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Massively dilated small intestine as a severe complication of ineffective treatment of Crohn's disease

Monstrualnie poszerzone jelito cienkie jako ciężkie powikłanie nieskutecznego leczenia choroby Leśniowskiego–Crohna

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Abstract

This case report describes a 17-year-old boy previously hospitalised in Belarus, with significant dilatation of the small intestine in the course of stricturing-type Crohn's disease. Upon admission, the boy was severely malnourished. Magnetic resonance enterography revealed stenosis at the level of the distal ileum with massive prestenotic dilatation of the loops. During the gastrointestinal passage examination, signs of subobstruction of the gastrointestinal tract and dilatation of several ileal loops were noted. Surgical treatment was recommended, but the parents opposed the decision. Six months later, the boy was hospitalised again due to an exacerbation of the disease. After obtaining parental consent, ileocaecal resection was performed. The patient was discharged in good condition. Biological therapy was initiated. This case report highlights the importance of appropriate treatment of Crohn's disease. Decisions regarding surgical intervention can be difficult to accept for parents, so, understandably, they require the support of a hospital psychologist.

Keywords: surgery, Crohn's disease, biological therapy, paediatrics, prestenotic dilation

Streszczenie

W artykule przedstawiono opis przypadku 17-letniego chłopca, uprzednio hospitalizowanego na Białorusi, ze znacznym poszerzeniem jelita cienkiego w przebiegu postaci zwężającej choroby Leśniowskiego–Crohna. Przy przyjęciu chłopiec był skrajnie niedożywiony. Enterografia rezonansu magnetycznego ujawniła zwężenie na poziomie dystalnego odcinka jelita krętego z masywnym prestenotycznym poszerzeniem pętli. Podczas pasażu przewodu pokarmowego ujawniono cechy podniedrożności i znaczne rozdęcie kilku pętli jelita krętego. Podjęto decyzję o leczeniu operacyjnym, co spotkało się ze sprzeciwem rodzica. Pół roku później chłopiec był ponownie hospitalizowany z powodu zaostrzenia choroby. Po uzyskaniu zgody rodzica wykonano resekcję krętniczo-kątniczą. Pacjent został wypisany w stanie ogólnym dobrym. W dalszym postępowaniu wdrożono leczenie biologiczne. Opis przypadku podkreśla znaczenie odpowiedniego leczenia choroby Leśniowskiego–Crohna. Decyzja o interwencji chirurgicznej jest trudna do zaakceptowania przez rodziców, dlatego podejmowanie takich decyzji wymaga wsparcia psychologa szpitalnego.

Słowa kluczowe: operacja, choroba Leśniowskiego–Crohna, leczenie biologiczne, pediatria, prestenotyczne rozdęcie

INTRODUCTION

Crohn's disease (CD) is one of the inflammatory bowel diseases (IBD). It is characterised by chronic inflammation leading to progressive intestinal damage. The exact aetiology of CD remains unclear. In recent years, there has been a steady increase in the number of CD cases, especially among children and young adults. The prevalence of CD is estimated at 31–71:100,000 individuals under 20 years of age. The most common locations (53%) of CD lesions include the ileum and colon, though they may occur in any segment of the gastrointestinal tract. In 16% of children and adolescents, isolated ileocaecal disease is observed, while only 4% have disease limited to the terminal ileum[1]. Persistent inflammation resulting from delayed diagnosis, lack of treatment, or inappropriate therapy leads to complications such as strictures, perforations, and fistulas in any part of the gastrointestinal tract[2]. The Montreal classification, introduced in 2005, distinguishes different phenotypic features of CD, classifying them by age at diagnosis, lesion location, and clinical course, differentiating between inflammatory, penetrating, and stricturing forms[3]. The clinical presentation of CD in adolescents is similar to that observed in adults. However, the presence of the disease during this critical developmental period, due to the risk of malnutrition, may result in growth disturbances, delayed puberty, and an increased risk of psychosocial issues[1]. The treatment aims to achieve deep clinical remission, understood as the healing of the mucosal lesions. Established treatments include nutritional, pharmacological, and surgical approaches. Pharmacotherapy comprises aminosalicylates, glucocorticosteroids, immunosuppressants, antibiotics, and biological therapy with anti-tumour necrosis factor (TNF)-alpha antibodies (infliximab, adalimumab). Early identification of patients at high risk of severe disease course and complications is crucial. This group of patients should be considered for prompt initiation of biological therapy[4]. According to our knowledge, similar guidelines for CD treatment are followed in Belarus. The case involves a patient previously hospitalised in Belarus with massive dilatation of the small intestine caused by ineffective treatment of the stricturing form of CD.

