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CASE REPORT / ПРИКАЗ БОЛЕСНИКА

Spontaneous perforation of sigmoid colon in a child with acute lymphoblastic leukemia

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SUMMARY

Introduction Perforation of the sigmoid colon is rare in children and its descriptions in medical literature are infrequent.

Case Outline In a 13-year-old boy with acute lymphoblastic leukemia, a ten-month course of chemotherapy was accompanied by many complications: parasitic infestation (*Enterobius vermicularis*), lung candidiasis, esophageal candidiasis, steroid diabetes, anaphylactoid reaction to L-asparaginase, febrile neutropenia, mucositis, anemia, thrombocytopenia, enterocolitis, and respiratory distress syndrome. During reinduction treatment, consisting of dexamethasone, vincristine, doxorubicin, and crisantaspase, he complained of abdominal pain and, upon radiographic examination, was found to have pneumoperitoneum. Because of suspicion of abdominal hollow organ perforation, he was subjected to explorative laparotomy, which yielded the diagnosis of perforation of the sigmoid colon.

Conclusion After an extensive review of the published reports on sigmoid perforation, all associated conditions that could possibly induce perforation – such as Hirschsprung's disease or foreign body – were systematically excluded in our patient. Although typhlitis was the first diagnostic hypothesis, this was excluded by intraoperative findings, histopathology, and perforation site. To the best of our knowledge, this is the first report of a spontaneous perforation of the sigmoid colon in a child with acute lymphoblastic leukemia.

Keywords: sigmoid perforation; children; immunosuppression; chemotherapy

INTRODUCTION

Perforation of the sigmoid colon is an acute surgical condition rarely reported in children. It is difficult to diagnose preoperatively and is associated with high mortality. By searching the literature, we found just two reports of sigmoid perforation in patients subjected to immunosuppressive treatment or organ transplant [1, 2].

CASE REPORT

We report a 13-year-old boy referred to our hospital for treatment of acute lymphoblastic leukemia (ALL). The treatment was carried out according to the ALL IC-BFM 2009 Protocol. He was assigned to the high-risk group due to poor treatment response at days 8 and 15. During induction treatment, the child was beset with many complications: parasitic infestation (*Enterobius vermicularis*), lung candidiasis, esophageal candidiasis, steroid diabetes, febrile neutropenia, mucositis, anemia, thrombocytopenia, enterocolitis, and respiratory distress. While undergoing the fourth chemotherapy block, he had an anaphylactoid reaction to L-asparaginase, and this drug was subsequently substituted by crisantaspase (Erwinase). In the course of the fifth block, pancytopenia and mucositis ensued, while during the sixth block he suffered from febrile neutropenia, enterocolitis and respiratory distress syndrome that necessitated respiratory support (Figure 1).

THERAPY	INDUCTION	CONSOLIDATION-HIGH RISK BLOCKS						REINDUCTION	MAINTENANCE
QUANTITY OF APPLIED L-ASP DOSES	6-aminohydrolase	1 A	1 A	1 A	1 A	3 crisantaspase	3 crisantaspase	3 crisantaspase	
Weeks	I	XVI	XX	XXIV	XXVIII	XXXII	XXXVI	XL	XLV
SIDE EFFECTS	parasitosis, steroid diabetes, lung candidiasis, EPGC				anaphylactic reaction to L-ASP	febrile neutropenia, mucosytis, anemia, thrombocytopenia	neutropenia, enterocolitis, RDS, CI	Sigmoid colon perforation	

Figure 1. BFM ALL-IC 2009 Protocol with most frequent side effects of each phase recorded in our patient

EPGC – esophagogastroduodenal candidiasis; L-ASP – L-asparaginase; RDS – respiratory distress syndrome; CI – cardiac insufficiency; A – aminohydrolase

