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LETTER

Pulmonary hemorrhage, due to rupture of small muscular arteries, in an autopsy case of systemic lupus erythematosus with antiphospholipid antibodies

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Dear Sir

Pulmonary hemorrhage is a rare, devastating, and frequently fatal manifestation of systemic lupus erythematosus (SLE) with mortality rates of 70–90% [1]. Diffuse alveolar hemorrhage (DAH) in SLE is usually characterized by immune complex deposition and pulmonary capillaritis associated with a neutrophil-mediated disruption of alveolar and capillary basement membranes [2]. Development of vasculitis usually is not reported in DAH. A distinctive microangitis characterized by acute inflammation and necrosis of alveolar capillaries, arterioles, and small muscular arteries also has been described in four patients only [3]. In this letter, we describe pulmonary hemorrhage, due to ruptures of small muscular arteries by fibrinoid necrosis with immune complex depositions, in an autopsy case of SLE with antiphospholipid antibodies.

A 17-year-old Japanese woman was admitted because of high-grade fever. Renal dysfunction, pancytopenia, positive tests for anti-nuclear antibody (640-fold) and anti-ds-DNA antibody (3,920 U/mL) led to diagnosis of systemic lupus erythematosus. The level of complement titer (CH50) was below the detection limit (<10 U/mL) and circulating immune complex (C1q method) was remarkably increased (48.2 mg/dL). A complication of secondary APS was suspected because of spot bleeding of her fingers, prolongation of activated partial thromboplastin time, and positive tests for lupus anticoagulant and anti-cardiolipin-b2- glycoprotein I complex antibody. Anti-phosphatidylserine (PS)/prothrombin (PT)-IgG antibody, [4] reported to be predictive of thrombosis in patients with SLE, [5] was also remarkably increased (76 U/mL).

Despite methylprednisolone pulse treatment under systemic heparinization, she suffered from oliguric acute renal failure and severe bilateral pulmonary edema on day 6 with increased fibrin/fibrinogen degradation products (FDP) (36.5 μg/mL) and thrombin-antithrombin III complex (32.7 ng/mL). We suspected sudden onset of pulmonary embolism, but there were no findings suggesting this in a contrast study by computed tomography and lung perfusion scintigraphy. Although we started continuous hemodiafiltration under systemic heparinization after a double filtration plasmapheresis, she was attached to a ventilator because of acute respiratory distress syndrome (ARDS) on day 10 and developed hemoptysis on day 13. Three times a week immunoabsorption with repeated methylprednisolone pulse and cyclophosphamide pulse treatments reduced anti-ds-DNA antibody from 3,920 U/mL to 220 U/mL, anti-PS/PT-IgG antibody from 76 U/mL to 3.6 U/mL, and FDP

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from 36.5 to 3.1 μg/mL. Nevertheless she died from severe hemoptysis on day 19.

Autopsy revealed blood-filled lungs and microscopic studies of the lungs showed DAH and ruptures of small muscular arteries by fibrinoid vasculitis (Fig. 1a, b). Immune complex deposition, including C1q was revealed by immunohistochemical study (Fig. 1c). Microscopic studies of the kidneys revealed diffuse global proliferative lupus nephritis with fibrinoid necrosis of efferent and afferent arterioles, correspond to Class IV-G (A) in the classification of glomerulonephritis in systemic lupus erythematosus revisited [6].

Pulmonary hemorrhage in this case was resistant to multiple treatments. Efficacy of plasmapheresis has only been supported by non-controlled and/or retrospective studies [7]. However, Erickson et al. reported dramatic improvement in three pulmonary hemorrhage patients who underwent intensive plasmapheresis combined with steroids and cyclophosphamide [8]. Rather than simple plasma exchange we performed double filtration plasmapheresis and immunoabsorption. It remains unclear which technique is preferable in plasmapheresis, but plasmapheresis is thought to be one of the most potent adjunctive therapies.

