

CASE REPORTS

Segmental pneumatosis cystoides coli: computed tomography-facilitated diagnosis

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ABSTRACT

Background: Intestinal pneumatosis is a rare entity of unclear etiopathogenesis characterized by the presence of gaseous cystic or linear collections within the intestinal wall. Intestinal pneumatosis may be primary and idiopathic in origin or, more frequently, it accompanies various clinical conditions. Rarely, the development of intestinal pneumatosis is attributed to the pharmacotherapy with different drugs.

Case report: This is a case report of cystic pneumatosis limited to the large intestine with predominant clinical presentation of chronic watery diarrhea in a 64-year-old man suffering from diabetes mellitus treated with metformin and acarbose. The patient had been referred to the outpatient gastroenterology clinic for further investigation of numerous polyp-like lesions found on colonoscopy. There was no history of cigarette smoking, drug abuse or extraintestinal complaints. The patient was in a good general condition and his laboratory tests were normal. No relevant abnormalities were found on chest X-ray, esophagogastroduodenoscopy or abdominal ultrasound, but computed tomography showed intramural gas-filled bubbles in the cecum and splenic flexure without signs of perforation or any other significant pathology in the abdominal cavity. The final diagnosis of pneumatosis cystoides coli (PCC), possibly related to treatment with acarbose, was established. On a follow-up visit after discontinuation of acarbose the patient reported no complaints and remained asymptomatic for the next 12 months.

Discussion: To conclude, drug-related PCC should be considered in a differential diagnosis of gastrointestinal symptoms and/or polyp-like lesions disclosed on colonoscopy in diabetic patients treated with acarbose.

Key words: Intestinal pneumatosis. Diabetes mellitus. Acarbose. Adverse effect. Computed tomography.

INTRODUCTION

Intestinal pneumatosis is a rare entity of unclear etiopathogenesis characterized by the presence of gaseous cystic or linear collections within the gastrointestinal wall, mainly subserosal in the small intestine and submucosal in

the colonic wall (1,2). Intestinal pneumatosis may be primary/idiopathic in origin or, more frequently, it accompanies various clinical conditions. Rarely, the development of intestinal pneumatosis is attributed to the pharmacotherapy with different drugs, predominantly anticancer and immunosuppressive agents or monoclonal antibodies.

CASE REPORT

A 64-year-old Caucasian male with unremarkable family history and type 2 diabetes mellitus treated with oral agents had been referred to the outpatient gastroenterology clinic for further evaluation of numerous polyp-like lesions up to 2 cm in diameter extending from the cecum to the splenic flexure of the colon found on colonoscopy performed because of watery diarrhea, flatulence and diffuse but mild abdominal pain without fever or significant weight loss for 6 months before endoscopic examination (Fig. 1). In addition, a small solitary sigmoid diverticulum without signs of inflammation was observed. Histopathological evaluation of biopsy specimens disclosed chronic mild non-specific colitis.

The patient denied drug and alcohol abuse, smoking cigarettes and taking nonsteroidal anti-inflammatory drugs. His past medical history was positive for appendectomy and elective surgery for bilateral inguinal hernia in childhood. Except for occasional mild backache due to degenerative bone disease, the patient had been healthy until 8 years earlier, when he was diagnosed type 2 diabetes mellitus and started treatment with acarbose (150 mg daily) and metformin (1.5 g daily) with good tolerance and blood glucose control. The patient had not been taking any other pharmacological agents on a daily routine in the last few months. There was no history of extraintestinal, including respiratory system-related complaints.

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Fig. 1. Colonoscopy image of polyp-like lesions in the large intestine.

