Pneumatosis Intestinalis Associated with Immune-suppressive Agents in a Case of Minimal Change Disease

Byoung Geun Han, Jae Myoung Lee, Jae Won Yang, Min Soo Kim, and Seung Ok Choi

Department of Nephrology, Yonsei University Wonju College of Medicine, Wonju, Korea.

We report treatment of a 38-year-old man with minimal change disease (MCD) who developed pneumatosis intestinalis (PI) during administration of immune-suppressive agents. His immunosuppressive medication had been tapered to 15 mg/day of prednisolone. MCD was steroid-resistant type. Abdominal examination and laboratory studies were not clinically remarkable. Radiologic findings were consistent with PI. Abnormal air accumulation was noted in the bowel, peritoneum, mediastinum and retroperitoneum. Conservative therapy with oxygen and metronidazole improved the PI symptoms. In 1993, a case of PI with nephrotic syndrome following steroid treatment was reported in Japan. However this is only the second case reported in the literature, and the first in English.

Key Words: Pneumatosis intestinalis, minimal change disease, steroids

INTRODUCTION

Pneumatosis intestinalis (PI) is a relatively rare, benign condition characterized by the accumulation of submucosal or subserosal gas-filled lesions in the gastrointestinal tract. Cases of PI have been described in patients who have bowel necrosis, mucosal disruption or obstructive lesions of the gastrointestinal tract, chronic obstructive pulmonary disease, collagen-vascular disease, acute leukemia, congenital immunodeficiency, and acquired immunocompromised states, and after organ transplantation. The cause or pathogenic mechanisms are uncertain.

In this study, we describe a case of PI, where air accumulated in the peritoneum, mediastinum and retroperitoneum as well as bowel, in a patient with minimal change disease (MCD) who received steroid therapy and discuss the factors that contributed to the development of PI in this patient.

CASE REPORT

A 38-year-old man was referred to our nephrology section with generalized edema. Up until 7 months prior to our consultation, he had been well until he first developed the above symptom. At that time he had visited local clinics and urinalysis had showed proteinuria (3014 mg/day). A steroid (prednisone 50 mg/day) had been administered for 4 months on the assumed diagnosis of nephrotic syndrome without pathologic diagnosis. One month prior to first admission at our hospital, generalized edema was again noted and diuretics were initiated.

On first admission, his blood pressure was 130/70 mmHg with a regular heart rate of 85 beats per minute. Pretibial pitting edema (2 positive) was noted. The hemoglobin concentration was 16.5 g/dL, the white blood cell count 7.08 x 10^9/L, and the platelet count 291 x 10^9/L. The prothrombin and partial thromboplastin times were within normal limits. Blood chemistry revealed a total serum protein of 4.0 g/dL, albumin 1.4 g/dL, AST 47 U/L, ALT 24 U/L, triglyceride 749 mg/dL, cholesterol 389 mg/dL, BUN 29.2 mg/dL, and creatinine 1.3 mg/dL with normal serum electrolyte. The serum Ig A was 205 mg/dL, Ig G 230 mg/dL and Ig M 105 mg/dL. The serum C3...
and C4 were 140.4 and 32.2 mg/dl, respectively. In a 24-hour specimen of urine, 7161 mg of protein and 1599 mg of creatinine were found. The tests for antistreptolysin O, ANA, VDRL, hepatitis B surface antigen and antibody, hepatitis C virus antibody and rheumatoid factor were all negative. The chest roentgenogram and abdominal ultrasonogram taken on admission were normal. There was no evidence of heart or liver disease. A renal biopsy was performed. The pathologic diagnosis was MCD.

We began treatment with high dose steroid therapy (prednisolone 60 mg/day). Forty days later, he presented with aggravating generalized edema with ascites and dyspnea. On second admission, laboratory findings showed increased BUN (81 mg/dl) and creatinine level (2.6 mg/dl). Nevertheless, high dose steroid treatment was continued for a total of 8 weeks and then tapered. At approximately 4 months after the commencement of steroid therapy, the patient complained of abdominal discomfort. Prednisolone was 20 mg/day. An abdominal X-ray demonstrated irregular and atypical scattering of a gas-shadow in the whole abdomen (Fig. 1). On the third admission, his vital signs were stable. He didn’t complain of abdominal pain. The abdomen showed tympanic distension with sluggish bowel sounds. However, there was no abdominal guarding or tenderness. The hemoglobin concentration was 11.0 g/dl, the white blood cell count 9.44 × 10⁹/L, and the platelet count 292 × 10⁹/L. The prothrombin and partial thromboplastin times were within normal limits. Blood chemistry revealed a total serum protein of 4.2 g/dl, albumin 1.9 g/dl, AST 15 U/L, ALT 24 U/L, triglyceride 295 mg/dl, cholesterol 423 mg/dl, BUN 22.3 mg/dl, and creatinine 0.9 mg/dl. We decided to delay surgical exploration due to a suspicion of the possibility of PI because of the lack of acute abdominal signs.

