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Case report

Pneumocystis cystoides intestinalis with pneumoperitoneum and pneumoretroperitoneum in a patient with extensive chronic graft-versus-host disease

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Summary:

***Pneumatosis cystoides intestinalis* is a rare finding of intramural gasfilled cysts in the bowel wall and sometimes free air in the abdomen. A few conditions are reported to cause this disease, one of them being immunosuppression. We describe a 50-year-old Caucasian male with extensive chronic graft-versus-host disease (GVHD) of the gut and skin who developed PCI with pneumoperitoneum and pneumoretroperitoneum. To our knowledge, this is the first report of PCI occurring in a patient with active chronic GVHD which resolved spontaneously.**

Keywords: *Pneumatosis cystoides intestinalis*; chronic graft-versus-host disease

Pneumatosis cystoides intestinalis (PCI) is a rare disorder consisting of multiple intramural gas collections in the bowel wall. Patients are either asymptomatic or present with diarrhea, pain, tenderness, vomiting and flatulence. The pathogenesis of this abnormality is still unknown. It is associated with chronic obstructive pulmonary disease, necrotizing enterocolitis in premature infants, intestinal obstruction, ischemic bowel disorders, bacterial and viral infections[1] and drug therapy.[2] In contrast to other gastrointestinal diseases PCI is a benign finding and usually resolves spontaneously. It responds well to conservative therapy. Rarely, PCI is observed after allogeneic bone marrow transplantation (BMT) where fatalities have been reported in patients receiving immunosuppression.[3,4] We describe a patient with myelodysplastic syndrome given an allogeneic marrow graft. He experienced extensive chronic graft-versus-host disease (GVHD) and developed PCI 8 months after BMT.

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Case report

A 50-year-old Caucasian male who was diagnosed with myelodysplasia, subtype chronic myelomonocytic leukemia, underwent BMT after conditioning with cyclophosphamide and fractionated total body irradiation (12 Gy) at our institution. He received 3.2×10^8 nucleated bone marrow cells/kg body weight from his HLA-identical sibling. GVHD prophylaxis consisted of cyclosporin A and a short course of methotrexate according to the Seattle protocol.[5] During aplasia, he experienced fever and *Staphylococcus aureus bacteremia*. On day +16 the patient developed acute GVHD grade II of the skin that resolved with corticosteroids (2 mg/kg/day). Two months after transplantation, he received pre-emptive gancyclovir therapy because of cytomegalovirus (CMV) reactivation. Five weeks later extensive GVHD of skin required treatment with steroids. Seven months after BMT, herpes encephalitis was diagnosed which resolved with acyclovir therapy. Another course of pre-emptive gancyclovir for CMV reactivation was also administered.

One month later the patient presented with diarrhea, slight diffuse abdominal pain and flatulence. Parenteral nutrition and electrolyte and fluid infusions were started. Colonoscopy showed signs of diffuse mucosal irritation. On histological examination biopsy specimens from two regions of the colon showed individual crypt cell necrosis, crypt abscesses with cell flattening and degeneration consistent with GVHD grade II.[6] CMV infection was ruled out by *in situ* hybridization. Stool cultures revealed no bacterial, viral or fungal infection. Steroids were added to the continuous immunosuppressive treatment with cyclosporin. The latter was replaced by FK506 since no clinical improvement with cyclosporin was seen after 2 weeks. A few days later the patient experienced relief of pain and a normalization of bowel habit. On routine chest X-ray on day +292, a large amount of free air between the liver and the right hemidiaphragm was seen (Figure 1). A contrast enhanced computed tomography scan of the abdomen demonstrated intramural gas collections, free intra- and retroperitoneal air and abdominal distension (Figures 2 and 3). The patient was switched to oral nutrition and steroids were reduced. His symptoms resolved within 10 days and he was

