CASE REPORT

Successful treatment of pneumatosis intestinalis with associated pneumoperitoneum and ileus with hyperbaric oxygen therapy

Evan Calabrese,¹ Peter JM Ceponis,² Bruce J Derrick,² Richard E Moon^{2,3}

¹Center for In Vivo Microscopy, Duke University, Durham, North Carolina, USA

²Center for Hyperbaric Medicine, Duke University, Durham, North Carolina, USA

³Department of Anesthesia, Duke University Medical Center, Durham, North Carolina, USA

Correspondence to

Dr Evan Calabrese,
edc15@duke.edu

Accepted 17 May 2017

SUMMARY

Pneumatosis intestinalis (PI), or the presence of air in the bowel wall, is a rare disorder that is associated with a variety of underlying diseases, including connective tissue disorders. PI presents on a spectrum from asymptomatic to bowel obstruction and acute abdomen. In general, treatment of PI consists of treating the underlying disease. Both normobaric and hyperbaric oxygen have been used to treat PI directly. Here we report a symptomatic scleroderma-related case of PI that responded clinically to hyperbaric oxygen therapy. This report adds to a growing body of literature supporting a role for hyperbaric oxygen therapy in symptomatic PI.

BACKGROUND

Pneumatosis intestinalis (PI) is a rare disorder characterised by the presence of gas in the bowel wall.^{1–3} This condition and its variants, termed pneumatosis intestinalis cystoides, intestinal emphysema, bullous emphysema, pneumatosis coli and lymphoneumatosis, may occur anywhere along the gastrointestinal tract in patients of all ages.^{3,4} PI can manifest as either a primary condition, or secondary to an underlying problem, such as gastrointestinal disorders, infection, ischaemia, pulmonary disease, rheumatological disorders or medication effects.^{3–5} The pathogenesis of PI is not well understood, but bacterial, mechanical, gaseous and nutritional factors are proposed.^{3–8} The fact that many different systemic conditions are associated with PI suggests a multifactorial pathogenesis, which may differ based on the condition.

Patients with incidental PI findings may be asymptomatic. Otherwise, nausea, vomiting, abdominal distension, constipation, diarrhoea, pain or inability to tolerate oral intake are possible symptoms.^{2,3} Severe cases can manifest gastrointestinal bleeding, bowel obstruction, peritonitis and associated systemic symptoms. The diagnosis of PI is typically made with abdominal radiographs or CT and, less commonly, abdominal ultrasound.⁶ Findings include intramural radiolucent gas collections in the bowel wall, luminal distension and pneumoperitoneum, although the significance of the latter is a matter of debate.^{2,3,6,9,10}

Identification of PI on radiography mandates a thorough investigation for an associated condition. Consideration of life-threatening causes, such as intestinal ischaemia/infarction, is particularly

important. Early evaluation for associated conditions helps identify potentially fatal complications and guides therapy for managing the underlying disease.

Treatment options for PI are limited. Medical management includes bowel rest, antibiotics, parenteral feeding and treatment of the underlying disease process. Surgical intervention may be necessary in the setting of an acute abdomen or failure of medical management. Both normobaric^{11,12} and hyperbaric oxygen (HBO₂)¹³ therapies have been used to treat PI not responding to conservative measures.^{3,14} Cases documenting the effective use of HBO₂ therapy for PI have been published and are the subject of a recent review.³ Here we present a case of PI complicated by ileus and pneumoperitoneum in a patient with underlying scleroderma. Clinical improvement occurred shortly after initiation of HBO₂ therapy, providing further evidence that HBO₂ therapy may be beneficial for treating PI.

CASE PRESENTATION

A female patient in her late 60s presented to a scheduled outpatient clinic appointment for evaluation of a possible connective tissue disease in the setting of a chronic pericardial effusion. Positive serologies included elevated antinuclear antibody titre $\geq 1:2560$ and antimitochondrial antibodies at 1:160. Remaining serologies were negative (rheumatoid factor; anti-scl70, antithyroglobulin, anti-dsDNA, anticardiolipin, anti-ribonucleoprotein(RNP), anti-smith(sm), anti-Ro and anti-La). Medical history included hypertension, type 2 diabetes mellitus, gastro-oesophageal reflux disease, Raynaud's phenomenon and chronic rectal prolapse repaired by complete proctectomy and colostomy. In the clinic visit, the patient described progressive dyspnoea over weeks, as well as increasing nausea, vomiting, abdominal distension and inability to tolerate oral intake in the preceding days. Normal tolerance to fluids and solid food had progressed to vomiting and infrequent sips of water. She denied fevers, chills, night sweats, weight loss, but endorsed decreased ostomy output. Her condition prompted immediate referral to an emergency department (ED) for evaluation. Physical exam in the ED revealed a non-tender but distended, tympanic abdomen with present bowel sounds and no fluid wave. Pertinent investigations were abdominal CT (figure 1) and plain radiographs (figure 2C)

