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Coexistence of mesenteric fibromatosis and Crohn's disease in a child – a novel case

Współwystępowanie fibromatozy krezkowej i choroby Leśniowskiego–Crohna u dziecka – opis nowego przypadku

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ABSTRACT
Desmoids are benign tumours originating from connective tissue. Their uncontrolled growth can threaten organ function, especially in the abdominal location, when presenting as mesenteric fibromatosis. There have been only a few case reports of the coexistence of mesenteric fibromatosis and Crohn's disease. All of them were in adults, mostly with potential risk factors for desmoid tumours including female sex, oestrogen intake and abdominal surgery.
We present, to our knowledge, the first paediatric case of the coexistence of both conditions. A 15-year-old boy was operated on due to an obstruction of the gastrointestinal tract. Preoperative radiological examination suggested a tumour causing intussusception. Intraoperatively, a tumour and a significant length of infiltrated ileum were resected. Histopathological examination confirmed a desmoid tumour in the course of mesenteric fibromatosis and Crohn's disease. The patient has been treated pharmacologically since.
Further research is needed to explain their origin and simultaneous appearance in children.
Keywords: desmoid tumour; mesenteric fibromatosis; Crohn's disease; child; paediatrics.

ABSTRAKT
Guzy desmoidalne to łagodne guzy wywodzące się z tkanki łącznej. Ich niekontrolowany rozrost może zagrażać funkcjonowaniu otaczających organów, szczególnie w lokalizacji brzusznej, gdy występują w przebiegu fibromatozy krezkowej. Opublikowano tylko kilka przypadków współwystępowania fibromatozy krezkowej z chorobą Leśniowskiego–Crohna. Wszystkie te przypadki dotyczyły osób dorosłych, w większości obciążonych czynnikami ryzyka predysponującymi do desmoidów, jak płeć żeńska, przyjmowanie estrogenów, operacje brzuszne w wywiadzie. Według autorów, w pracy zaprezentowano pierwszy przypadek współwystępowania tych jednostek chorobowych u dziecka. Piętnastoletni chłopiec operowany był z powodu niedrożności przewodu pokarmowego. Wynik przedoperacyjnego badania radiologicznego wskazywał na guz powodujący wgłobienie. Śródoperacyjnie stwierdzono guz oraz znaczącej długości zmieniony odcinek jelita, które wycięto. Badanie histopatologiczne potwierdziło guz desmoidalny w przebiegu fibromatozy krezkowej oraz chorobę Leśniowskiego–Crohna. Pacjent od tego czasu jest leczony farmakologicznie.
Dalsze badania naukowe są konieczne do wyjaśnienia przyczyn i jednoczesnego występowania fibromatozy i choroby Leśniowskiego–Crohna u dzieci.
Słowa kluczowe: guz desmoidalny; fibromatoza krezkowa; choroba Leśniowskiego–Crohna; dziecko; pediatria.

INTRODUCTION

Desmoid tumours originate from connective tissue. They are very rare, with an incidence reaching two to four cases per million per year. The peak rates are seen at between 25–35 years of age with a slightly higher prevalence in women. There is no clear aetiological factor, although higher oestrogen concentrations in young women, familial adenomatous polyposis (FAP) or history of surgical interventions on the bowel are some of the possible causes [1]. Although desmoids are considered benign, their uncontrolled growth can threaten the functioning of the surrounding organs, including causing intestinal obstruction, especially in the abdominal location, when presenting as mesenteric fibromatosis [2]. The clinical picture of Crohn's disease (CD) may also include progressive intestinal obstruction. In both conditions the final diagnosis is confirmed in a histopathological examination. There have been just a few cases published of the coexistence of the described pathologies in adult patients, mostly with predisposing factors. We present presumably the first case of a child with a postoperative histopathological finding of mesenteric fibromatosis and CD.