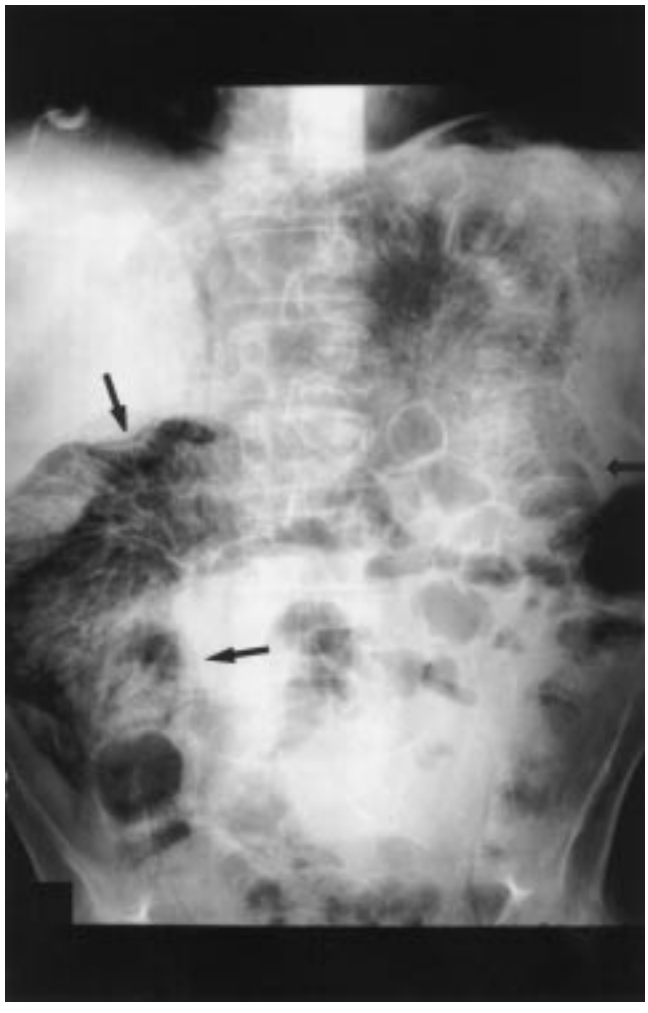

Figure 1 Plain abdominal radiograph performed on day +292 after transplantation showing intramural gas collections (arrows) suggestive for diffuse *Pneumatosis cystoides intestinalis*; in addition, free retroperitoneal gas is present.

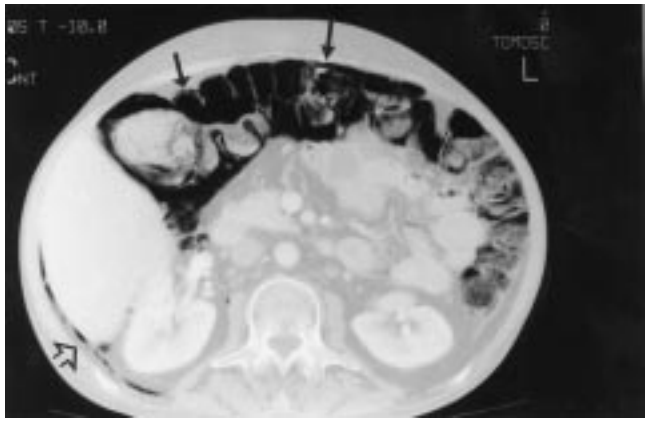

Figure 2 Contrast-enhanced CT of the abdomen performed on day +293 after transplantation at the level of the renal hila reveals multiple gas-filled cysts and streaky air collections (arrows) in the bowel wall of the transverse colon (image displays window settings optimized to demonstrate air). Additionally, small amounts of free intra- and retroperitoneal gas are present, notably behind the liver (open arrows).

