Primary Biliary Cirrhosis Associated with Ulcerative Colitis

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症　　例

Primary Biliary Cirrhosis Associated with Ulcerative Colitis

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Abstract A rare case of concurrent primary biliary cirrhosis and ulcerative colitis is described in a 61 year-old Japanese male. Primary biliary cirrhosis was diagnosed on the basis of characteristic histologic findings and a positive serum mitochondrial antibody test. Ulcerative colitis was diagnosed from typical findings on colonoscopy and the histologic features of a sigmoid colon biopsy specimen. This is the 12th report of a patient presenting with the combination of primary biliary cirrhosis and ulcerative colitis. The potential autoimmune relationships on the basis of these conditions are discussed.

Key words: Primary biliary cirrhosis, Ulcerative colitis

Introduction

Association of primary biliary cirrhosis with ulcerative colitis has been reported in only eleven cases. We describe the case of a Japanese male with both diseases who presented with liver dysfunction and watery diarrhea, and responded well to steroid therapy.

Case Report

A 58 year-old Japanese male developed generalized, persistent pruritus in 1990. In 1992 liver dysfunction was discovered, so he was admitted to our hospital for further evaluation.

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Laboratory data on admission included a hemoglobin of 13.2 g/dL and a white blood cell count of 3900/μl, with a normal differential. Serum concentrations of hepatic enzymes were as follows: asparate aminotransferase (AST) 112 IU/L, alanine aminotransferase (ALT) 74 IU/L, alkaline phosphatase (ALP) 1644 IU/L, and gammaglutamyl transpeptidase (γ-GTP) 467 IU/L. The serum concentration of total bilirubin was 1.7 mg/dL, and that of direct bilirubin was 1.1 mg/dL. Serologic markers for viral hepatitis types B and C were absent. The anti-mitochondrial antibody titer was 1 : 160, but neither anti-nuclear nor anti-smooth muscle antibodies were detected.

Analysis of a liver biopsy specimen obtained in October 1992 demonstrated expansion of nearly all portal areas by lymphocyte and histiocyte infiltrates (Fig. 1). Varying degrees of paucity of the interlobular bile ducts were

noted. A few portal areas contained granulomas and some had hyperplastic ductules. Fibrosis without nodule formation was also present. Microorganisms were not identified.

On the basis of these findings the patient was diagnosed as having primary biliary cirrhosis, stage 3 (Scheuer classification)[20]. He was discharged and followed up as an outpatient. In November 1993, he was readmitted for complaints of abdominal fullness and watery diarrhea. Serum concentrations of hepatic enzymes included AST 63 IU/L, ALT 61 IU/L, ALP 915 IU/L, and γ-GTP 299 IU/L. His total bilirubin concentration was 1.5 mg/dL, and that of direct bilirubin was 0.8 mg/dL. An erythrocyte sedimentation rate was 21 mm/hour. Computed tomography revealed mild liver atrophy and ascites, although a space-occupying lesion was not observed. He was treated with furosemide, 40 mg/day. Two weeks later, watery diarrhea associated with blood and mucus in his stool appeared. On sigmoidoscopy, friable and edematous colonic mucosa with a loss of vascularity was observed in a continuous 20 cm segment (Fig. 2a). A biopsy sample of the sigmoid colon demonstrated moderate to marked acute inflammation with crypt abscesses limited to the mucosa (Fig. 3). He was diagnosed as ulcerative colitis, and was managed medically with intravenous injections of prednisolone (50 mg/day). His abdominal symptoms dramatically improved and the diarrhea resolved. Subsequent examination of stool revealed no occult blood. Three months

