Sclerosing Mesenteritis Presenting as Protein-losing Enteropathy: a Fatal Case

Takashi Kida¹, Kentaro Suzuki¹, Tatsuo Matsuyama¹, Mika Okita¹, Yutaka Isozaki¹, Naoyuki Matsumoto¹, Shigeyuki Miki², Yasutaka Nagao¹, Kenji Kawabata¹, Masataka Kohno⁴ and Hirokazu Oyamada¹

Abstract

Sclerosing mesenteritis is a rare, benign disorder characterized by non-specific and chronic inflammation of the mesenteric adipose tissue. The disease usually presents with gastrointestinal symptoms and abdominal masses. The long-term prognosis is favorable, but it often becomes severe. In the present report we describe a 77-year-old man who presented with diarrhea, massive ascites and an abdominal mass. The rapid deterioration of the general condition of the patient limited invasive examinations and left the primary disease unclear. Despite symptomatic therapy, malnutrition and hypovolemia were prolonged, and he died. The definitive diagnosis of sclerosing mesenteritis and the cause of the fatal outcome were disclosed at autopsy. This case indicates that sclerosing mesenteritis is a potentially-fatal disease and the need for aggressive treatment should be discussed.

Key words: sclerosing mesenteritis, retractile mesenteritis, panniculitis, protein-losing enteropathy


Introduction

Sclerosing mesenteritis is a rare, idiopathic, benign disorder of unknown etiology characterized by non-specific and chronic fibrous inflammation of the mesenteric adipose tissue (1). Patients usually present with abdominal pain, bloating and distention, diarrhea, weight loss, palpable abdominal masses, etc. (1-4). Because its clinical manifestations are non-specific, the diagnosis of sclerosing mesenteritis is very difficult. Clinically, a definitive diagnosis is established by means of a surgical or imaging-guided biopsy (1-3). The disease is generally self-limiting, and the long-term prognosis is good (1-4).

In this report, we describe an unusual, fatal case of sclerosing mesenteritis presented with diarrhea, massive ascites and an abdominal mass. He was diagnosed as having protein-losing enteropathy, but the primary disease remained unclear until he died. The definitive diagnosis of sclerosing mesenteritis and the cause of the fatal outcome were disclosed at autopsy. This case indicates that sclerosing mesenteritis is a potentially-fatal disease.

Case Report

A 77-year-old man (height 161 cm, weight 47 kg) presented with abdominal distention and diarrhea which had continued for about 6 months. His symptoms gradually became exacerbated, and finally he was admitted to our hospital (Matsushita Memorial Hospital, Osaka, Japan) by ambulance.

His past medical history was significant for pulmonary tuberculosis, chronic obstructive pulmonary disease, hypertension, chronic heart failure, and chronic renal failure. There was no history of chronic liver disease, and his current medications included diuretics. He had no familial history of...
autoimmune disease or any form of malignancy.

Physical examination revealed slight fever, hypotension (80-100/50-60 mmHg), abdominal distention with massive ascites, and bilateral pitting edema of the lower extremities. No palpable mass was observed. There were no stigmata of liver dysfunction or peritonitis, and no significant interval change in his cardiac function.

Laboratory findings (Table 1) indicated chronic inflammatory responses, liver damage, renal dysfunction, and malnutrition. A 24-hour urine collection revealed that creatinine clearance was 17.5 mL/min, and urinary albumin excretion was 26.8 mg/24 hr. Abdominal paracentesis with ascitic fluid analysis demonstrated that his ascites were transudates, and there was no sign of bacterial infection or malignancy. Adenosine deaminase measurement and polymerase chain reaction of ascitic fluid were negative for peritoneal tuberculosis. Malnutrition induced by protein-losing enteropathy (PLE) was suspected. Extensive investigations were performed with symptomatic therapy including diuretic, albumin preparation, and thyroid hormone.

Abdominal CT (computed tomography scanning) revealed massive ascites and a mass with calcification in the small bowel mesentery (Fig. 1). Gastroscopy showed just atrophic gastrointestinal mucosa. Colonoscopy was also performed and it revealed scarring in the ileocecum, but the histology of colon biopsy showed that there was only nonspecific inflammation.

