Pneumatosis Cystoides Intestinalis Following Lupus Enteritis and Peritonitis

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Abstract

We describe a case of systemic lupus erythematosus (SLE) with enteritis and peritonitis who later developed pneumatosis cystoides intestinalis (PCI). A 35-year-old woman with SLE relapsed with enteritis and peritonitis. Prednisolone (PSL) effectively improved her symptoms. However, 6 weeks later, she developed PCI. Tapering of PSL, administration of intravenous cyclophosphamide, prokinetic agents and antibiotics, bowel rest with intravenous hypernutrition therapy and hyperbaric oxygen therapy successfully improved PCI. Although PCI is a rare complication of SLE, the present case suggests that lupus enteritis could be a risk factor for PCI, and that high-dose PSL could cause additional insult to PCI.

Key words: pneumatosis cystoides intestinalis, systemic lupus erythematosus, enteritis, peritonitis, cyclophosphamide, prednisolone


Introduction

Pneumatosis cystoides intestinalis (PCI) is an uncommon disorder characterized by the presence of gas within the walls of the gastrointestinal tract (1). PCI occurs in diverse conditions, such as obstructive pulmonary disease and intestinal disease including obstruction, inflammation and ischemia. PCI is also found in connective tissue diseases, especially in systemic sclerosis (SSc) (2). We report a case of systemic lupus erythematosus (SLE) complicated with PCI following enteritis and peritonitis.

Case Report

A 35-year-old woman was admitted to our hospital in August 2003 for abdominal pain and distension. Three years earlier, she was diagnosed with SLE complicated with pleuritis, pericarditis, proteinuria, hemolytic anemia, a high titer of anti-double-stranded-DNA antibody (anti-ds-DNA Ab) and positivity for anti-nuclear antibody (ANA). She was also diagnosed with interstitial pneumonia (IP). The initial therapy of prednisolone (PSL) at 60 mg/day was effective. The dose was subsequently tapered to 10 mg/day. Tacrolimus (3 mg/day) was started in January 2003 after worsening of IP and produced positive response. However, tacrolimus was discontinued in May 2003 after a request by the patient.

On admission, body temperature was 37.3°C. Clinical examination showed abdominal distension, decreased bowel sound, and tenderness on the right hypogastric region without rebound tenderness. Laboratory findings were leukocyte count 7,400/μL, hemoglobin 14.5 g/dL, C-reactive protein 0.8 mg/dL, erythrocyte sedimentation rate 18 mm/h, lactate dehydrogenase 350 IU/L, total bilirubin 1.6 mg/dL, direct bilirubin 0.7 mg/dL, creatine kinase 80 U/L, C3 63 mg/dL, C4 9 mg/dL, total complement (CH50) 23 U/mL, ANA×5,120 (homogeneous and speckled pattern), anti-ds-DNA Ab 9 IU/mL, anti-single-stranded-DNA Ab 30 IU/mL, antinucleoprotein Ab 3,898 U/mL, anti-cardiolipin-β2GP1 Ab <1.2 U/mL, anti-cardiolipin Ab IgG 1.4 U/mL, anti-cardiolipin Ab IgM 1.2 U/mL, proteinase 3-antineutrophil cytoplasmic antibody <10 EU, myeloperoxidase-antineutrophil cytoplasmic antibody <10 EU, haptoglobin 45 mg/dL, positive for direct Coombs test and negative for indirect Coombs test. A plain X-ray of the abdomen showed little gas and unclear iliopectos shadow (Fig. 1A). Enhanced computed tomography (CT) of the abdomen showed thickened intestinal wall from the distal ileum to ascending colon...
Figure 1. Radiographic findings on admission. A: A plain X-ray of the abdomen showed little gas and blurred iliopsoas shadow. B: Enhanced CT of the abdomen showed thickening of the intestinal wall extending from the distal ileum to the ascending colon (arrows) and ascites (arrowheads).

Figure 2. Radiological findings in mediastinal emphysema. A: Mediastinal emphysema was not detected in chest X-ray. B: Chest CT showed mediastinal emphysema (arrows).

and ascites (Fig. 1B). Enteritis and peritonitis after discontinuation of tacrolims and the low compliment level suggested the relapse of lupus activity. The dose of PSL was increased to 60 mg/day. This resulted in resolution of abdominal pain and disappearance of the abnormal CT findings immediately. Four weeks after 60 mg/day PSL, cyclophosphamide (CPA) was administered intravenously at 750 mg and PSL was tapered.

