Acute Respiratory Distress Syndrome Manifested by Leptospirosis Successfully Treated by Extracorporeal Membrane Oxygenation (ECMO)

Chen-Yi Liao, Ren-Jy Ben, Hau-Ming Wu, Shih-Kun Chang, Mei-Yu Liu, Hsien-Kuo Chin and Yen-Cheng Yeh

Abstract

Leptospirosis is recognized as a zoonotic disease that is emerging worldwide. Severe manifestations are associated with high morbidity and mortality rates and may therefore pose an important risk to public health, especially in certain high prevalence areas like Taiwan. The severe pulmonary form of leptospirosis is a lesser known entity and is characterized by intra-alveolar hemorrhage and can lead to acute respiratory failure with resistant hypoxemia, which leads to high mortality rates despite maximally invasive mechanical ventilation and adequate treatment. We herein present a case of severe leptospirosis complicated by massive pulmonary hemorrhage, which was successfully managed by extra corporeal membrane oxygenation.

Key words: leptospirosis, severe pulmonary form of leptospirosis (SPFL), extracorporeal membrane oxygenation (ECMO)

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Introduction

Leptospirosis is a zoonotic disease with protean manifestations caused by pathogenic spirochetes of the genus *Leptospira*. This dynamic group of bacteria consists of over 250 known serovars, which survive in warm and moist conditions. Leptospira can be carried and excreted by a wide range of mammalian species, which can serve as vectors. Infection can be acquired either through direct contact with animals, or through environmental contamination by animal urine. Leptospirosis is distributed worldwide, with the majority of clinical cases occurring in tropical areas such as southern Taiwan. Leptospirosis may be complicated by renal failure, uveitis, pulmonary hemorrhage, acute respiratory distress syndrome (ARDS), myocarditis, and rhabdomyolysis (1, 2). Mortality rates in hospitalized patients with leptospirosis range from 4 to 52% (3-5). Severe, potentially fatal illness characterized by jaundice and renal failure and bleeding (“Weil’s disease”) occurs in a minority of patients. Severe pulmonary disease, characterized by pulmonary hemorrhage, has emerged as the most serious complication of leptospirosis that may be underdiagnosed in highly endemic regions like Taiwan and is particularly difficult to treat due to hypoxemia resistant to mechanical ventilation. Early discovery of severe pulmonary form of leptospirosis (SPFL) and support for the patient through the critical period by the use of extra corporeal membrane oxygenation (ECMO) may play an important role in patient survival rates (6).

Case Report

A 32-year-old male fruit seller who was had previously been in good health presented to the emergency department with a two-day history of fever of unknown origin. He experienced a nonproductive cough, arthralgia and myalgia with pain in his neck and behind his eyes. A physical examination revealed high body temperature (40.5°C), rapid heart rate and a peripheral vascular redness of both sclera was observed. Laboratory investigation revealed a mild thrombocytopenia of 92×10^3/μL (normal 150 to 400), leukocytosis of 11.2×10^3/μL (normal 4.0 to 11.0) with marked...
An examination of arterial blood gases after ECMO revealed a pH of 7.529, pCO₂ of 40.5 mmHg and pO₂ of 124.9 mmHg with FiO₂ of 40%. After 10 days of aggressive therapy, including subsequent blood transfusion units of fresh frozen plasma (24 units), single donor platelet (4 units) and packed red blood cell (12 units), the patient was successfully extubated and he left the hospital in good condition. A paired serology study 2 weeks later during the convalescent phase with a microscopic agglutination test subsequently disclosed *Leptospira santarosai* serovar *Shermani* in a single serum specimen with 1:100 dilution and *Leptospira interrogans* serovar *Bataviae* in a single serum specimen with 1:200 dilution from an initial conversion of seronegativity (since admission) indicating seropositivity for leptospirosis. In a patient with clinical findings consistent with the disease, a single titer exceeding 1:200 or serial titers exceeding 1:100 is suggestive of leptospirosis and a 4-fold rise in titer between acute and convalescent specimens is considered to be a positive diagnostic result. The patient’s blood culture remained negative for leptospirosis. Once the diagnosis was explained to the patient he enlightened us as to how he had caught it: the week prior to becoming ill, he had walked barefoot through the surface water at a fruit market, and an uneven skin lesion had become infected.

