CASE REPORT

Pneumatosis Cystoides Intestinalis after α-Glucosidase Inhibitor Treatment in a Patient with Interstitial Pneumonitis

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Abstract

A 56-year-old woman was admitted to our hospital for treatment of non-specific interstitial pneumonitis (NSIP). The patient started prednisone treatment, but one month later treatment with voglibose, an α-glucosidase inhibitor (α-GI), was started because of prednisone-induced diabetes mellitus. One week later, a massive volume of free air below the diaphragm was detected by a chest X-ray examination. An abdominal CT examination demonstrated pneumatosis coli and the patient was diagnosed with pneumatosis cystoides intestinalis (PCI). Voglibose was discontinued and parenteral nutrition and oxygen inhalation were initiated. Radiographic findings of PCI disappeared within 7 days. We encountered a rare case of PCI, that was associated with α-GI treatment.

Key words: pneumatosis cystoides intestinalis, α-glucosidase inhibitor, non-specific interstitial pneumonitis

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Introduction

Pneumatosis cystoides intestinalis (PCI) is a very rare disease characterized by the presence of multiple gas-filled cysts in the submucosal or subserosal wall of the small and/or large intestine. PCI has been reported to be associated with several diseases, such as collagen disease (1), pulmonary disease and ischemic bowel disease, and also with transplantation (2-4), drug therapy (particularly prednisone therapy), chemotherapy and immunosuppression (2, 5). Recently, treatment with α-GI, a new hypoglycemic agent that can suppress postprandial hyperglycemia, has been reported to be related to PCI (6-8). α-GI delays absorption of carbohydrates in the small intestine through antagonism and inhibition of α-glucosidase activity. The drug has side effects of abdominal distention and increased flatus due to increased levels of intestinal gas, which is attributed to fermentation of undigested carbohydrates by intestinal bacteria, resulting in the formation of metabolites such as carbon dioxide, methane and hydrogen. Here, we describe a case of PCI after the patient was treated with α-GI and prednisone. This case suggests that PCI should be listed as a side effect of α-GI treatment.

Case Report

A 56-year-old woman was admitted to our hospital because of exertional dyspnea, which she had suffered from for several months. She was diagnosed with NSIP in June 2003. At the age of 45, she underwent a hysterectomy for uterine myoma. Both a computed tomography (CT) examination and a respiratory function test showed that NSIP was worsening. Prednisone (50 mg per day) was started in January 2004. One month later, her general condition had improved. A chest X-ray and CT examination showed an improvement of interstitial pneumonitis, and no abnormalities were detected. Hence, we tapered the prednisone dose (40 mg per day) and then maintained it at this level. At that time, the patient started 600 mg per day of voglibose because of development of prednisone-induced diabetes mellitus. She had no abdominal symptoms, except that a bub-
A blaring sound was occasionally noticeable. Seven days after she had started voglibose treatment, a routine chest X-ray examination was performed, and this revealed free air below the diaphragm. Her temperature was 36.4°C, blood pressure was 112/72 mmHg, heart rate was 72 with a regular sinus rhythm, and heart sounds were clear, although fine crackles were detected. The abdomen was mildly distended and soft, but the bowel sound was normal. Neither tenderness nor muscular guarding was detected. Laboratory examinations indicated no abnormal findings, including WBC and CRP. An X-ray examination of the abdomen revealed noticeable gaseous distention around the ascending colon (Fig. 1).

Computerized tomography (CT) of the chest revealed pneumomediastinum and pneumopericardium. Abdominal CT revealed pneumatosis of the ascending and transverse colon and pneumoretroperitoneum (Fig. 2). Portal venous gas was not detected. Contrast enhancement CT revealed a lot of air around the ascending colon, but there was no leak of contrast materials to cystic areas of gas. A barium enema examination revealed many cystic areas of the ascending colon. Colonoscopy showed multiple sessile polypoid lesions that were covered with mucosa of normal appearance in the ascending colon and terminal ileum (Fig. 3). Voglibose was discontinued when a diagnosis of PCI was made, and fasting was imposed and parenteral nutrition and oxygen inhalation (1 ml/min) were initiated. One week later the flatulence and abdominal distention had improved, and the cystic gas had disappeared.

Discussion

PCI is poorly understood, but is known to be associated with gastrointestinal or systemic diseases, such as acute and/or chronic inflammatory gastrointestinal disease, chronic obstructive pulmonary disease, and collagen disease. Moreover,
chemotherapy and immunosuppressive drug therapy, such as prednisone and cyclosporine (CyA) treatment, may predispose patients to PCI (2, 3, 5).

Although the mechanisms underlying PCI are still poorly understood, either a mechanical or a bacterial theory is generally accepted (2). The mechanical theory proposes that gas diffuses into the bowel wall from either the intestinal lumen or the pulmonary airway. The bacterial theory proposes that gas-forming bacilli enter the submucosa through mucosa and produce gas within the intestinal wall.

PCI has been associated with pulmonary disease in the absence of gastrointestinal disorder. Hence, Heng et al suggested that severe cough can lead to alveolar rupture, resulting in diffusion of air along blood vessels into the mediastinum, through the diaphragm, along major vessels in the mesentery, and into the bowel wall, which could explain the occurrence of PCI in patients with chronic obstructive pulmonary disease (10). In our case, the patient had suffered from a cough for a long time, and occurrence of latent PCI is therefore a possibility. However, we were unable to find any reports that refer to a relationship between PCI and NSIP.

Ammons et al reported that 3 of 103 renal transplant patients treated with prednisone and CyA developed PCI (2). In this report, it was suggested that some medications may shrink Payer’s patches, with resultant loss of structural integrity of bowel mucosa, allowing entry of gas into the bowel wall. Galm et al reported PCI in patients who had undergone chemotherapy, and suggested that PCI may be a rare complication of cytostatic or immunosuppressive treatment (5). In the present case, we used prednisone (50 mg/day) for a month, and a chest X-ray examination showed no signs of PCI before voglibose treatment were started. Hence, we believe that not only immunosuppressive therapy but also voglibose treatment may have a synergistic relationship with the occurrence of PCI.

Recently, several reports have mentioned that the α-GI, voglibose or Acarbose, might be a causative factor for PCI in Japan (Table 1) (6-9). It is generally understood that α-GI causes flatulence, because it suppresses absorption of carbohydrates in the colon, and intestinal bacteria then generate a large volume of gas by carbohydrate fermentation.

In the present case, the patient had been suffering from cough because of long term NSIP, and hence there was some possibility of a small amount of gaseous distention in her intestine. α-GI treatment may induce an increased gas volume, resulting in elevation of the internal pressure of the intestine and an increase in the permeability of the intestinal mucosa. Our histological examination of a biopsy specimen showed the presence of gas under epithelial cells and interepithelial lesions (Fig. 4). Electron microscopy of the ascending colon epithelium showed loose intracellular junctions (Fig. 5). These findings may indicate that the origin of the gas is the intestinal lumen, with leakage to submucosal lesions. If the leak is not through a fistula but through filtration of the intestinal epithelial cells, the gas composition in the intestinal wall may be different from that of the intestinal tract lumen, as reported previously (11).

In conclusion, we encountered a rare case of PCI, that was associated with α-GI treatment. It is important to consider PCI when α-GI is administered.
References


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