CASE REPORT

A 17-year-old boy, diagnosed with CD in 2017 and previously treated with azathioprine (AZA), mesalamine, and systemic steroids, was admitted to the Paediatric Ward in Poland at the beginning of January 2021 due to weakness, abdominal pain, and decreased appetite. The parents, together with the boy, had moved to Poland to provide him with better treatment conditions. On admission, his condition was severe. The boy was dehydrated and severely malnourished (body mass index, BMI 15 kg/m^2). His height was 173 cm (44th percentile), and his weight was 49 kg (5th percentile). Physical examination revealed muscle atrophy, pale pink and dry skin, dental caries, a markedly distended abdomen, palpation tenderness in the left upper and mid-abdomen, intermittently audible metallic bowel sounds with local absence on the left flank, ankle swelling, and visible complications of steroid therapy (facial plethora and purple striae on the back). Peritoneal signs were negative. He scored 60 points on the Paediatric Crohn's Disease Activity Index (PCDAI), indicating high disease activity. Laboratory tests showed haemoglobin 8.7 g/dL (normal value: 12.5–16.1 g/dL), red blood cell count 3.3 × 10^6/μL (normal value: 4.2–5.6 × 10^6/μL), haematocrit (HCT) 35.6% (normal value: 36–47%), C-reactive protein (CRP) 9.07 mg/L (normal value: <5 mg/L), hypoproteinaemia (41.9 g/L) (normal value: 64–83 g/L), hypoalbuminaemia (19.27 g/L) (normal value: 32–45 g/L), deficiencies in folic acid, vitamin B_{12}, vitamin D (12.5 ng/mL) (normal value: 30–80 ng/mL), and iron (1.2 μmol/L) (normal value: 5.83–34.5 μmol/L). Pancreatic enzymes were elevated: serum amylase 250 U/L (normal value: 28–100 U/L) and urine amylase 1,158 U/L (normal value: 16–491 U/L). Because the patient did not present any clinical symptoms of pancreatitis and imaging showed no pancreatic abnormalities, AZA treatment was only temporarily discontinued and then resumed. The elevated amylase was interpreted as pancreatic involvement during disease exacerbation. Serological tests for coeliac disease were negative. Colonoscopy revealed persistent inflammation of the caecal mucosa with localised fibrosis. Treatment included fluid and antibiotic therapy (metronidazole and amoxicillin with clavulanic acid) and continuation AZA and mesalamine. Due to persistent inflammatory changes in the caecum, dystrophy, and metabolic disturbances, the boy was urgently transferred to the Department of Paediatric Gastroenterology and Hepatology for further diagnostics and treatment. Upon admission to the hospital, the boy's condition was still severe, with the same physical signs as previously described. The initial ultrasound (US) performed in the emergency department had limited diagnostic value due to significant intestinal gas and marked distension of the intestinal loops, without clear identification of which segments were involved. A subsequent US performed in the Department of Gastroenterology was also diagnostically challenging, as the massively dilated small intestine mimicked the large intestine and was described as such (Fig. 1). Further imaging, including magnetic resonance (MR) enterography, was performed. A stricture in the distal ileum with massive prestenotic dilation of loops up to approximately 9.5 cm was observed, within which signs of active inflammation were present. A fistula between the ileal loops and the inferior surface of the caecum was also described (Fig. 2). For possible preoperative evaluation, a gastrointestinal transit examination with non-barium contrast was ordered, revealing features of subocclusion and significant distension of several ileal loops (up to approximately 9.5 cm), occupying an area of about 36 × 26 cm within the abdominal cavity. It was not possible to determine conclusively whether the contrast medium passed through the terminal ileum or via a fistula

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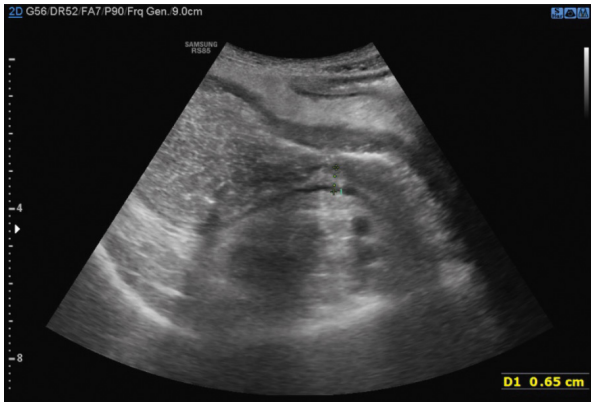

