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BRIEF COMMUNICATION

Massive Intra-Alveolar Hemorrhage Caused by *Leptospira* Serovar Djasiman in a Traveler Returning From Laos

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Leptospirosis is one of the most common pathogens responsible for life-threatening tropical disease in travelers. We report a case of massive intra-alveolar hemorrhage caused by *Leptospira* serovar Djasiman in a 38-year-old man returning from Laos, who was cured with antibiotics and salvage treatment with extra-corporeal membrane oxygenation.

Leptospirosis is one of the most common zoonoses worldwide, probably emerging and grossly underreported, especially in tropical areas.[1] The spectrum of illness is extremely broad, ranging from paucisymptomatic, self-resolving acute influenza-like syndrome to severe multisystem disease with high mortality rates. Leptospirosis is the third pathogen responsible for life-threatening tropical disease in travelers within the Geosentinel network,[2] and is most frequently reported in travelers returning from Asia.[3] Pulmonary involvement is not uncommon,[4] and has been associated with a 20% mortality rate as reported in a recent multicentric study from Greece.[5] Literature review identified intra-alveolar hemorrhage as the most severe pulmonary manifestation of leptospirosis.[6] We report a case of massive intra-alveolar hemorrhage caused by *Leptospira* serovar Djasiman in a traveler returning from Laos, who required extra-corporeal membrane oxygenation (ECMO).

Case Description

A 38-year-old man was admitted in the emergency department of Saint-Malo, western France, for high-grade fever of acute onset, arthralgia, and malaise. The patient had returned 2 days earlier from a 2-year trip in Laos, where he worked in rural areas, visiting farms and rice fields. A few hours after admission, he developed shortness of breath, massive hemoptysis, and shock. He received intravenous crystalloid and vasopressor and was intubated. Laboratory values were remarkable for deep thrombocytopenia (platelet count: 30 Gg/L), disseminated intravascular coagulation, elevated liver enzymes (two times upper normal values), acute renal failure, lactic acidosis (arterial lactates, 5.6 mmol/L), and hematuria. Disseminated patchy alveolar consolidations were observed on chest X-ray (Figure 1). Bronchial fibroscopy found massive intra-alveolar hemorrhage, and 200 mL of fresh blood was aspirated from the bronchial tree (Figure 2). Minimal $PaO_2 : FiO_2$ ratio was 34 mmHg under protective ventilation with FiO_2 100%, and a positive end expiratory pressure of 10 cm H_2O. Transthoracic echocardiography showed no significant abnormality. The patient was placed on veno-venous ECMO 2 hours after being intubated, and empiric antibacterial treatment was initiated with ceftriaxone and doxycycline. The patient received eight packs of red blood cell concentrates.

Blood cultures were sterile and bronchoalveolar lavage yielded no pathogen. The patient also tested negative for human immunodeficiency virus, malaria, dengue, legionellosis, and a panel of viruses potentially responsible for hemorrhagic fevers in southeast Asia. Two distinct samples of blood were positive for

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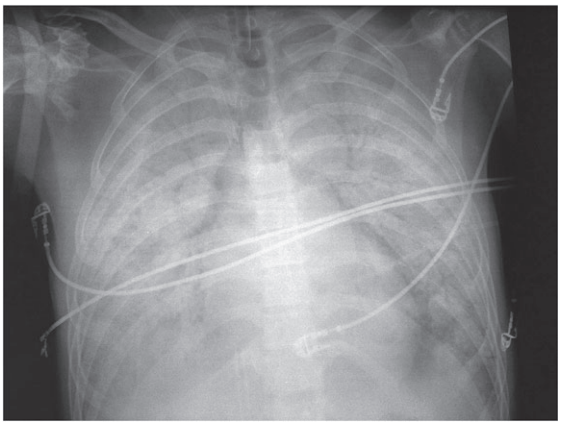

Figure 1 Chest X-ray after initiation of extracorporeal membrane oxygenation: Bilateral patchy alveolar consolidations and spontaneous pneumomediastinum.