CrossMark

To cite: Calabrese E, Ceponis PJM, Derrick BJ, et al. *BMJ Case Rep* Published Online First: [please include Day Month Year]. doi:10.1136/bcr-2017-219209

Figure 1 CT scan (coronal reformat) of the patient prior to hyperbaric oxygen therapy. White arrows indicate pneumatosis intestinalis — pockets of air tracking within the bowel wall. An asterisk marks the patient's chronic pericardial effusion.

revealing extensive PI, small volume pneumoperitoneum and moderately distended loops of the small bowel thought to represent a developing ileus. The patient was admitted to the hospital with a working diagnosis of scleroderma with associated pericardial effusion and secondary PI.

Her early hospital course was notable for inability to tolerate oral intake, increasing abdominal distension and obstipation with reduced ostomy output. A surgical consult on hospital day 4 recommended serial abdominal exams and conservative management. Despite intravenous hydration and elimination of oral intake, serial abdominal exam revealed increasing non-tender abdominal distension with absent bowel sounds (figure 2A). Serial abdominal radiographs again revealed dilated loops of bowel, multiple air-fluid levels and persistent PI.

TREATMENT

Metronidazole 500 mg intravenously every 8 hours was initiated on hospital day 6, and methylprednisolone 10 mg intravenously daily was started on hospital day 8. On hospital day 10, there was complete cessation of ostomy output, and total parenteral nutrition (TPN) was initiated. By hospital day 14, with no improvement in symptoms, the hyperbaric medicine service was consulted. Given the patient's lack of improvement thus far in her hospital course, the patient's high risk of morbidity and mortality, and the relatively low risk of treatment with case reports documenting potential benefit, the decision was made to initiate a trial of HBO₂ therapy. Daily HBO₂ therapy was conducted in a multiplace chamber at 2 atmospheres absolute (ATA) for 2 hours per session once daily on hospital days 15–17.

Figure 2 Photographs (A,B) and plain radiographs (C,D) of the patient before (A,C) and after (B,D) hyperbaric oxygen therapy. Magnified insets of the intestinal wall are included for both radiographs (C,D). Both abdominal distension and radiographical pneumatosis intestinalis were markedly reduced after treatment. Maximum abdominal circumference decreased from 111.5 cm to 102 cm after three hyperbaric oxygen treatments.

OUTCOME AND FOLLOW-UP

The patient tolerated HBO₂ well aside from mild bilateral otic barotrauma during the first treatment. After three HBO₂ sessions, the patient's symptoms had markedly improved such that abdominal distension was diminished from a circumference of 111.5 cm to 102 cm (figure 2B). At this point, the patient was able to tolerate a level 3 National Dysphagia Diet, TPN was discontinued and ostomy output had resumed. Radiography revealed a markedly reduced PI gas pattern and decreased distension of bowel loops (figure 2D). On hospital day 20 she was discharged to a skilled nursing facility.

DISCUSSION

Here we report an autoimmune-related case of PI that responded clinically to HBO₂ therapy, further supporting the conclusions of a recent review.³

Like a small number of previous reports, the PI in this case was felt to be secondary to scleroderma.^{15–19} However, our patient differs both in her severity of symptoms and in the rapid resolution of symptoms after only a few HBO₂ sessions. For example, PI cases in patients with scleroderma described by Togawa *et al* required 5 and 8 HBO₂ treatments for full symptomatic relief, respectively, with the latter patient requiring ongoing TPN. Shimada *et al*²⁰ treated a patient with PI twice daily for 30 days, and achieved clinical and endoscopic resolution of the lesions. They also reviewed the Japanese literature on patients with PI with different underlying diseases, revealing a range of 3–60 HBO₂ treatments leading to improvement or resolution in 15/15 patients with one documented recurrence.²⁰ Frossard *et al*²¹ administered 17 treatments to a patient with non-scleroderma PI, including multiple Comex 30 hyperbaric treatments (50:50 heliox gas mixture) typically reserved for severe decompression illness.²² There is also a case report of pneumatosis coli and diarrhoea resolving after an 8-week tapering regimen of HBO₂ therapy.²³ Ongoing resolution of bowel wall gas cysts in PI after HBO₂ therapy is documented for 6 months to 9 years after HBO₂, although immediate recurrence is also documented.^{21 24} In one case report of postoperative PI following emergent laparotomy with ileostomy, a single HBO₂ session was sufficient to resolve symptoms.²⁵

