A Rare Case of Benign Pneumatosis Intestinalis with Portal Venous Gas and Pneumoperitoneum Induced by Acarbose

Amihai Rottenstreich, Yahel Agmon and Ram Elazary

Abstract

Alpha glucosidase inhibitors have been shown to be associated with pneumatosis intestinalis (PI) in recent reports. We herein report the case of a 73-year old man who received treatment with an alpha glucosidase inhibitor (acarbose) and presented with acute abdomen. A computed tomography scan demonstrated PI in addition to intrahepatic portal air and pneumoperitoneum. During exploratory laparotomy, we found no evidence of hollow organ perforation or bowel necrosis. The patient recovered after conservative treatment with cessation of the alpha glucosidase inhibitor. This is the first report to describe the combination of PI with portal venous gas and pneumoperitoneum caused by an alpha-glucosidase inhibitor.

Key words: pneumatosis intestinalis, portal venous gas, alpha glucosidase inhibitors, pneumoperitoneum


Introduction

Pneumatosis intestinalis (PI) is a rare condition characterized by the accumulation of gas in the bowel wall. PI has been reported to be associated with a variety of disorders, ranging from benign conditions to abdominal sepsis and death (1). Although its etiology remains unclear, several theories have been suggested, including mechanical, bacterial and respiratory mechanisms. The simultaneous presence of portal venous gas has also been shown to correlate with increased morbidity and mortality (2).

During the last decade, the use of alpha glucosidase inhibitors to treat type 2 diabetes mellitus has been found to be associated with the onset of PI (3).

We herein present a case involving treatment with acarbose, an alpha glucosidase inhibitor, as the probable cause of PI with pneumoperitoneum and portal venous gas mimicking intestinal necrosis. This is the first case report to describe the administration of an alpha glucosidase inhibitor as the cause of portal venous gas in association with PI and pneumoperitoneum.

Case Report

A 73-year-old man with a medical history of ischemic heart disease, type 2 diabetes mellitus associated with target organ failure (retinopathy and nephropathy), hyperlipidemia, hypertension and recurrent urinary tract infections had used acarbose at a dose of 50 mg q8h for type 2 diabetes mellitus. He subsequently presented to the emergency department (ED) complaining of repeated vomiting and constipation starting the morning of admission. He denied chest or abdominal pain, diarrhea, fever or urinary discomfort. His vital signs were normal. A physical examination revealed diffuse abdominal tenderness without signs of additional peritoneal irritation. Bowel sounds were present, and the results of a digital rectal examination were normal, with stool in the rectum. Blood tests showed a white blood cell count of 21,000/mm and C-reactive protein level of 10 mg/dL as well as acute renal impairment (creatinine: 2.1 mg/dL). Metabolic acidosis with a pH of 7.3 and lactic acid level of 4.43 mmol/L were also noted. An erect chest radiograph demonstrated free air under the diaphragm (Fig. 1). Computed tomography scans of the chest, abdomen and pelvis were therefore conducted, which demonstrated pneumatosis intestinalis in the ileum and ascending colon (Fig. 2A, B, respectively).
Pneumatosis intestinalis, first described in 1730 by DuVer-roni, is defined as the presence of gas within the wall of the small or large bowel (4). More than 60 etiologies have been identified; however, 15% of cases are considered to be primary or idiopathic (5).

Three main theories have been proposed for the pathogenesis of PI. The mechanical theory postulates that PI develops as a result of increased intraluminal pressure which allows gas to infiltrate the bowel wall via mucosal defects (6). In contrast, the bacterial theory postulates that PI occurs when the submucosal localization of fermenting bacteria (e.g., clostridia and Escherichia coli) leads to the production of gas that subsequently accumulates in the submu-
cosa, while the pulmonary theory suggests that gas freed by the rupture of alveoli travels through the mediastinum and retroperitoneum into the bowel wall (6, 7).

The overall incidence of PI has been reported to be as low as 0.03%, according to an autopsy series (8). However, due to the increased use of CT scans, the reported incidence has recently reached 0.3% (9).

