.3u/l) in patients with destructive pancreatitis. The degree of the enzyme level corresponds to the degree of destruction of the pancreas. The imaging methods have shown the following:

1. *Abdominal imaging* is an objective method for the assessment of pathological changes within the pancreatic tissue. It offers a rapid and useful diagnosing of early pancreatitis and its intraabdominal complications (fig. 1). Ultrasound changes may predict clinical changes and may persist after normalization of hemodynamic indices. The ultrasound examination revealed the enlargement of pancreas, no clear-cut margins, and an increased echogenicity in the early stages of acute destructive pancreatitis. Free liquid collection was determined within both the omental bursa at the onset of the disease and small basin with dynamic assessment (fig.2).

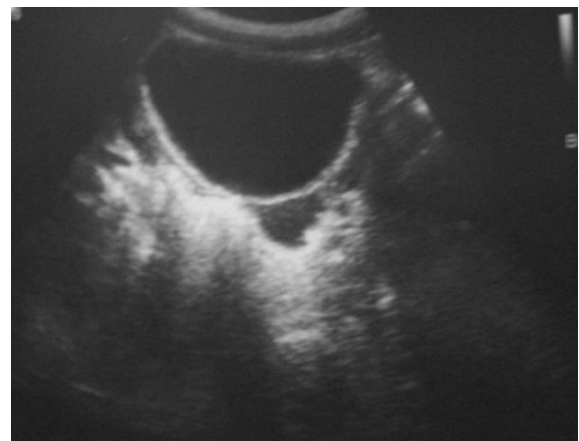


Fig. 2. The presence of free liquid in the small basin

Pancreatic pseudocysts and changes in the adjacent organs have been detected in complicated forms of pancreatitis. These usually occur two weeks after the onset of the disease during the aseptic necrosis stage of the pancreas.

2. *CT scanning and MRI.* Computed abdominal tomography was the "gold standard" method for patients with pancreatic necrosis that allowed assessing the degree of pancreatic destruction (inflammation, necrosis), localization and the necrotic zones:

- CT has detected the lesions and zones of pancreatic involvement for post-traumatic pancreatitis,
- CT has shown the pancreatic destructions and intraperitoneal complications (abscesses, pseudo-cysts) and complications in the nearby organs for advanced stages of destructive pancreatitis (fig. 3, fig. 4).

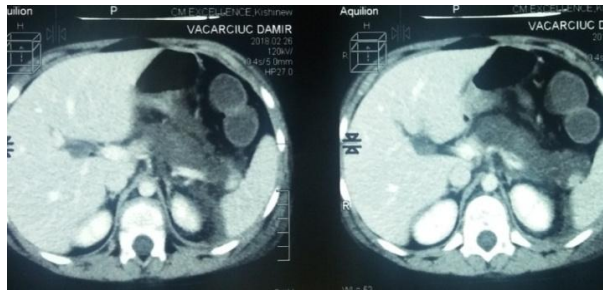


Fig. 3. Hemorrhagic pancreonecrosis

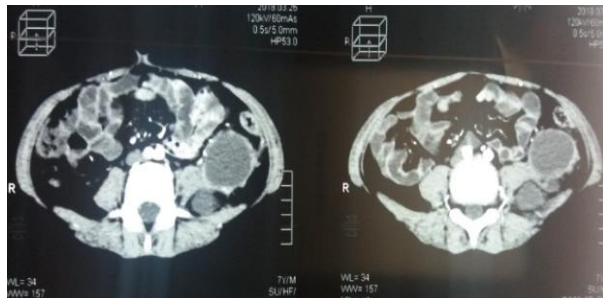


Fig. 4. Pancreatic pseudo-cysts

Results and discussion

MRI review of the study group was performed to evaluate the changes in pancreatic parenchyma and restore the destructive process within the pancreas at distance. It was also possible to assess the evolution of volume processes (pseudo-cysts, abscesses), as well as to restore tissue integrity of the pancreas.

CT and MRI have provided clear indications for surgical treatment and volume of surgical intervention.

Abdominal ultrasound performed 4 weeks after the onset of acute destructive pancreatitis has shown a subsequent restoration of the pancreas margins and resorption of intraperitoneal fluid.

The laparoscopic procedure was carried out on 5 patients that proved to be an efficient method of diagnosing severe destructive pancreatitis. However, laparoscopy does not allow, in all cases, a complete examination and assessment of the involved area of the pancreas, peritoneum and retroperitoneal space.

Of the total number of children admitted with acute pancreatitis, destructive forms were found in 25% cases. In about 10% cases, destructive pancreatitis was complicated by pseudo-cysts of different localizations (2 patients) and external pancreatic fistulas (2 patients). The mortality rate was 1.3% in destructive forms of pancreatitis. No postoperative lethal outcomes have been registered. All children with acute pancreatitis required conservative medical treatment, which included fighting off the pain syndrome and intestinal paresis, as well as management of the electrolyte disturbances.

Conservative treatment mandatorily included fasting (5 to 7 days), inhibition of gastric secretion, neuro-peptides (sandostatin) and protease inhibitors (contradictory, Gordox). The empiric therapy with antibiotics was performed, using aminoglycosides, generations III-IV cephalosporins (1, 7). Depending on the clinical form of destructive pancreatitis, patients required differential surgical treatment (laparotomy, laparoscopy, and ultrasound-assisted puncture) (1, 3, 10).

Emergency surgical treatment is indicated in cases of obvious surgical acute abdomen as in cases of enzyme peritonitis, free fluid within the abdominal cavity, uncertain diagnosis of pancreonecrosis. Eight patients with destructive pancreatitis from the study group underwent surgical treatment.

The median laparotomy and the drainage of the omental bursa and abdominal cavity was carried out in 3 cases, whereas laparoscopy with drainage of the omental bursa and abdominal cavity was performed in 5 cases. Pancreatic pseudo-cysts were found in 2 cases followed by ultrasound-assisted puncture and drainage and showing good results at distance (the diameter was less than 5 cm over 6 months after the disease onset).

Conclusions:

1. The most common causes of destructive pancreatitis in children resulted from pancreas traumas and pancreatobiliary disorders.
2. It is highly important to choose the appropriate approach and methods of surgical treatment in children with severe destructive pancreatitis.
3. The major diagnostic findings include tests on serum amylase and lipase levels, abdominal ultrasound, computed tomography and laparoscopy.
4. The early complex conservative and surgical treatment that is carried out in severe destructive pancreatitis may prevent the development of serious complications

REFERENCES

1. Bai H.X., Lowe M.E., Husain S.Z. What have we learned about acute pancreatitis in children? *J. Pediatr. Gastroenterol. Nutr.* 2011; 52:262-70.
2. Coffey M.J., Nightingale S., Ooi C.Y. Serum lipase as an early predictor of severity in pediatric acute pancreatitis. *J. Pediatr. Gastroenterol. Nutr.* 2013; 56(6):602-8.
3. Cofini M., Favoriti P., Quadrozzi F. Acute pancreatitis in pediatric age: our experience on 52 cases. *Minerva Pediatr.* 2014; 66(4):275-80.
4. Haugaard M.V., Weltegren A., Hillingsø J.G., Gluud C., Penninga L. Non-operative versus operative treatment for blunt trauma in children. *Cochrane Database Syst. Rev.* 2014; 12(4):164-78.
5. Lucidi V., Alghisi F., Dall'Oglio L., D'Apice M.R., Monti L., et al.. The etiology of acute recurrent pancreatitis in children: a challenge for pediatricians. *Pancreas.* 2011; 40(4):517-21.
6. Mao E.Q., Tang Y.Q., Fei J., Qin S., Wu J., et al.. Fluid therapy for severe acute pancreatitis in acute response stage. *Chin. Med. J.* 2009; 122(2):169-73.
7. Meyer A., Coffey M.J., Oliver M.R., Ooi C.Y. Contrasts and comparisons between childhood and adult onset acute pancreatitis. *Pancreatol.* 2013; 13(4):429-35.
8. Suzuki M., Sai J.K., Shimizu T. Acute pancreatitis in children and adolescents. *World J. Gastrointest. Pathophysiol.* 2014; 5(4):416-26.
9. Александрович Ю.С., Пшениснов К.В. Инфузионные антигипоксанты при критических состояниях у детей. *Общая реаниматология.* 2014; X(3):61-76.
10. Бельмера С.В., Разумовского А.Ю., Корниенко Е.А., Приворотского В.Ф. *Болезни поджелудочной железы у детей.* Медпрактика. М. 2015; 86-112.

