

A Case of Pneumatosis Intestinalis Associated with Antipsychotic Medication

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Pneumatosis intestinalis (PI) is an uncommon but important condition characterized by the accumulation of gases in the submucosa or subserosa of the gastrointestinal wall. The clinical course of PI represents a wide spectrum of conditions and outcomes that range from benign to life-threatening. Although controversy exists about the exact cause of PI, mucosal integrity, intraluminal pressure, gases, and bacterial flora are thought to have interactive roles in the formation of PI. Antipsychotic drugs are known to decrease bowel motility inducing constipation and ileus, ultimately increasing the intraluminal pressure which rarely results into PI. In Korea, several cases of PI caused by various etiologies have been reported. However, there has been no report of PI associated with antipsychotic drugs. We report a rare case of PI who was taking antipsychotic drugs due to schizophrenia.

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Key words: Pneumatosis intestinalis, Constipation, Antipsychotic drugs

Introduction

In pneumatosis intestinalis (PI), a rare but important condition, gases are found in a linear or cystic form in the submucosa or subserosa of the bowel wall.¹ The significance of PI depends on the nature and severity of the underlying conditions. PI encompasses a wide spectrum of conditions and outcomes, ranging from benign diseases to abdominal sepsis and death.² Although controversy exists regarding the exact cause of PI,³ mucosal integrity, intraluminal pressure, bacterial flora, and intraluminal gases are thought to have interactive roles in its formation.² An elevation of intraluminal and transmural pressures is important in developing gases accumulation in the gastrointestinal wall.

Antipsychotic drugs can cause decreased gastrointestinal

motility manifested as constipation, ileus, and colonic pseudo-obstruction.^{4,5} Constipation, a common adverse effect of antipsychotic drugs, can sometimes be severe enough to lead to ileus. Furthermore, impaired intestinal motility is one of the representative etiologic factors to increase the intraluminal pressure. In Korea, several cases of secondary PI associated with various conditions have been reported, but there is none regarding PI associated with antipsychotic drugs until now.

We report a case of PI of the small intestine in a patient who took the antipsychotic medication for schizophrenia.

Case report

A 37-year-old man was admitted to the emergency room (ER) for 3 days of abdominal pain and several times of hematochezia for a day. He had a history of schizophrenia for 16 years without any other remarkable medical or surgical history. He had been slightly psychotic but behaving well under control.

His psychiatric symptoms worsened 1 month before admission to the ER, so he was taken to the psychiatric hospital where he was treated with olanzapine 15 mg bid,

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Figure 1. Plain film of the abdomen. Distended small/large bowel loops and intramural gases paralleling the course of the bowel loops are observed.

divalproex sodium 625 mg bid, haloperidol 1.5 mg bid, and propranolol 20 mg bid.

Although the psychotic problems were improving, constipation was developed as a main problem during the treatment period, passing stool only once or twice a week.

On the day of admission to the ER, blood pressure, pulse rate, respiratory rate, and the temperature were 90/60 mmHg, 108 times/min, 20 times/min and 36.6°C, respectively. On physical examination, the abdomen was rigid and distended with hypoactive bowel sounds, but without definite direct or indirect tenderness. The laboratory findings showed hemoglobin = 17.9 g/dL, leukocytes = 5,330/mm³ (86.5% neutrophils) and platelets = 110,000/mm³, blood urea nitrogen = 13.1 mg/dL, creatinine = 1.7 mg/dL, C-reactive protein (CRP) = 57.8 mg/L, and lactate = 1.3 mmol/L (0.5-1.6). The electrolytes were Na = 139 mmol/L, K = 4.9 mmol/L, Cl = 102 mmol/L, and tCO₂ = 25 mmol/L. Autoimmune markers such as antinuclear antibody (ANA), anti-DNA antibody, and anti-neutrophil cytoplasmic antibody (ANCA) were negative.

Stool cultures for ova, parasites, and routine pathogens showed no evidence of infection.

The plain abdominal radiograph revealed the distended small and large bowel loops with intramural gases paralleling the course of the bowel loops (Fig. 1). Abdominopelvic computed tomography (CT) showed distended small and large bowel loops and linear collection of gases in the submucosal layer of the jejunum and ileum with an air-biliary gram in the liver (Fig. 2A-C).

He was treated with high oxygen (10 L/min with a mask), bowel rest, hydration with total parenteral nutrition, and broad-spectrum antibiotics. After hydration, serum creatinine and CRP were normalized with prophylactic antibiotics. Mesenteric angiography and capsule endoscopy, which were performed to evaluate underlying vasculitis or pathognomonic mucosal change of the bowel on the eighth day after his admission, showed unremarkable findings. On the ninth day after his admission, repeated abdominopelvic CT scan demonstrated completely resolved PI in the bowel loops and air-biliary gram in the liver (Fig. 3).

