Evaluation of HBO$_2$ therapy in pneumatosis cystoides intestinalis.

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Pneumatosis cystoides intestinalis (PCI) is a disease characterized by retention of gas in the intestinal wall. Retention of gas can be caused by three mechanisms; gas entry through the intestinal mucosa, gas dissection from the pulmonary alveoli and bronchi, and gas generation in the mucous membrane. Since gas in cysts is composed almost entirely of nitrogen, hyperbaric oxygen therapy (HBO$_2$) is effective for treating PCI due to the oxygen windows effect. However, PCI, caused by a mechanism involving pulmonary alveoli or branches, can become aggravated by HBO$_2$. Therefore, we propose modifying HBO$_2$ protocols for cases that do not require an invasive treatment. This study describes favorable results obtained in 2 PCI cases after HBO$_2$ therapy according to our protocol.

INTRODUCTION

Pneumatosis cystoides intestinalis (PCI) is a rare disease characterized by gas retention in the intestinal wall. Due to the small number of cases, therapeutic methods have been chosen regardless of the mechanism of development in many cases. This study describes selection of therapies based on the mechanism of development and cautions on treatment.

Mechanisms of gas retention

Gas retained in the intestinal wall is brought about by either entry of gas from outside or generation of gas in the tissue. Smith et al. (1) demonstrated histologically that increased fragility of the intestinal mucosa and increased intraluminal pressure of the intestine cause rupture of the mucous membrane through which intestinal gas leaks out into the wall to form air bubbles there. On the other hand, Keyting et al. (2) observed by roentgenology that air injected into the canine mediastinum dissected along vessels and formed PCI. Furthermore, they succeeded in making a cyst within the intestinal wall by injecting air after insertion of a catheter into the region of origin of the porcine mesenteric artery, thus demonstrating that PCI can be produced in the intestinal wall through dissection of the mediastinum, retroperitoneum and mesentery following rupture of the bronchial wall. In addition, Yale et al. (3, 4) demonstrated that PCI can be produced in the intestinal wall by injection of Clostridium perfringes into the rat intestinal wall. These findings indicate gas retention in the wall may be induced by three mechanisms; a) gas entry via the intestinal mucosa, b) gas entry via the pulmonary alveoli and bronchi, and c) gas generation within the intestinal wall caused by infection with gas-producing bacteria.
TREATMENT

Gas in the intestinal wall is composed mostly of nitrogen (5, 6). In any of the three mechanisms, an elevated partial pressure of oxygen around bubbles will reduce bubbles because of the oxygen window effect (7). In fact, there are many reports about successful use of HBO$_2$ (8-10). However, for mechanism a), gas may move through the disrupted mucosa due to necrosis of the intestinal wall (11-13) and, therefore, intestinal resection becomes the treatment of choice. In mechanism b) cases, the disease may be aggravated when gas, absorbed under a hyperbaric atmosphere, reaches the intestinal wall and expands there during decompression. Therefore, HBO$_2$ may not always be the treatment of first choice for PCI. Thus, the therapeutic options for PCI can be summarized as follows: In asymptomatic cases, the patient's course is followed without treatment. For symptoms associated with the peritoneal irritation, it should be considered that the condition requires invasive treatment. Oxygen therapy is performed on the cases that do not require an urgent surgical intervention. Although HBO$_2$ is more effective than normobaric concentration oxygen inhalation, it should be performed carefully due to possible aggravation which could theoretically occur as described above. Antibiotics should be administered concurrently, whenever bacterial infection is suspected (Fig. 1). This paper reports the results of treatment in 2 patients with PCI selected according to the guidelines mentioned above.

### Case 1

The patient was a 38-year-old woman. In 1996 she went to a local clinic with the chief complaint of diplopia and was diagnosed with myasthenia gravis. Since no symptom other than diplopia was noted, she received no treatment at the time. She developed muscle weakness of the extremities and dyspnea in 1998. With worsening of the disease, she presented to our hospital in 2000. She was treated with drugs including steroids and underwent thymectomy.