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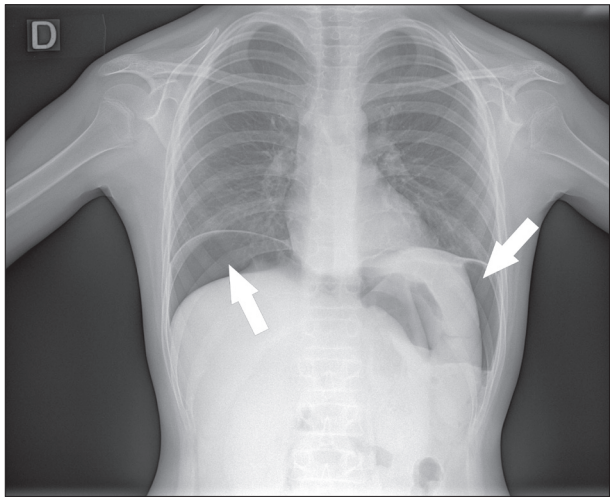

Figure 2. Plain abdominal X-ray image showing hydroaeric levels (arrows)

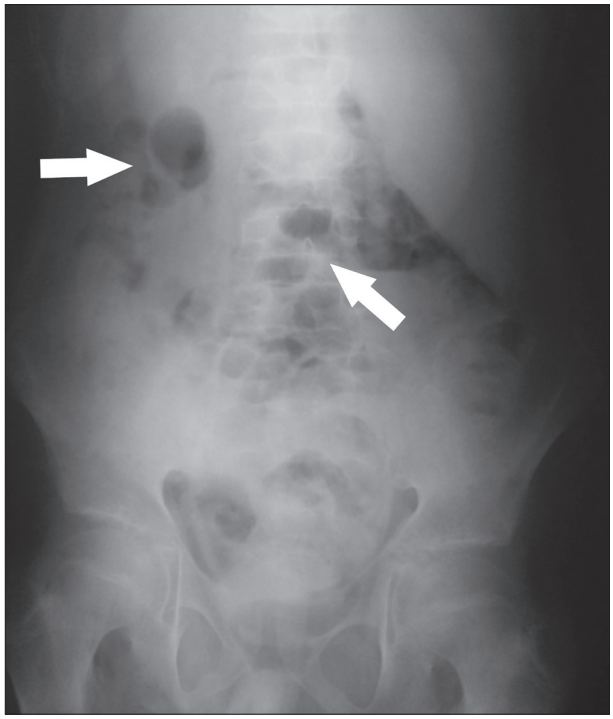

Figure 3. Chest X-ray image showing air in the peritoneal cavity (arrows)

Twenty-two days before the perforation of the sigmoid colon, reinduction treatment was initiated. He received fluconazole, trimethoprim/sulfamethoxazole, ranitidine, ondansetron, dexamethasone, vincristine, doxorubicin, and a total of three crisantaspase doses before the onset of perforation. On the 20th day of the reinduction phase, the child complained of suprapubic pain, which resolved spontaneously. On day 22, he still felt abdominal pain, but had regular stools and no vomiting. Physical examination showed a soft abdomen, painless upon both superficial and deep palpation. Plain abdominal (Figure 2) and chest (Figure 3) X-ray images demonstrated the existence of air in the peritoneal cavity, raising suspicion of hollow organ perforation. This was confirmed by abdominal computerized tomography scan with contrast, undertaken in order

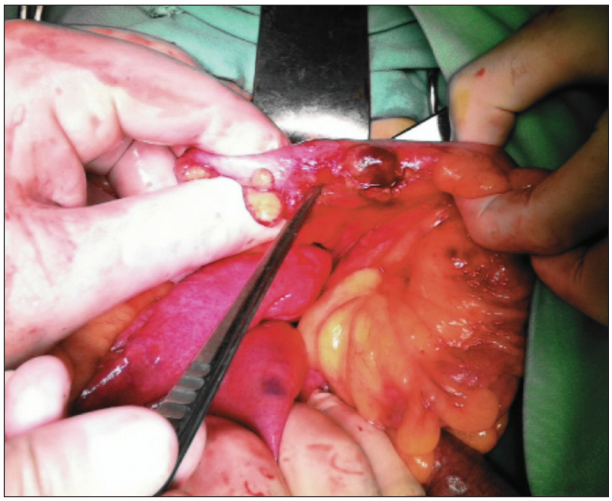

Figure 4. Intraoperative photography showing perforation site with surrounding tissue necrosis

to pinpoint the site of perforation, showing the presence of pneumoperitoneum without peritoneal fluid accumulation. Proximal small bowel segments were found to be filled by a rather dense content, while distant ones contained air. However, the site of perforation could not be identified.