Fig. 1. Ultrasound of the abdomen and retroperitoneal space; a 5-cm section of narrowed small intestine with prestenotic dilatation

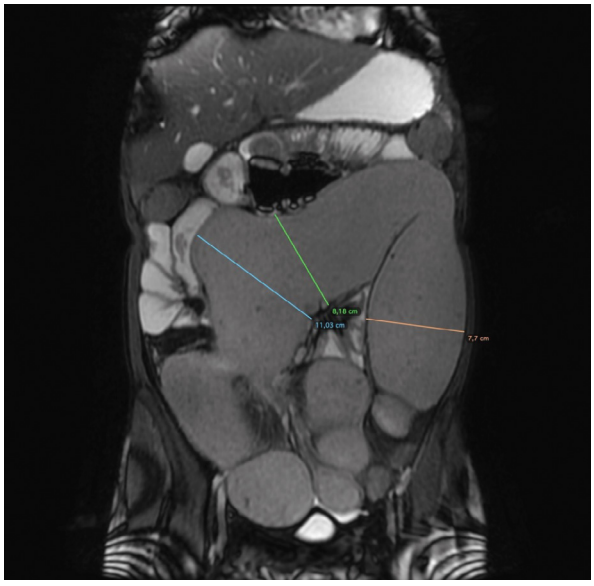

Fig. 2. Magnetic resonance enterography

connecting to the inferomedial wall of the caecum (Fig. 3). During hospitalisation, exclusive enteral nutrition (EEN) supplemented with Modulen IBD was initiated. After central access was established, parenteral nutrition (PN) based on Kabiven was started. Electrolyte and protein imbalances were corrected. Treatment included AZA, mesalamine, and prednisone. Additional tests were ordered to assess eligibility for biological therapy; however, contraindications to TNF-alpha treatment (stricturing form, features of small-bowel subocclusion) and low inflammatory activity suggested that surgical treatment should be considered first. The patient was in optimal condition, with improved nutritional and protein status (serum albumin: 19.27 g/L vs. 39.71 g/L; total protein: 41.9 g/L vs. 64.9 g/L; CRP: 9.07 mg/L vs. 0.49 mg/L). Despite several explanatory discussions, parental consent for the proposed treatment was not obtained. At the parents' request, the boy was discharged for further follow-up in the gastroenterology outpatient clinic before completing the diagnostic and therapeutic process.

Fig. 3. Gastrointestinal transit study; the sixth passage image, taken approximately after 5 hours, shows persistent anchorage and significant distension of the loops of the ileum, which together occupy an area of 36 × 26 cm. It was not possible to visualise the terminal ileum and the ileocaecal valve, making it impossible to clearly assess whether the passage of the contrast from the distended ileal loops occurs through the terminal ileum or through the fistula connecting to the inferomedial wall of the caecum

Six months later, the boy was urgently readmitted to the Department of Paediatric Gastroenterology and Hepatology due to a severe exacerbation of the underlying disease. During hospitalisation, PN based on Kabiven was initiated, mesalamine and AZA therapy was continued, intravenous antibiotic therapy with metronidazole was introduced, several albumin transfusions were administered, and intravenous iron was given. Inflammatory markers gradually decreased (CRP: 25.75 mg/dL vs. 5.67 mg/dL), protein–electrolyte imbalances were corrected (serum albumin: 28.4 g/L vs. 41.15 g/L; total protein: 55.3 g/L vs. 60.6 g/L), and weight gain was achieved (45.8 kg vs. 51.40 kg). Another surgical consultation was conducted, after which the parents consented to the proposed treatment. The boy was transferred to the Department of Paediatric Surgery for further treatment. A 50-cm segment of inflamed intestinal loops was resected, and an end-to-end anastomosis was performed. No perioperative or postoperative complications occurred. US of the abdomen performed before discharge revealed non-dilated intestinal loops, with normal thickness and clear peristalsis. Tests qualifying the boy for biological therapy were carried out. He was discharged from the hospital

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in good condition. His most recent hospitalisation was for the initiation of biological therapy with adalimumab. EEN enriched with Modulen IBD was continued. Currently, the patient's clinical condition is stable, and he remains in remission. After turning 18, he was transferred to adult care.