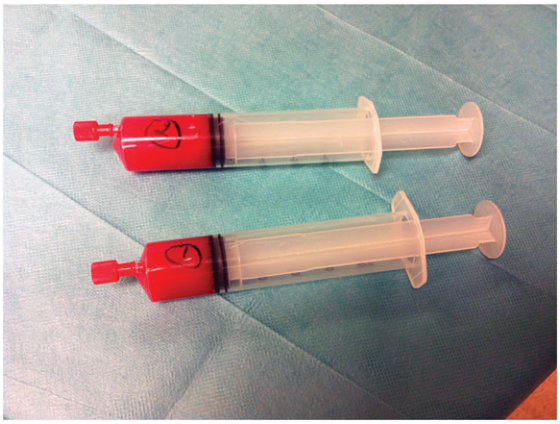

Figure 2 Fresh blood aspirated from bronchial tree during fibroscopy.

leptospirosis by polymerase chain reaction, and antibacterial treatment was stepped down to amoxicillin, for 7 days. The patient became afebrile the day after admission, and he was weaned from vasopressive agents on day 2, from ECMO on day 9, and from mechanical ventilation on day 12. He was discharged home on day 20, after which he returned to Laos with no residual complaint 3 weeks after the discharge. Serological testing for *Leptospira* sp. was negative on admission [IgM enzyme-linked immunosorbent assay (ELISA) < 1/200, Martin & Pettit microagglutination test was negative for all serovars tested] and strongly positive on day 18 (IgM ≥ 1/6400 on ELISA; Martin & Pettit microagglutination test was positive for *Leptospira* serovar Djasiman at a dilution of 1/800, while all other pathogenic serovars were positive at ≤1/100).

Discussion

Intra-alveolar hemorrhage is one of the main causes of death due to leptospirosis, an infectious disease that usually *promptly* resolves with antibiotics, or even spontaneously. Despite its reputation of "benign" illness,[7] some patients will develop shock, diffuse hemorrhage, and/or acute respiratory distress syndrome within a few hours. The pathophysiology of severe pulmonary hemorrhage syndrome is consistent with acute respiratory distress syndrome with diffuse lung injury, impaired gas exchange, and hemodynamic impairment leading to septic shock and multi-organ failure. Massive hemoptysis can arise simultaneously with other respiratory symptoms during the acute phase of illness, as was the case in this observation, or remain inapparent until patients are intubated.

The cataclysmic progression of leptospirosis in selected cases may be associated with specific serovars, host factors, or a combination of both.[8] *Leptospira* serovar Djasiman has been rarely identified, mostly in Asia,[9,10] and has not been associated with severe presentation of leptospirosis to date. Recent development of innovative technologies for life support should improve the prognosis of fulminant respiratory leptospirosis: Indeed, most *Leptospira* sp. pathogenic for humans remain susceptible to penicillin, so that disease control is only a matter of time once active antibacterial treatment is initiated. ECMO is a life-saving intervention that has been previously reported as salvage treatment during leptospirosis in three patients with acute respiratory distress syndrome and/or massive alveolar hemorrhage.[11–13] In the observation reported herein, the patient totally recovered in less than 2 weeks, although he would have died shortly after admission if he presented 2 decades earlier, before the advent of ECMO.

Given the increased incidence of leptospirosis in travelers, which can be life-threatening even in patients without comorbidities, effective means of prevention would be most welcome. Immunization with inactivated vaccines that are currently available provides short-lived immunity and protects against only a low proportion of serovars. Avoidance of high-risk exposures, including immersion in freshwater and walking barefoot, would decrease the risk in travelers, as would appropriate protective measures (eg, wearing boots, goggles, etc.), but these are difficult to apply in tropical environments. Of note, weekly doxycycline has been shown to be effective for leptospirosis prophylaxis in military personnel who underwent jungle training: This should be taken into account when designing antimalarial prophylaxis in settings at risk of both diseases.

Declaration of Interests

The authors state that they have no conflicts of interest to declare.

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