Pseudotumorous Pancreatitis Associated with Ulcerative Colitis

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Abstract

Pancreatitis is believed to be one of the uncommon extraintestinal manifestations of ulcerative colitis (UC). A 66-year-old woman who had been treated for UC for eight months was admitted to our hospital because of epigastralgia. Laboratory examinations revealed elevated pancreatic enzymes. Because differentiation of pseudotumorous pancreatitis from pancreatic cancer was difficult by the imaging findings, she underwent a distal pancreatectomy. Histologically, the tumorous lesion was composed of fibrosis with lymphocytic infiltration. We concluded that this case was pseudotumorous pancreatitis as an extraintestinal manifestation of UC.

Introduction

Although ulcerative colitis (UC) primarily involves the intestinal tract, it may also affect extraintestinal organs such as the skin, eyes, joints, and hepatobiliary tree. Although several case reports of UC-related pancreatitis have been published during past years, its pathological findings are rarely reported in the literature (1). We encountered a case of UC-associated pseudotumorous pancreatitis proved by resection.

Case Report

A 66-year-old woman was transferred to our hospital with complaints of bloody diarrhea, fever, and abdominal pain on May 26, 1997. Routine laboratory data including amylase were normal except for leukocytes of 11,300/µl (normal 3,500–8,000/µl) and C-reactive protein (CRP) of 9.4 mg/dl (normal <0.2 mg/dl). Results of stool cultures were negative; parasites were not found. Colonoscopy revealed diffuse, continuous colitis with absent vascular pattern, friability, and contact bleeding involving the total colon. Biopsy specimens of the colonic mucosa showed mucosal inflammation and crypt abscess formation. The endoscopic and histologic features were consistent with a diagnosis of UC. Abdominal ultrasonography showed no swelling of the pancreas and no dilatation of the main pancreatic duct (MPD).

She was treated with oral 5-aminosalicylic acid (5-ASA) (2,250 mg/day) without benefit for two weeks. Therefore, prednisolone of 60 mg/day was initially administered. She made a rapid clinical recovery and became asymptomatic after two weeks. Follow-up colonoscopy showed a recovery, and then prednisolone was tapered to 10 mg/day. She remained asymptomatic with normal laboratory data thereafter. Meanwhile she was treated with oral prednisolone of 10 mg and 5-ASA of 2,250 mg/day.

She was re-admitted to our hospital on January 28, 1998 because of sudden epigastralgia four days before. Neither she nor her family had any history of habitual alcohol consumption, pancreatitis, or gallbladder disease. On physical examination, blood pressure was 110/60 mmHg, pulse 72/min, and she was afebrile. Examination of the head, neck, skin, chest, heart, and extremities was unremarkable. The abdomen was soft and flat. There was localized tenderness in the epigastrium. Laboratory examinations showed hemoglobin of 11.3 g/dl, platelets of 420,000/µl, white blood cell count of 8,300/µl, and CRP of 1.9 mg/dl. Blood chemistry tests revealed aspartate aminotransferase of 24 IU, alanine aminotransferase of 23 IU, alkaline phosphatase of 236 IU, albumin of 3.7 g/dl, globulin of 2.7 g/dl (γ-globulin 11.4%), total bilirubin of 0.4 mg/dl, direct bilirubin of 0.3 mg/dl, serum amylase of 1,900 IU (pancreatic % 97%) (normal 70–185 IU), urine amylase of 11,740 IU (pancreatic% 99%) (normal <430 IU), lipase of 14,020 IU (normal <200 IU), elastase I of 2,695 ng/ml (normal <380 ng/ml), total cholesterol of 207 mg/dl (normal 110–220 mg/dl), triglyceride of 103 mg/dl (normal 30–150 mg/dl), calcium of 9.2 mg/dl (normal 8.4–10.0 mg/dl), and phosphorus of 4.0 mg/dl (normal 2.2–4.2 mg/dl). Serum carcinoembryonic antigen was <1.0 ng/ml (normal <2.5 ng/ml) and carbohydrate antigen 19–9 was 40.2 ng/ml (normal <37 IU). Immunoglobulin G, A, M, E, and D were all within normal limits. Autoantibodies including antinuclear antibody, SS-A and SS-B antibodies, mitochondrial antibody, and smooth muscle antibody were all negative.

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Figure 1. Contrast-enhanced CT scan of the abdomen revealed a low-density lesion in the body of the pancreas.

Figure 2. ERCP showed an obstructed MPD and normal biliary tracts.

Figure 3. A surgical specimen showed fibrotic changes with lymphocytic infiltration to the pancreatic ducts and acinar cells (HE stain, ×25).

Negative. Abdominal and endoscopic ultrasonography showed swelling of the pancreatic body and slight upstream dilatation of the MPD, without masses in the pancreas. A contrast-enhanced abdominal computed tomography (CT) scan demonstrated a low-density lesion 3.0 cm in diameter in the body of the pancreas in the early phase (Fig. 1), and low-density in the late phase. An endoscopic retrograde cholangiopancreatography (ERCP) and magnetic resonance cholangiopancreatography (MRCP) showed an obstruction of the MPD in the pancreatic body with slight upstream dilatation of the MPD and normal biliary ducts (Fig. 2). Incidentally ERCP was performed when the patient became asymptomatic and the serum pancreatic enzymes values were normal. Abdominal angiography was normal.