Case Report

Iatrogenic injury of the common bile duct during laparoscopic cholecystectomy in children

Danci A.¹, Jalba A.², Ambros I.²

Public Institution State University of Medicine and Pharmacy “Nicolae Testemițanu”,
Laboratory of Hepatic Surgery¹
Department of Pediatric Surgery, Orthopedics and Anesthesiology²
Chisinau, Republic of Moldova

Abstract

Leziunea iatrogenică a ductului biliar comun în timpul colecistectomiei laparoscopice la copil

Autorii prezintă un caz clinic de leziune iatrogenă a ductului biliar comun în timpul colecistectomiei laparoscopice, rezolvat prin operație reconstructivă – hepaticojejunostomie de ansă Roux in Y cu evoluție clinică favorabilă. Monitorizarea clinică și ecografică la distanță la 2 ani postoperator nu a relevat semne de stenoza a anastomozei bilio-digestive sau angiolită de reflux, iar pacientul rămâne în stare satisfăcătoare.

Cuvinte cheie: colecistectomie, laparoscopie, duct biliar comun, leziune iatrogenă, hepaticojejunostomie, copii

Abstract

The authors present a clinical case of the iatrogenic injury of the common bile duct during laparoscopic cholecystectomy, managed by reconstructive surgery – Roux en Y hepaticojejunostomy with favorable evolution. The clinical and ultrasound follow up after 2 years postoperatively revealed no signs of stenosis of the biliodigestive anastomosis or reflux cholangitis, and the child's condition remains satisfactory.

Keywords: cholecystectomy, laparoscopy, laparoscop, common bile duct, iatrogenic injury, hepaticojejunostomy, children

Correspondence: svetlana.sciuca@usmf.md; mob. +373 79471374

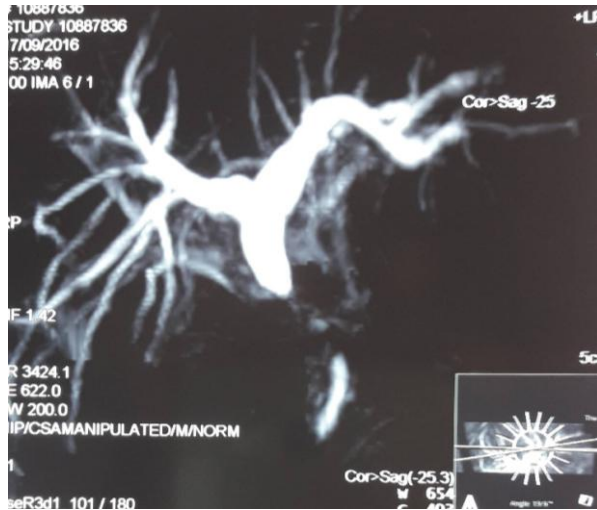
Background

At the moment the laparoscopic cholecystectomy, due to its safety and efficiency, represents the “gold standard” in the treatment of cholelithiasis [10]. Bile duct injury (BDI) is one of the most dangerous complications of cholecystectomy with a great potential of morbidity and mortality. According to literature data

the incidence of the BDI during gallbladder surgery ranges between 0,1-1,7% [4, 8, 11, 12, 13]. The BDI during laparoscopic surgery is determined by some factors such as wrong interpretation of the Calot triangle anatomy, surgeon's lack of experience, deficient anatomy of the hepatobiliary region etc. [1, 3, 11, 16, 17].

Case report

The child F.I. 9 years old was admitted on September, 12, 2016 with the diagnosis: Cholelithiasis. Acute calculous cholecystitis, which has been confirmed by abdominal ultrasound exam. The laparoscopic cholecystectomy was performed on September, 15, 2016. 24 hours postoperatively a mild jaundice occurred (Total bilirubin - 2,57 mg/dL), that became more prominent 48 hours postoperatively (Total bilirubin - 6,2 mg/dL).



The Magnetic Resonance Cholecystopancreatography (MRCP), performed on 17.09.2016, attested a funnel-shaped obstruction of the common bile duct in the middle 1/3, which was 16 mm long (12 mm from the bifurcation) (fig. 1).

According to Bismuth classification the diagnosis of E2 BDI (< 2cm from the hepatic biliary duct bifurcation) was established (Fig. 2).



Fig. 1. MRCP. Clamping of BDI and excision of a segment of common bile duct. The injury mechanism: intraoperatively the common bile duct was ventrally elevated and misinterpreted as cystic duct, and the surgical clip was wrongly applied on it.

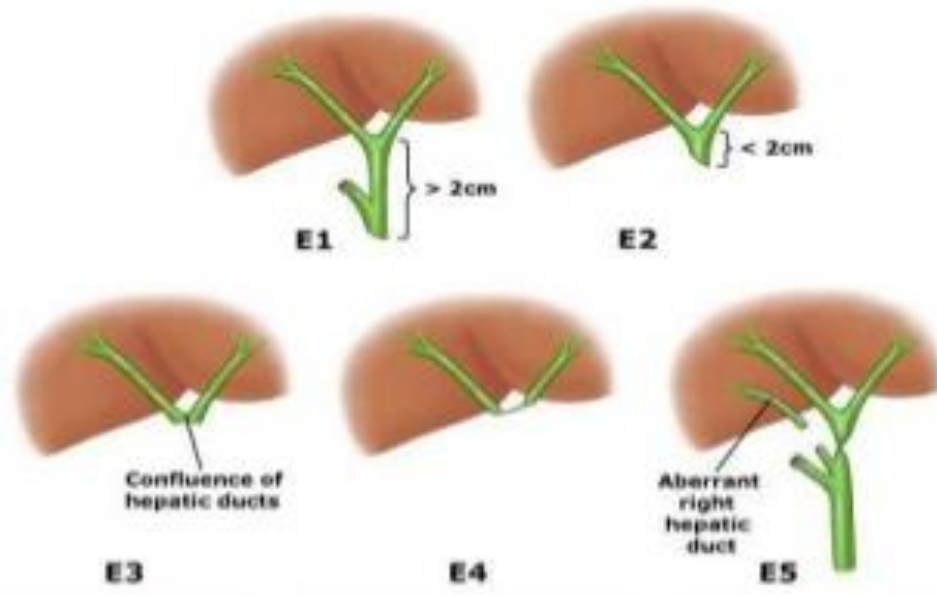


Fig 2. Bismuth BDI Classification

86 hours postoperatively the patient underwent open surgery – Roux-en-Y hepaticojejunostomy with Volker biliojejunal anastomosis stenting and drainage of the subhepatic space. The length of the Roux loop and of the jejunum from the Treitz ligament to the terminolateral jejunojunal anastomosis was approximately 40 cm altogether (fig. 3).

On the 11th day postoperatively (28.09.2017) an intestinal fistula opened, being an evidence of partial biliodigestive anastomosis dehiscence (fig. 4).

The next 9 days the child was at a total parenteral nutrition, the fistula closed on the 08.10.2016 and the enteral feeding was restarted. On the 17.10.2016 (30 days after reconstructive surgery) after subhepatic

drain removal with Volker stent in place the patient was discharged. On 19.10.2016 he was urgently readmitted because of accidentally exteriorization of the Volker stent (fig. 5).

The Volker stent was removed. On the 25.10.2016 the child was discharged with recommendations. Abdominal ultrasound exam after 1 month had shown that the biliary ducts were not distended, the hepatic parenchyma had no pathology.

The ultrasound exam performed 1 year after discharge has shown that the biliary ducts are not distended, there is a lack of signs of cholangitis, the hepatic parenchyma is homogenous. The lifestyle and food regimens without restrictions were recommended.

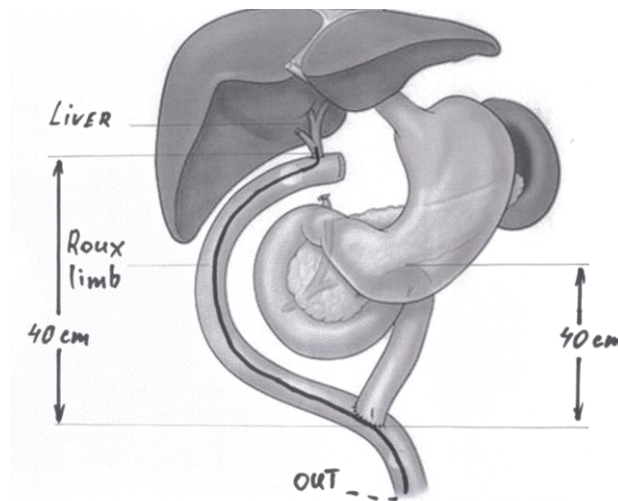


Fig.3. Roux-en-Y hepaticojejunostomy with Volker stenting of biliodigestive anastomosis



Fig. 4. Fistulography through Volker stent. Partial dehiscence of the biliodigestive anastomosis.