**Discussion**

Leptospirosis appears to be underestimated in Taiwan, which lies in the path of many tropical storms and typhoons that bring extremely heavy rainfall and flooding. The disease affects at least 10% of patients with multiple organ dysfunction (7). Although it is considered to be the most geographically widespread zoonotic disease, it is a sporadic disease, that restricted to risk exposure associated with specific occupational groups, such as farmers, field agricultural workers, miners, and abattoir and sewer workers, as well with people participating in outdoor recreational activities. We hypothesize that our patient, as a fruit seller, acquired leptospirosis while being exposed to contaminated fresh water due to his habit of walking barefoot around an area with wild rodents and that he initially presented as rapid progressive hemoptysis after the ruling out of other possible cause. In Taiwan, *Leptospira santarosai* serovar *Shermani* is the most frequently isolated serovar, causing both renal and systemic infections (8). Lung involvement occurs in 20 to 70% of cases, and the clinical severity ranges from, cough, hemoptysis, different grades of dyspnea to SPFL and even acute respiratory distress syndrome (9). Alveolar hemorrhage and ARDS are two of the most fatal conditions associated with leptospirosis (10-12). Pulmonary symptoms are found independently or concurrently with renal and hepatic manifestations. This suggests that SPFL is a different form of leptospirosis, rather than a form of Weil’s disease with apparent pulmonary symptoms. SPFL is characterized by profuse intra-alveolar hemorrhage and is seen in less than 5% of patients, and has now surpassed renal failure as a cause of death among patients in Taiwan and other parts of the world.
Figure 2. Temperature, Pulse rate, and Respiratory rate chart.

world (13). The mortality of severe leptospirosis caused by cardiac and renal failure is roughly ranges from 5 to 15%, while SPFL and respiratory failure causes fatalities in >50% (14, 15). In a cohort of 26 Spanish patients, 7 patients presented with hemoptysis and only 3 patients had an ARDS, which was always associated with multiple organ failure (15). Our case report underlines the finding that ARDS can be the manifestation of the disease even in the absence of significant renal or hepatic involvement. ARDS requiring mechanical ventilation is associated with a mortality rate as high as 30 to 60% (16). Respiratory symptoms usually appear between the 4th and 6th day of disease and may lead to death in less than 72 hours (12, 16). Capillary injury in the lungs results in leakage and extravasation of blood cells. The inflammatory reaction, characterized by infiltration by monocytes and neutrophils, is surprisingly mild when compared with vascular damage. Pulmonary edema, fibrin depositions and proliferative fibrinoblastic reactions are seen frequently and further hamper respiratory function (7). These changes can lead to intra-alveolar hemorrhage and ARDS, which is often fatal. Different variables have been reported to be associated with poor prognosis in patients with leptospirosis and pulmonary involvement such as alveolar infiltrate on chest radiographs and cigarette smoking (15). Imaging typically reveals bilateral patchy alveolar infiltrates, which like large snow flakes, and areas of consolidation, as reported in the present case. Antibiotic treatment has to be started early, and supportive care with correction of dehydration, hypovolemia, hypotension, and electrolyte abnormalities is essential. Prompt management of renal and hepatic dysfunction and acute respiratory failure may decrease the mortality rate. In most mild cases, leptospirosis is self-limiting. Amoxicillin, ampicillin, doxycycline or erythromycin can reduce symptoms and prevent further progression; however, in a more severe manifestation like SPFL, treatment with cephalosporins or high doses of intravenously-administered penicillin is associated with more favorable outcomes. SPFL with hypoxemia and the characteristic resistance to mechanical ventilation have proven particularly difficult to treat. This has led to recent reports of novel approaches to treatment including the use of inhaled nitric oxide and desmopressin (17, 18). Although the benefits of corticosteroids in the treatment of ARDS are known, evidence for use of corticosteroids in pulmonary leptospirosis is confined to occasional case reports or small studies (19). Neither of these options were used in our case. Instead, the patient was successfully supported through the period of pulmonary hemorrhage by the use of ECMO. ECMO is a method of cardiopulmonary support that allows the lung to be relieved of its gaseous exchange function. Consequently, it is thought to minimize the degree of lung injury caused by mechanical ventilation with high FiO₂, high tidal volumes and increased airway pressures needed in severe respiratory failure. ECMO has been used more extensively as a potential bridge therapy in patients with severe ARDS, massive hemoptysis and critical tracheal stenosis (20). The benefits of ECMO use in SPFL and associated ARDS are still under evaluation (21-23). The importance of careful case selection has also become clear. Our patient was referred early because problems with ventilation and refractory hypercapnia had been indicated due to massive hemoptysis.

Leptospirosis is a zoonosis with a wide range of clinical manifestations that can cause severe morbidity and mortality if left untreated. The disease is endemic in tropical regions, but may be increasing in temperate regions due to global warming and areas with recent flooding where a primary diagnosis of dengue may delay appropriate treatment. In recent years, SPFL seems to have emerged as a distinct manifestation with high mortality rates. ECMO should be considered early as a treatment option in adult patients with severe respiratory failure, especially if the underlying cause is infective and therefore ultimately curable.

The authors state that they have no Conflict of Interest (COI).
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