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CASE REPORT / ПРИКАЗ БОЛЕСНИКА

Autoimmune intestinal leiomyositis as a rare cause of chronic intestinal pseudo-obstruction in children – case report with literature review

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SUMMARY

Introduction Chronic intestinal pseudo-obstruction represents a group of rare disorders characterized by impaired gastrointestinal motility in the absence of mechanical bowel obstruction. These disorders can be primary or secondary, with autoimmune intestinal leiomyositis falling into the latter category. This condition is observed in adolescence and adulthood but is very rarely seen in children, especially in infancy.

Case outline A nine-month-old male infant was hospitalized due to persistent vomiting, abdominal bloating, and distension. After diagnostic evaluations and failure of conservative treatment measures, surgical formation of an ileostomy was performed. During the procedure, intestinal samples were obtained, revealing T lymphocyte infiltration of the intestine. Immunological blood analyses showed elevated serum immunoglobulins and smooth muscle autoantibodies. Combined with histological findings and elevated inflammatory markers, a diagnosis of autoimmune intestinal leiomyositis was established. Immunosuppressive therapy was initiated, leading to normalization of inflammatory markers and resolution of clinical symptoms. After four years of immunomodulatory therapy, the ileostomy was closed, and intestinal biopsies showed no inflammatory infiltrates. Five years later, the boy remains free of gastrointestinal symptoms, with normal growth and development.

Conclusion Although a rare condition, autoimmune intestinal leiomyositis is an important differential diagnostic entity in chronic intestinal pseudo-obstruction. Early disease recognition with intestinal biopsies, coupled with prompt and aggressive immunosuppressive therapy, enables favorable therapeutic outcomes.

Keywords: child; autoimmune intestinal leiomyositis; immunosuppression

INTRODUCTION

Chronic intestinal pseudo-obstruction (CIPO) refers to a group of rare, heterogeneous, and debilitating disorders marked by impaired gastrointestinal motility in the absence of mechanical blockage. The etiology may be primary (sporadic or familial), which is more prevalent in children, or secondary, associated with various metabolic, endocrine, toxic, infectious, or immune conditions [1]. There are only few studies, but suggested incidence is one per 40,000 live births in the United States [2].

The clinical presentation varies depending on the segment of the gastrointestinal tract involved, with common symptoms including abdominal distension, vomiting, and abdominal pain. The variability in the age of onset, disease severity, and underlying causes makes establishing clear diagnostic criteria challenging. To address this, an expert group led by The European Society for Pediatric Gastroenterology Hepatology and Nutrition (ESPGHAN) published evidence- and consensus-based guidelines to standardize the diagnosis and management of pediatric patients with CIPO [3].

These guidelines served as a crucial reference in managing our patient, diagnosed with autoimmune enteric leiomyositis – a rare condition presenting in early infancy with CIPO. With only a handful of similar cases reported in the literature, this disorder is characterized by lymphocytic infiltration of the intestinal muscular layer causing intestinal inflammation with dysmotility and is often associated with poor prognosis.

Here, we presented the case with follow up of an infant with autoimmune intestinal leiomyositis, who demonstrated a favorable therapeutic response to an immunosuppressive regimen, achieving clinical, immunological, and histological remission.

CASE REPORT

A nine-month-old male presented to the emergency room with subocclusive symptoms, including abdominal distension, bloating, and vomiting. The patient's medical history was unremarkable except for chronic constipation, and there was no family history of chronic gastrointestinal or autoimmune diseases. On admission, laboratory findings revealed elevated inflammatory markers: erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP)

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and hypoalbuminemia. Complete blood count and electrolytes were normal. Thyroid function tests were also normal. Cytomegalovirus and Epstein–Barr virus infections were ruled out using serological markers. Immunological evaluation demonstrated positivity for antinuclear antibodies and anti-smooth muscle antibodies (ASMA), accompanied by elevated gamma immunoglobulins (Table 1). Celiac serology was within the normal range. Imaging studies included a plain abdominal X-ray, which showed dilated small bowel loops with air-fluid levels, and an abdominal ultrasound, which revealed intestinal aperistalsis. A barium enema examination was normal.

