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Case report

Pneumatosis cystoides intestinalis, a rare case in a pediatric patient following allogeneic hematopoietic stem cell transplantation: CT findings and literature review ☆

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ABSTRACT

Pneumatosis cystoides intestinalis (PCI) is a rare condition characterized by the presence of gas-filled cysts in the subserosa or submucosa of the bowel wall. It is associated with various disorders including chronic obstructive pulmonary diseases, autoimmune disorders, and organ transplantation. PCI has also been observed following Hematopoietic Stem Cell Transplantation (HSCT), associated with chemotherapy, acute Graft versus Host Disease (GvHD), immunosuppression, and infections. Computed tomography (CT) provides an easy diagnosis because it highlights the presence of air bubbles in the intestinal wall and possible pneumoperitoneum. We report the case of a patient with severe acquired medullary aplasia undergoing allogeneic HSCT with subsequent development of cutaneous GvHD and an incidental finding of PCI during a CT scan of the chest in absence of gastrointestinal symptoms. Our work aims at clarifying a possible complication in pediatric patients undergoing HSCT to guide young or non-pediatric radiologists in the identification of this rare condi-

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tion, helping the clinician in the correct conservative management of these patients and reserving the surgical treatment only to specific complications.

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Introduction

Pneumatosis Intestinalis (PI) is a condition identified by the presence of gas within the bowel wall. It is considered a radiological finding, rather than a disease itself. According to Di Pietropaolo et al., PI is divided into 2 different conditions: life-threatening pneumatosis intestinalis and benign pneumatosis intestinalis [1]. Pneumatosis cystoides intestinalis (PCI) is a rare condition, belonging to benign pneumatosis intestinalis, and is characterized by gas-filled cysts in the submucosa and subserosa. The pathogenesis of PCI is unclear. However, some theories have been proposed [2]. PI has been divided into 2 subgroups: primary (idiopathic) and secondary [3]; the latter accounts for approximately 85% of cases and can be ascribed to several clinical conditions, such as chemotherapy, radiotherapy, inflammatory bowel disease, or GvHD. Clinical presentation can be variable: patients are either asymptomatic or present with diarrhea, pain, tenderness, vomiting, and flatulence. PI can be often identified by a simple x-ray of the abdomen, which demonstrates changes in the characteristics of the intestinal wall. However, CT is often necessary for the diagnosis and detection of complications that may be related to this condition, such as pneumoperitoneum. PCI is usually managed conservatively, while surgery is considered in case of complications.

We report a case in a pediatric patient with severe medullary aplasia who developed PCI following Allogeneic Hematopoietic Stem Cell Transplantation (allo-HSCT).

Case report

A 5-year-old male patient underwent allo-HSCT for severe Acquired Aplastic Anemia from Matched Unrelated Donor, after immune-suppressive therapy failure. His complications were lung and bowel aspergillosis resolved after treatment with antifungal agents. The only complication developed during hospitalization, documented by abdomen ultrasound, was febrile neutropenic enterocolitis on day 2 from transplant. The patient was discharged on day 25. After 43 days from transplant, high doses of systemic steroids were started for acute grade III skin GvHD; extracorporeal photopheresis was initiated on day +85, due to steroid dependence.

On day +91, a follow-up lung CT scan for previous invasive lung aspergillosis showed the presence of free air nuclei in the subphrenic and retropancreatic area (Fig. 1), as well as gas in the walls of the transverse colon and splenic flexure (Fig. 1). A plain abdominal radiograph confirmed the presence of pneumocystosis affecting the whole colon (Fig. 2). A CT scan of the abdomen with contrast medium was then performed in emergency, in the only portal phase. This showed extensive cystoid involvement of the walls of the cecum, ascending colon, and transverse colon with preserved vascularization of the intestinal wall (Figs. 3, 4, and 5), and the presence of small nuclei of intra and extraperitoneal free air, in the absence, however, of

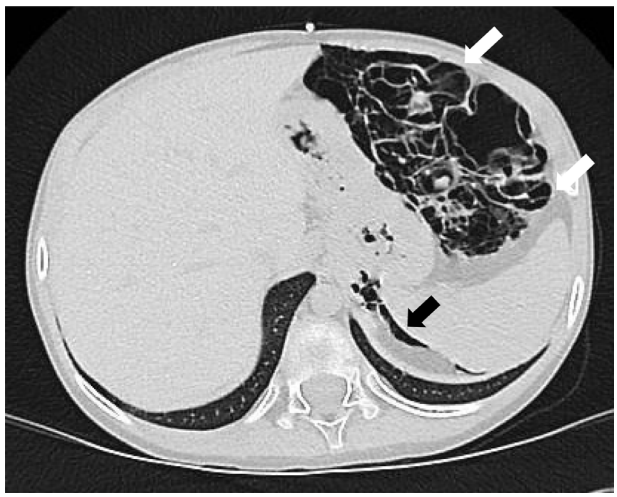

Fig. 1 – CT scan of the thorax. Axial view in lung window demonstrating free subphrenic air (black arrow) and massive pneumatosis intestinalis of the transverse colon and splenic flexure (withe arrow).