A 72 hours fecal alpha-1-antitrypsin (α1AT) clearance test was performed and the result was 93.3 mL/24 hour (normal, less than 20 mL/24 hour), which was compatible with PLE. To determine the leakage locus, the patient underwent protein-losing scintigraphy. Intravenously-injected 99mTc-HSA (technetium 99 m-labeled human serum albumin) revealed hot areas in the jejunoileum (Fig. 2). The underlying primary disease was not yet demonstrated, however, his general condition did not allow additional invasive examinations. His regular food intake was restricted by abdominal bloating (below 1,000 kcal per day). Despite continuous administration of albumin preparation, his serum albumin level was low (2.0 g/dL) and it decreased further after this preparation was replaced with enteral nutrition with elemental diets. His vital signs were stable, but hypovolemia progressed steadily.

On the 16th day after admission, the patient complained of abdominal pain of sudden onset, which increased and gradually extended. His vital signs could not be kept normal, and he died on the 20th day. Additional data of blood examinations before he died are shown in Table 2.

At autopsy, a massive amount of dirty ascites was found (5,800 mL). The mesentery, located at the broad small intestine, formed a nodular-thickened mass. The mass was retracted by itself and contained calcifications, corresponding to CT findings. There were two ulcerations in the small intestinal mucosa, one of which was perforated (Fig. 3, 4). Histological examination of the mesentery revealed diffuse necrotic fat tissue surrounded by proliferation of fibroblasts with infiltration of inflammatory cells (Fig. 5). It was partially progressed to fibrosis, and obliterated the small veins and lymphatics.

IgG4-immunohistochemistry of the mesentery was negative and there was no sign of peritoneal tuberculosis or peritonitis carcinomatosis. We concluded that the underlying disease was 'sclerosing mesenteritis' based on the histopathology.

### Discussion

Sclerosing mesenteritis is a rare, idiopathic, benign disorder characterized by chronic fibrosing inflammation of the mesenteric adipose tissue. Since the first article by Jura (5) in 1924, the disease was thought to have various histological features from case to case; fat necrosis, chronic inflammation, and fibrosis. In 1997, after a review of 84 cases, Emory et al concluded that these histological variants are based on a single pathological entity characterized by non-specific

<table>
<thead>
<tr>
<th>Table 1. Laboratory Data on the Admission</th>
</tr>
</thead>
<tbody>
<tr>
<td>Parameter</td>
</tr>
<tr>
<td>WBC</td>
</tr>
<tr>
<td>Hb</td>
</tr>
<tr>
<td>PLT</td>
</tr>
<tr>
<td>PT - INR</td>
</tr>
<tr>
<td>Fibrinogen</td>
</tr>
<tr>
<td>D-dimer</td>
</tr>
<tr>
<td>AT-III</td>
</tr>
<tr>
<td>Ferritine</td>
</tr>
<tr>
<td>BNP</td>
</tr>
<tr>
<td>Hyaluronate</td>
</tr>
<tr>
<td>TSH</td>
</tr>
<tr>
<td>Free T3</td>
</tr>
<tr>
<td>Free T4</td>
</tr>
<tr>
<td>TP</td>
</tr>
<tr>
<td>Alb</td>
</tr>
<tr>
<td>ALT</td>
</tr>
<tr>
<td>ALP</td>
</tr>
<tr>
<td>ChE</td>
</tr>
<tr>
<td>BUN</td>
</tr>
<tr>
<td>CRE</td>
</tr>
<tr>
<td>Na</td>
</tr>
<tr>
<td>K</td>
</tr>
<tr>
<td>Cl</td>
</tr>
<tr>
<td>T-Chol</td>
</tr>
<tr>
<td>CRP</td>
</tr>
</tbody>
</table>
Figure 1. Abdominal computed tomography shows massive ascites and a solid soft tissue mass with calcification in the small bowel mesentery.

Figure 2. Protein losing scintigraphy demonstrates protein leakage into the intestine. Intravenously-injected 99mTc-HSA (technetium 99m-labeled human serum albumin) exists in the jejun ileum after 24 hrs.

chronic inflammatory infiltration and fibrosis in the mesenteric fat, and “sclerosing mesenteritis (SM)” is the most appropriate umbrella term (1). This process also may lead to abdominal masses, mesenteric calcification, and the involvement of vessels. Because of its rarity, the clinical features and pathogenesis of SM remain uncertain (3). Some possible pathogenesis factors have already been reported, including autoimmunity, infection, trauma, surgery (4), paraneoplastic response (6), and IgG4-related disease (7).