DISCUSSION

According to the guidelines of the European Crohn's and Colitis Organisation (ECCO) and the European Society of Paediatric Gastroenterology, Hepatology and Nutrition (ESPGHAN), therapeutic management in children with CD should take into account age, the location of the gastrointestinal lesions, disease activity, the presence of growth retardation, weight loss or lack of weight gain, potential side effects of medications, and overall quality of life. Treatment begins with induction therapy to achieve clinical remission, followed by maintenance therapy to prevent relapse. For children with severe CD (with extensive involvement and ulceration) and the stricturing form, biological treatment should be used as induction therapy. In cases of active CD, antibiotic therapy should be considered in addition to biological treatment. Biological treatment administered concurrently with surgical management is the treatment of choice in patients with the most severe, fistulising form of the disease. In children presenting with symptoms of obstruction and/or prestenotic dilatation (distension), intestinal resection is required before initiating biological therapy[4]. Given the clinical picture, this approach was proposed for our patient. Before being hospitalised in Poland, he had been treated with mesalamine, AZA, and periodic prednisone-based steroid therapy (nine cycles in total). Biological treatment was not available to the boy, so his family, like many others, organised a public fundraiser to cover treatment costs. Without knowing the exact clinical picture of the patient at the beginning of the disease, it is difficult to determine what treatment would have been administered in Poland. However, given that the therapy used was ineffective and numerous complications developed, treatment modification was necessary. During the first hospitalisation in Poland due to disease exacerbation, antibiotic therapy, fluid therapy, and continued treatment with mesalamine and AZA were ordered. Although 5-ASA medications are still used in real-world practice, they are currently not recommended as therapy for patients with CD. According to the guidelines, 5-ASA treatment should be discontinued[4]. At the treating centre, EEN based on Modulen IBD, partial PN (Kabiven) were included, and water–electrolyte imbalance was corrected. Because of the malnutrition, narrowing of the terminal ileum with significant prestenotic distension, inflammation of the caecal mucosa with local fibrosis, and a fistula in the caecal region, the patient had indications for surgical intervention before the initiation of biological therapy. The described indications are consistent with reports in the literature. In children with CD, surgical management is recommended for three main circumstances: failure of medical therapy, growth retardation, and management of disease-related complications. The stricturing form of CD is the most common indication for surgical intervention. It is estimated that only 8% of patients with this form of the disease achieve remission with pharmacotherapy alone(1). In their study, Levine et al. examined 285 children with CD and found that 10.9% required surgery within two years of diagnosis. The main predictors of early surgery appeared to be the stricturing phenotype ($p = 0.001$) and PCDAI score >10 at week 12 ($p = 0.005$)[5]. In Belarus, although biological treatment is mentioned in the guidelines, access to it remains limited. On the website of the Ministry of Health of Belarus (http://minzdrav.gov.by/ru/sobytiya/podpisany-novye-programmy-po-okazaniyu-pomoshchi-detyam/), one can find a 2018 communication regarding CD treatment. It relates to the introduction of three treatment programmes by the Ministry in consultation with the Chance Foundation (http://www.eng.chance.by), including "Helping children with Crohn's disease and ulcerative colitis". Under this programme, children with CD were to be provided with "medications necessary for treatment that are not first-line drugs but have proven efficacy". On the Foundation's website, it is stated that the programme was implemented jointly with the Ministry of Health between 2018 and 2020. Its aim was to create a system to help prevent disability and achieve stable remission in children with chronically active inflammatory CD and glucocorticosteroid-resistant ulcerative colitis. The programme was designed to provide rapid and effective biologic treatment (with infliximab and adalimumab) to children with IBD. The Foundation's website also contains numerous fundraising announcements for the treatment of children diagnosed with CD between 2012 and 2017, with parents reporting that their children were offered a switch to adalimumab therapy, but the cost was beyond their means. Information published on the Foundation's website in 2018 reads: "To date, seven patients are receiving biological therapy in Belarus. Based on data from the Centre for Coeliac Disease and Gastroenterology, the estimated number of patients in need of this therapy is up to 15 per year". The case report shows that, due to the high cost and the possibility of obtaining the drug only through the Foundation's activities, access to biological therapy was difficult.