He gradually built up his oral intake, and psychiatric medications were adjusted to aripiprazole (25 mg), clonazepam (0.5 mg), benztropin (1mg), and propranolol (60 mg), combined with a laxative. After 6 months of follow-up, no sign of abdominal symptom or constipation was shown.

Discussion

Since its first description in 1783 by Du Vernoi, the pathogenesis of PI is poorly understood, but considered probably as multifactorial.^{6,7} Thus, various explanations have been offered for several decades and the breadth of pathologic conditions associated with PI formation suggests that its development is a multifaceted phenomenon.

PI can be classified as either idiopathic or secondary.^{8,9} Primary PI is defined when no coexisting condition is associated and secondary PI is reported with underlying conditions such as inflammatory bowel disease, gastrointestinal infections, paralytic ileus, chemotherapy, connective tissue

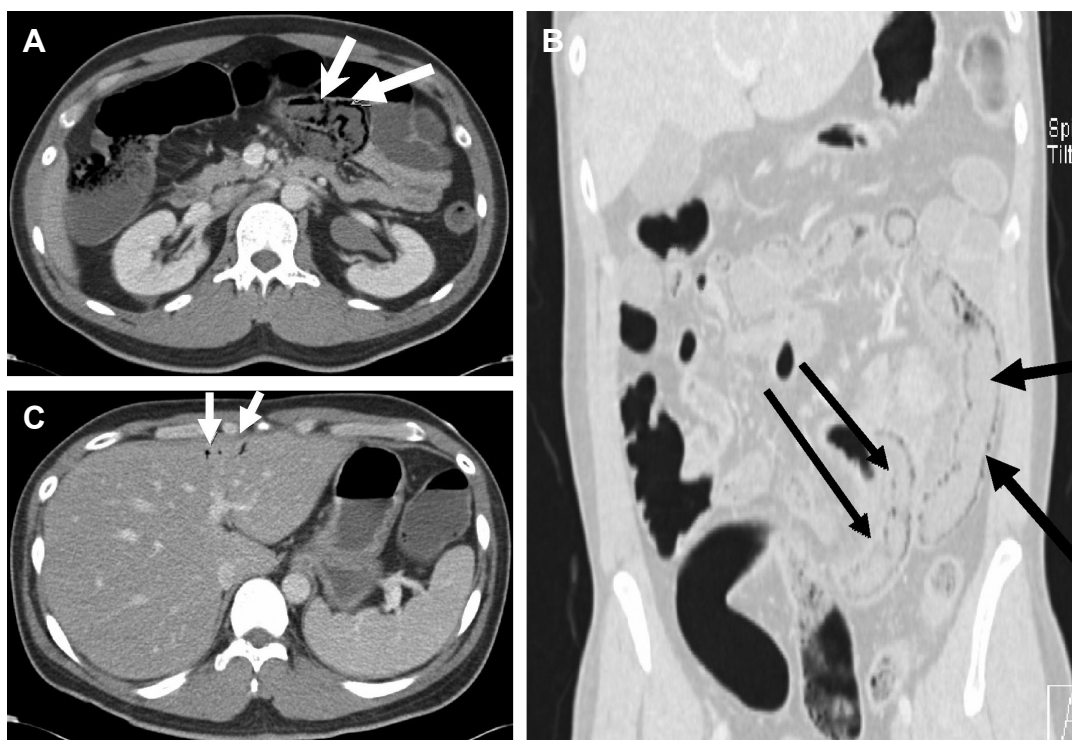


Figure 2. Abdominopelvic computed tomography scan. (A) A linear collection of gases are noted in the submucosal layer of the jejunum and ileum (arrows). (B) It presents fluid filled and distended small and large bowel loops and demonstrates a linear collection of gases. (C) It also shows the gases through the portal veins in the liver (arrows) and diffuse fat infiltration in liver with an air-biliary gram in left lobe.