Abdominopelvic CT scan confirmed a large collection of air located in the peritoneum, retroperitoneum and mediastinum. Abnormal gas collections were also noted in the intestinal wall protruding into the luminal contrast media (Fig. 2-4). Gas attenuation appeared consecutively on several cutting images, a finding highly suggestive of the linear type of PI. However, there were no significant pathologic lesions introducing PI on endoscopic gastroduodenoscopy and sigmoidoscopy. Barium enema demonstrated an extraluminal gas shadow in the right colon. There was no gross abnormality on the gastrointestinal protein losing scan. Fecal studies failed to reveal any enteric pathogens. He was treated with 100% oxygen inhalation and metronidazole. Steroid administration was stopped. At discharge 10 days later without significant gastrointestinal complication, we changed the immune-suppressive agent

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Fig. 1. Plain film of abdomen shows radiolucent air density in an unusual area.

Fig. 2. CT scan shows abnormal air attenuations in the mediastinum.
Fig. 3. CT scan shows abnormal gas collections in the peritoneum and retroperitoneum and throughout the bowel wall (width 400, level +20).

Fig. 4. Abnormal air density (open arrow) is noted in the intestinal wall protruding into the lumen in a window resetting (width 1600, level -550).

from corticosteroid to cyclosporin (300 mg/day). There was no evidence of PI recurrence for 9 months except for the proteinuria (11,176 mg/day). The patient was maintained on a 175 mg/day dosage of cyclosporin.

DISCUSSION

PI is characterized by multiple and diffuse collections of gas in the wall of the small and large intestines that be subdivided by linear or cyst-like type, depending on the localization. The gas may collect in the submucosa, subserosa, or may extend to other organs or spaces such as the stomach or peritoneum. Pneumoperitoneum may be stemmed from the result of bursting of the gas collections of the intestinal wall.

In our patient, barium enema and abdominopelvic CT scan showed that the appearance of the air density in the bowel wall was linear, not cystic. Characteristically, abnormal air density was also noted in the peritoneum, retroperitoneum and mediastinum on the radiologic studies.

In the majority of cases, including our own, PI is accidentally found on plain abdominal or chest roentgenogram. Radiologic findings can mimic a perforated abdominal viscus and cause a failure to distinguish between medical and surgical abdomen. Therefore, it is most important to get a correct diagnosis in order to prevent any unnecessary abdominal surgery. Any patient evidencing disease symptoms highly suggestive of PI may be treated with a conservative approach consisting of bowel rest, oxygen inhalation and/or antibiotic therapy. The gas collections in the intestinal wall usually resolve spontaneously. Surgical treatment may be rarely required even though PI is not in itself an indication.

The etiologic factor and its pathogenesis are still unknown. It is associated with several medical or surgical conditions as described in the introduction. Sequeira, summarizing the data from previously reported cases, reported that 33% of the patients had received steroids and 23% had received chemotherapy for their underlying disease. He insisted that immunosuppression caused by drugs or underlying disease was one of the two common factors. The other factor was an ulceration of the bowel mucosa.

In his review article, Andorsky suggested that the pathogenesis of PI was multifactorial, with the proposed factors being chemotherapy, radiotherapy, immunosuppressive therapy, opportunistic enteric infections and sympathetic reaction from an inflamed allograft after organ transplantation. He concluded that steroid was the most commonly used immunosuppressive agent, regardless of the type of organ transplanted or the particular clinical course, and could be a powerful PI causing factor due to the depletion of intestinal lymphoid tissue and loss of the integrity of the mucosal barrier that allows dissection of intraluminal air into the submucosal or subserosal layers.
Prompt diagnosis and proper therapy are essential for adequate management of PI patients being treated with immune-suppressive agents. If the patient is in an asymptomatic status, PI is probably of little clinical significance. However, it is necessary to approach the underlying disease, especially in patients in an immune compromised state or who are receiving immunosuppressive drugs. Prognosis most likely depends upon the underlying disease rather than the bowel cysts themselves.

In our case, PI occurred in the presence of preexisting MCD, which was being treated with high dose steroid therapy. Initially, on radiologic appearance, it was suspected that panperitonitis had developed from the bowel infarction by thromboembolic complication associated with hypoalbuminemia in nephrotic syndrome. However, there was no clinical evidence of bowel ischemia or peritonitis. Therefore, we would like to conclude by emphasizing the causative factor based on this case and our review of the available literature. The use of corticosteroid was the only presenting factor, which contributed to the development of PI in our patient. PI was completely recovered without complication. Prognosis was excellent, even though abnormal air was extensively noted in multiple areas.

REFERENCES