CASE REPORT

Disorders of the gastrointestinal tract were the cause of the admission of a 15-year-old boy to a gastroenterological department. The patient complained of recurrent strong girdling stomach pain in the left epigastrium. Symptoms had been present for over 1.5 months. Solid and fatty meals had been intensifying pain, so despite a correct appetite the boy limited his meals to bananas and liquid meals, reaching more than three litres of fluids per day. Pain was accompanied by bloating and sweating, with a body temperature of up to 38°C. While a detailed history was being taken the patient confirmed the variable consistency of stool without pus, blood or mucous in the previous six months. Patient had a history of severe allergy affecting the skin and gastrointestinal and respiratory tracts, obsessive-compulsive disorder, chronic anaemia, frequent conjunctivitis, recurrent episodes of zoster infection and elevated immunoglobulin E (IgE) levels up to 1765 IU/mL (normal concentration up to 100 IU/mL). There was a history of neoplasm in patient's family, with an unknown bowel disease of the father. It was impossible to get any further details as the patient has no contact with possibly affected relatives.

At the time of the admission both the patient's weight (37 kg) and height (155 cm) were below the third centile for his age. Cole's Index was 77% and confirmed severe malnutrition. Further clinical examination revealed cachexia, pale skin with atopic rash and subcutaneous nodules around the fingers, extended abdomen, normal peristalsis, without peritoneal signs. Laboratory results showed elevated C-reactive protein (up to 72.5 mg/L), iron deficiency anaemia, hypoproteinemia, hypoalbuminemia, elevated IgE and positive faecal occult blood test. Parasitic diseases were excluded and stool cultures were negative. Rectosigmoidoscopy did not reveal any pathological findings. Repeated abdominal X-rays showed extended intestinal loops and fluid levels in the left epigastrium, which supported a clinical picture of incomplete obstruction. Radiological barium passage presented an extended small intestine, but it was impossible to precisely identify the location of the obstruction. Abdominal ultrasound showed a massively affected intestine with thickened walls up to 6 mm, and congestion with extended loops with poor peristalsis in the area from the left epigastrium to the left hypogastrium. The surrounding adipose tissue was infiltrated. A limited amount of fluid was found in both iliac fossa with enlarged lymph nodes. In the left epigastrium a target sign was visualized, which suggested possible intussusception. Intussusceptum was identified as a well-defined solid lesion measuring 22×12 mm (Fig. 1).

The patient was qualified for surgery and transferred to the surgical department. Intraoperative findings included inflamed ileal loops (ca. 45 cm) with a centrally located tumour critically narrowing the lumen of the ileum, and enlarged mesenteric lymph nodes (Fig. 2). The lesion and the infiltrated part of ileum were resected, and a simple end-to-end anastomosis was conducted. Histopathological examination revealed mesenteric fibromatosis characteristics of the tumour and mesentery with the presence of spindle-shaped fibroblasts.

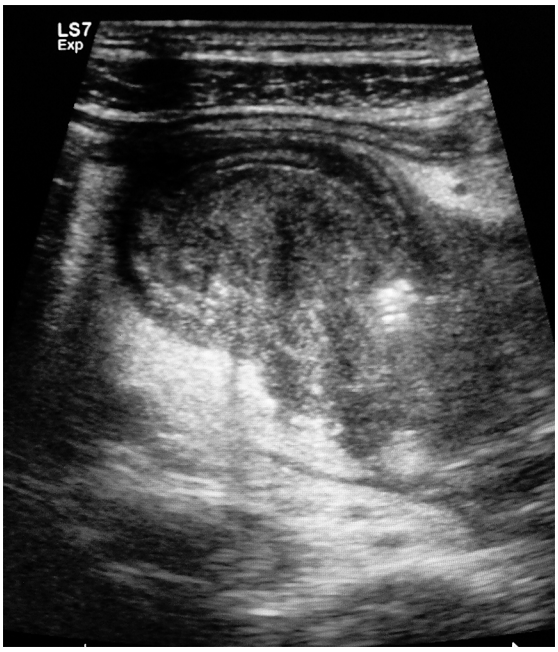

FIGURE 1. Ultrasound examination: a target sign suggesting intussusception caused by a tumor

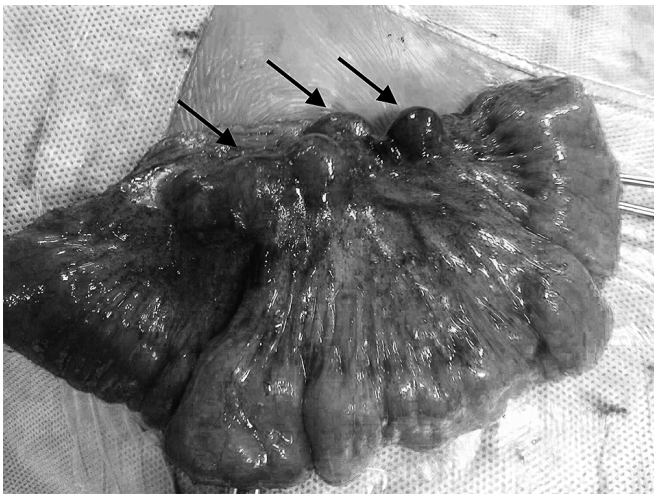

FIGURE 2. Intra-operative picture of an infiltrated intestine and mesentery with significantly enlarged lymph nodes (arrows)

