Forensic ramifications in diagnosing and treating high forms of the Hirschsprung’s disease

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Abstract: High forms of congenital megacolon sometimes present with an atypical clinical picture, as the irigographic exam gives inconclusive results. In case one is not familiar with the specific aspects of these cases, or does not observe the diagnosis protocols from medical literature, this could lead to serious diagnosis errors and repeated surgeries; this in turn will result in prolonged hospitalization and increased suffering for children, with negative ramifications on faeces continence. We present four specific cases of high form congenital megacolon, that were successfully dealt with in the Pediatric Surgery Clinic of the “M.S. Curie” Emergency Clinical Children’s Hospital in Bucharest, in the last 5 years, after serious initial diagnosis errors that were followed by severe complications and prolonged hospitalization.

Key Words: Hirschsprung disease, high form congenital aganglionosis, intestinal obstruction, sphincteral incontinence.

The Hirschsprung disease, or the congenital megacolon, is characterised by the absence of ganglion cells from the muscular plexus (Auerbach) and from the submucosal plexus (Meissner) at the distal colon level, with variable proximal extension, representing one of the most common causes of intestinal obstruction with infants.

The incidence of the disease is 1: 4400 - 1:7000 newborns, total colon damage representing 3-12 % of the cases [1].

The positive diagnosis can be established clinically, radiologically, by anorectal manometry; however, the exact diagnosis is obtained through the histopathological examination.

With total colon aganglionosis, the contrast agent irigography is inconclusive, the colon presenting a quasi-normal calibre most of the times; thus, the biopsy exam represents the golden standard in these cases.

The treatment of choice with the Hirschsprung’s disease is surgical and it involves completely removing the aganglionic area and rebuilding the continuity of the digestive tract. The success of the procedure depends on being able to identify exactly the aganglionic area during surgery. The macroscopic aspect in surgery is highly suggestive most of the times, but an exact diagnosis involves serial histopathological examination.

If the length of the aganglionic segment is underestimated, this could lead to the intersphincteral pull-through of a damaged colon fragment. As a result, the functional subocclusive-occlusive phenomena will be present even after surgery; a new surgical intervention will be needed, resulting in prolonged hospitalization and different degrees of faeces incontinence. On the other hand, if the length of the aganglionic segment is overestimated, this results in the unjustified excessive resection of a healthy colon segment, which amplifies the absorption disorders.
and increases the stool frequency. Thus, the period necessary for post surgery adjustment is also longer.

**OBJECTIVE**

Starting with the analysis of 4 specific cases of high form congenital megacolon, which were initially misdiagnosed, the paper aims to underline the importance of correctly assessing the length of the aganglionic area in order to avoid causing serious morpho-functional prejudices.

**Cases presentation**

**Case no. 1 – diagnosis: total congenital megacolon.**

The patient was admitted as a newborn with the symptoms of intestinal obstruction; he was misdiagnosed with common rectosigmoid congenital megacolon based solely on clinical and irigographic evidence. As a more objective histopathological examination of the length of the aganglionic area was not conducted, a series of incorrect therapeutic decisions followed. Multiple surgical procedures were performed – left colostomy, ileostomy, Duhamel abdominoperineal pull-through – leaving behind an aganglionic segment that developed negatively. When the patient was 4 years and 6 months old, he was admitted in the Pediatric Surgery Clinic of the "M.S. Curie" Emergency Clinical Children's Hospital Bucharest; here, with another surgery, the enteric lesions are correctly identified by serial biopsies of the colon and terminal ileum; the total congenital megacolon diagnosis was certified. A Soave abdominoperineal iterative pull-through of the terminal ileum was performed.

The patient has undergone a total of eight surgeries, which added up to 228 hospitalization days.

**Case no. 2 – diagnosis: total congenital megacolon.**

A female newborn with subocclusive syndrome was initially diagnosed with and treated for meconium ileus. She was readmitted in the emergency ward for intestinal obstruction; during surgery, it was interpreted as resulting from an inflammatory – adherent block through perforated appendix; appendicectomy, right anexectomy and cecostomy were performed. A subsequent negative development in the absence of a diagnostic biopsy led to further erroneous medical and surgical decisions: failed closure of the cecostomy, segmental enterectomy of the dilated ileal loop, with termino-terminal coloileal anastomosis, right hemicolecotomy, segmental resection of the terminal colon and left latero-lateral ileocolic anastomosis.

When admitted at the Pediatric Surgery Clinic of the "M.S. Curie" Emergency Clinical Children's Hospital Bucharest the child was cachectic (weighting 7 kg at the age of 24 months), and still presented the subocclusion symptoms. The histopathological examination of the biopitic fragment from the rectal muscular wall provided the correct diagnosis - congenital megacolon. The serial biopsies conducted afterwards exposed the spreading of the aganglionosis for the entire colon length, which required a Soave ileo-end-anal pull-through procedure.

The patient has undergone 7 surgical procedures by the time she was 4 years and 3 months old, which added up to 235 hospitalization days. At present she has partial facces continence.

