Crohn’s Disease and Primary Sclerosing Cholangitis: 
A Case Report and Review of the Literature

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Abstract

The comorbidity of Crohn’s disease (CD) and primary sclerosing cholangitis (PSC) is uncommon. Diagnosing such patients can be difficult, as illustrated by the following case. The combination of CD and PSC should be considered in patients with CD who have abnormal liver function. Because patients with PSC often present asymptomatically, all patients with CD should be screened for PSC by checking serum liver tests. Review of the literature suggests that there is an increased potential in these patients for the development of malignancy and long-term prognosis is poor. We conclude that patients diagnosed with a combination of CD and PSC should be managed with periodic colonoscopy, CA 19-9 investigation, early liver and bowel imaging, and liver biopsy. The treatment of CD associated with PSC remains unsatisfactory and the possibility of liver transplantation should be considered.

Key words: Crohn’s disease, primary sclerosing cholangitis, diagnose

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Introduction

The comorbidity of Crohn’s disease (CD) and primary sclerosing cholangitis (PSC) is rare, and properly diagnosing the two together is rather difficult. The following is a case of a 33-year-old patient diagnosed with CD associated with PSC, and a review of the literature on this topic.

Case Report

A 33-year-old man was referred to West China Hospital of Sichuan University for experiencing abdominal pain, bloody diarrhea and jaundice for one year. He had been diag-nosed with CD 12 years previously by colonoscopy with multiple biopsies in local hospitals 3 times. The patient’s colitis was managed well with sulfasalazine, steroids and metronidazole treatment.

One year earlier, however, the patient had a relatively severe exacerbation despite maintenance with mesalamine. For several months, he experienced intermittent fever, rectal hemorrhage, painless jaundice, and pruritus, and weight loss of 5 kg. He also experienced pain in his knees and elbows for a week.

Physical examination revealed a pale, thin patient. Spider naevi and palmar erythema were absent. There was moderate hepatomegaly with tenderness and stiffness on palpation. Otherwise, the abdominal examination was normal. There were no other abnormal physical findings.

Laboratory tests showed a Hgb of 56 g/dL, MCV 89 fl, HCT 24.5%, AST 94 IU/mL, ALT 72 IU/mL, ALP 958 U/mL, total bilirubin (TB) 117.1 μmol/L, direct bilirubin (DBIL) 101.2 μmol/L, erythrocyte sedimentation rate (ESR) 113 mm/h and C-reactive protein (CRP) 32.7 mg/dL. Screening for the various markers of viral hepatitis (A, B, C, CMV, EB, HS and VZ) was all negative. Non-organ specific auto-antibodies (ANAs, AMAs, AML, and anti-LKM1) were also negative. Laboratory studies showed the presence of the anti-neutrophilic cytoplasmic antibodies (ANCA) (+) and p-ANCA (+) (both 1:320). Stool cultures for pathogens shigella, salmonella, Vibrio cholerae, Mycobacterium tuberculosis, halophilic bacteria, and proteus were negative.

Ulcers and inflammatory polyps were noted from the transverse colon to the terminal ileum with a segmental pat-

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tern, via colonoscopy (Fig. 1). Colonic histopathology of biopsies demonstrated the inflammation involved the mucosa and submucosa, with granulomas found supporting the diagnosis of CD (Fig. 2).

A computerized axial tomography (CAT) scan of the abdomen revealed intrahepatic biliary dilatation and moderate hepatomegaly. A liver biopsy revealed the presence of a moderate portal and lobular plasmacytic inflammatory infiltrate with slight porta-portal and periductular fibrosis, along with an onion skin appearance and moderate ductular proliferation (Fig. 3). The suspected diagnosis of PSC was also confirmed by endoscopic retrograde cholangiopancreatography (ERCP). ERCP revealed stenosis of the intrahepatic bile ducts and multiple cystic expansions leading to an irregular string of beads appearance, considering cholangitis (Fig. 4).

The patient was treated with ursodeoxycholic acid (UDCA) and mesalamine with good response. He was discharged one month later without symptoms. After three months, his serum liver tests were normal.

**Discussion**

PSC is a disease of unknown etiology characterized by both intrahepatic and extrahepatic inflammation and fibrosis, frequently leading to biliary cirrhosis and hepatic failure. Based on the findings of a high frequency of HLA-B8 and HLA-DR3, along with common immune alterations in these patients, PSC is believed to be caused by genetic and immunologic factors (1, 2). Although PSC is also considered to be one of the hepatobiliary complications of CD, this entity is very uncommon. To the best of our knowledge, only 15 other cases of CD associated with PSC have been reported in the English language literature since the first case report completed by Atkinson and Carroll in 1964 (3) (Table). The percentage of CD patients with PSC has recently been estimated to be as high as 3.4%, and may be more prevalent than once thought (4).