Our patient was able to restart oral feeds and discontinue TPN, central venous access, nasogastric tube and the mobility restrictions imposed by these interventions shortly after completion of only three HBO₂ treatments. Confounders in defining a precise role for HBO₂ in our patient were concurrent treatment with methylprednisolone and metronidazole, as they can both treat PI symptoms.^{3 26 27} However, metronidazole has been reported to resolve symptoms in 1–5 days,^{28 29} while our patient did not improve until 11 days on this drug. Whether antibiotics have less efficacy in scleroderma-associated PI or improved effect with HBO₂ are unknown. The potential effect of methylprednisolone in this case is less clear, particularly at the low dose (10 mg/day) and because PI may be more likely to occur in patients with collagen vascular disorder on corticosteroid therapy.^{3 15 19}

HBO₂ therapy likely addresses some of the underlying pathophysiological mechanisms of PI. The gaseous lesions found in PI contain hydrogen produced by bacteria, and nitrogen. A possible mechanism for gas accumulation is counterdiffusion of these gases between the bowel lumen and capillary, allowing supersaturation of the bowel wall or mesentery with hydrogen.^{12 30–33} HBO₂ therapy effectively reduces the volume of various gas-filled body cavities,³⁴ related to the oxygen window, or the difference between arterial and tissue oxygen partial pressures. This

difference in partial pressure promotes diffusion of oxygen into the gas-filled cavities. Oxygen within the cavity is metabolised while hydrogen moves out of the cavity by diffusion. This process occurs more effectively with the greater diffusion gradients created by HBO₂ therapy as compared with normobaric oxygen. Typically, the bowel relies on coordinated stretch to regulate peristalsis.^{35 36} Distension of both the bowel lumen and the wall may disrupt this coordinated stretch process and alter bowel motility, but by removing luminal and bowel wall gas, HBO₂ therapy may help return bowel stretch closer to physiological parameters.

While identifying the underlying cause of PI is clearly important for both prognostic and therapeutic reasons, it is unclear how, or if, it affects response to HBO₂ therapy. The case report literature includes successful HBO₂ treatment of PI associated with several different conditions, including ischaemia, infection and rheumatological disease.^{15–21 23} This suggests that HBO₂ therapy may be effective regardless of underlying cause. In this case, HBO₂ was successful in treating PI that was most likely related to the patient's underlying connective tissue disease, as there was no evidence of other associated conditions.

No consensus guideline for treatment of PI is available. Togawa *et al*¹⁸ proposed the use of normobaric or hyperbaric oxygen in patients with symptomatic PI without peritonitis. Tahiri *et al*³⁷ suggested a treatment algorithm based on clinical, laboratory and imaging results, and considered HBO₂ therapy as appropriate in the absence of indications for surgery. A recent review of PI also proposed an algorithmic approach, advocating HBO₂ therapy at 2.5 ATA for 2 hours for at least three sessions in patients with symptomatic, 'non-alarming' PI.³ A large multi-centre retrospective trial yielded a clinical prediction rule that elevated lactate level with either hypotension/vasopressor requirement or peritonitis was associated with worse outcomes, but did not comment on intervention with HBO₂ therapy.³⁸ We propose that HBO₂ may be beneficial in PI when there is clinical deterioration, including inability to tolerate PO intake, leucocytosis and elevated lactate,³⁹ or imaging findings of portomesenteric venous gas, bowel dilatation, bowel wall thickening, ascites or mesenteric stranding.^{6 40} In the present case, three HBO₂ sessions at 2 ATA for 2 hours was sufficient to hasten recovery and hospital discharge after other conservative therapies failed to produce observable improvement.

Learning points

- ▶ Hyperbaric oxygen (HBO₂) therapy should be considered for moderate to severe pneumatosis intestinalis (PI) failing medical management and may be warranted prior to surgical intervention.
- ▶ A rigorously designed, randomised, controlled, double-blinded prospective trial would more conclusively define a role for HBO₂ in this disease.
- ▶ Unfortunately, such a trial is unlikely to occur given the rarity of PI and the limited access to hyperbaric oxygen facilities. As such, the case report literature remains a valuable source of treatment guidance for symptomatic cases of PI.