**Case no. 3 – diagnosis: subtotal congenital megacolon.**

The patient underwent surgery when he was 3 days old for intestinal obstruction, correctly interpreted as congenital megacolon; a right colostomy was performed, in the immediate vicinity of the caecum. As the length of the aganglionic area failed to be determined correctly through serial biopsies, erroneous therapeutic decisions were taken: Duhamel abdominoperineal pull-through of the left aganglionic colon, colic resection with colorectal pull-through (for an alleged stenosis), right colostomy closure, which failed as a stercoral fistula appeared at this level and the colostomy was maintained.

At 7 years old he is admitted at the Pediatric Surgery Clinic of the "M.S. Curie" Emergency Clinical Children's Hospital Bucharest. The correct evaluation of the spread of the aganglionic segment led to a Soave colorectal pull-through.

The patient has undergone a total of 5 surgical procedures, which added up to 132 hospitalization days.

**Case no. 4 – diagnosis: total congenital megacolon.**

A female patient with congenital megacolon in her father’s family history, having a 48-hour delay in meconium elimination, presented 7 episodes of enterocolitis; the irigography was inconclusive. When she was 2 years old she underwent an emergency procedure at the Pediatric Surgery Clinic of the "M.S. Curie" Emergency Clinical Children's Hospital Bucharest, for intestinal obstruction syndrome; during surgery the total congenital megacolon diagnosis was established; an ileocolostomy and subsequently a Soave abdominoperineal ileo-endo-anal pull-through were performed.

**DISCUSSIONS**

The Hirschsprung's disease or the congenital intestinal aganglionosis is a disease characterised by the absence of neural ganglions which affect the colon in various degrees. It is a congenital disorder with complex multigenic ramifications, characterised by incomplete penetration and multiple associated anomalies. The pathogenesis of the disease involves
mutations of several genes (more than 11) [2]. The mutation of the RET gene involved in the development of the enteric ganglia derived from the neural crest cells is responsible for 50% of the family history cases and 15-20% of the sporadic cases [3]. The Hirschsprung disease can appear as an isolated anomaly or in the

Figure 1. Typical irigography images for congenital megacolon

Figure 2. (a) – colon muscular fragment: the absence of the nerve ganglion cells from the muscular plexus, coloration HE, Ob. 10X. (b) - (photo detail a) colon muscular fragment: the absence of the nerve ganglion cells from the muscular plexus. Coloration HE, Ob. 20X

Figure 3. (a) mucosal and submucosal colon fragment; the absence of the nerve ganglion cells from the submucosal plexus. Coloration HE, Ob. 20X; (b) (photo detail a); the absence of the nerve ganglion cells from the submucosal plexus and the hyperplasia of nerve fibers. Coloration HE, Ob. 40X.
context of well-defined syndromes, associated with other congenital anomalies (Waardenburg syndrome, von Recklinghausen syndrome, type D brachydactyly, Smith-Lemli-Opitz syndrome).

The neurons and the glial cells that form the enteric nervous system are derived from the neural crest [4]. During the embriogenesis, the neurenteric cells migrate from the level of the neural crest to the proximal end of the digestive tube and then in the craniocaudal direction [5].

In the Hirschsprung's disease two main pathogenic theories are described. The first theory is about the deficiency in the migration of the neural crest cells; according to this theory, the earlier the gestation age at which the migration stops, the longer the aganglionic colon segment will be [6,7]. The second theory is the “hostile environment” theory, which postulates that the neural cells have a significant lower ability to adhere to smooth muscle cells [8].

Histopathologically, the disorder is characterised by the lack of ganglionic cells in the submucosal stratum (Meissner) and the muscular stratum (Auerbach) with the hypertrophy and the hyperplasia of the nervous fibres from the lamina propria and the muscularis mucosa. The aganglionosis area is to be found at the rectosigmoid level in most of the cases (58-81%). In 10-26% of the cases the aganglionosis is spread on a longer colon segment, in 3-12% it covers the entire large intestine (total colon aganglionosis), and in a very small percentage (under 3%) the small intestine is involved [9,10,11,12,13].

The positive diagnosis is established clinically, radiologically via anorectal manometry and especially by means of biopsy and histopathological examination. 90% of the cases are diagnosed in the neonatal period [14,15,16], the main symptom being represented by the delay with which the meconium is eliminated in the first 48 hours since birth. However, this symptom can be absent in 6-42% of the cases [17,18].

Other symptoms can be represented by constipation, abdominal distension, spontaneous vomiting in the first days of life. Some patients can also present with explosive diarrhea, within a history of constipation, suggestive for the enterocolitis diagnosis, which represents the most frequent cause of decease at the patients with the Hirschsprung’s disease. If it is not diagnosed and treated in due course, the enterocolitis in the Hirschsprung’s disease can present toxic megacolon complications – a severe disorder which endangers the patient’s life.

