Alveolar and serum antiphospholipid antibodies in acute respiratory distress syndrome associated with catastrophic antiphospholipid syndrome

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Bucciarelli and colleagues analysed the clinical and laboratory characteristics of patients with catastrophic antiphospholipid syndrome (APS) and acute respiratory distress syndrome (ARDS).¹ They found that ARDS is the dominant pulmonary manifestation of catastrophic APS.

In their discussion the authors report on the paper by Maneta-Peyret *et al.*,² who detected antilipid autoantibodies of the IgG class exclusively in the bronchoalveolar fluid (BALF) of patients with ARDS. These antibodies were directed against anionic phospholipids and reacted principally with phosphatidic acid. The antibodies showed significant binding on negatively charged phosphatidylserine and at a lower level on phosphatidylinositol in an enzyme linked immunosorbent assay (ELISA). These phospholipids occur in the pulmonary surfactant. Detection of antiphospholipid antibodies (aPL) in the BALF of patients with ARDS suggests involvement of autoimmune mechanisms in the pathogenesis of ARDS. However, it is difficult to determine if these antibodies are produced locally or provided from plasma owing to the increase in endothelial and epithelial permeability that occurs in ARDS.

In a previous study we found low titres (within the normal range) of IgG anticardiolipin, IgG anti- β_2 -glycoprotein I, IgG antiphosphatidic acid, and IgG antiphosphatidylserine antibodies in both the BALF and serum of patients with ARDS.³ However, one of 27 patients investigated had high levels of aPL in both BALF and serum. This patient had severe ARDS due to sepsis. The high aPL levels in serum, possibly triggered by sepsis, were associated with high aPL levels in BALF, which can be explained by high capillary-alveolar permeability. A computed tomographic (CT) scan showed widespread infarctions in brain, spleen, and kidney, and pulmonary thromboembolism, suggesting a diagnosis of catastrophic APS.

A previously reported patient with catastrophic APS and prominent respiratory failure with ARDS-like clinical picture⁴ had low aPL levels in BALF and high aPL levels in serum. This patient, however, had been treated with high dose methylprednisolone, bronchoalveolar lavage had been performed 5 days after onset of respiratory failure, and respiratory failure had improved at the time of bronchoalveolar lavage, suggesting low capillary-alveolar permeability. Previous studies did not indicate local production of any IgG subclasses in the respiratory tract,⁵ the strong correlation between serum and BALF IgG levels suggests that the BALF IgG derives from serum.⁶ These results do not support the hypothesis that aPL are produced locally in the alveolar space.

It is of interest to note that the diagnosis of catastrophic APS in the patient with high aPL in BALF³ was made retrospectively after careful re-examination of the CT scan, which showed pulmonary thromboembolism and widespread infarction in brain, spleen, and kidneys. The aPL were determined 1 year after collecting the BALF and serum,

which had been kept frozen at -80°C until analysis. At the time of diagnosis and treatment of ARDS due to bronchopneumonia, septic shock, and acute renal failure associated with squamous cell carcinoma of the bladder, we did not consider catastrophic APS as a possible diagnosis.

His past medical history included severe arterial hypertension, without, however, any evidence of thrombosis or other features of APS. Necropsy showed signs of severe general arteriosclerosis, and severe renal arteriolosclerosis. Arterial hypertension, severe arteriosclerosis, and carcinoma may be associated with the occurrence of aPL,^{7,8} which might be triggered by sepsis to become pathogenetic for developing catastrophic APS. According to the preliminary criteria for the classification of catastrophic APS,⁹ this patient can be classified as having probable catastrophic APS, because laboratory confirmation at least 6 weeks apart was impossible owing to the early death of the patient; he died within 48 hours after admission owing to progressive multiple organ failure (lung, circulation, kidney, liver, coagulation). Therefore, to exclude catastrophic APS, determination of aPL in patients with a similar history and who develop ARDS or multiple organ failure is recommended.

Competing interest: None.

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