Primary sclerosing cholangitis and sarcoidosis – an infrequent association

Avinash Murthy, Eva C. Foitzik, Jacquelyn Choate, Tipu Nazeer, David M. Chaletsky, Vinay Sood

Division of Gastroenterology, Albany Medical College, Albany, NY, USA
and Division of Gastroenterology, Pirmasens Hospital, Pirmasens, Germany

Discussion (continued)

Inflammatory bowel disease is strongly associated with PSC, nearly four-fifths of PSC will have inflammatory bowel disease (IBD). However only 2.5–7.5% of IBD have PSC. One series of case reports showed that PSC can occur in 5.7% of ulcerative colitis patients (UC). Sarcoidosis is a granulomatous systemic disease of probable autoimmune origin. Although familiar associations are reported for crohns disease and sarcoid case reports associating IBD and sarcoid are rare. Barr et al reported cases of sarcoidosis in 680 UC patients.

Primary sclerosing cholangitis and sarcoid should occur in the same individual by chance in 2–32 per one billion population. Thompson et al reported one case of sarcoidosis among 37 PSC patients, a case report, no other report of PSC has reported 5% sarcoidosis. Thus there must be a heritable unfound association between these entities.

Multiple cellular and humoral immunologic abnormalities are noted in PSC highlighting the role of immune-related process in its pathogenesis, they include presence of non specific auto antibodies, elevated serum levels of IgM, circulating immune complexes and complement activation. PSC is associated with other immunologically mediated diseases like angitis, lymphomatoid hypophysitis, immune deficiency syndromes, sicca syndrome, histiocytosis X, medial and retroperitoneal fibrosis. HLA-B8 and HLA-DR3 antigens are common in PSC and are associated with increased incidence of autoimmune disease.

Sarcoidosis likely results from an exaggerated immune response to a limited class of antigens (self or preserved) although no clear HLA locus has been associated with it. HLAA8 is associated with increased occurrence of osteoarthritis and arthritis in sarcoidosis. IBD and sarcoid both display areas of helper T lymphocytes in the disease sites, presence of circulating immune complexes, auto antibodies and heightened activity of circulatory and natural killer cells. An increased frequency of HLAA1, A8 and DR3 was shown among patients with UC and sarcoid by Barr et al.

Hence likely a immune related association between these entities is likely.

Sarcoidosis could mimic cholangiographic appearance of PSC if there are multiple granulomas in the extra hepatic and intrahepatic ducts. Secondary sclerosing cholangitis can occur due to recurrent episodes of bacterial cholangitis due to local obstruction. Sarcoid granulomas in portal hepatobiliary producing secondary sclerosing cholangitis is reported in at least one of the case reports. Also chronic ulcerative colitis may well mimic cholangiographic changes of the intrahepatic ducts seen in PSC.

In our patient diagnosis of PSC with UC later developing sarcoidosis is likely because he had UC, proven by biopsy and PSC well before he was diagnosed with sarcoid. His IgM was elevated keeping with the finding that in chronic cholestasis secondary to sarcoid IgM was normal, and showed an increase of more than 50% in PSC. Our patient had liver biopsy in 2001 which suggested probable PSC involving only small intrahepatic ducts, while repeat liver biopsy in 2003 was suggestive of hypereosinophilic syndrome as well as PSC, with eosinophil infiltration, periporal and portal fibrosis with possible bridging fibrosis without cholestatis. Cervical lymphnode excission biopsy in 2006 had shown follicular hyperplasia.

Patients IBD with or without PSC may later develop sarcoidosis although case reports with sarcoidosis producing PSC like biliary stricturing has been described; this latter conglomerate may constitute a different end of this curious association.

Conclusion

The association between primary sclerosing cholangitis and sarcoid may be important in evaluating patients with non specific symptoms of malaise and weight loss. Also the clinician should be aware of sarcoidosis complicating and mimicking a intrahepatic biliary cholestatic appearance. A trial of steroids might be beneficial in some patients although it has not yet been shown to reverse the cholestatic changes. Our patient was treated with oral steroids for neuro sarcoidosis and high dose ursofor his PSC; he continues to be seen in the clinic and is doing well.