VIA MEDICA

CLINICAL VIGNETTE

Acta Haematologica Polonica 2023
Number 2, Volume 54, pages 107–109
DOI: 10.5603/AHP.a2023.0020
ISSN 0001–5814
e-ISSN 2300–7117

Pneumatosis intestinalis after allogeneic hematopoietic cell transplantation

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Pneumatosis intestinalis (PI) is a radiographic sign showing the presence of gas in the subserosal and submucosal layers of the bowel wall [1, 2]. PI is not a disease itself, but rather a radiographic finding resulting from an underlying pathology [1, 2]. PI can occur as a complication following allogeneic hematopoietic cell transplantation (allo-HCT) in children. The risk factors include: conditioning chemotherapy or irradiation, antibiotic exposure, gastrointestinal (GI) infections with *Clostridioides difficile* or *Escherichia coli*, GI graft-versus-host disease (GvHD), and prolonged immune suppression [1–3].

PI presents as two different conditions: life-threatening PI and benign PI [1, 2]. Additionally, another entity, pneumatosis cystoides intestinalis (PCI), is a rare phenomenon belonging to the spectrum of benign PI, and is characterized by the presence of gas-filled cysts in the subserosa and submucosa [4, 5].

Pathogenetically, PI occurs as primary (idiopathic) (in 15% of cases) or secondary (in 85% of cases) [1, 4]. Clinical symptoms include diarrhea, vomiting, pain, tenderness, and flatulence [1, 2]. The diagnosis is usually made by computed tomography (CT), but sometimes it is identified by abdominal X-ray. PI is managed conservatively, and surgery is optional in cases of subsequent complications [1–4].

We present the case of a pediatric patient with secondary severe bone marrow aplasia who developed PI following a second allo-HCT.

A 5-year-old boy underwent allo-HCT for acute myeloid leukemia from a matched unrelated donor. Due to late secondary marrow aplasia, he had a second allo-HCT from another donor five years later, after conditioning with fludarabine, cyclophosphamide and thymoglobulin. GvHD prophylaxis included cyclosporin and methotrexate. His complications were cytomegalovirus infection, hypogammaglobulinemia, acute skin GvHD, and acute followed by chronic GI GvHD. He was treated with high-dose steroids, mycophenolate mofetil, anti-tumor necrosis factor (TNF) agent (etanercept), and extracorporeal photopheresis (ECP). 12 months after the second allo-HCT, he developed a mediastinal pneumothorax and the presence of free air nuclei in the subphrenic area was detected. In a CT scan, gas was found in the expanded intestinal wall of the transverse colon, the sigmoid colon and the descending colon, as well as in the peritoneal cavity (Figure 1). He was treated with antibiotics, total parenteral nutrition, immunoglobulins and blood products. No surgery was necessary. Two months later, all CT symptoms from the GI tract had resolved.

The probable mechanism of developing PI after allo-HCT is chemotherapy and immunosuppression, which can induce atrophy of the Peyer's patches [2, 4]. This can lead to the loss of integrity and focal damage of the bowel mucosa [4]. Subsequently, gas migration occurs into the submucosal and subserosal regions [4]. On the other hand,

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Received: 23.02.2023 Accepted: 26.02.2023 Early publication date: 09.04.2023