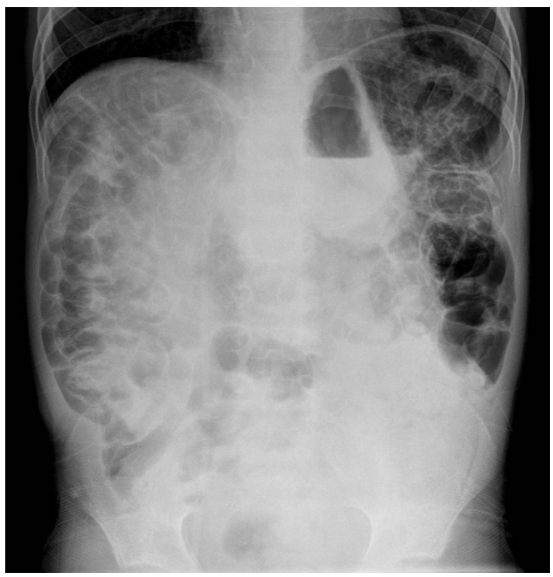

Fig. 2 – Plain abdominal radiograph shows an intramural gas collection of the cecum and colonic wall suggestive for diffuse pneumatosis cystoides intestinalis.

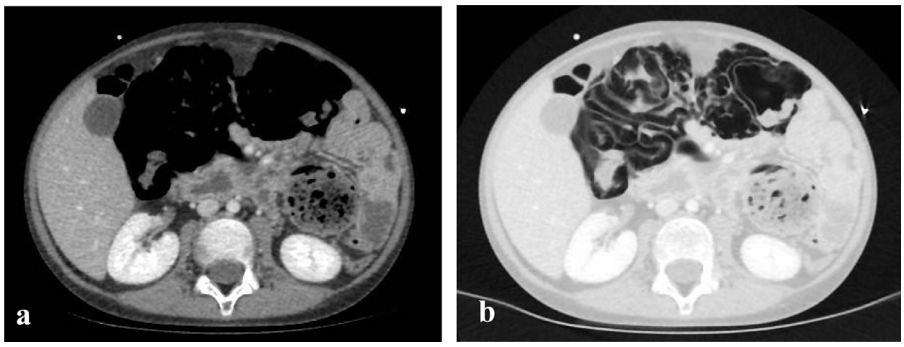

Fig. 3 – Axial abdomen contrast-enhanced CT images in the soft-tissue window (A) and lung window (B) confirm the presence of pneumatosis cystoides intestinalis of the transverse colon and hepatic flexure.

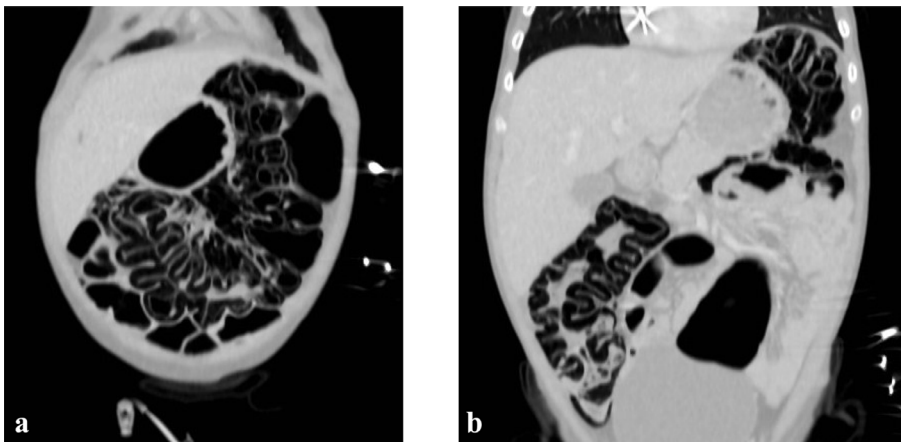

Fig. 4 – Coronal reconstruction of abdomen contrast-enhanced CT images in lung window shows the presence of pneumatosis cystoides intestinalis of the cecum, ascending and transverse colon, hepatic and splenic flexure.