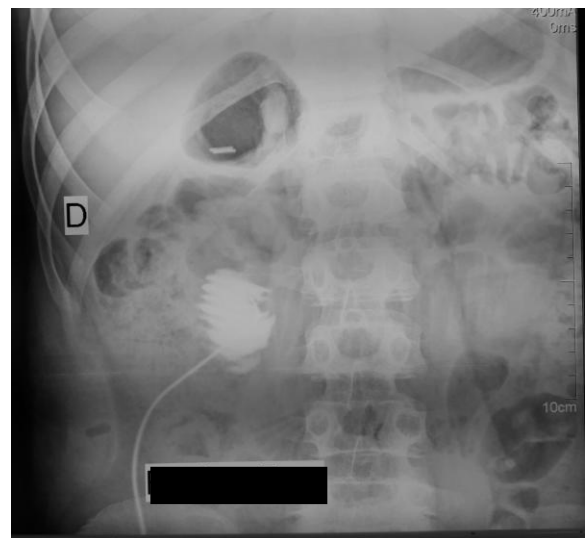


Fig. 5. Fistulography through Volker stent. Accidental exteriorization of the stent.

Discussion. The most frequent cause of the BDI during laparoscopic cholecystectomy is wrong interpretation of the Calot triangle anatomy by the surgeon [10]. The BDI is determined mainly by laparoscopic approach factors themselves (lack of direct perception, poor tactile feedback, lack of full manual maneuverability because of 2D image), as well as by surgeon's insufficient training and by topographic anatomy risk factors [2]. The most important factor responsible for the BDI during laparoscopic cholecystectomy is the position of the surgeon at the beginning of "learning curve" [5, 6]. However, an important role in the BDI occurring is played by phlogistic deterioration of the local topographic anatomy, caused by acute cholecystitis, significant adhesive processes due to chronic inflammation of gallbladder, all of these being responsible for 15-35% of the BDIs [1, 13]. Diverse abnormal anatomic variants of biliary ways (short cystic duct, cystic duct connected to the right hepatic biliary duct etc.) may also serve as a background for the BDI during cholecystectomy [1, 13].

The mechanisms of the BDI during laparoscopic cholecystectomy include: incomplete surgical dissection of the cystic duct and Calot triangle, application of surgical clips on the common bile duct which was mis-

interpreted as cystic duct, transection of the common bile duct [10, 14]. The optimal option for the correction of the BDI is considered the Roux-en-Y hepaticojejunostomy, although there are endoscopic and radiologic alternatives [1, 4, 5, 6, 7, 15].

Conclusion:

1. The anatomic and physiologic peculiarities of children should be always considered during laparoscopic cholecystectomy. The diameters of their biliary ducts are 2-3 folds smaller than in adults. This fact may lead to erroneous interpretation of the Calot triangle anatomy – the common hepatic and bile ducts may be easily misinterpreted as cystic ducts.

2. The biliary ducts wall in children is thinner than in adults that is why the reconstructive surgery may be more difficult as far as anastomosis sutures application is concerned, which, in turn, could affect the quality of biliodigestive anastomosis.

3. The postoperative evolution of children is less predictable, and the probability of the accidental stent removal is higher than in adults.

4. The incidence rate of cholelithiasis in children is smaller than in adults, and, respectively, the learning curve of specialized pediatric surgeons is chronologically longer.

REFERENCES

1. Ahrendt S.A., Pitt H.A. Surgical therapy of iatrogenic lesions of biliary tract. *World J. Surg.* 2001; 25(10):1360-5.
2. Azagra J.S., De Simone P., Goergen M. Is there a place for laparoscopy in management of postcholecystectomy biliary injuries? *World J. Surg.* 2001; 25(10):1331-4.
3. Babel N., Sakpal S.V., Paragi P., Wellen J., Feldman S., Chamberlain R.S. Iatrogenic bile duct injury associated with anomalies of the right hepatic sectoral ducts: a misunderstood and underappreciated problem. *HPB Surg.* 2009; 2009:153269.
4. Barbier L., Souche R., Slim K., Ah-Soune P. Long-term consequences of bile duct injury after cholecystectomy. *J. Visc. Surg.* 2014; 151(4):269-79.
5. Brandabur J.J., Kozarek R.A. Endoscopic repair of bile leaks after laparoscopic cholecystectomy. *Semin. Ultrasound CT MR.* 1993;14(5):375-81.
6. Connor S., Garden O.J. Bile duct injury in the era of laparoscopic cholecystectomy. *Br. J. Surg.* 2006; 93(2):158-68.
7. Davidoff A.M., Branum G.D., Meyers W.C. Clinical features and mechanisms of major laparoscopic biliary injury. *Semin. Ultrasound CT MR.* 1993;14(5):338-45.
8. Gadacz T.R. U.S. experience with laparoscopic cholecystectomy. *Am. J. Surg.* 1993;165(4):450-4.
9. Huang X., Feng Y., Huang Z. Complications of laparoscopic cholecystectomy in China: an analysis of 39,238 cases. *Chin Med. J. (Engl).* 1997;110(9):704-6.
10. Lee V.S., Chari R.S., Cucchiari G., Meyers W.C. Complications of laparoscopic cholecystectomy. *Am. J. Surg.* 1993; 165(4):527-32.
11. MacFadyen B.V. Jr., Vecchio R., Ricardo A.E., Mathis C.R. Bile duct injury after laparoscopic cholecystectomy. The United States experience. *Surg. Endosc.* 1998; 12(4):315-21.
12. Nuzzo G., Giuliani F., Persiani R. The risk of biliary ductal injury during laparoscopic cholecystectomy. *J. Chir. (Paris).* 2004; 141(6):343-53.
13. Parmeggiani D., et al. Biliary tract injuries during laparoscopic cholecystectomy: three case reports and literature review. *G. Chir.* 2010; 31(1-2):16-9.
14. Pulitanò C., Parks R.W., Ireland H., Wigmore S.J., Garden O.J. Impact of concomitant arterial injury on the outcome of laparoscopic bile duct injury. *Am. J. Surg.* 2011; 201(2):238-44.
15. Siegel J.H., Cohen S.A. Endoscopic treatment of laparoscopic bile duct injuries. *Gastroenterologist.* 1994; 2(1):5-13.
16. Wu Y.V., Linehan D.C. Bile duct injuries in the era of laparoscopic cholecystectomies. *Surg. Clin. North Am.* 2010; 90(4):787-802.
17. Zhou L.K., Prason P. Mechanical and preventable factors of bile duct injuries during laparoscopic cholecystectomy. *Hepatogastroenterology.* 2012; 59(113):51-3.



MINISTERUL SĂNĂȚII, MUNCII ȘI PROTECȚIEI SOCIALE
AL REPUBLICII MOLDOVA

Criptorhidia la copil

Protocol clinic național

PCN-330

Chișinău, 2018

CUPRINS

ABREVIERILE FOLOSITE ÎN DOCUMENT

PREFAȚĂ

A. PARTEA INTRODUCȚIVĂ

- A.1. Diagnosticul
- A.2. Codul bolii (CIM 10)
- A.3. Utilizatorii
- A.4. Scopurile protocolului
- A.5. Data elaborării protocolului
- A.6. Data următoarei revizuirii
- A.7. Lista și informațiile de contact ale autorilor și ale persoanelor care au participat la elaborarea protocolului:
- A.8. Definițiile folosite în document

B. PARTEA GENERALĂ

- B.1. Nivel de asistență medicală specializată de ambulator
- B.2. Nivel de asistență medicală spitalicească

C. 1. ALGORITMI DE CONDUITĂ

- C.1.1. Algoritmul de diagnostic al pacientului cu criptorhidie
- C.1.2. Algoritmul de tratament al pacientului cu criptorhidie

C. 2. DESCRIEREA METODELOR, TEHNICILOR ȘI A PROCEDURILOR

- C.2.1. Clasificarea
- C.2.2. Factorii de risc
- C.2.3. *Conduita pacientului* cu criptorhidie
 - C.2.3.1. Anamneza
 - C.2.3.2. Examenul fizic
 - C.2.3.3. Investigații paraclinice
 - C.2.3.4. Diagnosticul diferențial
 - C.2.3.5. Criteriile de spitalizare
 - C.2.3.6. Tratamentul
 - C.2.3.7. Evoluția
 - C.2.3.8. Supravegherea pacienților

D. RESURSELE UMANE ȘI MATERIALE NECESARE PENTRU RESPECTAREA PREVEDERILOR PROTOCOLULUI

- D.1. Policlinica consultativă pentru copii și femei
- D.2. Secția de urologie

E. INDICATORII DE MONITORIZARE A IMPLIMENTĂRII PROTOCOLULUI

ANEXE

Anexa 1. Informație pentru părinți

BIBLIOGRAFIE

Aprobat prin ședința Consiliului de experți proces verbal nr.2 din 18.04.2018

Aprobat prin ordinul Ministerului Sănătății, Muncii și Protecției Sociale al Republicii Moldova nr.829 din 02.07.2018 cu privire la aprobarea Protocolului clinic național „Criptorhidia la copil”

Elaborat de colectivul de autori:

Boris Curajos	doctor habilitat în științe meicale, profesor universitar, USMF „Nicolae Testemițanu”, Catedra Chirurgie, Ortopedie și Anesteziologie Pediatrică
Jana Bernic	doctor habilitat în științe meicale, conferențiar universitar, USMF „Nicolae Testemițanu”, Catedra Chirurgie, Ortopedie și Anesteziologie Pediatrică
Victoria Celac	doctor în științe medicale, șef secție urologie IMSP IMC
Vera Dzero	doctor în științe medicale, colaborator științific, USMF „Nicolae Testemițanu”, Laboratorul infecții chirurgicale la copii,
DI Anatol Curajos	medic ordinator, secția urologie, IMSP IMC, Centrul Național Științifico-Practic de Chirurgie Pediatrică „Academician Natalia Gheorghiu”
Victor Roller	colaborator științific, Laboratorul infecții chirurgicale la copii, USMF „Nicolae Testemițanu”
Ion Zaharia	medic urolog, secția urologie, IMSP IMC, Centrul Național Științifico-practic de Chirurgie Pediatrică „Academician Natalia Gheorghiu”
Eugen Ghețul	medic ordinator, secția urologie, IMSP IMȘIC, Centrul Național Științifico-Practic de Chirurgie Pediatrică „Academician Natalia Gheorghiu”
Larisa Seu	medic ordinator, secția urologie, IMSP IMȘIC, Centrul Național Științifico-Practic de Chirurgie Pediatrică „Academician Natalia Gheorghiu”
Adrian Revenco	doctorand, USMF „Nicolae Testemițanu”






Coordonator:

Eva Gudumac – doctor habilitat în medicină, profesor universitar, academician al AȘRM, Om emerit

Recenzenți

Victor Ghicavii	catedra Farmacologie și Farmacologie clinică USMF „Nicolae Testemițanu”
Valentin Gudumac	catedra medicina de laborator USMF „Nicolae Testemițanu”
Gh. Curocichin	catedra medicina de familie USMF „Nicolae Testemițanu”
Iurie Osoianu	Compania Națională de Asigurări în Medicină
Maria Cumpănă	Consiliul Național de Evaluare și Acreditare în Sănătate
Dumitru Saghin	Agenția Medicamentului și Dispozitivelor Medicale

Protocolul a fost discutat și aprobat

Denumirea/instituția	Persoana responsabilă - semnătura
Comisia științifico-metodică de profil „Chirurgie”	
Agenția Medicamentului și Dispozitivelor Medicale	
Consiliul de Experti al MS RM	
Consiliul Național de Evaluare și Acreditare în Sănătate	
Compania Națională de Asigurări în Medicină	

ABREVIERILE FOLOSITE ÎN DOCUMENT

AMP	asistența medicală primară
MSRM	Ministerul Sănătății al Republicii Moldovei
ECG	Electrocardiograma
i.m.	Intramuscular
i.v.	Intravenos
USG	Ultrasonografie
USMF	Universitatea de Stat de Medicină și Farmacie „Nicolae Testemițanu”

PREFAȚĂ

Protocolul clinic național „Criptorhidia la copil” a fost elaborat de un grup de medici ordinatori, colaboratori științifici sub conducerea dnei Eva Gudumac, doctor habilitat în medicină, profesor universitar, academician al AȘRM, Om Emerit, șefa catedrei Chirurgie, Ortopedie și Anesteziologie Pediatrică USMF „Nicolae Testemițanu”, Centrul Național Științifico-practic de Chirurgie Pediatrică „Academician Natalia Gheorghiu”.

A. PARTEA INTRODUCȚIVĂ

A.1. Diagnosticul: Criptorhidia la copil

Exemple de diagnostice clinice:

1. Anomalie congenitală de dezvoltare a organelor genitale externe masculine. Criptorhidia inghinală unilaterală.
2. Anomalie congenitală de dezvoltare a organelor genitale externe masculine. Criptorhidia inghinală bilaterală.
3. Anomalie congenitală de dezvoltare a organelor genitale externe masculine. Criptorhidia abdominală unilaterală.
4. Anomalie congenitală de dezvoltare a organelor genitale externe masculine. Criptorhidia abdominală bilaterală.

A.2. Codul bolii (CIM 10): Q 53

A.3. Utilizatorii:

- Oficiile medicilor de familie (medic de familie și asistenta medicală de familie);
 - Centrele de sănătate (medic de familie);
 - Centrele medicilor de familie (medic de familie);
 - Instituțiile/secțiile consultative (urologie);
 - Asociațiile medicale teritoriale (medic de familie, pediatru, urolog);
 - Secțiile de copii ale spitalelor raionale și municipale (pediatru, urolog);
 - Secția urologie, IMSP Institutul Mamei și Copilului.
- Notă:* Protocolul la necesitate poate fi utilizat și de alți specialiști.

A.4. Scopurile protocolului:

1. A îmbunătăți calitatea examinării clinice, paraclinice și a tratamentului copiilor cu criptorhidie.
2. A îmbunătăți diagnosticarea și acordarea asistenței necesare a pacienților cu criptorhidie.
3. Ameliorarea calității tratamentului chirurgical al pacienților cu criptorhidie.
4. Încadrarea copilului în societate.

A.5. Data elaborării protocolului: 2018

A.6. Data următoarei revizuirii: 2020

A.7. Lista și informațiile de contact ale autorilor și ale persoanelor care au participat la elaborarea protocolului:

Numele	Funcția deținută
Dna Eva Gudumac	academician AȘM, doctor habilitat în medicină, profesor universitar, Om emerit Director Clinică Chirurgie Pediatrică în Centrul Național Științifico-practic Chirurgie Pediatrică „Academician Natalia Gheorghiu”, șef Catedră Chirurgie, Ortopedie și Anesteziologie Pediatrică USMF „Nicolae Testemițanu”
DI Boris Curajos	d.h.ș.m., conferențiar universitar, Catedra Chirurgie, Ortopedie și Anesteziologie Pediatrică, USMF „Nicolae Testemițanu”, Director Clinică Urologie Pediatrică, USMF „Nicolae Testemițanu”, Centrul Național Științifico-practic Chirurgie Pediatrică „Academician Natalia Gheorghiu”
Dna Jana Bernic	d.h.ș.m., conferențiar universitar, Catedra Chirurgie, Ortopedie și Anesteziologie Pediatrică, USMF „Nicolae Testemițanu”
Dna Victoria Celac	d.ș.m., Șef secție urologie, IMSP IMȘIC
Dna Vera Dzero	d.ș.m., colaborator științific, Laboratorul infecții chirurgicale la copii, USMF „Nicolae Testemițanu”
DI Ion Zaharia	medic urolog, Clinica de Urologie Pediatrică, Centrul Național Științifico-practic de Chirurgie Pediatrică „Academician Natalia Gheorghiu”, IMSP IMȘIC
DI Anatol Curajos	Ordinator, medic urolog, Clinica de Urologie Pediatrică, Centrul Național Științifico-practic de Chirurgie Pediatrică „Academician Natalia Gheorghiu”, IMSP IMȘIC
DI Victor Roller	colaborator științific, Laboratorul infecții chirurgicale la copii, USMF „Nicolae Testemițanu”
DI Eugen Ghețeu	medic ordinator, secția urologie, IMSP IMȘIC, Centrul Național Științifico-Practic de Chirurgie Pediatrică „Academician Natalia Gheorghiu”

Dna Larisa Seu	medic ordinator, secția urologie, IMSP IMșiC, Centrul Național Științifico-Practic de Chirurgie Pediatrică „Academician Natalia Gheorghiu”
DI Adrian Revenco	doctorand, USMF „Nicolae Testemițanu”

A.8. Definițiile folosite în document

- **Definiție:** Criptorhidia se consideră o malformație congenitală, ce se manifestă prin retenția testiculului pe traiectul migrării lui în scrot, testicul ascuns, obscur (cryptos = ascuns). Testiculul criptorhid poate fi atrofic, ectopic sau necoborât. Pe de altă parte testiculul care nu se află în scrot poate fi palpabil (ectopic, necoborât), ori nepalpabil (atrofic, necoborât).
- **Clasificare:**
 1. Testiculul necoborât reprezintă 93% din totalitatea testiculelor criptorhide. El este situat în afara scrotului, dar pe „axa anatomică de coborâre”. Testiculul necoborât poate fi palpabil ori nepalpabil (testicul abdominal și uneori cel situat în canalul inghinal). Testiculul necoborât palpabil poate fi retractil (poziție extrascrotală intermitentă datorată unui reflex cremasteric puternic) sau sigur necoborât (abdominal, în canalul inghinal, prescrotal, suprafasial = reclinat pe aponevroza oblicului extern).
 2. Testiculul ectopic (4% din testiculul criptorhid) este situat în afara axei anatomice de coborâre: perineal, femural ori pubian. Testiculul ectopic este totdeauna palpabil și de obicei calitativ mai bun decât testiculul necoborât.
 3. Atrofia testiculară este rară (3% din testiculul criptorhid), rezultând în urma torsionii perinatale.
- **Cauzele:**
 1. Anomalia gubernaculului. Gubernaculul este o "coardă" fibroasă între polul inferior al testiculului și epididimului, pe de o parte, și scrot, pe de altă parte. Gubernaculul nu trage testiculul în scrot, îl direcționează doar. Absența ori anormalitatea gubernaculului (de structură ori de poziție) poate fi cauza de necoborâre ori de ectopie.
 2. Presiune intraabdominală redusă. Pacienții cu Prune Belly sindrom au testicul necoborât abdominal bilateral. Cei cu gastroschizis au incidența crescută de criptorhidism.
 3. Testiculul anormal. Această ipoteză derivă din observația că infertilitatea este mai ridicată la cei cu criptorhism, chiar după orhidopexia neproblematică.
 4. Dereglări endocrine. Cel mai probabil cauza criptorhismului este o dereglare endocrină. Procesul coborârii testiculului este influențat de o serie de hormoni: gonadotropina corionică umană, testosteronul, dihidrotestosteronul, calcitonin gene related peptide, factorul de creștere epidermală și hormonul luteinizant.

