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Case Report

Pneumatosis Cystoides Intestinalis: Report of a New Case of a Patient with Arthropathy and Asthma

Abstract

Pneumatosis cystoides intestinalis (PCI) is an uncommon entity without the characteristics of a disease by itself and it is characterized by the presence of gas cysts within the submucosa or subserosa of the gastrointestinal tract. Its precise etiology has not been clearly established and several hypotheses have been postulated regarding the pathogenesis. Since it was first described by Du Vernoy in autopsy specimens in 1730 and subsequently named by Mayer as Cystoides intestinal pneumatosis in 1825, it has been reported in some studies. PCI is defined by physical or radiographic findings and it can be divided into a primary and secondary forms. In the first instance, no identifiable causal factors are detected whether secondary forms are associated with a wide spectrum of diseases, ranging from life-threatening to innocuous conditions. For this reason, PCI management can vary from urgent surgical procedure to clinical, conservative treatment. The clinical onset may be very heterogeneous and represent a challenge for the clinician. We report the case of a 54-year-old woman with PCI associated with arthropathy and asthma and a long-lasting steroid therapy. Our purpose is to underline the correlation of PCI with arthropathy and asthma. Moreover we would like to describe the difficulties to diagnose this entity, avoiding a misdiagnosis and therefore an incorrect therapy.

Introduction

Pneumatosis cystoides intestinalis (PCI) is an uncommon entity characterized by the presence of multiple gas cysts within the submucosa or subserosa of the gastrointestinal tract. The precise etiology has not been clearly established and several hypotheses have been postulated regarding its pathogenesis. It has been divided into two forms: primary or idiopathic and secondary to a wide spectrum of other diseases, ranging from life-threatening to innocuous conditions. The first pathologic description of PCI has been attributed to Du Vernoy, a French pathologist who described it during an autopsy dissection in 1730 [1]. Subsequently it was named by Mayer as Cystoides intestinal pneumatosis in 1825 and Gazin et al. [2], described the first clinical report in a patient who underwent surgery in 1946. The correlation to asthma has been described only in four papers [3-6]. No previous studies have ever hypothesized a possible association with arthropathies as in our case. This paper describes a case of PCI in a patient who suffered from arthropathy and asthma and had a long-lasting history of steroid therapy. Our purpose is to underline the possible correlation between the PCI and these diseases. We would like to stress the difficulties in the correct identification of PCI, avoiding a misdiagnosis and an incorrect therapeutic treatment. It

would be desirable to provide guidelines that summarize a multidisciplinary approach to PCI to support a decision-making process. It may help to reduce the rate of benign forms of PCI that are unnecessarily subjected to exploratory surgery, and to shorten the delay in surgical procedures for patients who would profit from early intervention, as in cases with acute complications such as bowel necrosis, perforation, peritonitis, intestinal occlusion and multiple comorbidities like in our case.

Results

A 54-year-old woman suffering from multiple and recurrent intestinal subocclusive episodes, presented to our hospital for severe, generalized abdominal pain, nausea, vomiting, and constipation, without episodes of melena and fever. For several decades her past medical history consisted of hypertension, hyperlipidemia, obesity correlated to hypothyroidism, asthma exacerbated by smoke and arthropathy with severe gonarthrosis. Due to the latter diseases, she had been taking a steroid daily therapy for several years (for asthma, inhaled budesonide: a dose of 160 mcg/day; for gonarthrosis, intraarticular *methylprednisolone* 120 mg/week). On physical examination, abdomen was distended with no bowel sounds and with a generalized pain upon palpation.