The clinical manifestations of PI range from incidental findings with a benign course to severe life-threatening complications, such as bowel ischemia (5). Approximately half of patients diagnosed with PI can be managed conservatively (10). Moreover, pneumatoperitoneum, once considered an indication for surgical intervention, has also been reported to have a benign nature in selected patients with PI, likely reflecting rupture of PI-associated intramural blebs (11). These observations create a dilemma for the surgeon in determining whether emergency surgery is indicated.

Several factors have been identified as poor prognostic indicators in affected patients, including the presence of metabolic acidosis, a high APACHE II score and a serum lactate level above 2.0 mmol/L (11). The most ominous prognostic factor described to date is the presence of portal venous gas, which is associated with a 91% rate of transmural bowel infarction and 72% mortality rate (2). The location of PI may also aid in identifying the need for surgical intervention. Higher rates of transmural infarction and mortality have been demonstrated in patients with PI of the small bowel (12).

Wayne et al. suggested an algorithm for the management of PI and prevention of unnecessary non-therapeutic laparotomy. In particular, they designed a vascular disease score which takes into account the individual’s vascular risk, consisting of the smoking history, presence of diabetes, hypertension and/or dyslipidemia and history of coronary or peripheral vascular disease, in addition to the detection of abdominal pain on a physical examination and lactic acidosis on laboratory tests. The positive and negative predictive values are calculated to be 100% and 96%, respectively (6).

Recent reports have shown an association between PI and the use of alpha-glucosidase inhibitors. The proposed mechanism underlying this phenomenon is the inhibition of absorption of carbohydrates by this group of drugs, thus allowing bacterial flora to utilize these components for fermentation, thereby producing gas. Moreover, the autonomic neuropathy noted in some diabetic patients promotes peristaltic dysfunction, subsequently elevating the intraluminal pressure and consequently enhancing the invasion of gas into the bowel wall (3). Autonomic neuropathy occurs in association with other complications of diabetes mellitus as well as retinopathy and nephropathy, both of which were present in our patient.

A review of the literature yielded over 30 case reports of PI associated with treatment with alpha glucosidase inhibitors, including acarbose, voglibose and miglitol. However, the current case is the first reported case of PI associated with pneumatoperitoneum and the accumulation of portal venous gas caused by an alpha glucosidase inhibitor. The reported interval between the onset of PI and the first use of
an alpha glucosidase inhibitor ranges between seven days and 12 years (13, 14).

An interesting fact is that nearly all cases of this condition have been reported in Japan. This may be attributed to the fact that approximately one-third of the Japanese diabetic population is prescribed alpha-glucosidase inhibitors, which are less popular in Western countries (15). In fact, prescriptions of these drugs in Japan account for 98% of total sales of voglibose and 34% of those for acarbose (3). Providing conservative treatment after discontinuing the alpha-glucosidase inhibitor generally leads to the complete resolution of PI within 28 days (16).

In this report, the initial presentation of our patient included diffuse abdominal pain in addition to lactic acidosis, and it was decided to proceed to exploratory laparotomy. Applying the score suggested by Wayne et al., bowel ischemia should have been strongly suspected, with an immediate indication for laparotomy. Surgery was likely unnecessary in this patient, although this could be inferred only in retrospect after he improved under conservative treatment. Since other diseases associated with PI were excluded and an objective improvement was noted after discontinuing the dose of acarbose, we had little doubt that the radiological findings in this case were related to treatment with acarbose. We hypothesize that the accumulation of gas in the intestinal tract resulted in PI, while the rupture of intramural blebs and transition of the gas into the portal vein led to the development of pneumoperitoneum and portal venous gas accumulation, respectively. To the best of our knowledge, this is the first report to document the complete resolution of symptoms with conservative treatment in the setting of portal venous gas accumulation in association with PI and pneumoperitoneum.

In conclusion, the case described above illustrates the fact that the presence of portal venous air, pneumoperitoneum and PI, should not be perceived as diagnoses, but rather radiological findings. The clinical presentation, physical examination findings, laboratory data and a thorough anamnesis should be integrated meticulously when determining the cause and therapeutic approach in these complicated cases.

It is important to ask the patient about their medical history of diabetes mellitus and alpha glucosidase inhibitor therapy, as the latter has been found to be associated with the development of PI.

The authors state that they have no Conflict of Interest (COI).

References


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