Table 1. Laboratory and immunological panel at diagnosis and after immunosuppressive regimen when treating pediatric patient with autoimmune enteric leiomyositis

Parameters	Values at time of diagnosis	Values at ileostomy reversal	Normal values
CRP (mg/l)	77	< 0.5	< 3
ESR (mm/h)	55	5	≤ 10
Albumin (g/l)	21	35	22–47
IgG (g/l)	14.3	5.8	4.1–10.8
ANA	positive	negative	negative
ASMA	1/320	negative	negative

CRP – C-reactive protein; ESR – erythrocyte sedimentation rate; IgG – gamma immunoglobulins; ANA – antinuclear antibodies; ASMA – anti-smooth muscle antibodies

Due to the absence of clinical improvement with conservative management, including antibiotics, prokinetic agents and enemas, the patient underwent emergency laparotomy. Intraoperative findings revealed massively dilated, aperistaltic small bowel with normal vascularization and no evidence of mechanical obstruction. The macroscopic appearance of the large bowel was normal. Full thickness of small and large bowel biopsies was obtained, and a diversion of ileostomy was performed.

Histological examination of the small and large bowel demonstrated dense lymphocytic infiltration (CD3+, CD4+ T lymphocytes, predominant and less prominent CD8+lymphocytes) in *lamina muscularis mucosae* and evidence of myenteric ganglionitis without fibrosis (Figure 1). Hirschsprung disease (Congenital intestinal aganglionosis) was excluded through histological analysis of large bowel samples (Figure 1). In the meantime, genetic testing (whole exome sequencing) was obtained and no pathological mutations associated with CIPO were found.

Based on the symptoms, histopathological findings and the immunological profile, treatment with methylprednisolone (1 mg/kg/day for 10 days, followed by prednisone tapering) and azathioprine (2.5 mg/kg/day) was initiated.

This therapeutic approach resulted in clinical remission with regular bowel movements and resolution of inflammatory syndrome. Steroids were tapered and discontinued after six months, while azathioprine was continued for maintenance. Despite stable clinical and laboratory remission, the patient experienced a recurrence of occlusive symptoms two years later, necessitating a second laparotomy. Intraoperative findings revealed extensive adhesions from the ligament of Treitz to the terminal ileum, described as "intestines adhered like glue." Surgical adhesiolysis was performed with intestinal biopsies. Histological analysis suggested mild fibrosis in the *lamina muscularis mucosae* secondary to inflammation without evidence of current lymphocytic inflammation. Steroids were introduced and tapered for a period of three months and azathioprine continued.

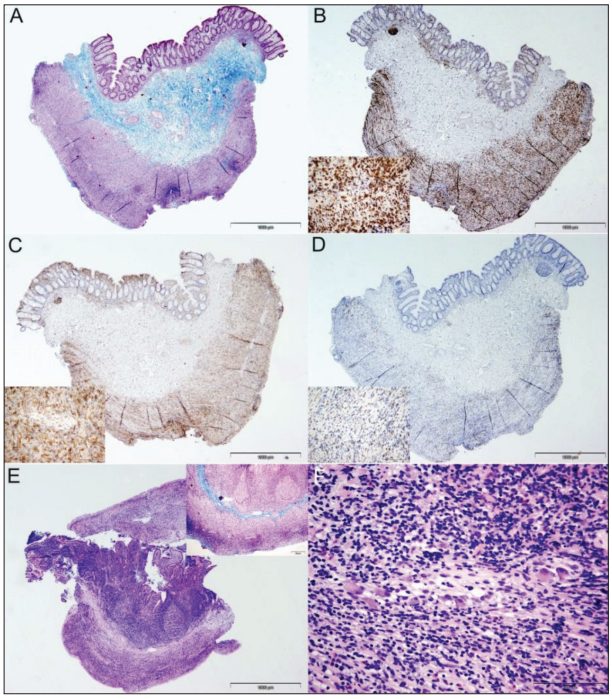

Figure 1. Histopathological evaluation of colon and ileal biopsies at diagnosis: A – biopsy of the colon showed no significant fibrosis (Masson-trichrome staining); B – CD3+ T lymphocytes infiltration of *lamina muscularis mucosae* and muscularispropria; C – CD4+ T lymphocytes infiltration of *lamina muscularis mucosae* and muscularispropria; D – CD8+T lymphocytes infiltration of *lamina muscularis mucosae* and muscularispropria; E and F – Terminal ileum biopsy showed similar histopathological features (H & E)