Test for fecal occult blood was negative. There was evidence of inflammation due to her abdominal symptoms and laboratory signs including elevated serum C-reactive protein levels (20 mg/dl; reference range: 0-0,5mg/dl) and leukocytosis (14×10^3 /ml; reference range: $3-9 \times 10^3$ /ml). Serum calcium (9,3 mg/dl; reference range: 8,80-10,20 mg/dl), kidney (creatinin: 0,8 mg/dl; reference range: 0,5-1,2 mg/dl) and liver function (ALT: 20U/L, reference range: 4-44U/L; AST: 22U/L, reference range: 8-38U/L) were normal. Computed tomography (CT) scan without intravenous contrast medium confirmed, at the splenic flexure, multiple air pockets consisting of isolated and clusters of bubbles thickening the intestinal wall. Moreover air-fluid levels were detected. At colonoscopy, several mucosal polypoid cystic bluish masses, 5 mm to 30 mm in diameter, were noted in the splenic flexure of the colon. These lesions were easily indented with gentle pressure and the overlying mucosa was soft and pinkish. Biopsies were not performed. The other colonic tracts were normal. Since the generalized peritonitis, after a multidisciplinary evaluation, the patient underwent laparoscopic left colectomy to avoid the risk of perforation. At gross examination, the surgical specimen showed numerous bubbles in the wall of the colon. They were single and in clusters and ranged from a few millimetres to 30 mm. in size (Figure 1). Microscopically, several cystic spaces were detected into the mucosa, submucosa and subserosa of the bowel wall. The cysts were partially lined by inflammatory cells including leukocytes, eosinophils, plasma cells, lymphocytes, foreign body cells and macrophages. In some portion of the cystic spaces no lining cells could be appreciated [Figure 2a,b]. Based on these morphological findings, histology was consistent with PCI. Moreover, a strong correlation with the long-lasting steroid therapy for arthropathy, severe gonarthrosis and asthma was suspected, inducing clinicians to decrease gradually the dose of drugs. The patients did not require any other specific treatment and she has remained asymptomatic for PCI since two years.

Conclusions

PCI is an uncommon entity, without the characteristics of a disease by itself, characterized by the following symptoms in decreasing order of frequency: diarrhea, abdominal pain, abdominal distension, bloody stool, constipation, weight loss, and tenesmus but many patients are asymptomatic [3,7]. These clinical presentation is caused by the presence of multiple gas-



Figure 1: Macroscopic appearance of surgical specimen showing the typical air bubbles along the entire colonic mucosa.

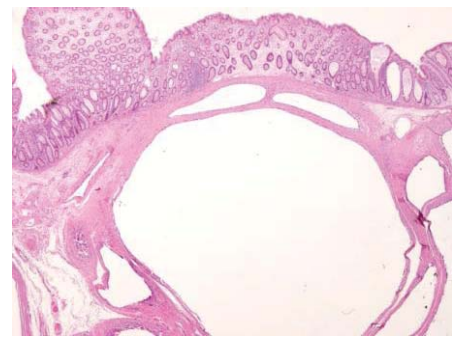


Figure 2a: Histological appearance: low power of Haematoxylin and Eosin stain showing variably sized cysts in the colonic wall.

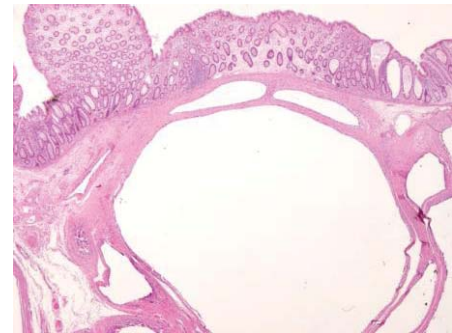


Figure 2b: Histological appearance: low power of Haematoxylin and Eosin stain showing typical macrophages and giant cells lining the cysts, filled of eosinophilic amorphous material or optically empty.

filled cysts within the submucosa or subserosa of the intestinal wall.

It can be divided into a primary or idiopathic (15%) form without identifiable factors and secondary (85%) when associated with predisposing factors [8].

In 1952, Koss observed that 15% of cases were primary or idiopathic PCI, while 75% were considered secondary PCI, and 10% had an unknown underlying disease. The majority of secondary PCI cases can be related to gastrointestinal disorders, followed by pulmonary, connective tissue, and hematological disease, immunosuppressed state, use of steroid and cytotoxic drugs [3,6,9-13]. PCI can also be observed in patients who undergo liver and bone marrow transplantation [14-15].