B. PARTEA GENERALĂ

B.1. Nivel de asistență medicală specializată de ambulator IMȘIC, Policlinica consultativă pentru copii

Descriere (măsuri)	Motivele (repere)	Pași (modalități și condiții de realizare)
I	II	III
1. Diagnosticul	Diagnosticarea precoce a criptorhidiei la copil permite inițierea tratamentului și reducerea complicațiilor	Obligatoriu: <ul style="list-style-type: none"> • Anamneza • Examenul obiectiv • Examenul de laborator <ul style="list-style-type: none"> <input type="checkbox"/> analiza generală a sîngelui <input type="checkbox"/> urina sumară • USG sistemului urinar • Diagnosticul diferențial
2. Decizia în selectarea tacticii de tratament: staționar sau ambulator	Tratamentul criptorhidiei este exclusiv chirurgical	Obligatoriu: <ul style="list-style-type: none"> <input type="checkbox"/> Toți copiii cu criptorhidie necesită tratament chirurgical
3. Tratamentul în condiții de ambulator	Profilaxia infecțiilor intercurrente	
4. Supraveghere	Va permite depistarea complicațiilor	Obligatoriu: <ul style="list-style-type: none"> <input type="checkbox"/> Dispensarizarea se va face în comun cu medicul specialist urolog-pediatru conform planului întocmit

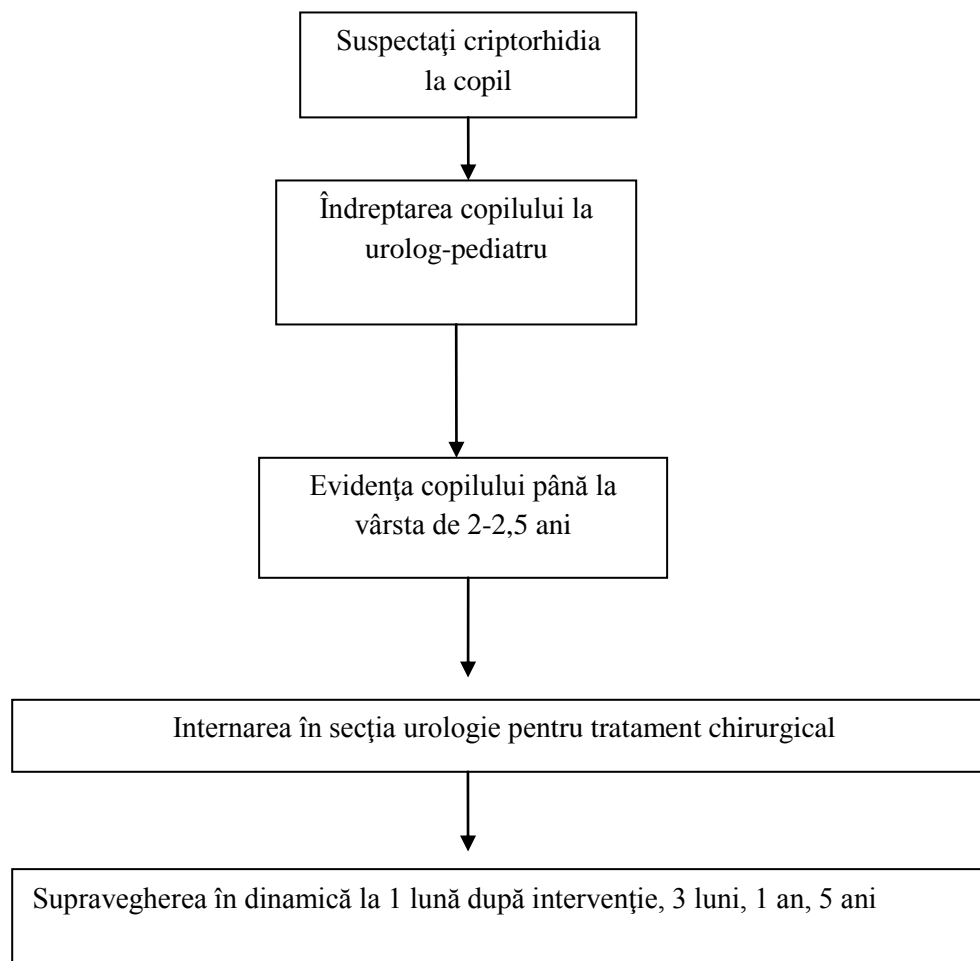
B.2. Nivel de asistență medicală spitalicească IMSP IMȘIC, secția urologie

Descriere (măsuri)	Motivele (repere)	Pași (modalități și condiții de realizare)
I	II	III
1. Spitalizarea	Vor fi spitalizați copiii care prezintă cel puțin un criteriu de spitalizare.	<ul style="list-style-type: none"> • Pacienții cu criptorhidie se vor spitaliza în secția de urologie a IMSP IMȘIC.
2. Diagnosticul		
2.1. Confirmarea criptorhidiei la copil	Diagnosticarea precoce a criptorhidiei permite inițierea tratamentului chirurgical la timp	Obligatoriu: <ul style="list-style-type: none"> <input type="checkbox"/> Colectarea anamnezei <input type="checkbox"/> Examenul obiectiv <input type="checkbox"/> Examenul de laborator <input type="checkbox"/> USG sistemului urinar <input type="checkbox"/> Diagnosticul diferențial

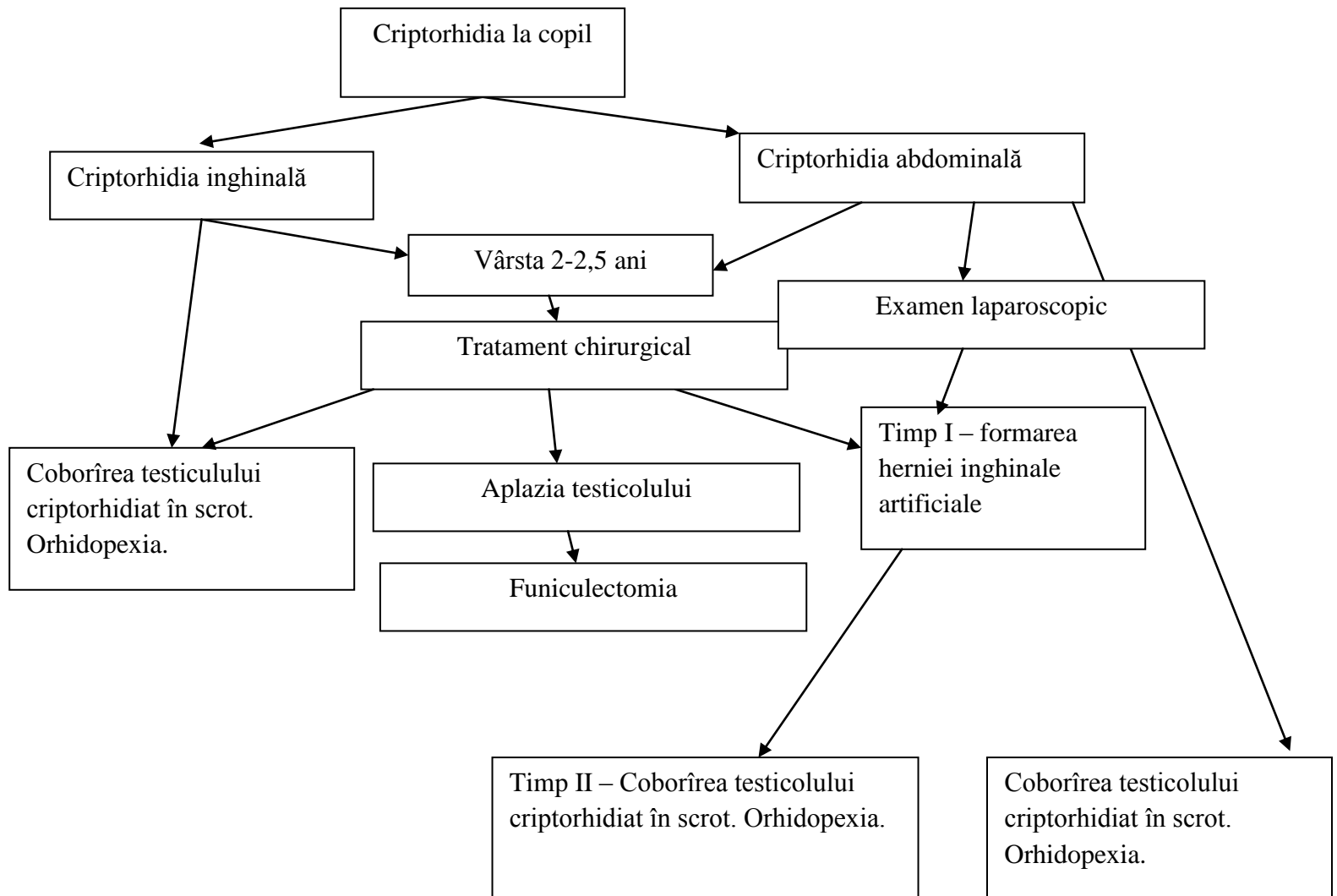
		Recomandabil: <input type="checkbox"/> Consultația altor specialiști (pediatru, neurolog etc.)
3. Tratament chirurgical	1. coborîrea testiculului 2. încadrare în societate	Obligatoriu: <input type="checkbox"/> Indicațiile pentru tratament chirurgical <input type="checkbox"/> Conduita preoperatorie <input type="checkbox"/> Intervenția chirurgicală <input type="checkbox"/> Conduita postoperatorie
4. Externarea	Starea satisfăcătoare a pacientului permite externarea.	Obligatoriu: <input type="checkbox"/> Evaluarea criteriilor de externare
4. Externarea, nivelul primar, tratament continuu și supraveghere	Evidența pacientului după manipulații chirurgicale cât și pe întreaga perioadă de creștere.	<input type="checkbox"/> Eliberarea extrasului care obligatoriu va conține: <input type="checkbox"/> Diagnosticul precizat desfășurat <input type="checkbox"/> Rezultatele investigațiilor efectuate <input type="checkbox"/> Tratamentul efectuat în staționar <input type="checkbox"/> Recomandări explicite pentru pacient <input type="checkbox"/> Recomandări pentru medicul chirurg-pediatru, urolog, medicul de familie