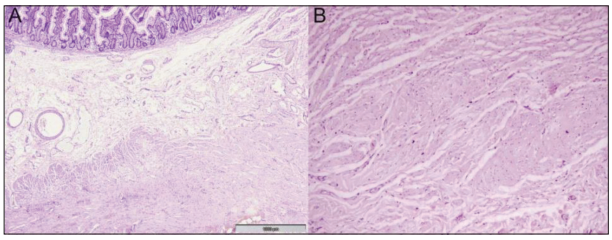

Figure 2. Ileal and colonic biopsy at ileostomy reversal; A – ileal biopsy adjacent to ileostomy revealed no inflammation in the intestinal wall (H & E); B – there were no signs of any pathological process in the muscular layer (H & E)

After a period of two years on azathioprine maintenance therapy, the patient remained clinically stable. Annual laboratory evaluations demonstrated normal inflammatory markers (CRP, ESR, and albumins), normalized gamma immunoglobulin levels and absence of histological inflammation on control intestinal biopsies. At the age of five, the ileostomy was successfully reversed. Intestinal biopsy revealed no inflammation in the intestinal wall (Figure 2). The patient is now a healthy, well-developed school-aged boy under regular medical follow-up.

The authors declare that the article was written according to ethical standards of the Serbian Archives of Medicine as well as ethical standards of institutions for each author involved. Informed consent was obtained from all the subjects involved in the study.

DISCUSSION

CIPO is a rare and severe disorder characterized by episodes of bowel obstruction without a fixed, lumen-occlusive lesion. It can be categorized as congenital or acquired [1, 2, 4]. Acquired causes of CIPO may result from toxic exposure, various infections such as Cytomegalovirus, Epstein–Barr virus, and human polyomavirus virus [5], or autoimmune inflammatory processes. CIPO due to autoimmune enteric lymphocytic leiomyositis with an autoimmune reaction to smooth muscles or nerves has been reported only a handful patients in medical literature [6, 7, 8].

Most patients have a history of preceding gastroenteritis, after which abdominal distension and intestinal ileus occur. In three analyzed case reports from literature, gastroenteritis preceded the onset of CIPO, but this was not the case for our patient [8, 9, 10]. For this reason, it is hypothesized that molecular mimicry between pathogens and T lymphocytes on one side and smooth muscles in the intestinal wall on the other side may play a role in the pathogenesis of this disorder [5]. Anti-Yersinia pseudo tuberculosis antibodies were detected in one infant [11].

Since diagnosing this condition requires full-thickness bowel biopsy to detect changes across all layers, this is not yet possible via endoscopy in children and requires surgical bowel biopsy. Histological analysis reveals a dense T lymphocyte infiltrate in the *lamina muscularis mucosae*, while the mucosa and submucosa are typically spared [3].

When analyzing the age of onset of autoimmune intestinal leiomyositis, around 80% of children present with symptoms in early childhood, but majority of them were older than our patient [12]. The majority was two, three, and five years of age, with more cases reported in adolescents and young adults [8, 9, 10]. Only one child under one year of age with autoimmune intestinal leiomyositis has been reported so far, with a very unfavorable disease course and outcome [11]. The predominance of female patients may be attributed to the autoimmune nature of this disorder.

In the personal medical histories of reported cases, we observed that two children had concomitant autoimmune diseases: autoimmune hepatitis and pure red cell anemia [8, 9]. This was not the case for our patient, as clinical analysis and immunological screening excluded associated autoimmune diseases. This difference seems from the fact that patients with comorbid autoimmune diseases were older, aged two and 3.5 years, respectively [8, 9]. Additionally, there were some cases of CIPO in adult patients with various autoimmune diseases [13].

Conversely, most patients (six out of eight), including our patient, showed significantly elevated anti-smooth muscle antibody titers. Two reported patients, as well as our patient, exhibited elevated inflammatory markers [9, 10]. These findings further confirm the autoimmune nature of the disease and, alongside bowel wall biopsy, contribute significantly to accurate diagnosis.

The most critical diagnostic tool remains histological analysis of the full-thickness bowel wall. All literature reports describe marginal or absent inflammation in the mucosa and submucosa, which was confirmed in our case. In all reported cases, including the one presented in this study, there was a massive T lymphocyte infiltrate in the *lamina muscularis mucosae*, sometimes accompanied by signs of fibrosis [8]. This histological finding is crucial for diagnosing autoimmune intestinal leiomyositis and, alongside clinical signs of bowel obstruction and elevated immunological parameters, forms an essential part of the diagnostic algorithm recommended by the ESPGHAN expert group [3].