The most frequent site of involvement is the ileum, followed by the colon, even if in nearly 20% of cases both of them are affected. Recently the incidence of colonic involvement is increased due to the use of colonoscopy and barium enemas [8]. In our case, a tract of the large bowel was affected; while the small bowel was spared. From a radiological point of view, three patterns of PCI have been described: a bubble-like or cystoid (i.e. bubbles of gas with a cystic appearance), linear (i.e. curvilinear or crescent shape) and circular or circumferential. In some cases more than one pattern may be present.

Although the exact etiology of PCI remains obscure, clinicians believe that it has a multifactorial etiology that could explain the cyst formation and the abnormal accumulation of gas into them. Several theories have been suggested. The most

important theories are: mechanical, pulmonary, bacterial, chemical and lymphatic. The mechanical theory is thought to be due to increased intraluminal pressure causing the intramural accumulation of gas [16,17]. The pulmonary theory (pulmonary diseases, such as chronic obstructive pulmonary disease, asthma, and interstitial pneumonia) is explained by pulmonary alveolar rupture producing a pneumomediastinum that dissects along the aorta and then along the mesenteric vessels to the bowel wall. In the bacterial theory, the gas is produced by gas-forming bacteria that enter the mucosal barrier through mucosal rents or increased mucosal permeability and produce the gas within the bowel wall. Indirect support for this theory was obtained by the successful treatment of PCI with antibiotics. The chemical theory, named also as nutritional deficiency theory, underlines that malnutrition can prevent the digestion of carbohydrates and increase bacterial fermentation in the intestine, producing large volumes of gas with distention and ischemia that induce the submucosal dissection. Recently Gui X et al. [18], have supposed an association of cystic spaces in PCI with dilatation of the lymphatic structures. We hypothesize that more than one theory can explain the pathogenesis of PCI in our case. In fact, severe asthma caused an increase in the intraluminal pressure in the gastrointestinal tract and that the long-lasting administration of high doses of steroid drugs reduced the number of lymphocytes in the gastrointestinal wall, impairing the bowel defense barrier system and making the intestinal wall susceptible to mechanical injury or to bacterial infection (*i.e. Clostridium difficile*), with decreased bowel movements and excessive intraluminal air product. In general, the diagnosis of PCI is usually based on endoscopy or plain radiography of the abdomen showing typical radiolucency in the form of grape-like clusters or honeycomb-shaped shadows along the wall of the intestine. Therefore the identification of PCI is usually not difficult and, after that, a prompt further evaluation, including concomitant CT scan, of the patient should be conducted. The appropriate therapy is related to the underlying cause of PCI. If the symptoms are not important, clinicians allow a conservative approach, such as gastrointestinal decompression, intestinal “rest”, parenteral nutrition, fluid and electrolyte supplementation and antibiotics but the most efficient treatment seems to be a combined therapy. Surgery is reserved to patients who do not respond to medical therapy or who develop complication such as intestinal obstruction or in cases with precancerous conditions [19]. In the current case, surgery was the best choice of management because of the recurrent episodes of intestinal sub occlusion worsened by pre-existent comorbidities. The variety of treatments reflect the poor knowledge regarding the complications of this disease. In the last years, some authors [20-22], have suggested a decision making algorithm after a diagnosis of PCI based on clinical, laboratory and radiological findings to better differentiate management of primary and secondary PCI. At first the medical history of the patient and his/her current treatment must be deeply investigated in order to acquire a complete clinical picture: in particular pulmonary, gastrointestinal, autoimmune, infectious, pulmonary, iatrogenic, drug-induced, or transplantation-related conditions, should be inquired. A thorough survey about