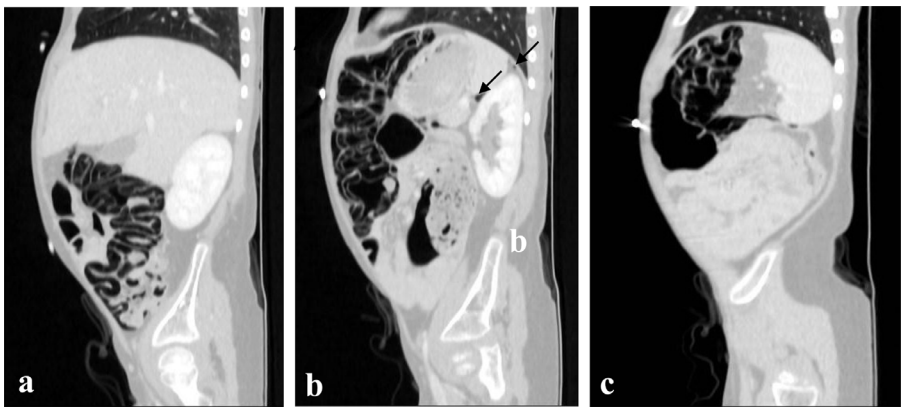

Fig. 5 – Sagittal reconstruction of abdomen contrast-enhanced CT images in lung window shows the presence of pneumatosis cystoides intestinalis of the cecum (A), ascending (A, B) and transverse colon (B, C), hepatic (A), and splenic (C) flexure and retroperitoneal free air (arrow in B).

free liquid and therefore due to the rupture of small subserosal bubbles.

Since there were no gastrointestinal symptoms, no elevation of inflammatory biomarkers as C-reactive Protein and procalcitonin, or signs of active gastrointestinal infection, and the bacterial/parasitological fecal cultures were negative, our patient was managed with medical conservative treatment. Therefore, the child was treated with bowel rest and total parenteral nutrition, radiological follow-up, and rapid steroid tapering/discontinuation.

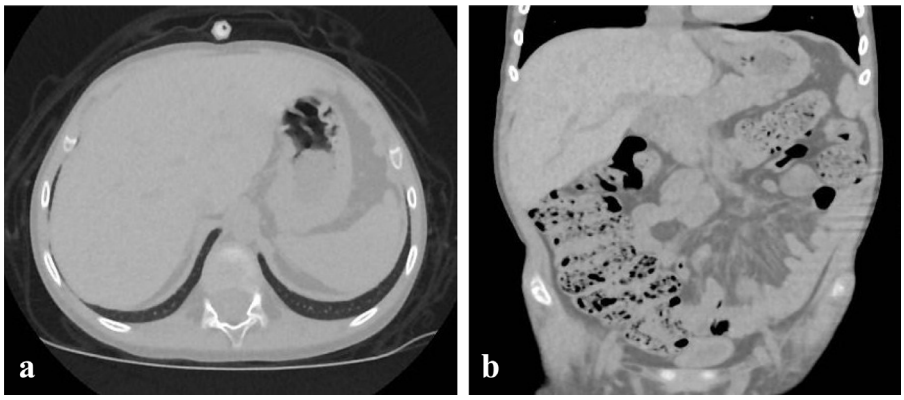

Fig. 6 – CT scan of the abdomen. (A) Axial view in lung window demonstrating the absence of free subphrenic air. (B) Coronal reconstruction of abdomen CT images in lung window shows the redintegration of intestinal walls.

There was evidence of progressive clinical improvement at the following checks until complete resolution about 2 months after diagnosis (Fig. 6).

Discussion

PCI is a rare condition characterized by gas-filled cysts in the intestinal submucosa and subserosa. First described by Du Vernoi in 1783, PI is often identified by abdominal radiographs or CT scanning. The precise etiology remains unknown, although PCI has been associated with surgery, pulmonary diseases, chemotherapy, acarbose, and ingestion of sorbitol [4]. Three plausible causes for PCI have been proposed: mechanical, bacterial, and pulmonary. According to the first theory, the gas present in the bowel is pushed through a mucosal defect into lymphatic channels and then distributed distally by peristalsis. The mucosal damage may be caused by blunt trauma, surgery, colonoscopy. In addition, lymphoid depletion induced by steroids and other immunosuppressive leads to atrophy of Peyer patches and mucosa thinning, this resulting in increased mucosal permeability, which in turn allows dissection of the gas into the bowel wall [5]. The pulmonary theory is demonstrated in patients with asthma and chronic bronchitis and implies that alveolar rupture results in the dissection of air along the pulmonary interstitium to the mediastinum and then through the retroperitoneal space coming then through the perivascular spaces in the intestinal wall [6]. According to the bacterial theory, submucosal localization of fermenting *Clostridia* and *Escherichia Coli* leads to gas production, which is retained by the submucosa and lymphatic channels. This theory is also supported by the resolution of pneumatosis with the use of metronidazole for bacterial overgrowth [7].