Moreover, multiple ulcerations of the mucosa and submucosa, transmural inflammation, and focal mucosal crypt abscess formation confirmed a coexisting CD. No neoplastic cells were found in resected reactive changed lymph nodes; instead foreign body-type multinucleate giant cells were identified. Reactive cells were found in the margins of examined specimen. There were no postoperative complications. The patient was referred to the gastroenterological department where the CD diagnosis was confirmed in further endoscopical examinations. Patient continues successful combined pharmacological treatment of CD including prednisolone and aziathioprine. In a one-year-long follow-up there was a noticeable weight gain with a lack of disruptive symptoms. As the patient was consulted with in another centre, histopathological examination

was re-evaluated and confirmed both diagnoses of the initial study. In addition Hiob syndrome was excluded in further immunological tests.

DISCUSSION

Desmoid tumours are in 60% of cases extra-abdominal, 25% affect the abdominal wall, and 8–15% are intra-abdominal. There are rare cases of desmoid type fibromatosis originating from the mesentery, referred to as mesenteric fibromatosis. Those tumours grow gradually, affecting the mesentery, omentum and retroperitoneal cavity. Clinical symptoms appear late, when the lesions reach significant volume, which often make a complete resection impossible [3, 4]. Abdominal presentation, although rare in the general population, affects 10–15% of FAP patients, reaching 20% in Gardner syndrome [5]. Our patient had no confirmation of FAP, and a rectosigmoidoscopy did not show any abnormalities. Unfortunately, it remains unclear what kind of bowel disease the patient's father was suffering from.

Although the exact aetiology of desmoids remains unknown, there are predisposing factors such as surgical interventions, female sex, pregnancy and other circumstances with high oestrogen levels. Digiacomo et al. presented two cases of young women taking oral contraceptives, with mesenteric fibromatosis arising from part of the bowel affected by CD [2]. Similarly to our male patient, both of these women had no history of previous surgeries. Bungay et al. presented presumably the first male case without surgical history with the coexistence of both conditions. However, that patient was a 50-year-old with over 15 years' history of irritable bowel syndrome – possibly undiagnosed CD. Bungay emphasizes the role of fibrogenic cytokine Transforming Growth Factor-beta (TGF-beta) in the pathogenesis of both diseases [1]. A spotlight should be pointed at the quite short duration of symptoms in our paediatric case. We shall continue to look for factors that could have induced the development of both pathologies at such a young age.

As muscle trauma, physiologically present in, e.g. pregnancy and parturition, is unavoidable during surgery, all of those factors predispose desmoid development. Reitamo et al. observed desmoids in young patients after numerous abdominal operations [6]. Israel et al. presented the dramatic case of an aggressive mandibular tumour in a young man, accompanied by recurrent and escalating inflammatory bowel disease followed by an ileocolectomy. An aspiration biopsy of the mass in the mandible confirmed a desmoid tumour. On the basis of histopathological examination CD was also confirmed. The patient later followed an unsuccessful, several-years-long chemotherapy with further progression of the tumour growth affecting the thorax and causing further disability. The authors suggest that initial tooth extraction started the process [7]. In the presented case report there was no history of surgical interventions.

