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LETTER TO THE EDITORS

Severe small bowel pneumatosis in adult heart transplant recipient

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Dear Sirs,

We are here reporting the case of a female patient, aged 50 years, who underwent heart transplantation for refractory heart failure due to amyloidosis (AL type) with cardiac involvement.

Indication to heart transplantation in such a case is much controversial; however, the patient was enrolled in a pilot study of heart transplantation, followed by a planned short-term bone marrow transplant, because of apparently isolated cardiac involvement without evidence of other organ implication. Heart transplantation and early postoperative course were uneventful, and only an episode of acute rejection was recorded and treated with steroids. In the two following months, Clostridium difficile colitis and CMV systemic infection were diagnosed and treated with oral vancomycin and i.v. ganciclovir, respectively. Although CMV infection was treated effectively, the patient developed two recurrent episodes of Cl. difficile colitis. The first recurrence was treated with vancomycin and the second with human immunoglobulins as part of an experimental trial. However, patient presented abdominal distension with abdominal pain, signs of intestinal malabsorption and constipation.

For this reason, 4 months after surgery, the patient was admitted to Multivisceral Transplant Unit (Padova University Hospital), to evaluate the intestinal dysfunction. On admission, the main clinical feature was a remarkable abdominal distension, with mild pain and mild muscle wasting. Cardiac function and cognitive function were normal. Immunosuppressive therapy was based on cyclosporine and steroids.

Laboratory tests showed signs of mild malabsorption with low serum proteins (37.6 g/l), hypoalbuminemia (21 g/l), coagulopathy (Prothrombin time 65%) and anaemia with iron deficiency (Hb 8.2 g/dl, iron 5.0 μmol/l). Intestinal inflammatory activity was confirmed by elevated CRP (45.1 mg/l), high ferritin levels (1165 μg/l, normal values 10–120 μg/l) and elevated inflammatory faecal markers, such as faecal calprotectine (>2100 μg/g, normal values <50 μg/g).

Abdominal X-ray confirmed pneumatosis of the small bowel with retroperitoneal free air; therefore, abdominal CT scan was performed showing the distension of small bowel with impressive diffuse intestinal wall pneumatosis, the presence of free air in the retroperitoneum and pneumoperitoneum, with associated subcutaneous emphysema (Fig. 1a). Small bowel NMR was also performed, showing air in the mesentery and retroperitoneum, no pneumoperitoneum, but a diffuse small intestine wall thickening with an abnormal quantity of gas cyst formation within the wall was seen.

Few days after admission, rettosigmoidoscopy showed an endoscopic pattern compatible with pseudomembraneous colitis. Histological examination on rectal biopsies confirmed intestinal amyloidosis.

Microbiological tests confirmed a relapse of systemic CMV infection (CMV-DNA 33 069 copies/ml), whereas Cl. difficile toxins A and B were negative in several stool samples. She was treated again with ganciclovir (250 mg twice a day) and the CMV-DNA subsequently became negative. Metronidazole and ciprofloxacin were also administered with the hypothesis of potential negative effect of microbacterial intestinal overgrowth, and vancomycin was added considering the number of Cl. difficile recurrent infections and patient comorbidity.

The patient underwent 14 sessions of hyperbaric oxygen therapy (HBOT) (2,5 ATA for 90 min daily), with improvement of the abdominal features. At the end of HBOT sessions, oral feeding was restarted with gradual reduction of parenteral feeding. The abdomen was normal with regular stools. A control CT scan was performed 4 weeks after admission, showing the complete resolution of the cysts with gas within the intestinal wall (Fig. 1b).

Unfortunately, few days later, the 3rd recurrence of Cl. difficile infection was diagnosed, and fidaxomycin 200 mg twice a day for 10 days was started, with complete resolution of the infection in few days.

The patient was retransferred to Cardiothoracic Department where she underwent cardiac biopsy which showed mild acute rejection classified as 1R (according to 2006

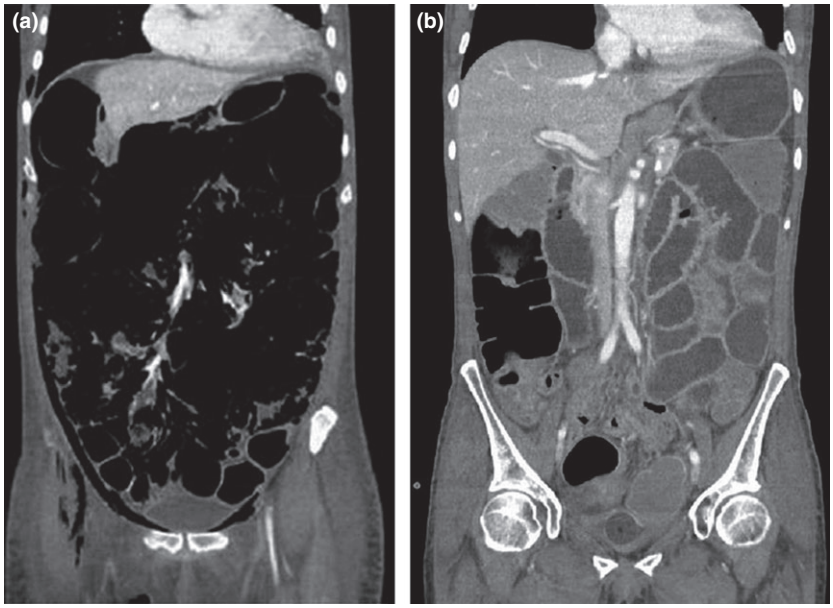

Figure 1 (a) Abdominal CT scan showing distension of small bowel with impressive diffuse intestinal wall pneumatosis, free air in the retroperitoneum and pneumoperitoneum, with associated subcutaneous emphysema. (b) Abdominal CT scan showing the resolution of the cysts with gas within the intestinal wall after hyperbaric oxygen therapy.

ISHLT classification), with no indication to antirejection treatment.

In summary, this is a rare case of small bowel pneumatosis in heart transplant recipient with systemic amyloidosis. Intestinal pneumatosis is a rare complication after organ transplantation [1] and, to date, only 12 cases of intestinal pneumatosis after heart transplantation are reported [2–6]. Amyloid *per se* is not a common cause of intestinal pneumatosis; however, intestinal amyloidosis often causes malabsorption, chronic intestinal dysmotility with development of nausea, dysphagia and constipation and favouring opportunistic infections [7,8]. We speculated that intestinal amyloidosis could have facilitated the development of diffuse pneumatosis, which was probably caused by CMV infection and recurrent Cl. difficile colitis.

Hyperbaric oxygen therapy is reported as an adjuvant therapy in some cases of intestinal pneumatosis [9]. In this case, the rationale to use HBOT to treat the small bowel pneumatosis was due to the fact that oxygen is toxic to the anaerobic intestinal bacteria and that the contents of the gas cysts are primarily nonoxygen gases, and the movement of gas follows the partial pressure gradient between the cavity and the bloodstream. The high concentrations of oxygen leaded by HBOT increase the partial pressure of oxygen in the venous blood and decrease the partial pressure of nonoxygen gases, favouring the exit of gas from the cavities [10].

Antibiotic therapy and antiviral therapy were useful to control Cl. difficile colitis and CMV infections and to reduce bacterial gas production, with regulation of intestinal flora. These therapies, in association with hyperbaric oxygen therapy, improved the clinical features of this interesting case.

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