Around December 2001, abdominal pain and chronic diarrhea developed and PCI was diagnosed based on X-ray (Figure 2), endoscopic and pathological findings. Since a large dose of steroids had been administered, gas could have entered into the intestinal wall through weakened mucous membranes of the intestines or bronchi. Retention of gas in the wall could have been caused by infection with gas-generating bacteria. Considering these two possible mechanisms of gas retention, in addition to the absence of symptoms of peritoneal irritation, it was determined

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**Fig. 1.** Suggested treatment algorithm

<table>
<thead>
<tr>
<th>Absent</th>
<th>Symptoms</th>
<th>Present</th>
<th>Administration of antibiotics in cases of infection</th>
</tr>
</thead>
<tbody>
<tr>
<td>Present</td>
<td>Intense peritoneal</td>
<td>Present</td>
<td>Ventrotomy</td>
</tr>
<tr>
<td>Normobaric oxygen</td>
<td>Absent</td>
<td>Not improving</td>
<td>HBO$_2$</td>
</tr>
<tr>
<td>Not improving</td>
<td>HBO$_2$</td>
<td>Remain tolerable</td>
<td>Observation</td>
</tr>
<tr>
<td>Remains severe or intolerable</td>
<td>HBO$_2$</td>
<td>Remain tolerable</td>
<td>Observation</td>
</tr>
</tbody>
</table>

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http://rubicon-foundation.org
that there was no need for emergency invasive treatment. HBO₂ was performed carefully due to possible aggravation of condition. Special attention was paid during the decompression period. HBO₂ therapy was carried out at 2 ATA for one hour nine times and at 2.8 ATA for 2 hours twelve times. Abdominal pain and diarrhea gradually abated. X-ray (Figure 3) and endoscopy revealed almost complete resolution of PCI. She recovered well enough to be able to eat, and her central venous catheter for nutrition was removed.

Case 2

The patient was a 53-year-old woman. She had been treated with steroids and other drugs for scleroderma, myositis and rheumatoid arthritis for approximately ten years. Nausea after dinner began to occur from September 2002. Because nausea gradually worsened and vomiting after dinner persisted, she was admitted to this hospital in October 2002. Computed tomography (Figure 4) and endoscopy revealed intestinal gas retention around the duodenum and constriction at the same site, respectively, resulting in the diagnosis of PCI. The constriction was so marked that it was impossible to pass an endoscope through the duodenum. We judged that there was no need for urgent invasive treatment due to absence of peritoneal irritation. HBO₂ was carefully performed to avoid aggravation because the patient had been treated with a large dose of steroids as in Case 1. Therapy at 2 ATA for one hour was performed five times. Vomiting resolved after two sessions of therapy, and nausea also disappeared after five sessions (Figure 5).
DISCUSSION

Koss et al. (14), who reviewed the literature on PCI for the first time and classified the disease into primary and secondary causes. Various other kinds of classification were subsequently proposed (15, 16). Pear (17) adopted four categories: 1) bowel necrosis, 2) mucosal disruption, 3) increased mucosal permeability, and 4) pulmonary disease. This classification has two advantages from the viewpoint of selection of therapy. The first advantage is that PCI caused by intestinal necrosis (the only type of PCI requiring emergency surgery) is classified independently. The second advantage is that PCI caused by pulmonary disease (PCI requiring HBO₂ therapy under strict management) is also classified independently. However, it is sometimes difficult to classify patients in clinics. In patients with PCI complicated with scleroderma, for example, elevated intestinal pressure due to hypoperistalsis, disruption of the enteric mucosa and bronchial wall, and vulnerability to infection all produced by the use of steroids, along with interstitial pneumonia as a complication, are commonly found.

Signs of abdominal irritation that arise from PCI itself include nausea, vomiting, abdominal pain, diarrhea and a feeling of abdominal distension. In most cases, signs of peritoneal irritation are not present. In the past, X-rays taken for other purposes have often revealed findings of pneumatosis intestinalis or free gas in patients without any symptoms (18). A small quantity of gas in the intestinal wall produces no particular symptom, and patients who have no complaint can be left untreated with only observation of their clinical course. A large quantity of gas might overstress the intestinal wall, thereby causing intestinal constriction, hypoperistalsis, or malabsorption with symptoms of nausea, vomiting, diarrhea and abdominal distension. If the symptoms persist for a long period, treatment becomes necessary. If PCI is caused by bowel necrosis in association with notable signs of peritoneal irritation, treatment of the primary disease, resection of the necrotic intestine, becomes necessary.