In our case, emaciation and symptoms of mechanical bowel obstruction caused by a tumour suggested an ongoing malignancy. Recognition of an intra-abdominal desmoid and coexisting CD was accidental. As both conditions may cause obstruction, a simple barium passage may lead to defining indications for surgical treatment. Thorough preoperative visual diagnostic measures may help in planning surgical strategy regarding assessing surrounding organ position. Endoscopy may indicate the length of the affected part of the gastrointestinal tract. In our case a simple X-ray followed by barium passage and ultrasound revealed the tumour and surrounding infiltration. The decision concerning explorative laparotomy was made. During the surgery a portion of the bowel was selected for resection based on a macroscopic intraoperative assessment of the infiltration. The tumour was resected with wide margins of intestine and later histopathological examination revealed it was strongly affected by CD inflammation process up to resection margins. Wide local excision with negative pathologic margins is known to be an effective treatment option for desmoids. When the disease involves vital organs it can be difficult to perform a complete removal. Incomplete resection of a lesion is responsible for increasing the chances of local recurrence. Alternative applied pharmacotherapy, especially in the mild cases and recurrences, includes non-steroidal anti-inflammatory drugs, anti-oestrogens and chemotherapeutics [8, 9].

Shivaram et al. published an interesting clinical quiz where an unknown condition was affecting a 13-year-old boy. A routine CD pharmacotherapy was introduced after a barium study showing the affected bowel correlating with disturbing symptoms. After months of ineffective treatment (including prednisolone and azathioprine) the patient had a classical resection of the changed terminal ileum, which was later histopathologically discovered to be mesenteric fibromatosis [10]. Ultrasound finding of an unequivocal tumour determined the decision concerning laparotomy in our case. Our patient had both diagnoses confirmed by pathologists. What is more, his condition significantly improved after the surgery when a similar CD pharmacotherapy was applied.

We present the novel case of a paediatric patient with coexisting mesenteric fibromatosis and CD without known predisposing factors. Our patient's history is of great importance for future studies on unclear aetiology of both rare conditions. Further analysis of the possible impact of CD in the development of desmoid tumours is highly reasonable. Moreover, our case should raise awareness of this rare disease in the differential diagnosis process of bowel obstruction.

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COMMENT

The paper discusses the course of illness in a 15-year-old boy with histopathologically confirmed Crohn's disease and mesenteric fibromatosis in the part of a tumor-obstructed small intestine resected due to blockage. Mesenteric fibromatosis is a form of desmoid tumor developing in the mesentery.

It is the first description of coexistence of these two conditions in children. So far rare cases of such coexistence have been reported in adults.

Each of these diseases has its different genetic origin. Typical of Crohn's disease are mutations in the *NOD2/CARD15* gene, while in patients with desmoid mutations in the catenin gene (*CTNNB1*) or the adenomatous polyposis coli gene (*APC*) [1] are observed. Therefore, a desmoid risk group are patients with familial adenomatous polyposis (FAB) in whom its incidence is 1000 times higher (it is diagnosed in 12–15% patients with FAB). Mesenteric desmoid tumors are known to be the second leading cause of death in FAB patients [2].

Desmoid tumors have an annual incidence of 2–4 cases per million. An average age at diagnosis is 40 years, but the disease is also diagnosed in younger patients (10–40 years) [3]. The etiology of these tumors is unknown, but genetic, hormonal (estrogens, pregnancy) and physical factors (trauma) play a role in their development [4]. Desmoid tumors are also referred to as: aggressive fibromatosis, deep fibromatosis, desmoid fibromatosis, familial infiltrative fibromatosis, hereditary desmoid disease and musculoaponeurotic fibromatosis.

Desmoid tumors are rare tumors developing from fascia cells or musculo-tendonous tissue. Typically, they are single tumors, although some people have multiple ones. The tumors can occur anywhere in the body. They are locally invasive because they infiltrate adjacent organs and tissue, damaging their structure. They cannot be radically resected, which results in the recurrence of the disease. However, they are known to be likely to recur even when totally resected. Unresectable or recurrent desmoids are treated with hormonal (anti-estrogen) therapies, with nonsteroidal anti-inflammatory drugs (NSAIDs), interferon, chemotherapy (vinblastine, methotrexat) and radiotherapy [5].

The presented description contains the following interesting issues:

— the development of a desmoid in a male – desmoids are more common in females (2:1) as in their pathogenesis an important role is played by hormones, particularly by estrogens,

— no injury or preceding surgery that are known factors triggering the desmoid development, unless we consider prior Crohn's disease to be such a factor.

According to the description of the patient's status, the boy was severely undernourished (Cole's index was 77%; weight and height were below the third centime for age) with abnormal laboratory results (CRP – 72.5 mg/L, iron deficiency, anemia, hypoproteinemia, hypoalbuminemia, positive fecal occult blood test), which indicated high probability of severe Crohn's disease.

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