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## Parenteral use of recombinant activated factor VII during diffuse alveolar hemorrhage secondary to leptospirosis

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Dear Sir: Diffuse alveolar hemorrhage (DAH) is a rare but serious event, with 50% mortality in patients who require mechanical ventilation. Recently, local or systemic administration of recombinant activated factor VII (rVIIa) has been successfully used for treatment of DAH [1, 2].

A 53-year-old man without any medical history was admitted to the emergency room with cholestatic

jaundice associated with a flu-like syndrome evolving for 48 h. Laboratory data showed severe cholestasis and hepatic cytolysis, acute renal failure, and isolated thrombopenia (19 G/l), without coagulation abnormality. Computed tomography (CT) scan revealed multiple disseminated pulmonary micronodules mainly in the right lung and a small left pleural effusion. No radiologic explanation was found for the cholestasis.

Shortly thereafter, acute respiratory failure occurred secondary to a DAH. The patient was intubated because of severe hypoxemia (Fig. 1) leading to cardiac arrest. External cardiac massage and epinephrin injections allowed restoration of sinus rhythm. At  $FiO_2 = 1$ , pH was 7.0, arterial lactate was 13 mmol/l, and  $PaO_2$  was 37 mmHg. Transfusion of 3 fresh frozen plasma, 1 platelet concentrate, and 3 red blood cells units was started because of acute severe anemia (Hb of 5.4 g/dl) and persistent bleeding from the lungs. The patient also received an injection of 1 mg/kg methylprednisolone.

Diffuse alveolar hemorrhage and severe hypoxemia were refractory ( $PaO_2/FiO_2 = 40$ ) despite use of

neuromuscular blocking agents, inhaled NO, prone positioning, and endotracheal administration of epinephrin. Then a single bolus of 105  $\mu\text{g}/\text{kg}$  rVIIa was administrated intravenously.

Immediately after the treatment (4 min), bleeding stopped, without any recurrence. No other administration of rVIIa was needed. Inhaled NO was stopped after 48 h, and  $FiO_2$  gradually decreased. Extubation was possible after 17 days.

No neoplastic or autoimmune diseases were found during the etiological investigations. However, serology returned highly positive for *Leptospira icterohaemorrhagiae*.

The patient left the intensive care unit (ICU) after 3 weeks. Biological data and chest X-ray were normalized. After 4 months, the patient returned to normal activity.

## Discussion

Leptospirosis-associated DAH is usually treated with corticosteroids along with symptomatic treatment. To date, desmopressin has been the only hemostatic agent reported for treatment of DAH due to leptospirosis [3].

rVIIa is an approved, though expensive, treatment for bleeding episodes in patients with hemophilia A or B. Studies using rVIIa in multiple life-threatening bleeding situations have recently been published, widening the range of its potential indications.

Although local administration of rVIIa has been successfully used for DAH treatment [4], we used the systemic route because of blood abundance in the endotracheal tube and ventilatory difficulties. Administration of rVIIa was therefore the only alternative therapy and quickly stopped the intra-alveolar bleeding.

Since the introduction of rVIIa, there have been continuing safety



**Fig. 1** Chest radiograph after intubation, showing bilateral patchy alveolar opacities corresponding to DAH

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concerns because of its thrombogenic properties. Indeed, several thrombotic complications have been reported after rVIIa administration, including myocardial ischemia and deep vein thrombosis [5]. Despite their rarity (1–2%), these adverse effects should be kept in mind. In this case, no thrombotic event happened after the rVIIa treatment during the ICU stay.

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