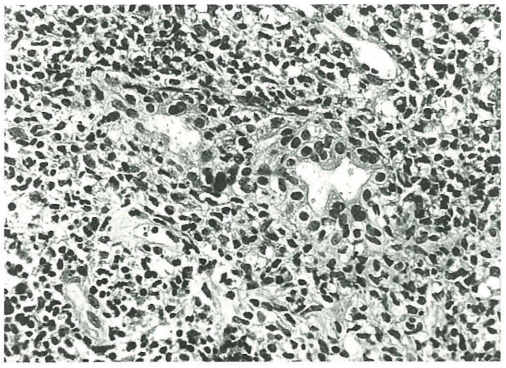
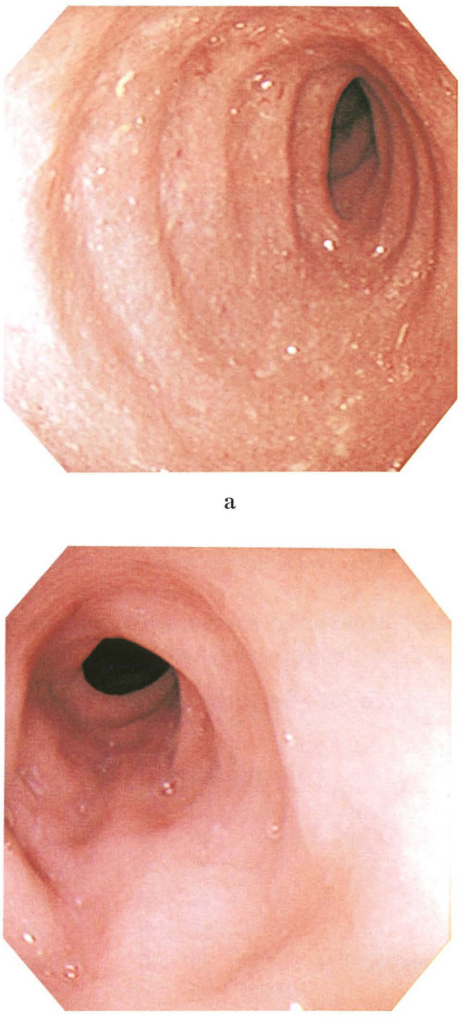


Fig. 1 The histological findings of the liver show intermediate sized bile ducts infiltrated by chronic inflammatory cells. (HE stain, 480×)



a

b

Fig. 2 (**a**) Sigmoidoscopy shows friable and edematous colonic mucosa with a loss of vascularity. (**b**) Three months later, repeat sigmoidoscopy demonstrates resolution of the ulcerative colitis.

later, repeat sigmoidoscopy demonstrated resolution of the ulcerative colitis (Fig. 2b). The primary biliary cirrhosis had not markedly changed.

Discussion

Primary biliary cirrhosis is associated with several extrahepatic autoimmune diseases including Sjögren's syndrome, rheumatoid arthritis, and Hashimoto's disease[9)21)26)]. However, an association with inflammatory bowel disease, either ulcerative colitis or Crohn's disease is not widely recognized. Other hepatobiliary diseases commonly found in association with ulcerative colitis include hepatic steatosis, primary sclerosing cholangitis, and chronic active hepatitis[7)8)13)16)19)27)]. However, primary biliary cirrhosis is a less common complication of ulcerative colitis than primary sclerosing cholangitis, and an association between primary biliary cirrhosis and ulcerative colitis has been reported in only eleven previous cases.

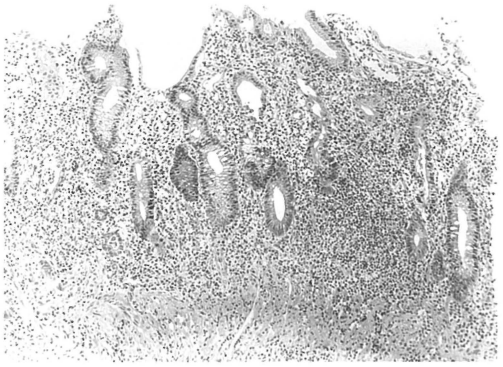


Fig. 3 The histological findings of the sigmoid colon show moderate to marked acute inflammation with crypt abscesses limited to mucosa. (HE stain, 140×)

The clinical features of these patients including our own are summarized in Table 1. Though many of patients with primary biliary cirrhosis are middle-aged woman, five of the 12 reported cases of concurrent primary biliary cirrhosis and ulcerative colitis have occurred in men. Three of these 12 patients were younger than 30 years. The colitis in patients with concurrent primary biliary cirrhosis and ulcerative colitis was less severe than that typically seen in isolated ulcerative colitis. Eight of the 12 patients had left-sided colitis and proctitis. Those who had primary sclerosing cholangitis, in contrast, tend to manifest a pancolitis. Twenty-five to 50% of the reported patients with primary sclerosing cholangitis and ulcerative colitis have undergone total colectomy,