For this reason, treatment involves immunosuppressive medications, including steroids and immunomodulators. Previous reports have described the use of these immunosuppressive drugs with variable success [14]. The youngest patient, under one year of age, succumbed to the disease despite steroid therapy [11]. In contrast, most patients with autoimmune intestinal leiomyositis underwent prolonged steroid therapy with a relapsing disease course, requiring extended hospitalization [9, 10]. Additionally, there are abundant literature data about intestinal transplantation in CIPO patients, but autoimmune pathogenesis was not predominant etiology, so we cannot recommend this surgery as a therapy of choice [15, 16].

In our case, initial treatment began with steroids and azathioprine, with steroids discontinued after six months, while azathioprine maintenance therapy continued, as recommended by Oton et al. [6]. Our patient responded well to both initial immunosuppressive therapies and maintenance treatment with azathioprine. After two years, he experienced one relapse of intestinal pseudo-obstruction requiring surgical intervention (adhesiolysis) but subsequently achieved histological remission while on immunomodulator, confirmed at the time of ileostomy closure.

When comparing the clinical course of previously reported autoimmune intestinal leiomyositis cases with our patient, we observe a favorable course in our patient. He had fewer relapsing obstruction episodes, successful ileostomy closure, and achieved histological remission with minimal fibrotic tissue, due to the prolonged inflammatory process. This favorable course resulted from early, aggressive, and prolonged immunosuppressive treatment, as recommended by Ruuska et al. [9].

What stands out in our case is that our patient is the youngest reported with autoimmune intestinal leiomyositis who responded well to immunosuppressive therapy, leading to favorable clinical, laboratory, and histological outcomes.

This case highlights the critical role of combining steroids and azathioprine in managing very early-onset autoimmune leiomyositis effectively.

Although rare, autoimmune enteric leiomyositis should be an important consideration in the differential diagnosis of CIPO, regardless of the patient's age or sex. Accurate

diagnosis relies on a high index of clinical suspicion, supported by full-thickness biopsy findings of T-cell infiltration and ASMA positivity in most cases. Early recognition and timely initiation of therapy, before the development of fibrotic lesions, are critical for improving patient outcomes.

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Аутоимуни интестинални лејомиозитис као редак узрок хроничне интестиналне псеудоопструкције код деце – приказ болесника са прегледом литературе

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САЖЕТАК

Увод Хронична интестинална псеудоопструкција представља групу ретких обољења која се карактеришу поремећеним мотилитетом дигестивног тракта у одсуству механичке блокаде црева. Обољења могу бити примарна или секундарна, а аутоимуни интестинални лејомиозитис припада групи секундарних обољења. Овај поремећај се виђа у адолесценцији и одраслом добу, а врло ретко код деце, поготову у одојачком узрасту.

Приказ случаја Мушко одојче узраста девет месеци је хоспитализовано због упорног повраћања, надимања и дистензије трбуха. Након обављене дијагностике и неуспеха конзервативних терапијских мера извршено је хируршко формирање илеостоме. Том приликом су узети узорци црева, који су показали интестиналну инфилтрацију Т-лимфоцитима. Имунолошке анализе крви су показале повишење серумских имуноглобулина и антитела на глатке мишиће, па је уз хистолошки налаз и повишење упалних параметара постављена дијагноза аутоимуног интестиналног лејомиозитиса. Ординирана је имуносупресивна терапија, на коју је дете одреаговало нормализацијом упалних параметара и смиривањем клиничке слике. Након четири године примене имуномодулатора затворена је илеостома, а узете биопсије црева показале су одсуство запаљенског инфилтрата. Пет година након дијагнозе, дечак је без дигестивних тегоба, уредног раста и развоја.

Закључак Иако је аутоимуни интестинални лејомиозитис ретка болест, представља важан диференцијално-дијагностички ентитет код хроничне интестиналне псеудоопструкције. Рано препознавање болести са биопсијама црева, раном и агресивном применом имуносупресивне терапије омогућава повољан терапијски исход.

Кључне речи: дете; аутоимуни интестинални лејомиозитис; имуносупресија