Pneumatosis Intestinalis With a Focus on Hyperbaric Oxygen Therapy

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Abstract

Pneumatosis intestinalis is a rare condition of air in the bowel wall. Pneumatosis intestinalis is most often secondary to another medical condition. The diagnosis is most often made radiologically with a computed tomography scan. The disease severity ranges from benign to life-threatening. Predictors of poor outcomes include pH less than 7.3, bicarbonate level of less than 20 mEq/L, lactate level of more than 2 mmol/L, and portal venous gas on imaging. Early recognition of life-threatening pneumatosis intestinalis is critical. Treatment options include bowel rest, antibiotics, surgery, and, more recently, the use of hyperbaric oxygen therapy. Hyperbaric oxygen therapy is extremely safe, and no reported complications in the literature when used for pneumatosis intestinalis. When surgery is not emergently needed, symptomatic pneumatosis intestinalis can be safely treated with hyperbaric oxygen with a high likelihood of success without any considerable adverse effects.

BACKGROUND AND EPIDEMIOLOGY

Pneumatosis intestinalis (PI) is defined as the imaging finding of air dissection into the bowel wall. Pneumatosis intestinalis is usually a sign of an underlying condition rather than a disease itself. It was first described by Duò Vernoi in 1730 and later subcategorized by Koss in 1952. A number of synonyms for PI have been used in the literature, including pneumatosis intestinalis cystoides, cystic lymphopneumatosis, peritoneal lymphopneumatosis, intestinal emphysema, bullous emphysema of the intestines, pneumatocele, pseudolipomatosis, gas cysts of the intestines, and intraluminal gas. For this review, we refer to it only as pneumatosis intestinalis. Pneumatosis intestinalis can occur in any age group: from neonates to the elderly. There is no gender predominance. The exact incidence of PI is unknown because most patients with PI are asymptomatic. An autopsy series reported...
an incidence of 0.03% in the general population. It can occur anywhere within the gastrointestinal tract from the esophagus to the rectum but frequently occurs in the intestine. A study by Jamart in 1979 localized PI to the small intestine in 42% of the cases, the large intestine in 36% of the cases, and both in 22% of the cases. Pneumatosis intestinalis is most often found incidentally in asymptomatic patients during routine imaging studies. Although some cases of PI are benign, other cases portend life-threatening illness including bowel necrosis and perforation.

Pneumatosis intestinalis is categorized as primary/idiopathic (15% of the cases) or secondary (85% of the cases) on the basis of prognosis, radiographic appearance, and the absence or presence of underlying disease. Radiologically, primary or idiopathic PI refers to air collections that are cystic in appearance and implies a chronic, benign idiopathic etiology. Secondary PI refers to radiologic findings of linear, microvesicular, or more circumferential appearing intramural gas and is associated with various associated diseases with a range of severity.

**PATHOPHYSIOLOGY**

The 2 main pathophysiologic explanations for PI are based on mechanical vs infectious processes. The mechanical theory suggests that PI results from increased intraluminal pressure that forces air into the bowel wall via mucosal defects. Supporting this theory is the association of PI with trauma, surgery, endoscopy, and bowel obstruction. Similarly, in pulmonary disease such as chronic obstructive pulmonary disease, it is theorized that ruptured alveoli propel dissection of air into the bowel wall. However, there are shortcomings to a purely mechanical explanation for PI, and several observations implicate an alternate, infection-based account. The infectious theory postulates that PI results from cysts formed by gas-producing organisms. The notably elevated hydrogen content in the intraluminal cysts is not explained by a mechanical theory alone, but hydrogen gas is a byproduct of bacteria. Furthermore, the injection of clostridium into the bowel wall in guinea pigs produces pneumatosis, but injection of air or saline alone does not. However, bacteria are rarely cultured from cystic spaces, and patients with PI frequently lack clinical signs and symptoms of infection such as fever or peritonitis.

A combined hypothesis proposes that PI develops from a synergism of mechanical and infectious processes; increased intraluminal pressure forces anaerobic organisms (or the gas they produce) into the bowel wall via mucosal defects.

**DIAGNOSIS, ETIOLOGY, AND COMPLICATIONS**

**Clinical Symptoms**

Most patients with PI are asymptomatic. When present, symptoms may vary on the basis of the location of PI but include nausea, emesis, abdominal pain, diarrhea, abdominal distension, constipation, bloody stool, flatus, loss of appetite, weight loss, and tenesmus.