A simple abdominal x-ray of a newborn can underline dilated intestinal loop with hydroaeric levels. The contrast agent irigography usually offers highly suggestive images for the diagnosis of the Hirschsprung’s disease (Figure 1): the distal colon has a reduced calibre; over it one can see a conical area with descending calibre, transitional, proximal of which the colon is highly dilated [19].

In the total colon aganglionosis, the contrast agent irigography is inconclusive; it does not offer positive diagnosis elements, as the colon has a normal calibre in 25-77% of cases.

The golden standard in the diagnosis for the Hirschsprung’s disease is represented by rectal biopsy (Figure 2). Swenson was the one that in 1959 created the technique of rectal biopsy in total stratum. Gherardi has proved in 1960 that in the Hirschprung’s disease the aganglionosis covers both the myenteric and the submucosal plexus. This observation has created the premises to conduct the submucosal aspiration biopsy (Figure 3). This technique is safe, can be performed without anesthesia and has a diagnostic accuracy of 99.7%.

The treatment for the Hirschsprung’s disease is surgical; along the years, standard techniques described by Swenson, Duhamel and Soave have been developed, yielding very good results. In 1998, De La Torre Mondragon presented a new surgical technique of transanal endorectal pull-through performed exclusively perineally [20].

In the recent years this type of procedure, laparoscopically assisted or not, has become the choice procedure in the treatment of the congenital megacolon [21].

In the common forms of the disease (rectosigmoid aganglionosis), the irigographical examination is usually highly suggestive; the rectal submucosal aspiration biopsy confirms the diagnosis; the surgical aspect of the concerned area is most of the times visible macroscopically (Figure 4).

The serial biopsies confirm the macroscopic evaluation, and the correctly performed surgical procedure leads to long term functional results.

In the total forms of aganglionosis there is a lack of specificity of the irigographic examination. This
is why in cases where the clinical picture is suggestive of Hirschsprung’s disease and the irigography is inconclusive, the rectal submucosal aspiration biopsy is mandatory; it protects the pediatric surgeon against serious subsequent therapeutic errors. At the same time, in these surgeries it is absolutely necessary to perform serial biopsies that will establish precisely the length of the damaged area and thus will help in outlining an appropriate surgical response.

The lack of availability of the extemporaneous biopptic exam forces the procedure to be split in two stages; the first one has a diagnostic objective, which is followed by the curative one, once the aganglionic area has been precisely delimited.

In Pediatric Surgery Clinic of the "M.S. Curie" Emergency Clinical Children's Hospital in Bucharest, starting from 2007, we have initiated the protocol of submucosal aspiration biopsy in cases where the Hirschsprung's disease is suspected, regardless of the aspect of the irigography.

The experience of the last six years, with the same surgical team, has led to a total of 31 cases of congenital megacolon. Out of these, 8 cases were initially treated in other hospitals; four represented extremely difficult cases; the initial diagnosis and treatment were incorrectly decided upon as the diagnosis protocol was not observed.

Thus in case number 1, serial biopsies were not performed, which led to a significant delay in establishing the exact diagnosis. Multiple interventions in the perineal area, the prolonged presence of petrified faecoliths in the rectal ampulla, the first Duhamel abdominoperineal pull-through procedure with an incorrect evaluation of the aganglionic area, all these required a second abdominoperineal pull-through. At present the patient presents with partial nocturnal faeces incontinence.

In the second case, the misdiagnosis based solely on the clinic and macroscopic aspects in surgery led to a chain of therapeutic errors that resulted in a very long period of hospitalization, the removal of the right annex and of a normal ileal area, an impressive chronic suffering and subsequent development, after the final surgery, of a partial faeces incontinence.

In the third case, the lack of initial serial biopsies led to a wrong diagnosis of the type of congenital megacolon and to a series of failed surgical procedures, and not least to the patient’s prolonged suffering (maintaining colostomy for 7 years) and partial faeces incontinence.

In the last case the repeated subocclusion situation was wrongly interpreted as enterocolitis, and a rectal aspiration biopsy was not conducted. Thus, the diagnosis was established much later, when the patient was 2 years old, following an occlusive episode.

CONCLUSIONS

The rectal biopsy gives the diagnosis of Hirschsprung’s disease, but it offers no information regarding the length of the aganglionic area.

In surgery, at older ages, the calibre difference between the dilated proximal colon and the aganglionic one is obvious; at younger ages this difference is sometimes difficult to identify and gives way to surgical management errors; thus the serial biopsies are mandatory as they establish exactly the spread of the aganglionic area.

Leaving behind an aganglionic area signifies conducting a curatively erroneous intervention in the area of the sphincteral complex, and that results in the persistence of the functional obstacle; a new procedure is required in the perineal area, which increases the risk of sphincteral faeces incontinence.

Sphincteral incontinence, growth disorders in a critical period for a child’s development, persistent intestinal transit disorders, hydroelectrolytic balance disorders, all these represent from a forensic perspective temporary or permanent morpho-functional prejudices, with impact on the quality of life; all these can be directly and causally linked to unjustified surgical procedures that were a consequence of the failure to apply the diagnosis protocol in the Hirschsprung’s disease.

References