Hepatic Manifestations of the Antiphospholipid Syndrome

Key words: autoimmune hepatitis, Sjögren's syndrome, Budd-Chiari syndrome, nodular regenerative hyperplasia

Antiphospholipid syndrome (APS) is characterized by the presence of antiphospholipid antibodies (anticardiolipin antibodies and/or lupus anticoagulant) in association with symptoms including venous/arterial thromboses, recurrent fetal loss and thrombocytopenia. Thrombotic episodes may occur at any part of the circulation system, hence, any organ may be involved. As for hepatic involvement, the most well known manifestation of APS is Budd-Chiari syndrome, which is caused mostly by obstruction of hepatic veins or inferior vena cava. Pelletier et al (1) have reported that of their 22 non-tumorous Budd-Chiari patients, 4 had antiphospholipid antibodies without other causes of hepatic vein thrombosis. Among these 4 patients, 2 seemed to have primary APS, i.e., no signs of other autoimmune diseases such as SLE. Thus, APS should be considered as a cause of unexplained Budd-Chiari syndrome. Another uncommon but important hepatic complication of APS is nodular regenerative hyperplasia (NRH). NRH is occasionally found in patients with SLE, and association with the presence of antiphospholipid antibodies has been documented. NRH has also been found in patients with primary APS (2, 3). Since NRH may lead to portal hypertension and variceal hemorrhage, it is important to detect its presence. MRI may be useful among the more noninvasive examinations. Other hepatic manifestations of APS include hepatic veno-occlusive disease, hepatic infarction, occlusion of small hepatic veins and portal hypertension (4).

Recently, possible association of autoimmune hepatitis and presence of antiphospholipid antibodies have been reported. Nagayama et al reported a case of a 57-year-old female, who presented with multiple cerebral infarctions and livedo reticularis (5). She had elevated transaminase activity, and showed positivity for antinuclear, anti-DNA, anti-smooth muscle, IgM anticardiolipin antibodies, and lupus anticoagulant. Liver biopsy revealed changes compatible with autoimmune hepatitis. The patient was successfully treated with ursodeoxycholic acid, anticoagulant and antiplatelet therapies. Kobayashi et al reported a 76-year-old female with autoimmune hepatitis (6). During treatment with prednisolone, the patient developed lung infarction, and subsequent examination revealed the presence of IgM anticardiolipin antibody. This patient was successfully treated with warfarin. In another case, reported by Pathmakanthan et al, a 24-year male developed

autoimmune hepatitis (7). Examinations prior to liver biopsy revealed a greatly prolonged APTT, and the patient was found to be positive for IgG anticardiolipin antibody and lupus anticoagulant. However, this patient showed no signs of thrombosis or any other symptoms suggestive of APS.

In this issue, Katayama et al (8) report a case of Sjögren's syndrome complicated with autoimmune hepatitis and APS.

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In previously reported cases of autoimmune hepatitis associated with the presence of antiphospholipid antibodies, antinuclear antibody was present, but the presence of anti-SS-A antibody or sicca symptoms have not been documented. Therefore, this case may possibly be the first documented case of autoimmune hepatitis with APS and Sjögren's syndrome. Their patient had autoimmune hepatitis, and Sjögren's syndrome confirmed by Schirmer's test and sialography. The patient showed positive for β_2 -GPI dependent anticardiolipin antibody and lupus anticoagulant. This patient did not show any signs of thrombosis, but marked thrombocytopenia, which responded favourably to 30 mg/day of prednisolone, was observed. Although not included in the recently proposed diagnostic criteria for APS (9), thrombocytopenia is a well known complication of APS. In addition, Katayama et al have found that serum sIL2R, IFN γ and GM-CSF were elevated in this patient, and suggested that Th0-Th1 cells may be activated in this patient. Of course, this may or may not be common in patients with this condition, and accumulation of similar cases is necessary.

Although Sjögren's syndrome is a well recognized complication of autoimmune hepatitis, association of APS and autoimmune hepatitis is not well known. As both are autoimmune diseases, a thorough survey of patients with autoimmune hepatitis may reveal a more close connection between these conditions.

When an APS patient is found to have liver dysfunction or portal hypertension, it may be purely coincidental, such as an association of HCV hepatitis, but may also be associated with APS in some way. These possibilities should always be considered.

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