On physical examination the patient was in a good general condition. Physical examination was remarkable only for the presence of postoperative linear abdominal scars. His body temperature was normal, heart rate regular at 72/min, blood pressure 110/80 mm Hg and BMI 24.6 kg/m². Breath sounds were normal with respiration rate of 12/min. His stool and blood tests including ESR, complete blood count, total bilirubin, GGTP, alkaline phosphatase, aminotransferases, amylase, glucose, glycated hemoglobin (HbA1c), electrolytes, creatinine, lipemia and gasometry were normal with good long-term diabetes control. No relevant abnormalities were found on chest X-ray, abdominal ultrasound and esophago-gastroduodenoscopy. However, computed tomography (CT) showed intramural gas-filled collections in the cecum and splenic flexure without evident thickening of the intestinal wall or signs of perforation as well as a few small hepatic cysts and a solitary 14 mm renal cyst without any other significant pathology in the abdominal cavity (Fig. 2). The final diagnosis of pneumatosis cystoides coli (PCC) was established. The patient was suggested discontinuation of acarbose, an α -glucosidase inhibitor found to be rarely related to intestinal pneumatosis, under the supervision of diabetologist. On a follow-up visit 4 weeks later the patient reported no complaints and sufficient blood glucose control. He did not agree to second-look colonoscopy but a check-up CT revealed remission of previously described PCC-related lesions (Fig. 3) and the patient remained asymptomatic for the next year.

DISCUSSION

PCC is a subtype of intestinal pneumatosis characterized by the presence of gaseous cystic collections within

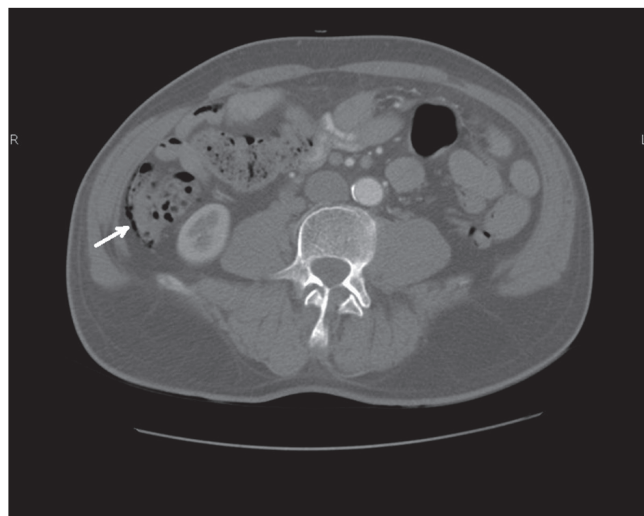


Fig. 2. Axial contrast-enhanced CT scan showing gas-filled intramural lesions in the right-sided part of the large intestine.



Fig. 3. Follow-up axial contrast-enhanced CT scan showing remission of previously described lesions in the large intestine.

the colonic wall. The true incidence of PCC in general population remains unknown, but intestinal pneumatosis is found in 0.03-0.2% of autopsies, predominantly in males (3). PCC may be idiopathic (15%) or it accompanies various clinical conditions of digestive system (peptic ulcer, pyloric stenosis, Crohn's disease, appendicitis, necrotizing enterocolitis, bacterascites) or respiratory (chronic obstructive pulmonary disease, cystic fibrosis), autoimmune (dermatomyositis, scleroderma), inflammatory, infectious (*Clostridium difficile*, HIV) diseases or trauma (4,5). Development of PCC is rarely attributed to pharmacotherapy with different agents, including α -glucosidase inhibitors (6).

Although the pathomechanism of PCC remains unclear, mechanical or bacterial theory is usually quoted. The first although currently highly questionable concept is the diffusion of gas from ruptured alveoli through the mediastinum, the diaphragmatic orifices and then along the mesenteric vessels into the intestinal wall (7). Alternatively, gas may diffuse from the intestinal lumen into its wall due to increased intraluminal pressure in the presence of mucosal injury (8). The bacterial theory suggests that gas-producing bacteria enter intestinal wall in the presence of increased mucosal permeability and form gas collections there (9).

Patients are usually asymptomatic and PCC is found accidentally during unrelated diagnostic imaging or surgery. However, occasionally PCC manifests with life-threatening conditions deserving prompt diagnosis and intensive treatment (3,10).