From the beginning of October, she developed anorexia. At the end of October, chest CT revealed mediastinal emphysema, although the patient did not have any respiratory symptoms and chest X-ray showed no obvious changes than before (Fig. 2A and B). Radiological examination of the abdomen showed multiple linear and cystic radioluencies in the ascending colon, and CT showed multiple areas of intraluminal gas accumulation (Fig. 3A and B). Free air was not detected. Based on these findings, she was diagnosed with PCI and mediastinal emphysema. Physical examination and laboratory tests did not showed any signs of infections or lupus activity: normal stool, negative fecal occult blood tests and normal complete blood counts, blood biochemistry test, CRP, complements and autoantibody levels. PSL was tapered by 5 mg/week to 10 mg/day, and monthly intravenous CPA therapy was continued (Fig. 4). She was also treated with bowel rest and received intravenous hypernutrition therapy, 3 g/day of kanamycin and 50 μg/day of octreotide, together with hyperbaric oxygen therapy (HBO). She became constipated and auscultation of the abdomen indicated decreased bowel sound, suggestive of impaired movement of intestine. Accordingly, she was treated with 30 mg/day metoclopramide, 15 mg/day mosapride and 600 mg/day erythromycin. In spite of these treatments, improvement of the pneumatosis was not obvious for the first one month. However, when the dose of PSL was tapered to 20 mg/day, pneumatosis turned to dramatically improve, and she started eating at 2 months after the above treatment. Antibiotics and prokinetic agents were gradually tapered, and she remains free of recurrence.

**Discussion**

Although it is reported that abdominal symptoms occur in
more than 50% of SLE patients during the course of their disease (3), PCI is a rare complication in SLE. A thorough search of the PubMed database identified only 14 reported cases of PCI associated with SLE (Table 1) (2, 4-16). Pathological analysis was conducted in only seven of these cases, and vasculitis was found in 6 cases (5, 6, 10, 11, 13, 15). The other case was diagnosed with vasculitis by angiography (8). Considered together, PCI might be a complication associated with vasculitis in at least half of these cases. In terms of the background conditions including autoantibody and symptoms of SLE, we cannot find any common features to suggest the risk of PCI (Table 1). However, Laing et al also reported a case of PCI after high-dose PSL therapy for bowel vasculitis, suggesting that high-dose PSL therapy for bowel vasculitis could be a risk for PCI. Eight cases developed remission: 3 were spontaneous (4, 9, 12), 2 by oxygen therapy (8, 14), 1 by steroid therapy (13) and 2 by CPA (10, 15). PCI was speculated in one case to be caused by CPA therapy (14). However, since high-dose methylprednisolone was also used in the same patient, it is not clear whether CPA was associated with development of PCI.

In the present case, PCI developed after lupus enteritis and peritonitis. The area of PCI was consistent with the region involved with lupus enteritis. Therefore, PCI might be caused by injury of the mucosa and immune barrier due to lupus enteritis presumably by vasculitis, and also by impaired healing due to PSL therapy. Overlap with SSc is the other possible explanation for the cause of the PCI, since our case was complicated with interstitial pneumonia. However, systemic sclerosis was not observed in this patient. Moreover, although the cause of PCI in SSc is thought to be the impaired movement of the intestine, our case did not show any sign of impaired movement of intestine before the onset of the PCI. Furthermore, the fact that improvement of PCI occurred after the tapering the dose of PSL to 20 mg/day suggests that the cause of PCI was not due to SSc but rather the PSL therapy after the lupus enteritis.

The mediastinal emphysema was considered to have developed secondary to PCI, since the emphysema was much more moderate compared with PCI. When a cyst ruptures in the retroperitoneal space, pneumoretroperitoneum occurs, and may lead to mediastinal emphysema (2, 17).
Development of PCI was speculated to be due to increased intraluminal pressure, mucosal injury, and production of gas from bacteria in the mucosa (1). Therapeutic strategy for PCI should be determined for each individual case as it depends on various factors and the background condition. Oxygen inhalation or HBO is reported to promote removal of the gas from the cysts (18). Antibiotics are effective in reducing bacterial overgrowth and gas production by anaerobic bacteria (19). To improve the impaired intestinal movement and reduce intraluminal pressure, prokinetic agents such as cisapride, metoclopramide, dinoprost and erythromycin are used (20). It is reported that octreotide is also effective in the treatment of abnormal motility and bacterial overgrowth in SSc (21). In SSc, the cause of PCI is thought to be the impaired intestinal movement which increases the intraluminal pressure and bacterial overgrowth. Therefore prokinetic agents, bowel rest and antibiotics are frequently used for the treatment of PCI in SLE. In SLE, it is important to select the appropriate therapeutic strategies according to the cause of PCI such as vasculitis, infection, fragility and bowel movement, based on thorough investigation. In the present case, the most important problem was high-dose PSL. Therefore, tapering of PSL with monthly intravenous CPA therapy was first conducted. Bowel rest, HBO, and the use of prokinetic agents and antibiotics also contribute to the improvement of the condition.

Although PCI is a rare complication in SLE, the present case suggests that lupus enteritis could be a risk factor for PCI, and that high-dose PSL could cause additional insult to PCI.

Table 1. Reported Cases of PCI in SLE

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<tr>
<th>First author</th>
<th>Age</th>
<th>Sex</th>
<th>Abdominal pain</th>
<th>Abnormal motility</th>
<th>Intestinal air present before the onset of PCI</th>
<th>Symptoms at the onset of PCI</th>
<th>Pathogenesis</th>
<th>PCI Treatment of PCI</th>
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References


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