Contributors EC and PC performed literature review. EC wrote the manuscript and made the figures. PC, BD and RM each provided guidance, edited the manuscript and contributed to revisions.

Competing interests None declared.

Patient consent The patient did personally agree and provide written consent to publish this report (consent form provided); however, consent was not obtained using the BMJ consent form. Prior to submission we attempted to contact the patient

to sign the BMJ form; however, we unfortunately learned that she had passed away from unrelated causes. Attempts to contact family were unsuccessful.

Provenance and peer review Not commissioned; externally peer reviewed.

© BMJ Publishing Group Ltd (unless otherwise stated in the text of the article) 2017. All rights reserved. No commercial use is permitted unless otherwise expressly granted.

REFERENCES

- Jamart J. Pneumatosis cystoides intestinalis. A statistical study of 919 cases. *Acta Hepatogastroenterol* 1979;26:419–22.
- Heng Y, Schuffler MD, Haggitt RC, et al. Pneumatosis intestinalis: a review. *Am J Gastroenterol* 1995;90:1747–58.
- Feuerstein JD, White N, Berzin TM. Pneumatosis intestinalis with a focus on hyperbaric oxygen therapy. *Mayo Clin Proc* 2014;89:697–703.
- Boerner RM, Fried DB, Warshauer DM, et al. Pneumatosis intestinalis. two case reports and a retrospective review of the literature from 1985 to 1995. *Dig Dis Sci* 1996;41:2272–85.
- Lock G, Holstege A, Lang B, et al. Gastrointestinal manifestations of progressive systemic sclerosis. *Am J Gastroenterol* 1997;92:763–71.
- Lassandro F, Valente T, Rea G, et al. Imaging assessment and clinical significance of pneumatosis in adult patients. *Radiol Med* 2015;120:96–104.
- Yale CE, Balish E, Wu JP, JP W. The bacterial etiology of pneumatosis cystoides intestinalis. *Arch Surg* 1974;109:89–94.
- Wu LL, Yang YS, Dou Y, et al. A systematic analysis of pneumatosis cystoides intestinalis. *World J Gastroenterol* 2013;19:4973–8.
- Knechtle SJ, Davidoff AM, Rice RP. Pneumatosis intestinalis. Surgical management and clinical outcome. *Ann Surg* 1990;212:160–5.
- Ooi SM, Sms O. Pneumoperitoneum in a non-acute abdomen-pneumatosis cystoides intestinalis. *Surg Case Rep* 2015;1:44.
- Forgacs P, Wright PH, Wyatt AP. Resolution of pneumocystic disease of the Colon with oxygen therapy. *Proc R Soc Med* 1973;66:687.
- Forgacs P, Wright PH, Wyatt AP. Treatment of intestinal gas cysts by oxygen breathing. *Lancet* 1973;1:579–82.
- Masterson JS, Frarkin LB, Osler TR, et al. Treatment of pneumatosis cystoides intestinalis with hyperbaric oxygen. *Ann Surg* 1978;187:245–7.
- Wyatt AP. Prolonged symptomatic and radiological remission of colonic gas cysts after oxygen therapy. *Br J Surg* 1975;62:837–9.
- Mueller CF, Morehead R, Alter AJ, et al. Pneumatosis intestinalis in collagen disorders. *Am J Roentgenol Radium Ther Nucl Med* 1972;115:300–5.
- Sato A, Hoshina Y, Shimizu H, et al. [Systemic sclerosis with various gastrointestinal problems including pneumoperitoneum, pneumatosis cystoides intestinalis and malabsorption syndrome]. *Ryumachi* 1995;35:927–33.
- Pruitt RE, Tumminello VV, Reveille JD. Pneumatosis cystoides intestinalis and benign pneumoperitoneum in a patient with antinuclear antibody negative systemic lupus erythematosus. *J Rheumatol* 1988;15:1575–7.
- Togawa S, Yamami N, Nakayama H, et al. Evaluation of HBO2 therapy in pneumatosis cystoides intestinalis. *Undersea Hyperb Med* 2004;31:387–93.
- Mizoguchi F, Nanki T, Miyasaka N. Pneumatosis cystoides intestinalis following lupus enteritis and peritonitis. *Intern Med* 2008;47:1267–71.
- Shimada M, Ina K, Takahashi H, et al. Pneumatosis cystoides intestinalis treated with hyperbaric oxygen therapy: usefulness of an endoscopic ultrasonic catheter probe for diagnosis. *Intern Med* 2001;40:896–900.