C. 1. ALGORITMI DE CONDUITĂ

C.1.1. Algoritm de diagnostic al pacientului cu criptorhidie



C.1.2. Algoritmul de tratament al pacientului cu criptorhidie



C. 2. DESCRIEREA METODELOR, TEHNICILOR ȘI A PROCEDURILOR

C.2.1. Clasificarea maladiei:

Caseta 1. I 1. Criptorhidia unilaterală 2. Criptorhidia bilaterală	II 1. Criptorhidia inghinală 2. Criptorhidia abdominală
---	--

C.2.2. Factorii de risc

Caseta 2. Factorii de risc în dezvoltarea criptorhidiei

- Prematuritate/greutate mică la naștere
- Istoric familial
Alte posibile asocieri :
- Factori maternali (vîrstă, naștere complicată, cezariană, preeclampsie)
- Etnie asiatică
Genetic
- Asocierea cu alte anomalii (hipospadie) are 12–25% incidență de anomalie cromozomială.
Criptorhidia izolată are 3–4% incidență de anomalie cromozomială.

C.2.3. Conduita pacientului cu criptorhidie

C.2.3.1 Anamneza

Caseta 3. Acuzele părinților copilului cu criptorhidie

- Absența testiculului în scrot de la naștere
- Testiculul coboară periodic în scrot (testicul retractil).
- Prezența în anamneză a hiperemiei scrotale, edemului, mărirea în volum, prezența unui hematom la naștere sau pe parcurs.

C.2.3.2 Examenul fizic

Caseta 4.

- Lipsa testiculului în scrot.
- Uneori în forma inghinală sau ectopică- dureri neînsemnate.
- La examinare clinică - important este a se preciza dacă testiculul e palpabil sau nu. Dacă este palpabil, se va stabili dacă e retractil, sigur necoborît, ori ectopic. Perioada bună de examinare este înaintea vîrstei de 6 luni: pînă la această vîrstă subcutanul este subțire, iar reflexul cremasterian slab (condiții bune de examinare). Pe de altă parte un pacient peste 6 luni cu testicul absent în scrot, dar care inițial avusese un testicul normal, este susceptibil a avea testicul retractil și nu testicul necoborît.
- Forma scrotului de partea criptorhidă poate sugera dacă testiculul este prezent: un hemiscrot normal este indiciu că testiculul se găsește probabil în regiunea inghinală (prescrotal, susprafascial, canal).
- Transiluminare negativă.
- Tehnica palpării - examinatorul stă de partea afectată. Palparea începe în regiunea inghinală în apropierea crestei iliace antero-superioare cu mîna stîngă pentru testiculul criptorhid drept și invers. Se exercită o presiune spre posterior (sacru), în timp ce mîna glisează spre simfiză (presiunea va fi menținută spre sacru și nu spre coapsă!), în acest timp cealaltă mîna palpează dinspre scrot spre canalul inghinal. Testiculul ectopic se descoperă prin examinarea atentă a regiunii perineale, femurale, ori prepubic.

Repetarea examinării evită investigații inutile și uneori costisitoare.

C.2.3.3. Investigațiile paraclinice

Tabelul 1.

Investigațiile paraclinice	Semnele sugestive pentru criptorhidie	Nivelul acordării asistenței medicale	
		Nivelul consultativ	AMS
Analiza sumară a urinei (Grad B Nivel II a)	norma	O	
Analiza generală a sîngelui (Grad B Nivel II a)	norma	O	
Ecografia sistemului urinar (Grad B Nivel II a)	Norma sau în cazul asocierii altor anomalii urogenitale	O	
Analiza biochimică a sîngelui (markeri ai afectării funcției renale) (Grad B Nivel II a)	norma	O	
Grupa de sînge și Rh factor (Grad B Nivel II a)			
ECG (Grad B Nivel II a)		O	
R-grafia panoramică a căilor urinare		R	R
Urografia intravenoasă		R	R
Scintigrafia renală		R	R
Tomografia computerizată, Rezonanța magnito-nucleară		R	R

Notă: O- obligatoriu, R-recomandabil.

C.2.3.4 Diagnosticul diferențial

Tabelul 2.

Retenție adevărată (criptorhidia)	Retracția	Ectopia
Scrotul sau hemiscrotul nu este dezvoltat, testiculul lipsește	Scrotul dezvoltat, testiculul situat suprapubian, ușor se coboară în scrot	Testiculul lipsește în scrot, dar se palpează în regiunea perineană, femorală sau prepeniană

C.2.3.5. Criteriile de spitalizare

Caseta 5. Criteriile de spitalizare a copiilor cu criptorhidie

- Lipsa unui sau ambelor testicule în scrot.
- Prezența patologiilor asociate ce pot determina criptorhidia.
- Prezența complicațiilor (torsione, traumă, malignizare).

C.2.3.6. Tratamentul

Caseta 6. Tratamentul hormonal

Ghonadotropinum chorionicum și rilizing-hormonul luteinizant (LHRH) pot fi utilizați individual ori combinat. GCU acționează pe celulele Leydig în timp ce LHRH acționează prin intermediul pituitarei. Hormonii nu vor fi administrați la pacienții cu hernii evidente (indicație operatorie absolută) sau la cei cu testicul ectopic.

Terapia durează 4 săptămâni consecutive. Succesul terapiei hormonale este apreciat în jur de 14%, pentru testicul necoborât unilateral, și virtual 100% pentru testiculul retractil.

Caseta 7. Conduita preoperatorie

- Organizarea corectă a regimului general;
- Alimentarea rațională; lichidarea infecției bacteriene în căile urinare și acțiunea asupra reacției imunopatologice;
- Terapie simptomatică;
- Examinarea obligatorie (examenul general al sîngelui, durata sîngerării, urina sumară, ECG, Grupa sîngelui și RH factor).

Caseta 8. Tratament chirurgical

Orhidopexia se practică între 9 și 18 luni vîrstă. După 9 luni nu se mai produce coborîrea spontană. Temperatura intraabdominală crescută poate degrada celulele germinale (a nu se amîna prea mult intervenția). Deoarece la vîrsta mică nu există conștientizarea sexului, este avantajos și din punct de vedere psihologic practicarea operației la această vîrstă . O indicație general acceptată a *orhiectomiei* testiculului nepalpabil este vîrsta pacientului peste 10 ani, în prezența testiculului contralateral normal. În aceste cazuri șansa testiculului necoborît de a contribui la fertilitate este minimală, în timp ce riscul malignizării este crescut, astfel orhiectomia fiind justificată.