CD associated with PSC occurs predominantly in middle-aged males, with a mean age of 39 years (range 20-40). The ratio of male to female patients is 2:1. The age of the onset of symptoms is younger than it is in general PSC patients (5). It is generally seen in patients who have extensive colonic disease (6). Although the pathogenesis remains unknown, a possible association between CD associated with PSC and immunological abnormalities has been suggested in earlier reports. In fact, 8 of 16 patients, including the current patient, displayed some immunological complications such as alopecia, autoimmune haemolytic anaemia, glomerulonephritis, autoimmune pancreatitis, granulomatous pneumonitis, and autoimmune hepatitis (AIH) (7-12, 16, 20) (Table). The present patient also complained of a bout of transient arthritis. One case of PSC has been reported in association with hepatitis C virus (HCV) infection (18), indicating that HCV may trigger PSC. Possible mechanisms for the association of PSC with CD include mucosal T cells that are recruited to the liver in response to aberrantly expressed endothelial-cell adhesion molecules and chemokines that are normally restricted to the gut. This mechanism might also explain why this disease is associated with site-specific liver
The medical management of CD associated with PSC treatment remains inadequate. Methotrexate (28), corticosteroids (29), cyclosporine (30), azathioprine, and 6-mercaptopurine (31) have not been proven beneficial. UDCA has been shown to improve liver biochemistry and histology, but has not been shown to alter the progression (32, 33). Infliximab therapy may be efficacious. Siemanowski and Regueiro (34) reported using infliximab in two patients with CD and PSC. Their serum liver tests improved one month after the first infusion of infliximab. However, its effect has not been proved by histopathology, and more evidence is required to support its routine use.

Endoscopic dilation with sphincterotomy or stenting can improve the symptoms and liver biochemistry levels for a small numbers of patients. However, the disease can lead to cirrhosis and ultimately liver failure. Liver transplantation may be considered at that time. For patients with end-stage PSC, liver transplantation remains the only effective treatment. One report described a CD patient with PSC who had an active terminal ileal ulcer that improved after liver transplantation (12). However, there are other reports of increased rates of colon cancer after liver transplantation (15). It remains unclear if this is due to longstanding immunosuppressive use or confounding variables such as long duration of disease.

The prognosis of CD associated with PSC is poor. The median survival rate, after diagnosis and without liver transplantation is approximately 12 years with a worse survival rate for those who were symptomatic at presentation (24, 35). The major cause of increased mortality is the occurrence of colorectal cancer, cholangiocarcinoma, hepatic failure, and hepatocellular carcinoma. Recent studies have found an increased prevalence of colonic dysplasia and cancer in patients with PSC and CD compared with those with only CD. It is possible that there was some contribution from the immunosuppressive therapy (10). This risk for cholangiocarcinoma and hepatocellular carcinoma is higher in
patients with PSC associated with CD than those with PSC alone with an estimated annual incidence of 0.5%-1% (17, 36). Two cases with diagnosed PSC associated with CD have been reported to have been complicated by the appearance of hepatocellular carcinoma (12, 17). Some practice guidelines have recommended that patients with PSC and CD should have periodic CA 19-9 testing, abdominal ultrasound examinations and annual surveillance colonoscopies with multiple random biopsies for the detection of dysplasia (37, 38).

Conclusion

In conclusion, the combination of CD and PSC is rare. The diagnosis of PSC should be considered in patients with CD who have abnormal serum liver tests of unknown etiology after the exclusion of common causes of hepatic damage such as viral and drug-induced hepatitis. Screening should be done with serum liver tests on all patients with CD, as patients with PSC often present asymptptomatically. We conclude that serum biochemical assessment of liver damage should be performed on all patients with CD, and if the results are abnormal, PSC should be suspected. The latter diagnosis can be confirmed by liver biopsy and cholangiography. Considering that the course of PSC is independent of CD, both liver biopsies and cholangiograms are needed in every patient with CD and PSC to evaluate the extent of the disease. In cases where clinical deterioration and weight loss are seen, early liver and bowel imaging along with liver biopsy should be performed. The long-term prognosis is poor, making it all the more important to be vigilant. Once the diagnosis is established, periodic colonoscopic surveillance and CA 19-9 should be completed, and possible inclusion in a transplantation program should be considered.

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

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