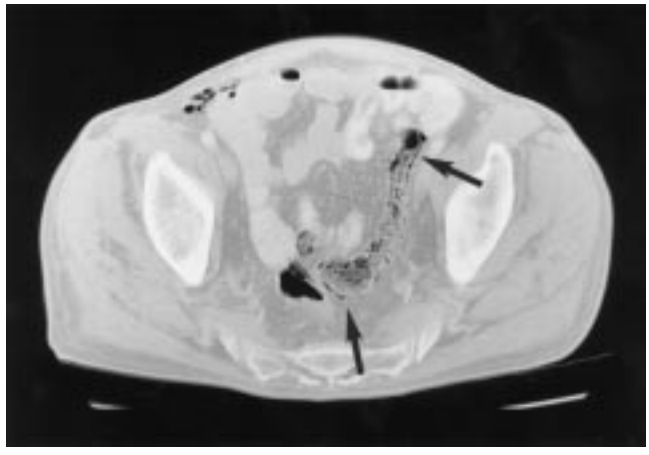

Figure 3 Contrast-enhanced CT of the abdomen performed on day +293 after transplantation at the level of the pelvis demonstrates extensive intramural gas collections in the wall of the sigmoid colon (arrows).

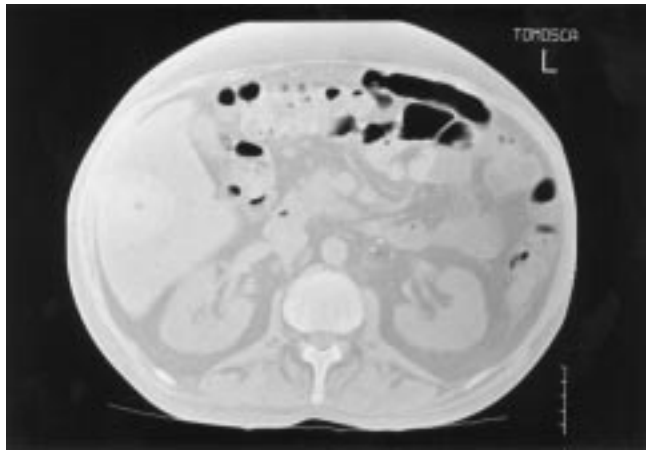

Figure 4 CT of the abdomen performed on day +410 after transplantation at the level of the renal hilum shows no evidence of *Pneumatosis intestinalis*, pneumoperitoneum or pneumoretroperitoneum.

discharged. Periodic X-rays of the abdomen in the outpatient department showed continuing resorption of free air. A computed tomography scan of the abdomen showed no more free air or intramural gas cysts 4 months after the diagnosis of PCI (Figure 4). At present the patient is in complete hematological remission with clinical signs of chronic limited GVHD 18 months after BMT.

Discussion

PCI is characterized by multiple mucosal, submucosal or subserosal gas collections in the bowel wall, with or without free air in the abdomen.[7,8] PCI has been reported in several clinical settings including necrotizing enterocolitis in premature infants, obstructive pulmonary disease, immunosuppression[9–12] or infections, and has a benign course. After BMT,[3,4,14] the occurrence of PCI has been repeatedly associated with acute GVHD, infections or immunosuppressive medication. In these patients fatal outcomes have been observed. We report a severely immuno-

compromised patient with extensive chronic GVHD who experienced multiple viral infections and episodes of graft-versus-host disease after BMT and had PCI with an uneventful course. In this patient neither bacterial nor viral infection could be detected at the onset of gastrointestinal symptoms. Gastrointestinal perforation was excluded. PCI was asymptomatic and resolved spontaneously over time. To our knowledge this is the first report of the occurrence of PCI in association with active chronic GVHD. The pathogenesis of PCI in this case remains speculative. Patients with chronic GVHD of the gut have mucosal damage in the bowel allowing intraluminal air under pressure to diffuse into the bowel wall. Peyer's patches could also be a locus of minor resistance due to decreased cellularity, and allow the entry of air into the bowel wall.[5] It has also been suggested that gas-producing bacteria could be the cause of PCI.

After intestinal perforation has been radiologically excluded, conservative treatment[13] of PCI is advisable including parenteral nutrition and a diet of low-flatulence-producing carbohydrates. In cases of concomitant infection appropriate antimicrobial therapy is beneficial in these patients.

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