Table 1 Reported Cases of Primary Biliary Cirrhosis Associated with Ulcerative Colitis

No.	Author	(Year)	Age	Sex	AMA titer	Symptom of PBC	Type of UC	Prior diagnosis	References
1	Kato et al.	(1985)	65	F	1 : 64	Asymptomatic	Pancolitis	UC	10
2	Bush et al.	(1987)	20	F	Positive	Asymptomatic	Proctitis	UC	3
3			22	M	1 : 160	Asymptomatic	Proctitis	UC	
4			44	M	1 : 320	Asymptomatic	Proctitis	UC	
5			28	F	1 : 200	Asymptomatic	Left-sided colitis	UC	
6	Akahoshi et al.	(1992)	49	F	1 : 320	Asymptomatic	Left-sided colitis	Simultaneous	1
7	Lever et al.	(1993)	40	M	1 : 160	Pruritus	Left-sided colitis	UC	12
8	Veloso et al.	(1993)	45	F	1 : 320	Pruritus	Proctitis	PBC	22
9	Satsangi et al.	(1996)	48	F	1 : 160	Asymptomatic	Pancolitis	UC	18
10	Koulentaki et al.	(1999)	58	M	>1 : 160	Asymptomatic	Pancolitis	UC	11
11			68	F	1 : 160	Asymptomatic	Pancolitis	UC	
12	This case		61	M	1 : 160	Asymptomatic	Proctitis	PBC	

PBC, primary biliary cirrhosis. UC, ulcerative colitis. AMA, antimitochondrial antibody.

compared with none of the primary biliary cirrhosis patients[5)12)17)25)].

The etiology of concurrent primary sclerosing cholangitis and ulcerative colitis has been considered, and the following pathogenetic mechanisms have been proposed: (1) a chronic low-grade portal infection caused by the ulcerative colitis leads to chronic biliary tract inflammation and fibrosis; (2) the primary sclerosing cholangitis associated with ulcerative colitis is caused by a reaction to toxic circulating bile acids released from the diseased colon; and (3) serum anticolon antibodies caused by ulcerative colitis cross-react with the portal tracts. Primary biliary cirrhosis and primary sclerosing cholangitis share a common feature in that the biliary system is involved in each of these inflammatory processes. Therefore, the possibility that primary biliary cirrhosis might accompany a number of disorders associated with ulcerative colitis is conceivable[1)4)6)24)].

Involvement of the immune system in the pathogenesis of autoimmune hepatobiliary disorders associated with ulcerative colitis is suggested by lymphocytic infiltration of the portal tracts, demonstration of circulating immune complexes and antibodies that react with bile ducts, alteration in the helper/suppressor T-lymphocyte ratio, and an enhanced HLA-DR display on biliary epithelium[2)14)15)22)23)].

In addition, concurrent autoimmune conditions are frequently associated with primary biliary cirrhosis such as Sjögren's syndrome, rheumatoid arthritis, systemic sclerosis, dermatomyositis, thyroiditis, as well as with ulcerative colitis such as primary sclerosing cholangitis, ankylosing spondylitis, uveitis. Thus, concurrent primary biliary cirrhosis and ulcerative colitis may represent an additional fundamental association between syndromes with an autoimmune etiology, though an uncommon one.

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(和文抄録)

潰瘍性大腸炎を合併した原発性胆汁性肝硬変

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潰瘍性大腸炎および原発性胆汁性肝硬変を合併した稀な1症例を経験したので報告する．症例は61歳，男性．抗ミトコンドリア抗体陽性および肝生検組織所見より原発性胆汁性肝硬変と，結腸内視鏡検査およびS状結腸組織所見より潰瘍性大腸炎と診断された．潰瘍性大腸炎を合併した原発性胆汁性肝硬変の報告は少なく，本症例を含め12例が報告されているのみである．両疾患の合併における自己免疫機序の関与について考察した．