- Frossard JL, Braude P, Berney JY. Computed tomography colonography imaging of pneumatosis intestinalis after hyperbaric oxygen therapy: a case report. *J Med Case Rep* 2011;5:375.
- Moon RE, Sheffield PJ. *Guidelines for treatment of decompression illness*, 1997:234–43.
- Lustberg AM, Fantry GT, Cotto-Cumba C, et al. Hyperbaric oxygen treatment for intractable diarrhea caused by pneumatosis coli. *Gastrointest Endosc* 2002;56:935–7.
- Grieve DA, Unsworth IP. Pneumatosis cystoides intestinalis: an experience with hyperbaric oxygen treatment. *Aust N Z J Surg* 1991;61:423–6.
- Castren EE, Hakeem AR, Mahmood NS, et al. Case of pneumatosis intestinalis and hepatic portal venous gas following a laparoscopic right hemicolectomy. *BMJ Case Rep* 2016;2016:bcr201614431.
- Tak PP, Van Duinen CM, Bun P, et al. Pneumatosis cystoides intestinalis in intestinal pseudoobstruction. resolution after therapy with metronidazole. *Dig Dis Sci* 1992;37:949–54.
- Costa M, Morgado C, Andrade D, et al. [Pneumatosis Coli treated with metronidazole and hyperbaric oxygen therapy: a successful case]. *Acta Med Port* 2015;28:534–7.
- Ellis BW. Symptomatic treatment of primary pneumatosis coli with metronidazole. *Br Med J* 1980;280:763–4.
- Jauhonen P, Lehtola J, Karttunen T. Treatment of pneumatosis coli with metronidazole. endoscopic follow-up of one case. *Dis Colon Rectum* 1987;30:800–1.
- Hughes DT, Gordon KC, Swann JC, et al. Pneumatosis cystoides intestinalis. *Gut* 1966;7:553–7.
- Read NW, Al-Janabi MN, Cann PA. Is raised breath hydrogen related to the pathogenesis of pneumatosis coli? *Gut* 1984;25:839–45.
- Florin TH, Hills BA. Does counterperfusion supersaturation cause gas cysts in pneumatosis cystoides coli. *and can breathing heliox reduce them?* *Lancet* 1995;345:1220–2.
- Rennenberg RJ, Koek GH, Van Hooft P, et al. Pneumatosis cystoides intestinalis, four cases of a rare disease. *Neth J Med* 2002;60:22–5.
- Van Liew HD, Bishop B, Walder P, et al. Effects of compression on composition and absorption of tissue gas pockets. *J Appl Physiol* 1965;20:927–33.
- Huizinga JD, Lammers WJ. Gut peristalsis is governed by a multitude of cooperating mechanisms. *Am J Physiol Gastrointest Liver Physiol* 2009;296:G1–G8.
- Bragg D, El-Sharkawy AM, Psaltis E, et al. Postoperative ileus: recent developments in pathophysiology and management. *Clin Nutr* 2015;34:367–76.
- Tahiri M, Levy J, Alzaid S, et al. An approach to pneumatosis intestinalis: factors affecting your management. *Int J Surg Case Rep* 2015;6C:133–7.
- DuBose JJ, Lissauer M, Maung AA, et al. Pneumatosis Intestinalis Predictive evaluation study (PIPES): a multicenter epidemiologic study of the Eastern Association for the surgery of Trauma. *J Trauma Acute Care Surg* 2013;75:15–23.
- Spektor M, Chernyak V, McCann TE, et al. Gastric pneumatosis: laboratory and imaging findings associated with mortality in adults. *Clin Radiol* 2014;69:e445–e449.
- Lee KS, Hwang S, Hurtado Rúa SM, et al. Distinguishing benign and life-threatening pneumatosis intestinalis in patients with Cancer by CT imaging features. *AJR Am J Roentgenol* 2013;200:1042–7.

Copyright 2017 BMJ Publishing Group. All rights reserved. For permission to reuse any of this content visit <http://group.bmj.com/group/rights-licensing/permissions>.
BMJ Case Report Fellows may re-use this article for personal use and teaching without any further permission.

Become a Fellow of BMJ Case Reports today and you can:

- Submit as many cases as you like
- Enjoy fast sympathetic peer review and rapid publication of accepted articles
- Access all the published articles
- Re-use any of the published material for personal use and teaching without further permission

For information on Institutional Fellowships contact consortiasales@bmjgroup.com

Visit casereports.bmj.com for more articles like this and to become a Fellow