Case report

Lethal pulmonary hemorrhage syndrome due to Leptosira infection transmitted by pet rat

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ABSTRACT

Human infection with Leptospira interrogans can be life-threatening. Multiple organ involvement frequently presents with liver and kidney failure, less commonly including severe hemolysis and pulmonary hemorrhage syndrome.

Here, we present a fulminant case of leptospirosis presenting with hemolysis and pulmonary hemorrhage. A formerly healthy 34 year old patient presented to a rural hospital with dyspnea and hemoptysis after a week of influenza-like symptoms. Initial assessment revealed severe sepsis, acute kidney failure and severe hemolysis.

Within the next 29 h, a multi-organ failure developed, which could eventually not be reversed despite mechanical ventilation, venovenous extracorporeal membrane oxygenation, continuous renal replacement therapy, plasmapheresis and extracorporeal cytokine absorbent therapy.

The diagnosis of leptospirosis was made after the patient died. The transmitting animal was a pet rat. Leptospirosis has to be considered in case of rapid multi-organ failure presenting with pulmonary hemorrhage.

Introduction

Leptospirosis is a zoonotic infectious disease with Leptospira interrogans bacteria. Transmission is typically caused by contact with urine of infected animals, mostly rodents [1,2]. While human infections with Leptospira interrogans are frequently mild presenting with influenza-like symptoms, 10% of patients present with sepsis including liver and kidney failure. This severe form of leptospirosis is known as Weil’s disease and reported mortality rates range from 10 to 15% [1,2]. In some patients, pulmonary hemorrhage develops, which is also known as severe pulmonary hemorrhage syndrome (SPHS), with reported mortality rates from 50 to 70% [1,3]. Detection of Leptospira by serological methods and PCR DNA analysis is the fastest and most sensitive diagnostic procedure, respectively [1].

Case report

A 34-year-old man without known pre-existing conditions was transferred to our intensive care unit located at a tertiary referral hospital with pulmonary hemorrhage and septic shock. The day before his transfer, he was admitted to a local hospital with acute dyspnea and hemoptysis. Seven days before first admission, he reported fatigue, back and abdominal pain with nausea and vomiting.

On initial presentation at the primary hospital, the temperature was 35.9 °C, the systolic blood pressure was 70 mmHg, the heart rate 100 beats per minute, the respiratory rate 19 breaths per minute and the oxygen saturation 60% breathing ambient air. He presented with jaundice, hemoptysis and abdominal pain over the right upper quadrant of his abdomen. Chest auscultation revealed ubiquitous coarse crackles and the chest X-ray showed bilateral patchy infiltrates. Blood tests showed a mild normochromic, normocytic anemia (hemoglobin 13.0 g/dL), bilirubin of 8.45 mg/dL, severe thrombocytopenia of 20 × 10⁹/L, acute renal failure with creatinine level of 4.9 mg/dL, as well as leukocytosis of 31 × 10⁹/L, elevated C-reactive protein and procalcitonin levels (Fig. 1).

The diagnosis of community acquired pneumonia with sepsis was made. The patient was transferred to the intensive care unit, blood cultures were obtained and an empiric antimicrobial therapy with piperacillin/tazobactam and ciprofloxacin was initiated. Hypoxia however aggravated despite non-invasive ventilation, which necessitated an
Fig. 1. Timeline of clinical course and laboratory tests performed. Blood tests performed are given with normal ranges. Due to hemolysis, several blood tests could not be performed. Blood gases derive from arterial blood. "NMH: not measurable, sample hemolytic."
endotracheal intubation 8 h after admission. The patient could not be sufficiently oxygenized despite high invasive mechanical ventilation necessitating extracorporeal membrane oxygenation (ECMO) therapy. Our ECMO team visited the patient in the primary hospital and implanted a venovenous ECMO and transferred the patient to our intensive care unit (Fig. 1).