The most common laboratory abnormalities in CD include elevated inflammatory parameters and deficiencies (hypovitaminosis and hypoalbuminaemia). In addition, microcytic anaemia, leucocytosis, thrombocytosis, and acidosis are frequently observed. Similarly, in the case of the described patient, there was an increase in inflammatory parameters, anaemia, decreased serum levels of iron, folic acid and vitamin B_{12}, hypoalbuminaemia, and hypoproteinaemia. For a definitive diagnosis of CD, endoscopic examination of the gastrointestinal tract is required. In this patient, endoscopy showed persistent inflammation of the caecal mucosa with local fibrosis[2,3]. Imaging studies are used to fully assess the intestine, including the presence of complications[2].

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Intestinal US (IUS) is the first-line tool to visualise disease activity (intestinal wall thickness, echo stratifications, hyperaemia on colour Doppler, mesenteric inflammatory fat, and lymphadenopathy). In addition to the standardised assessment of luminal and mesenteric features, the evaluation of complications is a fundamental component of IUS. Small-bowel strictures are defined by the presence of luminal narrowing <1 cm and dilation of proximal bowel loops >2.5 cm from the external wall to the external wall of the visualised bowel[6]. Parente et al., in an adult population study, showed that IUS's sensitivity, specificity, and positive predictive values for the detection of strictures were 79%, 98%, and 95% in non-operative CD patients, and 90%, 100%, and 100% in operative CD cases, respectively. In a recent review, sensitivity estimates for stricture diagnosis on IUS using various "gold standards" ranged from 68 to 100%, with corresponding specificities ranging from 0% in one study to 86–100% in all others[7]. In the case reported here, IUS was not sensitive enough to detect the intestinal structure and bowel dilatation due to the extremely dilated small intestine and large amounts of intestinal gas. The MR result, however, indicated multiple complications of CD – a stricture at the level of the distal ileum with massive prestenotic loop distension and a fistula between the ileal loops and the inferior surface of the caecum.

During the examination, special attention should be paid to the child's nutritional status, growth rate, and sexual maturation[3]. Weight loss is a common symptom preceding the diagnosis of IBD. It is estimated to occur in up to 80% of newly diagnosed paediatric patients with CD. Malnutrition, affecting up to 85% of individuals with IBD, results primarily from inadequate food supply (avoidance of food due to exacerbation of disease symptoms, dietary restrictions, loss of appetite), malabsorption, chronic inflammation, elevated levels of inflammatory mediators that increase catabolism, and drug-nutrient interactions. Laboratory markers of malnutrition primarily include anaemia and iron deficiency, folic acid, vitamin B_{12} and D deficiency, and hypoalbuminaemia. Anaemia (often due to a combination of iron deficiency and anaemia of chronic disease), affects up to 75% of paediatric patients with CD[8]. Among vitamin deficiencies, folic acid and B_{12} deficiency are most common. Both children and adolescents with CD are at risk of vitamin D deficiency, and levels should be regularly monitored, especially during steroid therapy[9]. In their cross-sectional study, Marcil et al. examined 590 patients with IBD (203 children and 387 adults). In both children (88.2%) and adults (70.8%), the most common form of IBD was CD. The prevalence of malnutrition in paediatric and adult patients was comparable. In the paediatric and adult cohorts, individuals with active CD were more likely to be malnourished. Growth stunting (moderate to severe) was observed in 14.3% of children with IBD. The prevalence of hypoalbuminaemia did not differ between the paediatric and adult IBD groups, but it was significantly higher among CD patients. Anaemia, iron deficiency, and elevated CRP levels, were significantly more common in paediatric patients compared with adults, whereas vitamin B_{12} deficiency was significantly less frequent in the paediatric population. In both adults and children, predictors of malnutrition were low albumin levels ($p < 0.006$) and active disease ($p < 0.03$)[8]. In addition, albumin level has been found to be a strong prognostic factor for postoperative complications[10]. In the present case, malnutrition was indicated by: BMI = 15 kg/m^2 (<5th percentile), weight = 49 kg (at 5th percentile), muscle atrophy, anaemia, iron deficiency, hypoproteinaemia, hypoalbuminaemia, and hypovitaminosis (folic acid, vitamin B_{12} and D deficiency). The vitamin D level was 12.15 ng/mL, indicating severe deficiency.