**Diagnosis**

Given the diversity of clinical presentation, the diagnosis of PI is radiologic. A computed tomography scan is the most sensitive imaging modality for detection and is prognostically useful when radiographic signs such as hepatoportal and portomesenteric venous gas are present. Both these findings portend a deleterious outcome. A study by Lee et al comparing CT findings in benign vs increased mortality PI noted that the presence of portomesenteric venous gas (P=.02), bowel dilatation (P=.004), bowel wall thickening (P<.001), ascites (P<.001), and peri-intestinal mesenteric stranding (P<.001) were all significantly associated with increased mortality PI. Plain radiography can detect PI, which appears as a radiolucency in the walls of the gastrointestinal tract. Pneumatosis intestinalis can also be detected on barium enemas as filling defects in contrast columns or linear delineations along the margins. Ultrasound may show linear or focal echogenic areas or a continuous echogenic ring within the bowel walls. Magnetic resonance imaging is infrequently used but can depict PI on gradient-echo images. In rare cases, cysts can be visualized endoscopically as polyps or submucosal tumors that release gas on biopsy. Evaluation with endoscopic ultrasonography can be helpful in diagnosing PI endoscopically.

**Associated Disease and Causes**

There are multiple diseases associated with PI (Table). The most common causes are related to gastrointestinal diseases, pulmonary diseases, rheumatologic diseases,
infectious diseases, medication-related diseases, and traumatic diseases secondary to endoscopic or surgical procedures.2,4,7,15,72

Laboratory Testing
Laboratory abnormalities are usually the result of the underlying disease causing the PI. Certain laboratory derangements are associated with poor outcomes. Clinical predictors of bowel necrosis and/or mortality in patients with PI include the following: pH less than 7.3, bicarbonate level of less than 20 mEq/L, lactate level of more than 2 mmol/L, amylase level of more than 200 U/L, and laboratory test results consistent with disseminated intravascular coagulation (prolonged prothrombin time, activated thromboplastin time, decreased fibrinogen level, elevated fibrinogen degradation products, and an elevated d-dimer level).3,8,34 Common laboratory markers such as white blood cell count, alanine aminotransferase, aspartate aminotransferase, and alkaline phosphatase have not demonstrated predictive efficacy for the presence of necrotic bowel or likelihood of survival.3,8

Complications
Complications are infrequent, occurring in approximately 3% of the cases. However, when complications occur, they are often life-threatening.73 Intestinal ischemia and perforation is the most feared complication and usually results in death if emergent surgery is not performed. Other complications include obstruction or volvulus related to large cysts compressing the bowel lumen or due to adhesions induced by the cysts. Less common complications include pneumoperitoneum, peritonitis, intussusception, and hemorrhage.2,72

TREATMENT

Medical Management
Patients who are asymptomatic or mildly symptomatic can be observed closely.33 Various nonsurgical treatment options have been attempted with varying success. Treatments include antibiotics, octreotide, metoclopramide, erythromycin, bowel rest, high flow oxygen, and hyperbaric oxygen (HBO) therapy. Antibiotics are used to target possible intraluminal bacteria, thereby reducing anaerobic production of hydrogen gas.23,72 Metronidazole has the largest use, although only a small body of evidence support its use.74,75 Treatment usually continues until documented resolution of the PI. Similarly, bowel rest is often recommended to decrease the available substrates for bacteria,33 and, likewise, an elemental diet has also been associated with the resolution of PI.76 However, elemental diets are not always well tolerated. Theoretically, hypomotility may increase intraluminal pressure and worsen PI. Accordingly,

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**TABLE. Causes of Pneumatosis Intestinalis**

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case reports document investigative therapy with octreotide or promotility agents, metoclopramide, and erythromycin, though data are limited.30

**Surgical Management**

Early surgical intervention should be considered in any patient with signs of perforation or predictors of poor outcomes.8 Any patient with laboratory abnormalities predictive of necrosis and mortality including a pH of less than 7.3, bicarbonate level of less than 20 mEq/L, lactate level of more than 2 mmol/L, amylase level of more than 200 U/L, or signs of disseminated intravascular coagulation should undergo emergent surgery. Similarly, patients who are immunosuppressed with underlying liver disease, sepsis, and hypotension are all at a higher risk of mortality from PI.34 Radiologically, the presence of portal venous gas is highly indicative of severe disease, and when present, mortality rates range from 37% to 75%.3,8,28,34 Other radiologic predictors of mortality include thickened or dilated bowel, peri-intestinal mesenteric stranding, ascites, and in some studies, the linear appearance of PI is associated with transmural bowel ischemia.3,8,15,16 Surgical intervention is particularly successful for pneumatosus in the setting of gastrointestinal tumors, underlying bowel obstruction, or bowel ischemia.3,8 Unfortunately, patients with these predictors of mortality are often poor surgical candidates.

