Management of Autoimmune and Cholestatic Liver Disorders

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• Autoimmune hepatitis • Biliary cirrhosis
• Sclerosing cholangitis • Overlap syndrome
• Cholestasis • Liver transplantation

The management of autoimmune and cholestatic liver disorders is a challenging area of hepatology. Autoimmune and cholestatic liver diseases represent a comparatively small proportion of hepatobiliary disorders, yet their appropriate management is of critical importance for patient survival. In this article, management strategies are discussed, including the indications and expectations of pharmacologic therapy, endoscopic approaches, and the role of liver transplantation.

AUTOIMMUNE HEPATITIS

Autoimmune hepatitis is an inflammatory liver disease of unknown cause. The disease can present with the onset of jaundice and marked elevation of amino liver transaminases. In some patients, autoimmune hepatitis may present as symptomatic, chronically elevated liver enzymes, or incidentally found cryptogenic cirrhosis, or more rarely, as acute fulminant liver failure.[1–4] Patients with autoimmune hepatitis typically have circulating autoantibodies at robust titers, elevated globulins, plasma cells, lymphocytic inflammation and periportal liver cell necrosis on hepatic histology.[1,5] An immune mediated injury in genetically susceptible persons, perhaps triggered or modulated by environmental agents, is believed to lead to liver damage in

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autoimmune hepatitis.[6–8] The syndrome, diagnosis, and natural history of autoimmune hepatitis have been reviewed in detail elsewhere.[1,2,9,10]

Management

In general, management strategies in patients with autoimmune hepatitis are individualized and tailored to the clinical, biochemical, and histologic severity. The classic presentation, with jaundice, systemic symptoms, marked elevation of alanine aminotransferase (ALT), aspartate aminotransferase, and elevated globulins in a young or middle aged woman, is typically treated with corticosteroids, or a combination of high doses of corticosteroids and antimetabolites (see later discussion). In contrast, autoimmune hepatitis presenting with acute liver failure may require urgent liver transplantation. Mild forms of autoimmune hepatitis may be more common than previously estimated. Low-level fluctuation of aminotransaminases, the presence of circulating autoantibodies, and mild histologic changes may only require observation, or low-dose pharmacologic monotherapy. More data are needed in this area.

A response to initial pharmacologic therapy is observed in 60% to 80% of cases, with a transplant-free survival at 10 years in excess of 90%. However, the survival advantage of medical therapy is more limited in patients with established cirrhosis (**Box 1**).

Pharmacologic Therapy

Of several agents with anti-inflammatory or immunosuppressive properties used for treatment of autoimmune hepatitis, corticosteroids and azathioprine have been the most extensively evaluated (see **Box 1**).[10–13] The indication to proceed with pharmacologic therapy is based primarily on the observation of an aggressive histologic picture on the liver biopsy, including interface hepatitis (also known as piecemeal or periportal necrosis). Patients with severe autoimmune hepatitis almost always have active interface hepatitis. Initial monotherapy with prednisone (or prednisolone) at doses of 40 to 60 mg/d in adults, is the preferred regime for patients with acute presentation of severe autoimmune hepatitis, when the prompt and potent anti-inflammatory effect of corticosteroids is needed.[14] In cases of moderate severity, lower doses of prednisone (15 to 30 mg/d), in combination with either azathioprine (50 to 150 mg/d) or 6-mercaptopurine (25 to 100 mg/d), can be employed as initial therapy. Whether monotherapy or in combination therapy, prednisone dose is gradually tapered over several weeks and months.

A common cause of relapse is an excessively rapid tapering of corticosteroids, leading to biochemical flare-ups or exacerbation.

The goal should be to achieve sustained biochemical remission (normalization of ALT) with the lowest possible dose of prednisone. Patients who achieve normal transaminases after a few weeks or months of therapy, should, in general, be maintained on therapy to complete at least 1 year of persistently normal ALT. A liver biopsy should

Box 1
Autoimmune and cholestatic liver diseases

Autoimmune hepatitis

Primary biliary cirrhosis

Primary sclerosing cholangitis

Overlap syndromes