Clinical Features and Pathogenesis of Catastrophic Antiphospholipid Syndrome

Key words: antiphospholipid antibodies, thrombosis, thrombocytopenia

The concept of antiphospholipid syndrome (APS) has been established (1). It is well-known that one of the clinical features in APS is arterial or venous thrombosis, and that the specificity of so-called antiphospholipid antibodies have diversity against their epitopes, as so-called antiphospholipid antibodies react to phospholipids as well as plasma proteins such as β₂-glycoprotein I and prothrombin (2-5). Antiphospholipid antibodies have been reported to be one of the acquired risk factors against thrombotic events.

Catastrophic antiphospholipid syndrome (CAPS) is defined by the clinical manifestations of sudden onset of multiple organ involvements including renal failure or acute respiratory distress syndrome in patients with primary or secondary APS (6-8). CAPS is characterized by microangiopathy, that is, occlusive vascular disease affecting predominantly small vessels of different organs, particularly kidney, lung, brain, heart, and liver. Therefore, the similarities and/or differences in the clinical features and the pathogenesis must be clarified to differentiate CAPS from thrombotic thrombocytopenic purpura (TTP) and other related generalized non-inflammatory thrombotic diseases (9).

In this issue of the Journal, Mizuno et al (10) describe an important case report of CAPS based on systemic lupus erythematosus (SLE).

Their patient showed clinical manifestations of central nervous system involvement, renal failure and adult respiratory distress syndrome. Also, she had thrombocytopenia, autoimmune hemolytic anemia, and high levels of IgG anticardiolipin antibodies. Moreover, postmortem microscopic examination revealed non-inflammatory thrombosis as indicated by occlusion of arterioles and capillaries with abundant hyaline thrombi and segmented subendothelial hyaline deposition in many organs. These findings were compatible with CAPS (6-8). In addition, infection such as pneumonia was found as a precipitating factor of CAPS, as reported previously.

Microangiopathy in patients with CAPS is similar to the finding in those with TTP, as this occlusive vasculopathy is mediated by the hypercoagulable state. It has been reported that this hypercoagulable state occurs due to activation of vascular endothelium (11). On the other hand, antiphospholipid antibodies such as IgG and IgM anticardiolipin antibodies are detected in sera from patients with TTP (12). Therefore, there is a possibility that clinical entities share clinical and pathological features between patients with CAPS and TTP.

There still remains three questions to be answered in the near future: 1) The specificity of so-called antiphospholipid antibodies should be examined in patients with TTP to determine the serological markers among these patients. 2) The dysfunction of von Willebrand factor-cleaving protease or antibodies to von Willebrand factor-cleaving protease has been reported in patients with TTP (13, 14). The activity of von Willebrand factor-cleaving protease in patients with CAPS should be analyzed to assess the possibility of this mechanism of thrombosis in such patients. 3) Plasmapheresis has been reported to be effective in both patients with CAPS and TTP (7, 8, 15), and plasmapheresis was performed in the patient of Mizuno et al (10). However, a precise prospective study has not been carried out. It will be necessary to determine the efficacy of plasmapheresis in these patients.

The case report of Mizuno et al (10) can facilitate resolution of these problems.

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References