Nutritional deficiencies can have serious consequences for IBD patients. They are associated with decreased immunity, and impaired muscle and respiratory function. One of the most common extraintestinal manifestations seen in childhood-onset CD is growth retardation. It occurs in up to 88% of children and often precedes gastrointestinal symptoms by several years[8]. Studies suggest an association between malnutrition and poorer clinical outcomes after surgery, including higher rates of infections, delayed wound healing, longer hospital stays, reduced response to pharmacotherapy, and an increased risk of reoperation and postoperative complications. Ladd et al. examined 516 patients with CD: 67.6% had no malnutrition, 18.8% had mild, 9.5% had moderate, and 4.1% had severe malnutrition. The authors found that a worsening degree of malnutrition correlated directly with an increased risk of complications at 30 days after surgery[10]. Appropriate early nutritional strategies can lead to better disease control, as well as restoration of normal growth, improved bone mineral density and normal sexual maturation[9]. In cases of malnutrition, EEN ought to take precedence over PN. Furthermore, it is important to avoid dehydration to reduce the risk of thrombosis[11]. In the case reported here, fluid therapy was applied, achieving compensation of water and electrolyte disturbances, EEN based on Modulen IBD was introduced, and oral therapy with iron, vitamin D, and B vitamins was initiated. Moreover, in accordance with the guidelines, partial PN (Kabiven) was administered due to the severity of changes in the small intestine and the presence of fistulas[11].

Many complications, such as obstruction, fistula formation, bowel perforation and haemorrhage, can occur in the course of CD. Among reported cases of patients with complications, those with such a severe disease course, especially with marked prestenotic bowel dilatation, are very rare. Protásio et al. described the case of a 10-year-old girl with severe CD, presenting with narrowing of the distal part of the ileum and intestinal and perirectal fistulae. Despite the use of infliximab, clinical improvement was achieved only after surgical resection of the stenosed bowel and fistulae, indicating that their presence was a limiting factor in the effectiveness of biologic treatment[12]. In their study, Biko et al. examined 11 patients (aged 11–20 years) with CD.

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One patient was found to have two colonic strictures, resulting in a total of 12 strictures assessed. Prestenotic dilation of the bowel near the site of the reported strictures was observed in eight of the 12 cases (67%), and in three of them involved a segment >5 cm. Surgical intervention was necessary in five of the 11 patients[13].

The proposed treatment for this patient was initially met with disapproval from the parents. This was primarily due to numerous concerns related to possible complications of surgical treatment and the need for an ostomy. Studies show that this complication is one of the most common concerns among CD patients and their families[14]. Sometimes, urgent stoma creation is a necessary solution to an emergency and complicated surgery under difficult circumstances, and caregivers should be informed of this. Caregivers' anxiety is often compounded by uncertainty about the course of the disease and fear about whether they can handle the day-to-day care for their child. Providing patients and caregivers with pre-operative education significantly reduces stress. This is especially important for paediatric patients, where education must be developmentally appropriate and take into account the family system[15]. If, despite proper communication with the caregivers, they still do not consent, it is always advisable to request the intervention of a hospital psychologist. This support is crucial because, as in the case of reported here, timely surgical intervention can improve the clinical picture and reduce symptoms.

Although many complications may occur during the course of CD, cases of such serious changes with prestenotic dilatation of the intestine are very rare. If appropriate treatment had been started promptly, there is a possibility that serious complications – and most likely the need for surgery – could have been avoided.

CONCLUSIONS

CD can progress with intestine strictures, which in turn lead to prestenotic dilatation of the intestine. In the case of the patient described, this dilatation mimicked the large intestine on imaging studies, resulting in significant diagnostic difficulties. The patient, due to the presented disease-related complications – fistula in the caecal region, stricture of the terminal ileum, and significant prestenotic dilatation of the ileum – required surgical treatment before initiating biological treatment. The decision to proceed with surgery is always difficult to accept for parents, who are mainly concerned about their child having a stoma, so it is understandable that such decisions require the support of a hospital psychologist. In Poland, due to the possibility of rapid initiation of biological treatment, it is possible to achieve CD control and avoid complications of ineffective treatment. In Belarus, however, access to appropriate CD treatment in children, including biological therapy, is limited, as indicated by the clinical course of the described patient. If CD is not treated effectively, complications such as malnutrition, growth retardation, and anaemia may occur.

Conflict of interest

The authors do not report any financial or personal connections with other persons or organisations which might negatively affect the content of this publication and/or claim authorship rights to this publication.

Author contribution

Original concept of study: MP, WK, JK, KBD. Collection, recording and/or compilation of data; analysis and interpretation of data; writing of manuscript: NN, MS, AS. Critical review of manuscript: JK, KBD.

Patient consent statement

The authors confirm that patient consent was obtained for the purposes of this article.

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