PCI has also been observed and reported after allo-HSCT [8–10]. The occurrence of PCI in this setting is thought to be associated with chemotherapy, pre-SCT conditioning, glucocorticoid therapy (prednisone and non-absorbable oral steroids such as beclomethasone dipropionate and budesonide), infections or infectious colitis, septic shock [9], and acute GvHD.

The probable mechanism in developing PCI after allo-HSCT is that chemotherapy and immunosuppression induce atrophy of the Peyer's patches, leading to the loss of integrity of the bowel mucosa and subsequent gas migration into the submucosal and subserosal regions. Another hypothesis is that gas-forming bacteria invade the bowel wall, producing intramural gas. Steroids may contribute to PCI development for their immunosuppressive properties, which predispose to infection and inhibit wound healing [11]. Some studies have suggested that glucocorticoid therapy alone may increase significantly the risk of PCI development [12].

PCI shows no typical clinic presentation. Patients may be asymptomatic or complain of pain and abdominal distension, diarrhea, and rectal blood loss associated with intestinal pseudo-obstruction [7,13,14]. The diagnosis of PCI may be identified by a simple x-ray of the abdomen showing a change in the characteristics of the intestinal wall. Plain radiography includes different patterns of radiolucency: linear, small bubbles, or multiple large cysts [15].

However, PCI is most commonly diagnosed with CT, which is more sensitive than plain radiography in distinguishing PCI from intraluminal air or submucosal fat. CT typically demonstrates a thickened bowel wall containing gas. In addition, it allows the detection of potential complications or additional findings such as altered contrast mucosal enhancement, dilated bowel, soft tissue stranding, ascites, and the presence of portal air [16].

PCI may cause various complications that may be intestinal or extra-intestinal. Intestinal complications are obstruction caused by the cysts (such as fecal impaction) and perforation from stercoral ulceration. The extra-intestinal complications are adhesions or compression of adjacent structures by large masses of cysts [17].

There is no standard treatment for PCI. Most of the PCI cases are usually managed conservatively, while surgical therapy is considered a second-line therapy chosen especially in patients with severe pain and in case of complications.

The appropriate therapy should be related to the underlying cause of PCI. Antibiotic treatment (such as metronidazole) is one of the choices for PCI to decrease anaerobic bowel flora and consequently the production of gas until clinical and

radiological resolution is achieved. Bowel rest and total parenteral nutrition, with electrolyte supplementation, have also been reported as possible treatments for PCI in conservative management. Inhalational or hyperbaric oxygen therapy has also been used to treat PCI. The rationale of oxygen treatment is based on increasing partial pressure of oxygen in the blood, raising thus the pressure gradient of the gas in the cysts. Cysts release gases contained within them and refill with oxygen which is then metabolized leading to resolution [18].

In our case, according to the literature review of PI case reports [19], the patient was managed with medical conservative treatment because there were no gastrointestinal symptoms, no elevation of inflammatory biomarkers, no signs of active gastrointestinal infection, and negative bacterial/parasitological fecal cultures. Therefore, the child was treated with bowel rest and total parenteral nutrition, radiological follow-up, and rapid steroid tapering/discontinuation, due to a probable association between immunosuppression and PI occurrence [20].

Conclusions

In conclusion, PCI is a rare condition that may occur following allo-HSCT. It is most commonly diagnosed with a CT scan, which is more sensitive than plain radiography. CT exam typically demonstrates a thickened bowel wall containing gas, and results in a highly sensitive detection of complications. The choice of treatment should be based on clinical symptoms, laboratory tests, and CT findings.

In our patient, multiple concomitant factors may suggest damaging of the intestinal mucosa, such as previous fungal infection followed by neutropenic typhlitis and systemic use of steroids.

Prompt diagnosis with CT scan and medical conservative treatment allow rapid resolution of PCI, while surgery should be reserved for complications, such as adhesions, obstruction, and perforation.

Patient consent

All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki declaration of 1975, and its late amandments. Additional informed consented was obtained from all patients for which identifyng information is not included in this article.

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