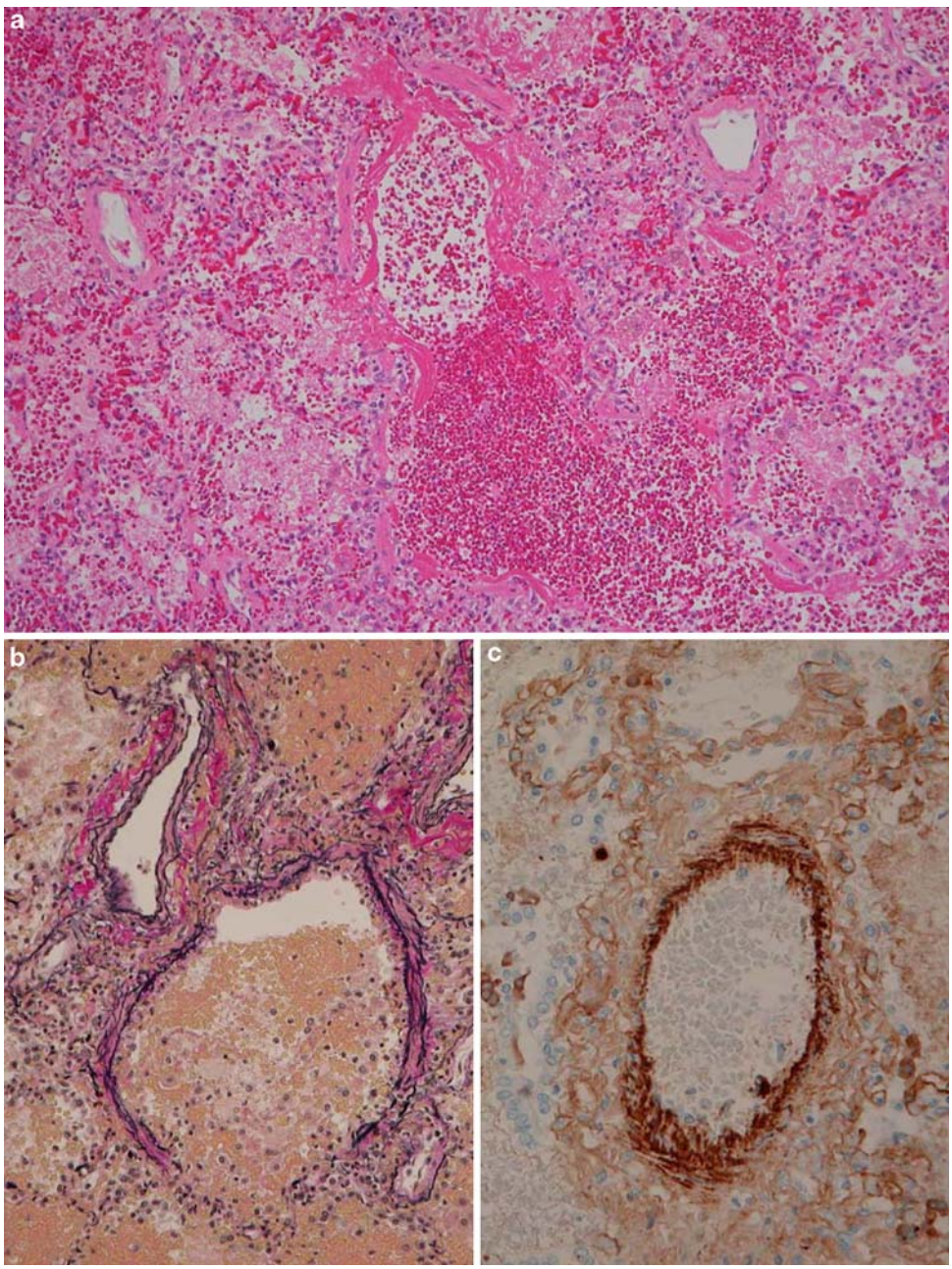

Fig. 1 Rupture of a small muscular artery of the lung with immune complex deposition. **a** H&E stain revealed diffuse alveolar hemorrhage and fibrinoid necrosis of a small muscular artery of the lung with inflammatory cells (×40). **b** Elastica-van Gieson stain revealed rupture of arterial elastic laminae (×100). **c** IHC study showed subendothelial deposition of C1q in a small muscular artery (×200)

Previous reports have shown antiphospholipid syndrome with hypoprothrombinemia by aPS/PT antibody had hemorrhagic tendencies [9, 10]. Although our case did not correspond to antiphospholipid syndrome with hypoprothrombinemia, because of normal prothrombin time, lupus anticoagulants might affect progression of pulmonary hemorrhage. We finally concluded that pulmonary capillaritis led, initially, to DAH and ARDS and she developed severe hemoptysis due to rupture of small muscular arteries by fibrinoid vasculitis.

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