**Oxygen Therapy, HBO Therapy and High Flow Oxygen Therapy**

Oxygen therapy has long been recognized as an effective therapy for PI, leading to cyst regression on imaging and symptom resolution.74 Forgacs et al13 in 1973 first demonstrated the successful use of high-concentration atmospheric oxygen therapy to treat PI. However, these patients required an arterial oxygen tension of 200 to 300 mm Hg. This was achieved only with a cumbersome close-fitting mask that had to be worn for 5 h/d for 7 days.77 In 1978, Masterson et al12 used HBO therapy for the treatment of PI. Hyperbaric oxygen therapy reduced the duration of oxygen exposure and the risk of toxicity.12 Hyperbaric oxygen therapy increases arterial oxygen tension, which forces oxygen into the hydrogen-containing cysts by diffusion from areas of high oxygen tension in the artery to low oxygen tension in the hydrogen-containing cyst. In turn, oxygen accumulating in the cysts increases the partial pressure of hydrogen in the cysts, which causes hydrogen to diffuse out of the high-pressure cyst into the low-hydrogen bloodstream.11-13,33,75 Cyst resolution follows as the oxygen leaves the cyst via reabsorption for use in cellular metabolism. In addition, increased tissue oxygenation from HBO may facilitate phagocytic activity and directly target the gas-producing organisms via anaerobic impairment.20,22,74

A number of case reports have been published supporting the efficacy of HBO. Shimada et al22 reviewed 15 cases of PI treated with HBO in the Japanese literature. In these cases, PI was secondary to asthma, trichlorethylene exposure, colon cancer, polymyositis, systemic lupus erythematosus, Sjögren syndrome, systemic sclerosis, and chronic idiopathic intestinal pseudo-obstruction.22 Most (11 of 15) of the case reports involved PI of the colon, most commonly the sigmoid colon. The standard treatment was HBO 2 to 3 atmospheres absolute (ATA) for 60 to 120 min/d. Treatment duration ranged from 3 to 33 days. Pneumatosis intestinals resolved in 11 patients and improved in the other 4 patients with no serious adverse effects in any patient. Recurrence of gaseous cysts occurred in 1 patient 9 months after treatment.22 Another case series in the Japanese literature by Togawa et al33 in 2004 reviewed 7 patients with PI using HBO and 20 patients using 1 ATA oxygen (non-HBO).33 Patients receiving 1 ATA oxygen had treatments ranging from 1 to 35 days (mean 14.6 days). In contrast, among the 7 patients who received HBO treatment, the duration was much shorter, ranging from 1 to 8 days (mean 4.7 days).33

There are no randomized controlled trials using HBO therapy in the treatment of PI given the rarity and potential severity of this entity. In review of the literature, there are 35 illustrative cases from the literature in which HBO therapy was successfully used in patients ranging in age from 10 months to 86 years.12,18,20,21,24-29,31-33,73,76,79-85 There were no reported complications. Initial resolution or improvement in symptoms was achieved in 31 of 35 (89%) patients. The overall ATA level, treatment time, and overall duration of treatments were variable among the case reports.

Given the safety and efficacy of HBO in the available case report literature, HBO may
be considered as a reasonable alternative to antibiotic therapy for PI, particularly when demonstrable evidence of infection is lacking. Although there are no controlled data addressing the efficacy of antibiotics, prolonged use of antibiotics is associated with multiple complications and adverse events. The Figure shows a treatment algorithm for patients presenting with PI.

CONCLUSION

Pneumatosis intestinalis is a rare condition that may be idiopathic or a sign of an underlying systemic disease. Given the potential severity of PI, early recognition of this condition is critical because delayed diagnosis may result in death. Treatment for symptomatic PI may include bowel rest, cessation of instigating medications, antibiotic therapy, surgery, and/or hyperbaric oxygen. Hyperbaric oxygen therapy appears to be a safe and effective means to treat PI, regularly achieving sustained improvement with limited adverse effects. Future studies are needed to determine the optimal ATA level, treatment time, and overall duration of therapy.

ACKNOWLEDGMENTS

Drs Feuerstein and White contributed equally to this work.

Abbreviations and Acronyms: ATA = atmospheres absolute; HBO = hyperbaric oxygen; PI = pneumatisos intestinalis

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REFERENCES


FIGURE. Treatment algorithm for pneumatisos intestinalis. ATA = atmospheres absolute; PVG = portal venous gas.