Oxygen is the treatment of choice for PCI itself. Since 90% of the intestinal gas is nitrogen, air bubbles can be reduced, by the oxygen window effect of increasing the partial
pressure of oxygen in the intestinal wall. According to this theory, HBO₂ therapy should be more effective in reducing bubbles in the intestinal wall than high-concentration oxygen inhalation at normal barometric pressure. However, when PCI is caused via the bronchi and alveoli, the absorbed high-pressure oxygen might expand after reaching the intestinal wall, resulting in worsening of the disease. We extracted cases of PCI with specific descriptions about their treatment and outcome in Japanese medical abstracts from 1991 to 2000 and compared the number of days of treatment necessary for improvement. The number of patients who received 1 ATA oxygen and HBO₂ therapy was 20 and 7, respectively, and the number of days of treatment was 1-35 (mean, 14.6) days in the former and 1-8 (mean, 4.7) days in the latter. Though this is a simple comparison with obvious sources of bias, the number of days of treatment with HBO₂ was shorter than with sea level oxygen, suggesting a practical therapeutic effect. In the report of Gagliardi et al. (19) who summarized useful data of 25 cases at his facility, 1 ATA oxygen therapy was performed in 9 cases, resulting in improvement in all cases and complete abatement in only 4 cases, leaving an impression of an insufficient effect of 1 ATA.

In cases when oxygen therapy is not beneficial and when PCI is secondary to intestinal necrosis (11-13), invasive treatment is necessary. However, ventrotomy has been performed for suspected intestinal perforation in many cases with an X-ray image of free gas due to bubble disruption as the only basis, even though there were no peritoneal signs (20, 21). More accurate assessment of the disease state should be made in order to avoid unnecessary ventrotomy. In our review of Japanese articles on PCI from 1991 to 2000, 106 cases with descriptions of treatment and possible mechanism.

![Figure 6](http://rubicon-foundation.org)

**Fig. 6.** Treatment according to mechanism in Japan (1991-2000). Only cases in which the gas source was suggested in the literature are included. When two or more mechanisms were presumed in a case, all of them were counted.

For PCI caused by gas entry through the intestinal mucosa or gas generation in the intestinal wall, ventrotomy is most often selected at a ratio of ventrotomy, to high-concentration oxygen therapy to HBO₂ of 4:2:1. However, for PCI caused by gas entry via the bronchi and alveoli, the use of HBO₂, which should be performed under strict observation, was comparable to those of adopting ventrotomy or high-concentration oxygen therapy. Furthermore, 20 out of 55 cases (37%) had no peritoneal signs and underwent ventrotomy, and 31 out of 46 cases (67%) had no change other than intestinal pneumatosis at ventrotomy. In these cases, oxygen should have been the treatment of first choice (Table 1).
Table 1: Treatment of pneumatosis cystoides intestinalis in Japan (1991-2000)

<table>
<thead>
<tr>
<th>Method</th>
<th>Number of cases</th>
<th>Recovery rate% (In literature)</th>
</tr>
</thead>
<tbody>
<tr>
<td>observation of clinical course</td>
<td>21</td>
<td>95</td>
</tr>
<tr>
<td>High concentration oxygen</td>
<td>30</td>
<td>92</td>
</tr>
<tr>
<td>Hyperbaric oxygen</td>
<td>11</td>
<td>100</td>
</tr>
<tr>
<td>Ventrotomy</td>
<td></td>
<td></td>
</tr>
<tr>
<td>1) resection of the intestine</td>
<td>38 (Peritoneal signs present 42%)</td>
<td>91 (2 deaths)</td>
</tr>
<tr>
<td>2) only ventrotomy</td>
<td>17 (Peritoneal signs present 22%)</td>
<td>85 (1 death)</td>
</tr>
</tbody>
</table>

* normal except for intestinal emphysema: 31 out of 46 cases (67%)

In addition, the common use of unnecessary ventrotomy is not restricted to Japan. Peter et al. (22) have also indicated a similar trend in many other countries.

Until now, the etiological mechanisms of PCI have not been taken into consideration in selection of therapy which, may have been arbitrary. We propose that the etiological mechanism for each case provides a clue to selection of appropriate therapy. Thus, PCI should be acknowledged as an indication for HBO₂ and be performed carefully in cases suspected to have developed PCI via the bronchi.

CONCLUSION

We make treatment recommendations for the management of PCI according to the classification of its etiological mechanisms. HBO₂ should be performed with caution when there is a possibility of aggravating of patient’s condition.

REFERENCES


