Pulmonary Hypertension and the Antiphospholipid Syndrome

It is now well known that symptoms such as arterial and venous thrombosis, recurrent fetal loss, central nervous system involvement and thrombocytopenia in patients with systemic lupus erythematosus (SLE) are associated with the presence of antiphospholipid antibodies. In addition, antiphospholipid antibodies can be found in patients with no other apparent autoimmune diseases and may cause cerebral infarction, myocardial infarction and other thromboembolic complications. The term “antiphospholipid syndrome” (APS) is given to these conditions.

Many studies have established the importance of anticycadioplin antibody (aCL) for predicting thrombotic symptoms and fetal loss in patients with SLE. More recent studies have shown that binding to cardiolipin of IgG class aCL found in patients with APS is dependent on the existence of a cofactor, namely β2-glycoprotein I (β2-GPI). The issue concerning the antigenic specificities of aCL is currently being studied by numerous laboratories.

Pulmonary hypertension (PH) is one of the most life-threatening complications of collagen diseases including systemic sclerosis, mixed connective tissue disease and SLE. In particular, PH in SLE often resembles the primary idiopathic type of PH, that is with clear lung fields and no apparent evidence of pulmonary thromboembolism. Occurrence of PH in SLE patients is considered uncommon, but one study suggests that this condition may be present in 14% of SLE patients (1). Although its pathogenesis is not clearly understood to date, abnormal vasospasm, platelet abnormalities, immune complex deposition in pulmonary vessels and defective fibrinolysis have been suggested as possible pathogenic factors. The association of antiphospholipid antibodies and PH is beginning to draw attention of many rheumatologists. This association in SLE patients was originally described by Asherson et al (2). In their series of 6 SLE patients with PH, 5 were positive for lupus anticoagulant activity. It is of interest that, of their patients, 3 were positive for Raynaud’s phenomenon, suggesting that abnormal vasospasm may also have contributed to the occurrence of PH in these patients. It is also of importance that PH has been reported to occur in patients with primary APS (3). Primary APS patients present with various thrombotic episodes without apparent underlying autoimmune diseases. Furthermore, a high incidence of antiphospholipid antibodies in patients diagnosed as “primary idiopathic” PH has been reported (4). Therefore, the presence of antiphospholipid antibodies should be considered in patients with primary PH.

In this issue of Internal Medicine, Yutani et al describe a case of SLE presenting with severe PH (5). The patient died despite aggressive treatment, and postmortem examination revealed fresh and organized thromboemboli in many of the small arteries. These small thrombi were thought to be the cause of PH in this patient. This condition should always be considered as a cause of PH in collagen disease patients, since this may be easily overlooked clinically. The cause of the thromboemboli in this patient is not completely clear but the hypercoagulative state due to APS may have played a role as the lupus anticoagulant assay was positive in this case. Although aCL (anti-β2-GPI antibody) and biological false-positive test for serological test for syphilis were not detected in this patient, this does not exclude the diagnosis of APS, since antiphospholipid antibodies are a heterogeneous population of antibodies with different specificities. The three tests mentioned above may detect different antiphospholipid antibodies, and should all be tested when APS is clinically suspected.

Finally, it should be emphasized that PH or pulmonary embolism may be present in patients with primary or secondary APS, who do not show any respiratory symptoms such as dyspnea or chest pain. When a patient is diagnosed as having APS, it is essential to examine the respiratory function and pulmonary blood flow of this patient even if the patient is free of symptoms suggestive of PH or pulmonary embolism.

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References