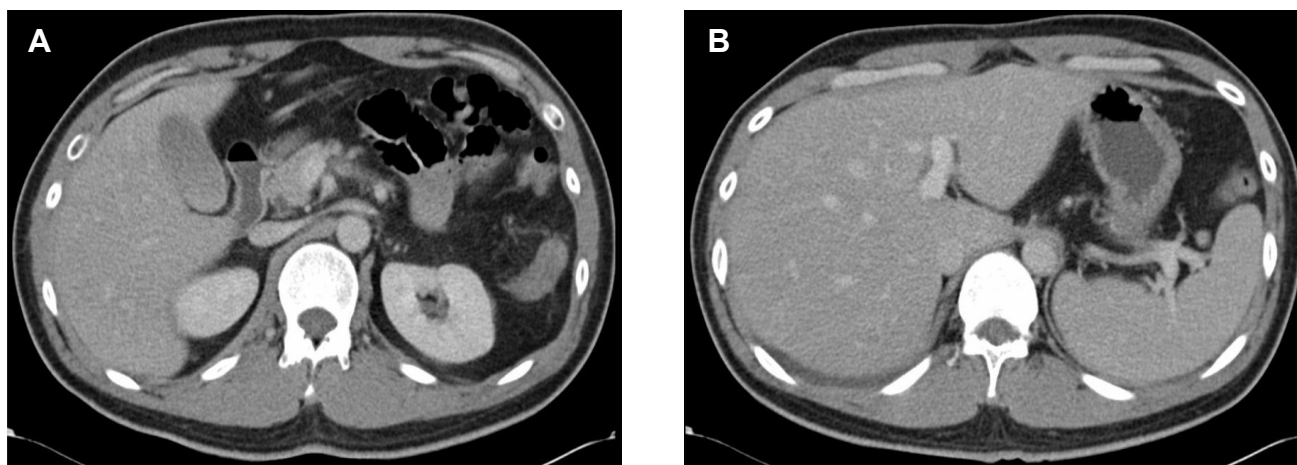


Figure 3. Follow-up abdominopelvic computed tomography scan. (A) Pneumatosis intestinalis through the mid small bowel loop is resolved. (B) The portal venous gases and air-biliary gram in the liver are also resolved.

disease, chronic obstructive pulmonary disease, and rarely malignancy. Certain medications are also known to be another cause of secondary PI, including antipsychotic drugs, chemotherapeutic agents, and sclerotherapeutic agents.

Many reports have discussed first-generation (typical)

antipsychotic drugs (haloperidol and chlorpromazine) to cause decreased gastrointestinal motility manifested as constipation, ileus, colonic pseudo-obstruction (Ogilvie's syndrome), esophageal atony, and bowel dilatation.¹⁰ The depression of intestinal motility was hypothesized to be caused by pheno-

thiazines and haloperidol, and is probably the consequence of their anticholinergic activity.⁴ This hypothesis was further supported by animal experiments showing the inhibition of intestinal movement by chlorpromazine which was diminished by pilocarpine (an agonist of muscarinic receptors) and the cholinesterase inhibitor, physostigmine.¹¹

In addition, some reports have shown that a man with schizophrenia developed paralytic ileus after receiving a combination of second-generation antipsychotics (clozapine, olanzapine, and risperidone).¹² The gastrointestinal dysmotility caused by the combination of the first (olanzapine) and second (haloperidol) generation antipsychotic therapy is followed by the intraluminal pressure elevation, which then force the gases to dissect into the wall of the bowel either through breaks in the mucosa or through the serosal surface tracking along the mesenteric blood vessels.¹

A case has been reported recently with an improvement in bowel habits after dose-reduction, and simplification of antipsychotic drugs was clinically important.¹³ Switching to an atypical antipsychotic could be another option, although this might be associated with an increased mortality in the elderly.¹⁴ Therefore, dose-reduction should be considered as the first attempted treatment for similar patients.

Our patient was evaluated for conditions such as autoimmune diseases like systemic lupus erythematosus or vasculitis, and other causes including inflammatory bowel disease, gastrointestinal infections, or paralytic ileus that may induce ischemic changes and mucosal injury. However, all of these examinations were negative. Since antipsychotic drugs are known to decrease bowel motility inducing constipation and ileus and ultimately lead to increased intraluminal pressure, we believed that the antipsychotic drugs of the patient were the cause of constipation, ileus, and finally PI. However, the hematochezia upon initial examination was considered to be caused by mild ischemic changes induced by ileus.

The possibility of bowel dysmotility should be regarded in patients who take antipsychotic drugs as it could cause the PI by decreasing bowel motility and inducing constipation and ileus.

In Korea, two cases of secondary PI associated with drugs have been reported including PI caused by prednisolone¹⁵ and by lactulose with underlying liver cirrhosis.¹⁶ However, there has been no report of PI associated with antipsychotic drugs until now. The present case is the first report in Korea that the antipsychotic drugs to cause the PI through decreased bowel motility.

We report a rare case of PI of the small intestine in a patient who has taken antipsychotic medication.

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