Considering the possibility of acute pancreatitis due to 5-ASA (though the clinical characteristics of this case were not consistent with that of 5-ASA pancreatitis), we discontinued the medication of 5-ASA after admission. The patient became asymptomatic and laboratory data were normalized with total parenteral nutrition in about 3 weeks. Because the above imaging findings failed to distinguish pseudotumorous pancreatitis from pancreatic cancer (the findings of CT, ERCP, and MRCP suggested pancreatic cancer), she underwent a distal pancreatectomy.

Macroscopically, sections of the specimen revealed a well-defined tumorous lesion with a 3.0 cm long narrowing of the MPD. Histological examination of the pancreatic tumorous lesion showed predominant CD 4 positive T lymphocytic infiltrates as well as decreased exocrine parenchyma and inter- and intralobular fibrosis. Most acini disappeared while some of the pancreatic ducts and Langerhans' islets were preserved (Fig. 3). The non-tumorous lesion of the pancreas was normal except for upstream dilatation of the MPD.

Discussion

UC is associated with numerous extraintestinal manifestations, including pancreatitis. However, pancreatic disease has never been clearly recognized as a manifestation of UC, and the pathogenesis of pancreatitis in UC is not understood. The association between pancreatic disease and UC was first suggested by Ball et al in 1950 (2). Since then, several cases of clinically significant pancreatitis have been reported in UC.
Patients (1, 3–8).

UC and pancreatitis are linked, although this may be a coincidence. This suggestion is supported by the absence of known causes of pancreatitis, including alcohol abuse, gallstones, underlying hepatobiliary complications, hyperlipidemia, hypercalcemia and drugs. Chronic pancreatitis and primary sclerosing cholangitis (PSC) have been reported in association with UC (9, 10). In the present case PSC was excluded by the absence of pruritus and jaundice, and the demonstration of normal intra- and extra-hepatic biliary ducts (10, 11). Gallstones, other hepatobiliary complications, hyperlipidemia, and hypercalcemia were not detected, but the use of corticosteroid and 5-ASA, both potential precipitants of pancreatitis, made it difficult to clearly establish the relationship between UC and pancreatitis.

Some reports have suggested that steroids could cause acute pancreatitis (12–14). However, corticosteroids might not be the etiologic culprit in most, if not all, of the cases. Steinberg and Lewis concluded that the evidence used to incriminate steroids as a cause of acute pancreatitis could be challenged as inconclusive on several aspects: First, none of the case reports or autopsy studies that single out corticosteroids as the etiologic agent has completely excluded other potential causes of pancreatitis. Second, no consistent pancreatic secretory or histopathologic changes appeared to be induced by corticosteroids in humans or in animals that would explain the pathogenesis of acute pancreatitis. Third, there does not appear to be any consistent relationship between the dose of steroids given or the duration of treatment and the onset of pancreatitis (15). Few cases of steroid-induced pancreatitis have been reported since then.

Some authors put forward the hypothesis that a correlation between acute pancreatitis and 5-ASA therapy might exist (16–21). The common characteristics of 5-ASA-induced pancreatitis are as follows: mild symptoms, onset within three weeks after taking 5-ASA, no abnormal findings in the imaging examinations, no reports which referred to the pathological findings. The clinical features in the present case were inconsistent with the above findings.

We excluded drug-induced pancreatitis by these findings, and the recognized causes of pancreatic insufficiency were excluded. We thus considered the pancreatic disease in this case as one of the extraintestinal manifestations of UC.

The histological findings of the resected specimen of UC-related pancreatitis cases are rarely reported in the literature (1, 3–8). Pathological specimens of UC-related pancreatitis demonstrate the presence of inter- and intra-lobular fibrosis with marked acinar regression (1). Autopsy studies in UC have revealed the presence of macroscopic or microscopic pancreatic lesions in 14% to 53% of 86 cases (2). The most common findings were chronic interstitial pancreatitis and pancreatic fibrosis. Microscopic findings of this case were similar to those of previously reported cases. One case report showed a pseudotumorous lesion like ours (1). Although the pathogenesis of pseudotumorous pancreatitis is unknown, an autoimmune mechanism is suggested as its cause (22).

### References

19. Fiorentini MT, Fraccia M, Galatola G, Barbotta A, De La Pierre M. Acute Immunohistochemical studies have demonstrated that the majority of infiltrating lymphocytes around the lesion are CD4 positive T cells in autoimmune disease (23, 24). In the present case, most of the lymphocytes surrounding the pancreatic ducts were CD4 positive T cells, suggesting an autoimmune mechanism of pancreatitis. Therefore, both pancreatic and colonic lesions in this case might be attributed to a common mechanism (autoimmunity). However, the characteristics of the present case were inconsistent with that of so-called ‘autoimmune pancreatitis’ (22).

Pancreatic lesion in UC has been discussed as a previously unrecognized ‘new’ kind of an extraintestinal manifestation due to systemic inflammation. Although the link between UC and pancreatitis remains obscure, this report serves as further evidence to support the relationship between UC and pancreatitis as an extraintestinal manifestation.