currently used medications should be administered, focused on cytotoxic, immunosuppressive, or corticosteroid drugs, and the use of lactulose, sorbitol, or glucosidase inhibitors. During the physical examination, the extent of the abdominal complaint should be evaluated. The examination must include bowel sounds, any palpable resistance indicative of an abdominal mass, and signs of peritonism. Routine laboratory tests should be performed. After these procedures, combining anamnestic, clinical, instrumental and laboratory findings, Khalil et al. propose three treatment options: emergency surgery, clinical observation followed by later, complete re-evaluation, and medical treatment of the underlying disease [21]. Currently conservative management is recommended in most patients and surgery is usually indicated when acute and life-threatening complications such as bowel necrosis, perforation, peritonitis or acute intestinal occlusion occur [23]. A laparoscopically assisted approach is a good indication in cases of PCI that are unresponsive to standard conservative treatment as in our case. We hope that, within a well-coordinate multidisciplinary team work, a precise algorithm could be incorporated into management and treatment guidelines for PCI, considering that etiology of PCI is often multifactorial and it is difficult to identify a definite cause in patients with multiple comorbidities. In conclusion, the observation of this case allowed us to highlight some important learning points regarding the management of PCI and correlation to other pre-existing pathologies. Although PCI was first described in 1738, it is still a poorly understood entity and further studies are required.

References

1. Du Vernoy JG (1730) Aer intestinorum tam sub extima quam intima tunica inclusus: observationes anatomicae: comment. Acad Acient Imp Petropol 5: 213-225. [Link: https://goo.gl/MxJgW9](https://goo.gl/MxJgW9)
2. Gazin AI, Brooke WS, Lerner HH, Price PB (1949) Pneumatosis intestinalis: roentgen diagnosis and surgical management. Am J Surg 77: 563-572. [Link: https://goo.gl/E2WL1U](https://goo.gl/E2WL1U)
3. Choi JY, Cho SB, Kim HH, Lee IH, Lee HY, et al. (2014) Pneumatosis intestinalis complicated by pneumoperitoneum in a patient with asthma. Tuberc Respir Dis 77: 219-222. [Link: https://goo.gl/RtMHZG](https://goo.gl/RtMHZG)
4. Culver GJ (1963) Pneumatosis intestinalis with associated retroperitoneal air. Report of a complication of severe asma. JAMA 186: 160-162. [Link: https://goo.gl/Rp3Dkt](https://goo.gl/Rp3Dkt)
5. Appere-De Vecchi C, De Jonghe B, Santoli F, Louboutin A, Outin H (2001) Severe acute asthma with bowel infarction and pneumatosis intestinalis in a young adult. J Asthma 38: 215-219. [Link: https://goo.gl/ldZDDE](https://goo.gl/ldZDDE)
6. Ezuka A, Kawana K, Nagase H, Takahashi H, Nakajima A (2013) Improvement of pneumatosis cystoides intestinalis after steroid tapering in a patient with bronchial asthma: a case report. J Med Case Rep 7: 163. [Link: https://goo.gl/l5E8YF](https://goo.gl/l5E8YF)
7. Jamart J (1979) Pneumatosis cystoides intestinalis. A statistical study of 919 cases. Acta Hepatogastroenterol 26: 419-422. [Link: https://goo.gl/N7sGst](https://goo.gl/N7sGst)
8. Hanna P, Kassir R, Tarek D, Bassile B, Saint-Eve P, et al. (2016) Pneumatosis cystoidis intestinalis presenting as bowel perforation, a rare entity. Int J Surg Case Rep 20: 7-9. [Link: https://goo.gl/tqYjkk](https://goo.gl/tqYjkk)

