Diagnosis and Treatment Strategy for Syncytial Giant Cell Hepatitis

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Syncytial giant cell hepatitis (GCH) is frequently found in neonates, but very rarely in adults, with an estimated incidence ranging from about 0.1% to 0.25% of all liver diseases in adults (1, 2). GCH in adults is a rare disorder characterized by severe icteric hepatitis, histologically defined by diffuse syncytial multinucleated hepatocytes, and often has a fulminant course (3, 4).

The diagnosis of GCH is based on the presence of the giant cell transformation of hepatocytes. Giant cell proliferation is a non-specific reaction to various stimuli, rather than a specific disease process (2, 5). The mechanism of giant cell formation is still unknown. However, two possible mechanisms involved in the formation of giant hepatocyte have so far been proposed: the fusion of individual cells to form a syncytium (1) and the failure of the cytoplasm to divide at the time of nuclear division (4).

Giant cell hepatitis is commonly found in various neonatal and infantile liver diseases, but is rarely found during the post-infantile period. Hepatitis with multinucleated giant cells in the liver tissue is called giant cell hepatitis, and it is often seen in neonatal viral hepatitis and biliary atresia (6). The hypotheses regarding its etiology suggest drug-induced disease (7) including that due to herbal remedies (8), hepatitis viruses (hepatitis A, B and C) (9), Epstein-Barr virus, variant A of human herpesvirus 6 (10) and paramyxoviruses (3, 11), ulcerative colitis (12) and autoimmune disorders (4), including autoimmune hepatitis (13).

GCH is a descriptive diagnosis of a unique pattern of reaction to several different insults. Therefore, the determination of the exact etiology of the underlying disorder, such as viral infection or an autoimmune reaction, is useful, because the prognosis generally depends on the underlying liver disease (14). However, it should be noted that no underlying process can be identified in many cases.

If the cause of giant cell hepatitis is infectious, then it can be treated with either antibiotics or antiviral therapies. There

are several case reports in the literature describing the effective treatment of GCH with ribavirin (15). In the case of autoimmune hepatitis, multinucleated giant cells are likely observed in the acute type or chronic type with exacerbation (16). The typical clinical features are a prolonged clinical course, severe cholestasis, and a progression to cirrhosis within a few months (17).

Phillips et al. reported that ten patients with GCH had either severe chronic active hepatitis or subacute hepatic failure not responding to corticosteroid treatment (3). Moreover, half of the patients died, while the other half of patients eventually underwent liver transplantation.

In this issue of Internal Medicine, Tajiri et al. document an elderly male with syncytial giant cell hepatitis who was successfully treated by immunosuppressants. They conclude that active immunosuppressive treatment may be beneficial in patients with adult syncytial giant cell hepatitis (18). Although immunosuppressive therapy with steroids and/or azathioprine has proven to sometimes be beneficial when used in the early treatment of some patients, frequent deaths or the need for liver transplantation have also been reported.

The first clearly documented case of post-infantile giant cell hepatitis proven to be positive for ANA, SMA and antibodies against liver membrane antigen (LMA), had marked hypergamma-globulinemia, and responded well to immunosuppressive therapy (13). Furthermore, Thaler et al. demonstrated the presence of hypergamma-globulinemia and the favorable response to immunosuppressive therapy in the treated patients, thus suggesting an underlying autoimmune disease (1). The clinical course of autoimmune hepatitis with GCH varies from the normalization of the hepatic histology to a progression to cirrhosis and liver failure. Immediate therapy after the diagnosis may prevent liver failure due to GCH. Moreover, prolonged treatment with corticosteroids and immunosuppressants is usually effective for rendering the cirrhosis inactive.

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