Laboratory analyses showed severe neutropenia (granulocyte number 0.3×10^9/l), highly elevated C-reactive protein (301 mg/l), increased fibrinogen concentration (6.2 g/l), low levels of albumin (6.2 g/l), chloride (97 mmol/l), and sodium (132 mmol/l), while bilirubin, lactate dehydrogenase, lipase, glucose, urea, creatinine, total protein, aspartate aminotransferase, alanine aminotransferase, urate, potassium, magnesium, calcium, phosphate, alkaline phosphatase, and amylase (both in the serum and urine) were in the reference ranges. Blood coagulation screening tests showed normal values: prothrombin time 13.1 s, activated partial thromboplastin time 24 s, D-dimer (latex) 335 ng/ml, antithrombin III 85%. Serological tests for fungal infections (anti-*Candida* and *Aspergillus* IgG and IgM, mannan and galactomannan) were negative. Oral food intake was discontinued and the following antibiotic treatment was instituted: ceftriaxone, amikacin, and metronidazole, then intravenous immunoglobulins, filgrastim, hydrocortisone, albumin, pantoprazole, intravenous rehydration. The child was initially stable, his abdomen was at chest level, soft and non-tender. A few hours later, the abdomen became mildly distended and painful upon deep palpation in the lower left quadrant. The child was shivering, his cardiac and respiratory rate increased, while blood pressure plummeted.

The decision was to perform a surgical exploration. It showed a perforation of about 3.5 cm in diameter at the junction of the sigmoid and descending colon, on the counter-mesenteric side (Figure 4). The transverse colon was filled with soft dense stool, which was evacuated. A colonic resection of 14 cm in length was performed, the resected bowel segments were anastomosed, and an ileostomy was made in the anterior abdominal wall. Histopathological findings of the colonic segment showed an

oval mucosal perforation. The surrounding mucosa and upper part of the submucosa were necrotic, and there was a dense inflammatory infiltrate underneath. The adjacent serosa was also inflamed. Outside the described region, the mucosa did not show any inflammation. No microorganisms were isolated.

Since it was decided that the reinduction phase of the treatment should not be continued, maintenance therapy was initiated on postoperative day 17. Ileostomy was closed four months later. The child is in stable remission of ALL.

DISCUSSION

In the articles referring to sigmoid colon perforation in children, it was most frequently a complication of Hirschsprung's disease, diverticulosis, sigmoid volvulus, or foreign body ingestion. Hirschsprung's disease is a common cause of functional intestinal obstruction and perforation in children, particularly in developing countries. Mabula et al. [3] reported on 110 patients with histologically confirmed Hirschsprung's disease treated at the University Children's Hospital in Tanzania, four of whom (3.6%) had suffered sigmoid perforation. Most of the patients had a short aganglionic segment at the rectosigmoidal junction. Six articles describe a connection of the presence of diverticula and sigmoid perforation. Hernández-Siverio et al. [4] presented a 10-year-old boy with acute sigmoid perforation that ensued as a complication of diverticulitis. They reported that this must be a rare occurrence, since they found no similar cases in literature in persons younger than 20 years. Five articles describe sigmoid perforation in children as a complication of sigmoid volvulus (SV). Even though it is rare in the general population, SV is significantly present in children due to Hirschsprung's disease. According to published data, the mortality rate of sigmoid perforation complicating SV is between 14% and 45% [5]. Accidental foreign body ingestion is also reported to be a cause of sigmoid perforation. Schroepfer et al. [6] reported a case of a 20-month-old boy who suffered perforation after having ingested a magnetic toy. Another report details a sigmoid perforation found by laparoscopic exploration in a 10-year-old boy who ingested a toothpick, while yet another published case involves a fishbone [7, 8]. Histopathological examination of our patient's sigmoid colon did not demonstrate Hirschsprung's disease, diverticulosis, SV, or foreign body ingestion. Notably, the patient did not suffer from constipation and was never subjected to colonic irrigation.

