

## **Best Practice in Diagnosis and Treatment**

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

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#### **Abstract**

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#### **Rolul anomalilor neuronale intestinale în geneza colostazei la copiii operați pentru malformații anorectale**

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

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

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#### **Abstract**

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

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

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## **Introduction**

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

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

## **Methods**

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

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

Clinically, special attention is paid to interviewing parents and the patients, assessing the child's psycho-emotional status and the socio-economic climate in the

family. The loco-regional examination (visual, instrumental) provided the respective information about the anal position (anal index), the dimensions of the anal orifice (dilatometry), the healing deformations, the prolapse of rectal mucosa, etc.

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

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

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

## **Results**

Based on the questioning the parents of the children in our study, it was found that colostasis began recently postoperatively. We note that a protective colostomy was applied to 40.0% of children recently postnatal, which until its liquidation ensured daily colonic evacuation. The specialized loco-regional examination allowed us to detect anal stenosis in 13.3% of cases, which clarified colostasis as a result of organic infra-rectal obstruction, some of which were resolved by conservative methods, others by surgical treatment (Diamond-shaped flapreconstructive anoplasty).

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

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

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

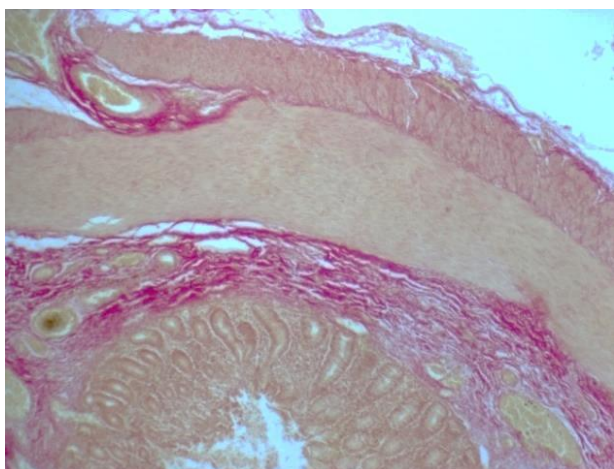
Radiological examination was used for differential diagnosis in 13 (86.6%) chronically constipated children, operated for ARM in the neonatal period and the first year of life. Simple radiological image of the lumbosacral area revealed congenital lumbosacral osteogenic defects (spina bifida and sacrococcygeal agenesis) in 13.3% of cases. Osseous defects detected in this segment of the

spine suggest for a possible anatomical and functional damage of the adjacent rectoanal and perineal neuromuscular apparatus with a possible dysfunctional influence that causes infra-rectal obstruction. The irigoscopy was performed to define the organic colonic parameters. At 9 (60.0%) children was appreciate left side megadolicocolon, 3 of them had a radiological area suspected for aganglionic zone.

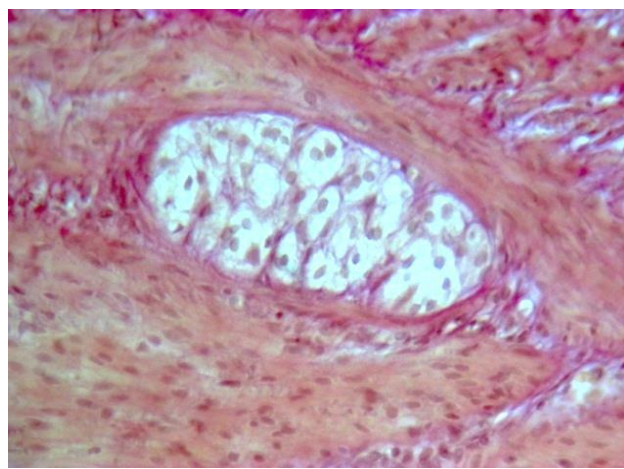
All children with organic changes of colon underwent for rectal biopsy (Swenson's procedure) with subsequent histomorphological examination.

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

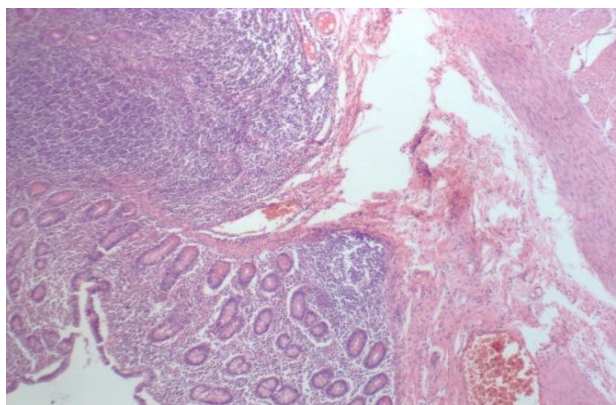
At 3 (5.6%) children, the intestinal nervous ganglions staining with hematoxylin-eosin did not visualize in the intermuscular and submucosal area, suspected for Hirschsprung's disease (fig. 3). For the confirmation of intramural innervation lesions in these children, we decide to define the AChE and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



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



**Fig. 2.** Auerbach's myenteric plexus consists mostly of resected colonic glial cells. Color. van Gieson.  $\times 40$



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

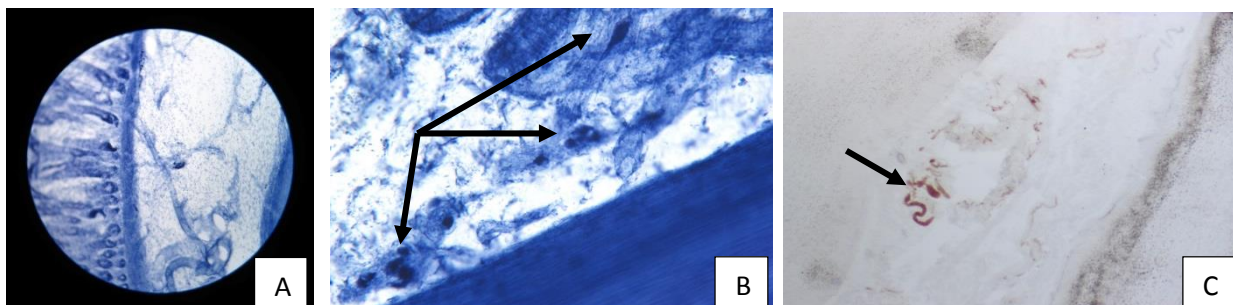


For the confirmation of intramural innervation lesions in these children, we decide to define the AChE and NADP activity (fig. 4). In 3 cases, the data analysis revealed congenital aganglionosis, which was characterized by absence of nervous ganglion in both plexuses of the colon, on a limited rectal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

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

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

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



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

*In conclusion*, we mention that lossing of the opportune moment for the early detection of IND and the overlapping of disorder of extrinsic innervation in the postoperative period conditioning major difficulties in

differential diagnostic for identify the cause of constipation in ARM, the solution of which requires the involvement of a multimodal clinical-paraclinical examination.

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