SM is more frequent in males during the 6th and 7th decades of life (3). The most common symptoms are abdominal pain, bloating and distention, diarrhea, weight loss, and a palpable abdominal mass (1-5). These are caused by the mechanical effect of the mesenteric mass encasing the intestines, blood vessels, and lymphatics. Therefore, SM-related complications include small bowel obstruction and ischemia, and superior mesenteric vein thrombosis (3). Also there are a few reports which present PLE (8, 9) and intestinal perforation (3), as in the present patient.

Laboratory parameters are often normal (3). Nonspecific abnormalities, including anemia and elevation of the erythrocyte sedimentation rate and C-reactive protein level, may be found. In the present patient, an increased plasma hyaluronate (HA) level was noted (1,178 ng/mL). This might have been based on the fibrous inflammation of the mesentery.

Because its clinical manifestations are nonspecific, the diagnosis of SM is difficult. A definite diagnosis of SM can be established only by surgical (10) or imaging-guided biopsy. The most consistent histological findings are the presence of fibrous tissue and a chronic inflammatory infiltrate (1). However, in fact, some cases were incidentally identified during surgery, CT examination, or autopsy (3, 6). Abdominal CT is expected to play an important role in diagnostic evaluation. The most common CT finding is a soft tissue mass in the small bowel mesentery (especially at the root of the small bowel mesentery). The following CT find-
The course of SM is generally favorable (1-4). Most cases have been reported as having a self-limiting benign course. Nevertheless, in about 20% of patients, it is associated with significant morbidity and a chronic debilitating course (3). A few fatal cases have been reported, as in the present patient (13, 14).

At present, there is no consensus as to the treatment of SM. Most patients are managed conservatively and about a half of them may not require any therapy (3). Some improved symptomatic cases treated with corticosteroids (15), azathioprine (16), cyclophosphamide (17), thalidomide and tamoxifen (3) have been reported, though to date there has been no randomized controlled trial. Surgical resection of the lesion is of little benefit, except in the case of bowel obstruction or perforation (18). Some authors recommend that asymptomatic or mild symptomatic SM may be left untreated and observed, and surgical resection is advocated for patients with severe complication or the possibility of malignancy (18). Others recommend aggressive immunosuppressive therapy with prednisolone and cytostatic agents to prevent progression of the lesion once the diagnosis is established (16).
In the present case, we did not use any immunosuppressant due to the possibility that his immunosuppression was based on an infection. We could not make a definite diagnosis and predict his outcome, because not only is SM itself rare but also comorbidity between SM and severe PLE is very rare. The prognosis of SM is usually good, but the rapid exacerbation of his general condition, which was greatly affected by PLE-induced malnutrition, and the limited invasive examinations, led to a fatal clinical course. Although there was no evidence of vasculitis in his mesentery and cutaneous tissues, and also he did not fill the diagnostic criteria of any connective tissue disease, his high titers of ANA might suggest the possibility of his immunological disorder. The pathogenesis of his protein losing was probably based on SM. It was speculated that the impaired intestinal lymph ducts had ruptured and subsequently leaked protein into the GI tract. In addition, stasis of the mesenteric veins had caused intestinal ischemia and reduction of portal blood flow. These mesenteric conditions might play a role in the pathogenesis of PLE. His massive ascites appeared to be based on hypoproteinemia, inflammation of mesentery, and block of portal blood flow due to mesenteric mass. The abdominal pain of sudden-onset before his death was caused by intestinal ischemic perforation. The suppurative peritonitis due to the perforation finally led to the failure of the general circulation.

In conclusion, SM should be considered in the differential diagnosis of patients with abdominal symptoms, abdominal masses and PLE. When encountering patients with suspected SM, we should follow up their symptoms carefully and make a bold decision for aggressive therapy involving immunosuppressive agents and surgical resection once their symptoms are severe or fatal complications appear. More case studies would help the establishment of diagnostic criteria and a therapeutic strategy of SM.

The authors state that they have no Conflict of Interest (COI).

References