Bowel amoebiasis, a protozoal infection, may be complicated by massive hemorrhage and colon perforation. Perforation due to amoebic infection is predominantly located in the right colon [9]. In our patient, clinical signs that could point to this potential cause of sigmoid perforation (diarrhea, fever, headache, vomiting) were not seen. A spontaneous sigmoid perforation has been described in a 17-year old boy, later diagnosed to have Ehlers–Danlos syndrome, clinically characterized by signs of arterial/bowel wall fragility or perforation, thin and transparent skin, severe hematomas, peculiar facial features (small ears, overemphasized eyes, narrow nose, thin lips, small chin) [10]. Our patient displayed no clinical feature corresponding to this syndrome.

Typhlitis, also known as typhloenteritis, cecitis, neutropenic enterocolitis, necrotic enterocolitis, and ileocecal syndrome, is an inflammatory condition of the cecum arising in immunocompromised patients with severe neutropenia undergoing intense chemotherapy. Although the cecum is most often involved, involvement of the terminal ileum, ascending colon and the appendix has been reported as well. However, a similar affection has not been described in the sigmoid colon. Nevertheless, typhlitis remains a complication to be considered in all immunocompromised patients with abdominal pain [11]. Although we did initially suspect typhlitis, radiographical, intraoperative, and histopathological findings did not confirm this diagnostic hypothesis in our patient.

L-asparaginase is an important component of chemotherapy used in the treatment of acute lymphoblastic leukemia in children. Although it is well tolerated, hypersensitivity reactions may occur in up to 30% of patients, limiting further use of the drug. Other significant toxic effects include reduced protein synthesis, pancreatitis, thrombosis, and liver dysfunction [12]. However, our patient did not have decreased antithrombin III concentration that would potentially induce thrombosis, and his coagulation screening tests were within reference values.

This is, to the best of our knowledge, the first report of sigmoid perforation in a child with ALL. Since all conditions reported to be a potential cause of sigmoid perforation were excluded, the explanation for this event remains elusive.

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Спонтана перфорација сигмоидног колона код детета са акутном лимфобластном леукемијом

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САЖЕТАК

Увод Перфорација сигмоидног колона је код деце реткост, а подаци у литератури о овом обољењу су оскудни.

Приказ болесника Код тринаестогодишњег дечака са акутном лимфобластном леукемијом десетомесечно лечење хемиотерапијом било је праћено бројним компликацијама: паразитоза (*Enterobius vermicularis*), плућна кандидијаза, езофагусна кандидијаза, стероидни дијабетес, анафилактоидна реакција на Л-аспарагиназу, фебрилна неутропенија, мукозитис, анемија, тромбоцитопенија, ентероколитис и респираторни дистрес синдром. Током реиндукционе фазе лечења, која се састојала од дексаметазона, винкристина, доксорубицина и крисантаспазе, јавио се абдоминални бол, а након радиографских испитивања констатован је пнеумоперитонеум. Због сумње на перфорацију шупљег интраабдоминалног органа учињен је оперативни захват, чиме је постављена дијагноза перфорације сигмоидног колона.

Закључак Код нашег болесника искључена су сва удружена обољења и стања која би могла довести до перфорације, као што су Хиршпрунгова болест и страно тело. Иако се најпре посумњало на тифлитис, оперативни налаз, хистопатологија и локализација перфорације су то искључили. Претрагом литературе у којој се помиње перфорација сигмоидног колона утврђено је да је ово први описани случај спонтане перфорације сигмоидног колона код детета са акутном лимфобластном леукемијом.

Кључне речи: перфорација сигмоидног колона; деца; имунокомпромитовани пацијенти; хемиотерапија