9. Koss LG (1952) Abdominal gas cysts (pneumatosis cystoides intestinorum hominis). An analysis with a report of a case and a critical review of the literature. *AMA Arch Pathol* 53: 523-549. [Link: https://goo.gl/8wLdNg](https://goo.gl/8wLdNg)
10. Doumit M, Saloojee N, Seppala R (2008) Pneumatosis intestinalis in a patient with chronic bronchiectasis. *Can J Gastroenterol* 22: 847-850. [Link: https://goo.gl/g8FDKK](https://goo.gl/g8FDKK)
11. Groninger E, Hulscher JB, Timmer B, Tamminga RY, Broens PM (2010) Free air intraperitoneally during chemotherapy for acute lymphoblastic leukemia: consider pneumatosis cystoides intestinalis. *J Pediatr Hematol Oncol* 32: 141-143. [Link: https://goo.gl/VXXO4K](https://goo.gl/VXXO4K)
12. Vendryes C, Hunter CJ, Harlan SR, Ford HR, Stein J, et al. (2011) Pneumatosis intestinalis after laparoscopic appendectomy: case report and review of the literature. *J Pediatr Surg* 46: e21-e24. [Link: https://goo.gl/F7tOBt](https://goo.gl/F7tOBt)
13. Khalid F, Kaiyasa H, Binfadil W, Majid M, Hazim W, et al. (2016) Pneumatosis intestinalis due to gastrointestinal amyloidosis: A case report & review of literature. *Int J Surg Case Rep* 23: 29-32. [Link: https://goo.gl/3QHDTz](https://goo.gl/3QHDTz)
14. Park CS, Hwang S, Jung DH, Song GW, Moon DB, et al. (2015) Pneumatosis intestinalis after adult living donor liver transplantation: report of three cases and collective literature review. *Korean J Hepatobiliary Pancreat Surg* 19: 25-29. [Link: https://goo.gl/X8jDO1](https://goo.gl/X8jDO1)
15. Galm O, Fabry U, Adam G, Osieka R (2001) Pneumatosis intestinalis following cytotoxic or immunosuppressive treatment. *Digestion* 64: 128-132. [Link: https://goo.gl/frmBsC](https://goo.gl/frmBsC)
16. Nancy Fu YT, Kim E, Bressler B (2013) Pneumatosis intestinalis after colonoscopy in a Crohn's disease patient with mucosal healing. *Inflamm Bowel Dis* 19: E7-E8. [Link: https://goo.gl/LcEROU](https://goo.gl/LcEROU)
17. Wertkin MG, Wetchler BB, Wayne JD, Brown LK (1976) Pneumatosis coli associated with sigmoid volvulus and colonoscopy. *Am J Gastroenterol* 65: 209-214. [Link: https://goo.gl/llJLJj](https://goo.gl/llJLJj)
18. Gui X, Zhou Y, Eidus L, Falck V, Gao Z, et al. (2014) Is Pneumatosis Cystoides Intestinalis Gas-Distended and Ruptured Lymphatics? Reappraisal by Immunohistochemistry. *Arch Pathol Lab Med* 138: 1059-1066. [Link: https://goo.gl/wjZk7U](https://goo.gl/wjZk7U)
19. Zhang H, Jun SL, Brennan TV (2012) Pneumatosis intestinalis: not always a surgical indication. *Case Rep Surg* 2012: 719713. [Link: https://goo.gl/z3WZmL](https://goo.gl/z3WZmL)
20. Tahiri M, Levy J, Alzaid S, Anderson D (2015) An approach to pneumatosis intestinalis: Factors affecting your management. *Int J Surg Case Rep* 6C: 133-137. [Link: https://goo.gl/sLKICF](https://goo.gl/sLKICF)
21. Khalil PN, Huber-Wagner S, Ladurner R, Kleespies A, Siebeck M, et al. (2009) Natural history, clinical pattern, and surgical considerations of pneumatosis intestinalis. *Eur J Med Res* 14: 231-239. [Link: https://goo.gl/Q7IfIs](https://goo.gl/Q7IfIs)
22. Greenstein AJ, Nguyen SQ, Berlin A, et al. (2007) Pneumatosis intestinalis in adults: management, surgical indications, and risk factors for mortality. *Journal of Gastrointestinal Surgery* 11: 1268-1274. [Link: https://goo.gl/N5myM9](https://goo.gl/N5myM9)
23. Gassend JL, Dimitrief M, Roulet D, Cherbanyk F (2016) Large bowel pneumatosis intestinalis: to operate or not to operate? *BMJ Case Rep* 1:2. [Link: https://goo.gl/4dUYdF](https://goo.gl/4dUYdF)