Autoimmune Hepatitis-Primary Sclerosing Cholangitis Overlap Syndrome Complicated by Crohn’s Disease

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Dear Sir

Autoimmune hepatitis-primary sclerosing cholangitis (AIH-PSC) overlap syndrome is characterized by features of both conditions. Association of AIH-PSC overlap syndrome with ulcerative colitis (UC) is well recognized but is rarely seen with Crohn's disease (CD). We report a case of a young African-American woman with AIH-PSC overlap syndrome complicated by CD that illustrates the approach to diagnosis and management of the condition. A brief discussion of the topic follows the case presentation.

Case Presentation

A 22-year-old African-American woman with a previous diagnosis of autoimmune hepatitis (AIH) was being successfully maintained on azathioprine (AZA) and prednisone when her serum transaminase and alkaline phosphatase levels abruptly rose. She was referred to an adult hepatology clinic. Magnetic resonance cholangiopancreatography (MRCP) revealed intra- and extrahepatic biliary dilation with scattered biliary strictures indicating primary sclerosing cholangitis (PSC). A diagnosis of AIH-PSC overlap syndrome was made and ursodeoxycholic acid (UDCA) was added. Percutaneous transhepatic cholangiography (PTC) with temporary biliary stenting was performed within a month of the new diagnosis for worsening cholestasis. Three months later, mycophenolate mofetil (Cellcept) was started for persistently increased transaminases. She finally began to respond with significant decrease in serum transaminase and alkaline phosphatase levels.

After 3 years of successful management, she developed diarrhea and abdominal cramping. Colonoscopy revealed extensive patchy mucosal inflammation throughout the colon and terminal ileum. Mucosal biopsies demonstrated extensive crypt distortion, focal cryptitis, increased chronic inflammation, fibrino-inflammatory exudates and erosion establishing a diagnosis of Crohn’s disease (CD) (fig. 1). Contrasted CT scan of the abdomen and pelvis revealed diffuse thickening of terminal ileum, cecum, ascending and transverse colonic wall and pericolic stranding consistent with active inflammatory bowel disease. It also demonstrated signs of liver cirrhosis (based on the increased caudate to right lobe ratio) as well as intra- and extrahepatic biliary dilation (fig. 2a, b). Budesonide 9 mg daily was added to treat active CD and prednisone was discontinued. She remained symptomatic with continued diarrhea and further deteriora-

Fig. 1. Hematoxilin and eosin (×10 magnification) stain of biopsy of the patient obtained from colonic mucosa demonstrates crypt distortion depicted here by a bifid crypt (long arrow) in addition to marked chronic inflammatory changes in the mucosa represented by increased lymphocytes, plasma cells and eosinophils (short arrow).
normalized. She did well during the next 6 months but then again gradually developed abdominal cramping, diarrhea and bloody stools. Methotrexate (MTX) was added to optimize the effect of adalimumab. The patient’s diarrhea and abdominal pain improved but only temporarily and the aminotransferase levels began to rise once again. As a result, both adalimumab and MTX were discontinued. To bypass the glutathione S-transferase mediated conversion of AZA to 6-mercaptopurine (6-MP) the patient was placed directly on 6-MP.

Currently, the patient is in remission on 6-MP 100 mg daily. AIH component of the overlap syndrome is being successfully controlled with mycophenolate mofetil. UDCA is being used for symptomatic treatment of PSC associated cholestasis. She was recently found to have recurrence of biliary stricturing (fig. 3) for which balloon dilation was performed during endoscopic retrograde cholangiopancreatography (ERCP). The patient has compensated liver cirrhosis. Liver transplantation has been discussed as a future option but due to normal hepatic synthetic function and good functional status, she has not been evaluated yet.

Discussion

AIH and PSC are distinct autoimmune hepatobiliary diseases [1, 2]. Patients who present with overlapping features of the two have the AIH-PSC overlap syndrome [2]. AIH and PSC may also occur in association with other autoimmune conditions, most notably ulcerative colitis (UC) [3]. CD however, in association with AIH-PSC overlap syndrome, is rarely encountered in clinical practice [3].

Our understanding of overlap among autoimmune hepatobiliary conditions including that between AIH and PSC is in flux. There is still controversy over whether AIH and PSC are distinct disease entities confined to the hepatobiliary tract or whether their occurrence alone or in combination heralds the presence of a more extensive autoimmune process [4].

There are established individual treatments for AIH as well as for PSC [5, 6]. The American Association for the Study of Liver Diseases (AASLD) recommends corticosteroids with or without AZA/6-MP as the first line treatment for AIH [5]. PSC generally responds poorly to medical treatment and therefore PTC or endoscopic balloon dilation with or without biliary stenting is frequently needed. In many cases, liver transplantation is eventually required [6].

As opposed to AIH and PSC, there are no definitive management guidelines for AIH-PSC overlap syndrome whether it occurs by itself or in association with either of the two IBD subtypes. The current trend is to treat each disease entity separately and adjust medications according to symptoms and side effects [5, 6]. Successful medical treatment may require a trial of several immune modulators and UDCA as well as endoscopic or surgical intervention. Each condition may influence the other in terms of disease course, therapeutic options and response to treatment as illustrated in our case presentation. Thus a close follow up of the patient with effective communication between the treating clinicians is essential.

Disclosures

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References