În caz de criptorhidie abdominală: orhidopexia în 2 timpi după prof. B.Curajos:

I Timp – hernie artificială cu ancorarea peritoneului în apropierea testicolului

II-lea Timp – coborîrea testicolului cu plastia herniei

Etapa postoperatorie

Caseta 9. Conduita postoperatorie

- Regim alimentar
- Examen obiectiv zilnic
- Preparate antipiretice: Paracetamolul – doza maximă 25 mg/kg
- La febră și dureri:
 - Sol. Metamizolum natricum 50% 2 ml 0,1 ml la 1 an de viață i.m.
 - Sol. Diphenhydraminum 1% 1 ml 0,1 ml la 1 an de viață i.m.
- Tratament local (pansamente)

C2.3.7. Evoluția

Caseta 10. Criterii de externare

- Normalizarea stării generale
- Lipsa febre, vomei
- Cicatrizarea primară a plăgii posoperatorii
- Lipsa complicațiilor postoperatorii

C.2.3.8. Supravegherea pacienților

Caseta 11.

- Evidența și monitorizarea periodică la medicul specialist
- Consultația repetată în clinica de specialitate la necesitate
- Monitorizarea postoperatorie în privința persistenței testiculare în scrot
- Monitorizarea pe termen lung în privința riscului de malignizare înaltă
- Auto-examinarea periodică

D. RESURSELE UMANE ȘI MATERIALE NECESARE PENTRU RESPECTAREA PREVEDERILOR PROTOCOLULUI

<i>D.1. Asistența medicală primară.</i>	<ul style="list-style-type: none">• medic de familie• asistenta medicului de familie
<i>D.2. Asistența medicală specializată de ambulatoriu. Policlinica consultativă</i>	Personal: <ul style="list-style-type: none">• pediatru• urolog-pediatru• asistente medicale• medic de laborator
	Aparate, utilaj: <ul style="list-style-type: none">• USG• cabinet radiologic• laborator clinic și bacteriologic standard
<i>D.3. Asistența medicală spitalicească. Secția de urologie</i>	Personal: <ul style="list-style-type: none">• urolog-pediatru• pediatru• neurolog• cardiolog• anesteziolog• medic imagist• asistente medicale• medic de laborator• R-laborant
	Aparate, utilaj: <ul style="list-style-type: none">• aparat de USG• cabinet radiologic• tomograf computerizat• cabinet radioizotopic• instrumente pentru examen radiologic• laborator clinic și bacteriologic standard

	Medicamente: <ul style="list-style-type: none"> • Preparate antibacteriene: Antibiotice: (Cefalosporine generația I-IV: Cefazolinum, Cefalexinum, Cefuroximum, Cefotaximum, Cefepimum etc.) • Peniciline semisintetice + acid clavulonic • Preparate antipiretice: Paracetamolom • Preparate antihistaminice: Diphenhydraminum, Chloropyraminum. • Metamizolum natricum
--	---

E. INDICATORII DE MONITORIZARE A IMPLIMENTĂRII PROTOCOLULUI

No	Scopul protocolului	Indicatorul	Metoda de calculare a indicatorului	
			Numărător	Numitor
1.	A îmbunătăți diagnosticarea pacienților cu criptorhidie	1.1. Ponderea copiilor care au împlinit vârsta de 1 an și au fost supuși examenului urologic în vârsta de 1 lună și 1 an, pe parcursul unui an din cei depistați intrauterin (în %)	1.1. Numărul copiilor care au împlinit vârsta de 1 an și au fost supuși examenului urologic la vârsta de 1 lună și 1 an pe parcursul ultimului an din cei depistați intrauterin x 100	Numărul total de copii care au împlinit vârsta de 1 an și au fost consultați de medicul urolog pediatru la policlinica consultativă de copii
		1.2. Ponderea copiilor suspecți la anomalia sistemului urogenital care au fost supuși examenului urologic în primele zile după naștere pe parcursul unui an (în %)	1.2. Numărul copiilor suspecți la anomalia sistemului urogenital care au fost supuși examenului urologic în primele zile după naștere pe parcursul ultimului an x 100	Numărul total de copii care au împlinit vârsta de 1 an și au fost consultați de medicul urolog pediatru la policlinica consultativă de copii
		1.3. Ponderea pacienților diagnosticați cu criptorhidie pe parcursul unui an (în %)	1.3. Numărul pacienților diagnosticați cu criptorhidie pe parcursul ultimului an x 100	Numărul total de copii care au împlinit vârsta de 1 an și au fost consultați de medicul urolog pediatru la policlinica consultativă de copii
2.	A îmbunătăți tratamentul pacienților cu criptorhidie	2.1. Ponderea pacienților cu criptorhidie supuși tratamentului chirurgical pe parcursul unui an, care au dezvoltat complicații postoperatorii în primele 10 zile după intervenție chirurgicală (în %)	Numărul pacienților cu criptorhidie supuși tratamentului chirurgical, care au dezvoltat complicații postoperatorii în primele 10 zile după intervenție chirurgicală pe parcursul ultimului an x 100	Numărul total de pacienți cu criptorhidie supuși tratamentului chirurgical pe parcursul ultimului an
		2.2. Ponderea pacienților cu criptorhidie care au dezvoltat dezvoltat complicații postoperatorii peste 3 luni după intervenție chirurgicală (în %)	Numărul pacienților cu criptorhidie care au dezvoltat dezvoltat complicații postoperatorii peste 3 luni după intervenție chirurgicală x 100	Numărul total de pacienți cu criptorhidie care se află la evidența medicului urolog pediatru la policlinica consultativă de copii
3.	A reduce rata complicațiilor la pacienții cu criptorhidie	3.1. Ponderea pacienților cu criptorhidie supuși corecției chirurgicale, la care a survenit complicații pe parcursul unui an (în %)	Numărul pacienților cu criptorhidie supuși corecției chirurgicale, la care a survenit complicații pe parcursul ultimului an x 100	Numărul total de pacienți cu criptorhidie supuși corecției chirurgicale pe parcursul ultimului an

Anexa 1. Informație pentru părinți

Acest ghid descrie asistența medicală și tratamentul copiilor cu criptorhidie în cadrul serviciului de sănătate din Republica Moldova. În ghid se explică indicațiile adresate pacienților cu HC, dar și familiilor acestora, părinților și tuturor celor care doresc să cunoască cât mai mult despre această maladie. Ghidul vă va ajuta să înțelegeți mai bine opțiunile de îngrijire și tratament al HC. Nu sunt descrise în detalii maladia, analizele și tratamentul necesar. Despre acestea veți afla de la medicul de familie.

1. Criptorhidia se consideră o malformație congenitală, ce se manifestă prin retenția testiculului pe traiectul migrării lui în scrot, testicul ascuns.

2. Care sunt cauzele criptorhidiei?

- Cauza apariției criptorhidiei se socot tulburările embriogenezei la a 7-14-a săptămână a sarcinei. Factorii care influențează embriogeneza și cauzează dezvoltarea criptorhidiei sunt modificările endocrin-hormonale în organismul mamei, bolile infecțioase etc.

3. Simptomele clinice: lipsa testicolului în scrot.

4. Diagnosticul se stabilește imediat după nașterea copilului.

5. La ce duce criptorhidia? Provoacă trauma psihică a copilului și a părinților. Temperatura intraabdominală crescută poate degrada celulele germinale.

6. Tratamentul criptorhidiei este exclusiv chirurgical la vârsta de 9-18 luni.

7. Supravegherea copiilor ce suferă de criptorhidie și care au suportat una sau mai multe intervenții chirurgicale de urolog, periodic 1 dată în lună, 3 luni peste 1 an și de la evidență copiii se scot peste 5 ani, în lipsa complicațiilor.

Respectați regimul tratamentului prescris, recomandările medicului și prezentați-vă la control la timp. Toate aceste măsuri sunt direcționate către însănătoșirea copilului D-voastră și previn dezvoltarea complicațiilor grave.

Anexa 2 Fișa standardizată de audit bazat pe criterii pentru criptorhidia la copil.