Upon arrival at the tertiary referral hospital, blood gases displayed a combined metabolic and respiratory acidosis and hypoxemia. A CT-scan showed extended confluent infiltrates compatible with severe adult respiratory distress syndrome (ARDS). Bronchoscopy revealed diffuse alveolar hemorrhage responsible for the hemoptysis.

Further blood tests demonstrated intravascular hemolysis with a drop of hemoglobin from 13.0 g/dL to 5.9 g/dL, reduced haptoglobin and increased lactate dehydrogenase. Coagulation was compromised with fibrinogen levels below detection limit of 30 mg/dL. In total, 10 packed red blood cells and 12 g fibrinogen were transfused within 12 h stabilizing the hemoglobin concentration at 7.0 g/dL. (Fig. 1). Urinalysis revealed muddy-brown casts and acanthocytes. Due to hyperkalemia, a continuous venovenous renal replacement therapy with citrate for anticoagulation was initiated. Since our patient reported gastrointestinal symptoms prior to hospital admission, plasmapheresis with suspected diagnosis of hemolytic uremic syndrome was initiated. The patient received a volume therapy of 13 L within 16 h including 2250 mL of 8.4% sodium bicarbonate and 10 packed red blood cells. Since all conventional therapy failed to stabilize the patient a rescue therapy with extracorporeal cytokine absorbent filter was connected to the venovenous dialysis machine and 1000 mg prednisolone were administered. Despite all therapeutic interventions, the patient died in fulminant multi-organ failure 17 h after admission to our hospital and 29 h after initial presentation.

Several differential diagnosis for hemolysis and diffuse alveolar hemorrhage were considered during the treatment of our patient. Fibrin monomers were negative excluding disseminated intravascular coagulation to be responsible for the hemolysis. Anti-glomerular basement antibodies could not be detected excluding Goodpasture syndrome. Anti-nuclear antibodies as well as anti-neutrophil cytoplasmic antibodies were negative excluding autoimmune disease. However, the peripheral blood smear detected 6–8% schistocytes. The ADAMTS-13 activity was reduced only mildly to 35% (normal range 50–110%) not pointing towards thrombotic thrombocytopenic purpura. The test result for the LipL32-PCR detecting Leptospira interrogans DNA in urine, blood and bronchoalveolar lavage samples returned 8 h after the death of our patient and 24 h after transferal to our hospital. Blood cultures and all other samples including urine and fluid from the bronchoalveolar lavage remained sterile.

Discussion

Leptospirosis is in the differential diagnosis of patients with sudden severe infection including liver and kidney failure. Leptospirosis is a zoonotic infection transmitted by urine (direct or diluted in water) of infected animals [1,2]. We identified the transmitting pet rat which the patient bought approximately 4 weeks before his admission. Leptospira interrogans serovar icterohaemorrhagiae strain 17 was detected in the kidney of the animal by local health authorities involved after diagnosis of leptospirosis.

In our patient, abdominal symptoms and hematemesis were the leading symptoms at presentation. Severe pulmonary hemorrhage in context of leptospirosis (SPHS) has mortality rates without ECMO therapy as high as 74% [3]. Plasmapheresis has been reported to be beneficial in Weil’s disease with kidney failure [4] as has been cortisone therapy in case of pulmonary leptospirosis [5]. Both therapies had been implemented combined with a beta-lactam antimicrobial and extracorporeal cytokine absorbent therapy. However these measures could not improve the outcome of our patient.

Conclusion

Leptospirosis potentially can be a life-threatening disease despite modern intensive care medicine including continuous renal replacement, plasmapheresis, extracorporeal cytokine absorbent and ECMO therapy. Diagnosis of leptospirosis is dependent on specific tests and has to be considered in case of multi-organ failure including liver and kidneys. Though typically transmitted by urine of rodents and domestic animals, pet rats can be vectors as well.

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Written informed consent was obtained from the patient for publication of this case report. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

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