A definite preliminary diagnosis of PCC requires a high index of suspicion. A detailed medical history concerning co-morbidities and their treatment as well as thorough physical examination are essential for making a distinction between primary and secondary PCC. Laboratory tests are usually normal in idiopathic asymptomatic PCC and may be unspecific in secondary pneumatosis. Endoscopic examinations may be either false negative in the presence of minor subserosal collections of gas or misleading with colonoscopic findings similar to polyposis or submucosal tumors. Occasionally, preliminary diagnostic mistake leads to unnecessary "polypectomies" and intestinal perforations. Therefore, abdominal imaging methods: abdominal ultrasound, radiography (plain radiographs, double contrast barium series, CT) and MRI may be crucial for the final diagnosis of PCC.

CT is regarded as the most useful diagnostic tool in this entity, additionally able to disclose other pathological changes in the abdominal cavity. It may be ordered as the first-line imaging in case of emergency, contraindications to endoscopic examinations or lack of consent to colonoscopy. CT scans reveal the presence of two types of intestinal pneumatosis: cystic and linear (multiple bubbles or linear collections of gas, respectively); but they sometimes show limited value in the diagnostics of accompanying intestinal ischemia or necrosis (11). On X-ray examinations cysts usually appear as radiolucent shadows resembling a bunch of grapes adjacent to the intestinal lumen.

In the case described diabetic enteropathy as a causative factor of complaints was regarded as highly improbable in the presence of a good, well-documented short and long-term diabetic control. In quest of potential triggering factors of PCC in this case, the WHO Adverse Drug Reactions database search was performed and it disclosed 176 reports on drug-related intestinal pneumatosis over ten years (2002-2012; total number of reports: 7,147,137), mainly attributed to treatment with anticancer and immunosuppressive drugs or monoclonal antibodies. Only 5 of them were related to treatment with acarbose, a competitive inhibitor of intestinal α -glucosidases that reduces

post-meal glycemia excursions by delaying the digestion and absorption of starch and disaccharides (12). It is approved for patients with type 2 diabetes mellitus in doses 25-100 mg before meals as monotherapy or in combination with other oral hypoglycemic drugs. Prominent adverse effects include flatulence, diarrhea and abdominal pain and result from appearance of undigested carbohydrates in the colon and their subsequent fermentation into short chain fatty acids, releasing gas. However, the patient had been taking acarbose for years with good tolerance before he developed abdominal symptoms so the mechanism behind the presence of gas in his large bowel wall remained unclear. In the absence of signs and symptoms of respiratory system disorders the pulmonary origin of that gas was highly unlikely. In addition, there were no data to suspect increased intraluminal pressure in the absence of diverticulosis, however there is a case report on PCC in the presence of solitary sigmoid diverticulum and corticosteroid therapy (2). Nevertheless, in our patient right-sided pneumatosis not extending the splenic flexure makes such causal connection improbable. Although the patient did not suffer from abdominal distention or flatulence for many years of treatment with acarbose, literature review (the majority of case reports originating from East-Asian countries), showed that coincidence between PCC and therapy with α -glucosidase inhibitors is possible, probably due to the drug-induced promotion of bacterial overgrowth (13-16). Therefore, the preliminary diagnosis of acarbose-related PCC was suggested.

At present, there is a general consensus that asymptomatic PCC does not have to be treated. As a result, when PCC is diagnosed incidentally, surgical removal of the colon is not indicated. On the other hand, causative treatment, conservative or surgical if necessary, is recommended in symptomatic patients and involves therapeutic means tailored according to PCC etiology, including oxygen hyperbaric therapy or antibiotics in individual cases (17,18). Review of the literature shows that in case of α -glucosidase inhibitor-related PCC, discontinuation of the drug is the treatment of choice that usually leads to the complete recovery within 5 to 28 days (6,19). Such therapeutic option proved to be successful also in the case of the patient described.

CONCLUSION

To conclude, with the increasing prevalence of diabetes mellitus a growing number of endoscopic examinations in these subset of patients may be expected. PCC should be considered in a differential diagnosis of gastrointestinal symptoms, especially watery diarrhea, in patients with medical history of type 2 diabetes mellitus treated with acarbose. In case of polyp-like lesions on colonoscopy presumed diagnosis of PCC may be confirmed by non-invasive radiographic imaging modali-

ties. CT is a valuable diagnostic tool in case of unclear endoscopic findings suggestive for PCC or the need to elucidate background responsible for the development of secondary PCC.

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