FIȘA STANDARDIZATA DE AUDIT BAZATĂ PE CRITERII CRIPTORHIDIA LA COPIL		
Domeniul prompt		Definiții și note
1.	Denumirea IMSP evaluată prin audit	
2.	Persoana responsabilă de completarea fișei	Numele prenumele, telefon de contact
3.	Perioada de audit	DD.LL.AAAA
4.	Nr FM a bolnavului	
5.	Medicul de reședință a pacientului	1 – urban; 2- rural
6.	Data de naștere a pacientului	DD.LL.AAAA sau 9 –nu-i cunoscută
7.	Sexul pacientului	1 – masculin; 2- feminin, 9 – nu este specificat
8.	Numele medicului curant	
9.	Patologia	Criptorhidia
INTERNAREA		
10.	Data adresării primare după ajutor	DD.LL.AAAA, necunoscut=9
11.	Data internării în spital	DD.LL.AAAA sau 9 –necunoscută
12.	Secția de internare	DMU – 1; secția de profil pediatri – 1; secția de profil chirurgical – 2; secția reanimare -3
13.	Durata internării în spital (zile)	număr de zile; necunoscut=9
14.	Aprecierea criteriilor de spitalizare	Aplicate: 0 – da; 1- nu, 9 – nu se cunoaște
15.	Tratament administrat la DMU În cazul răspunsului afirmativ indicați tratamentul (medicamentul, doza, ora administrării)	Administrat: 0 – nu; 1- da, 9 – nu se cunoaște

DIAGNOSTICUL		
16.	Data debutului simptomelor	DD.LL.AAAA; 0- pînă la 6 luni; 1- mai mult de 6 luni sau 9 –necunoscută
17.	Ecografia abdominală	După internare: 0 – nu; 1- da, 9 – nu se cunoaște
<i>În cazul răspunsului afirmativ indicați rezultatul</i>		
ISTORICUL MEDICAL AL PACIENTULUI		
18.	Internat în mod programat	nu=0; da=1; necunoscut=9
19.	Internat în mod urgent	nu=0; da=1; necunoscut=9
20.	Sătrea pacientului la internare	Satisfăcătoare=2; grav-medic=3; gravă=4; foarte gravă=5; extrem de gravă=6
21.	Complicații înregistrate la internare	nu=0; da=1; necunoscut=9
22.	Maladii concomitente	nu=0; da=1; necunoscut=9
TRATAMENTUL		
23.	Tratament chirurgical a fost efectuat	0 – nu; 1- da
EXTERNAREA ȘI MEDICAȚIA		
24.	Data externării	DD.LL.AAAA
25.	Complicații înregistrate pe parcursul tratamentului	nu=0; da=1; necunoscut=9
26.	Implimentarea criteriilor de externare	0 – nu; 1- da; 9 – nu se cunoaște
27.	Prescrierea recomandărilor la externare	0 – nu; 1- da; 9 – nu se cunoaște

BIBLIOGRAFIE

1. Curajos B.M. Orhidopexia în doi timpi la criptorhidism abdominal. *Buletin de perinatologie*. 2001; 2:55-6.
2. Curajos B.M. ș.a. Criptorhidismul la copii. *Anale științifice ale Universității de Stat de Medicină și Farmacie „Nicolae Testemițanu”*. 2007; 9:46-9.
3. Muntean D. ș.a. Dismorfismul sexual. Criptorhidismul. Cluj-Napoca. 1996.
4. Littman J.K, Smith A.M. The optimum time to operate for criptochidism. *Pediatrics*. 1974; 53(3):96.
5. Urology S.Tekgul, H.S. Dogan, E.Erdem et al. *Eur. Soc. Paed. Urol.* 2015.
6. Воложин В., Ерохин А. Крипорхизм. Москва. 1995.
7. Лопаткин Н.А. Руководство по урологии. Москва: Медицина. 2000. Том 1. 304 с.
8. Лопаткин Н.А. Урология. Учебник для медвузов. Москва: Медицина. 2004. 520 с.
9. Пугачев А.Г. Детская урология. Москва: „ГЭОТАР-Медиа”. 2009. 832 с.



Moldavian Journal of Pediatric Surgery

Stimați colegi!

Scopul revistei este publicarea celor mai recente performanțe științifice și a rezultatelor cercetărilor clinice bazate pe dovezi din sfera specialităților chirurgicale pediatrice și din alte domenii conexe, și educația medicală continuă. Revista apare cu regularitate, două numere anual, și inserează următoarele tipuri de materiale:

- articole originale
- articole de sinteză (review)
- lecții
- cazuri clinice
- tehnici chirurgicale și metode de tratament
- istoria medicinei și chirurgiei
- recenzii
- comentarii

Instrucțiuni pentru autor

Sunt acceptate articole în limba engleză. Manuscrisele vor fi însoțite de o declarație de copyright semnată de autori, care sunt responsabili de conținut și de standardele etice stabilite. După recenzare și declarația privind dreptul de autor al editorului, semnată de toți autorii, primul autorul va primi o confirmare de acceptare pentru publicare. Nu se acceptă lucrări publicate în alte reviste medicale.

Volumul articolelor nu va depăși 8-12 pagini (A4) pentru cercetări originale și de sinteză, 4-6 pagini pentru prezentările de cazuri clinice și 1 pagină pentru recenzii, comentarii. Lucrările vor fi tipărite în programul Microsoft Word, caractere Times New Roman 12, intervalul 1,5, câmpurile a câte 2 cm..

Articolul va începe cu autorii (numele, prenumele), titlul (se culege cu majuscule), departamentele și instituțiile afiliate la momentul când a fost efectuat studiul, orașul și țara.

Rezumatul articolului se va prezenta în limba engleză (250-350 cuvinte), cu menționarea obligatorie a titlului. Sub rezumat vor fi indicate 5-7 cuvinte-cheie.

Textul propriu-zis al articolului va include următoarele compartimente: actualitatea temei, scopul și obiectivele lucrării, material și metode de cercetare, rezultate obținute, discuții, concluzii, bibliografie.

Citățile se inserează cu cifre arabe în paranteze drepte (ex.: [3]). Referințele bibliografice vor cuprinde obligatoriu: autorii (numele și inițiala prenumelui), titlul articolului citat (în limba originală), revista (cu prescurtarea internațională), anul apariției, volumul, numărul paginilor (Ex.: Akhtar J., Skarsgard E.D. Associated malformations and the "hidden mortality" of gastroschisis. J. Pediatr. Surg. 2012; 47(2):911-6.).

Se permite includerea în text a figurilor și tabelor care se întitulează și se numerotează. Figurile vor fi obligatoriu în format TIFF sau JPEG, de calitate acceptabilă (rezoluția 300 dpi).

Articolele vor fi prezentate într-un exemplar tipărit (cu contrast bun) sau prin e-mail. Colegiul de redacție va considera obligatorie o recenzie asupra articolului din partea unui specialist recunoscut în domeniu. Se admit spre publicare nu mai mult de 2 lucrări de la fiecare prim-autor. Articolele, ce nu corespund cerințelor menționate mai sus, vor fi returnate autorilor pentru modificările necesare.

Versiunea online conține textul integral al articolelor și are acces liber

(Online version: www.SNCPRM.info.md).

Tel. de contact: tel. +373 69114780; +373 61055112; +373 67156999

e-mail: babuci@newmail.ru; sandujalba@gmail.com

Dear Colleagues!

The journal is focused on the publication of the latest scientific performances and the results of the evidence-based clinical research in the field of pediatric surgical specialties and other related fields, being also a means of continuous medical education. The journal publishes two issues per year. The following categories of papers are published:

- original articles
- brief reports
- lectures
- clinical cases
- surgical techniques and methods of treatment
- history of medicine and surgery
- reviews
- comments

Instructions for authors

The manuscripts of the submitted articles have to be accompanied by a copyright statement signed by the authors who are responsible for the content and ethical standards set. After providing the review and the copyright statement signed by all authors, the first author will receive a confirmation of acceptance for publication. Papers published in other medical journals are not accepted.

The article volume should not exceed 8-12 pages (A4) for original research and reviews, up to 4-6 pages - for clinical case presentations and 1 page - for comments. The papers should be printed in Microsoft Word, 12-point Times New Roman, 1.5 spacing, 2 cm margins. Articles in English are accepted.

Article structure:

Authors names (surname, initials)

Title (capitalized)

Affiliation (departments and institutions at the time the study was made)

City and country

The abstract has to be in English and contain 250-350 words, with the mandatory mention of the title. Immediately after the abstract, provide a maximum of 7 keywords.

The text of the article must include the following sections: novelty, purpose and objectives, material and methods of research, results, discussions, conclusions, references.

Citations are inserted with Arabic numerals in straight brackets (e.g. [3]). The references should include the authors (surname and first name initial), the title of the article (in the original language), the journal (with the international abbreviation), the year of publication, the volume, the number of pages. (e.g., Akhtar J., Skarsgard E.D. Associated malformations and the "hidden mortality" of gastroschisis, J. Pediatr. Surg. 2012; 47 (2):911-6).

It is allowed to include in the text numbered and entitled figures and tables. The figures will be compulsory in TIFF or JPEG format, having acceptable quality (300 dpi resolution). The articles must be submitted in a printed (good contrast) copy or by e-mail. A compulsory article review of a recognized specialist in the field is required to be submitted to the editorial board. No more than 2 papers from each of the first authors are allowed for publication. Articles that do not meet the above mentioned requirements will be returned to the authors for the necessary changes.

*The online version contains the full text of the articles and has free access
(Online version: www.SNCPRM.info.md).*

Tel: +373 69114780; +373 61055112; +373 67156999

e-mail: sandujalba@gmail.com, babuci@newmail.ru