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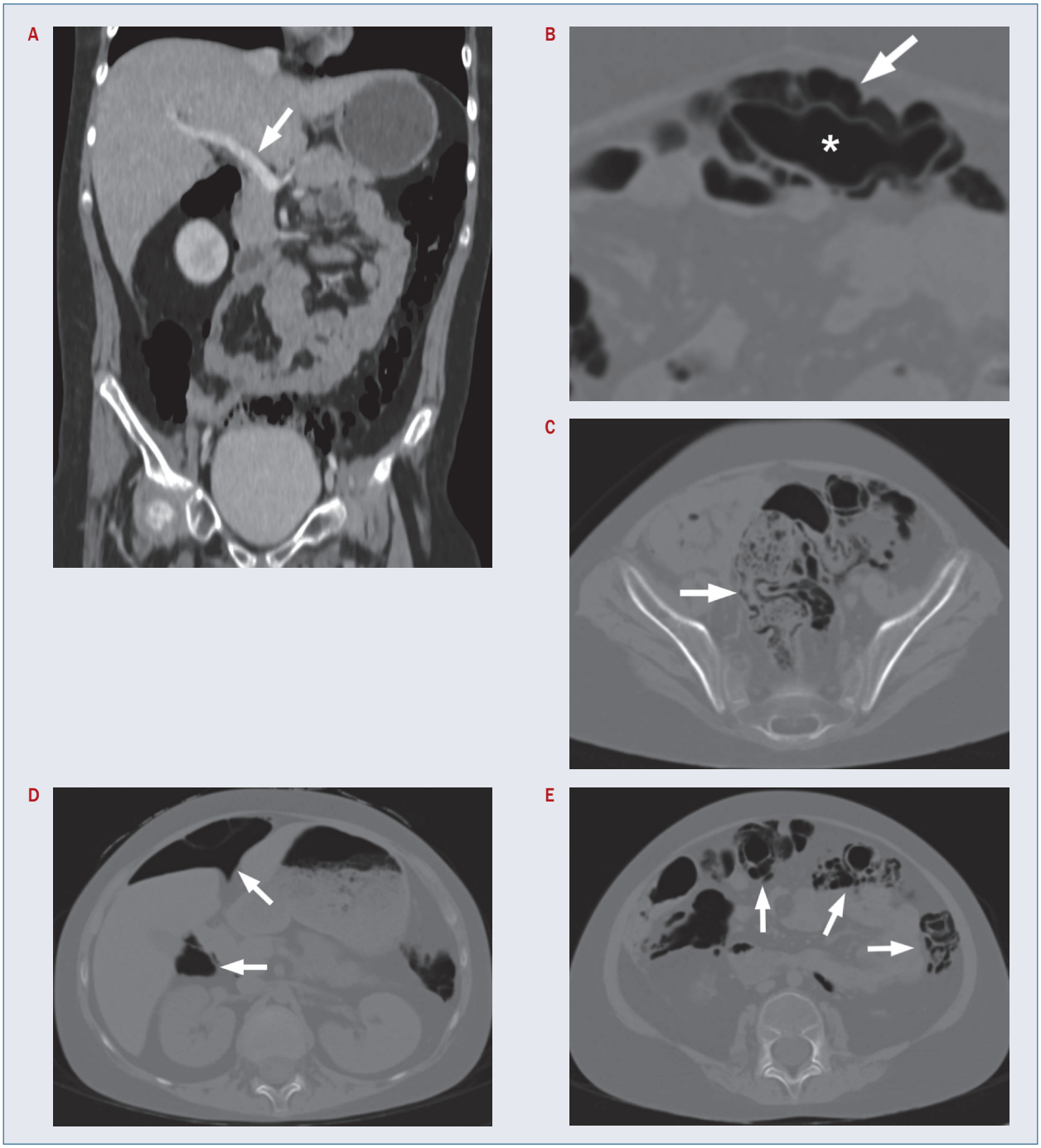

Figure 1. Pneumatosis intestinalis in computed tomography imaging: **A.** Contrast-enhanced computed tomography (CT). No evidence of gas in portal vein (arrow); **B.** Non-contrast-enhanced CT. Zoomed image of transverse colon. Gas in lumen of intestine (asterisk) and gas in expanded intestinal wall (arrow); **C.** Non-contrast-enhanced CT. Pneumatosis of sigmoid colon (arrow); **D.** Non-contrast-enhanced CT. Gas in peritoneal cavity (arrows); **E.** Non-contrast-enhanced CT. Pneumatosis of transverse colon and descending colon (arrows)

gas-forming bacteria or other immunosuppressive drugs such as steroids can contribute to PI development [1, 2]. PI shows no typical clinical presentation, and a definitive diagnosis is usually made by a CT scan [1–4]. There is no standard treatment for PI [1, 2]. In most cases, patients with PI are managed conservatively with wide-spectrum antibiotics, bowel rest and total parenteral nutrition [1–5]. Surgical therapy is considered as a second-line therapy which can be chosen in patients with other severe complications [1–5].

Acknowledgements
The authors thank the team of nurses chaired by Ewa Dembna for their excellent care of patients.

Authors' contributions
KC, TS — design of study. RD, MRP, KC — provision of clinical data. ZS — imaging. All authors — analysis of clinical data. TS, JS — literature search, analysis of data, writing of manuscript. All authors — critical revision and final approval.

Conflict of interest
All authors declared no conflict of interest.

Financial support
None.

Ethics
The work described in this article has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans; EU Directive 2010/63/EU for animal experiments; Uniform requirements for manuscripts submitted to biomedical journals.

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