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Case Report

A rare case report of leptospirosis with extensive alveolar hemorrhage

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Abstract: Leptospirosis is a zoonosis caused by a pathogenic Leptospira species of Spirochaetes. Recently, we managed a rare case of leptospirosis with diffuse alveolar hemorrhage. The patient had acute febrile illness, productive cough and massive hemoptysis. Before being diagnosed as leptospirosis, the patient was urgently treated with bronchial artery embolization. The patient had isolated severe pulmonary hemorrhagic leptospirosis instead of classic renal and hepatic involvement. A high index of suspicion of leptospirosis should be kept for patients with acute febrile illness and rapidly progressed alveolar hemorrhage in high risk population. Early diagnosis and management with high flow oxygen, antibiotics and intensive supportive therapy can prevent complications and mortality.

Keywords: Leptospirosis, massive hemoptysis, diffuse alveolar hemorrhage, bronchial artery embolization, antibiotic

Case report

A 58-year-old male with hypertension and diabetes type II, who was a farmer, began with symptoms of cough, expectoration after catching a cold on July 20th in 2015. He developed high fever from August 2nd and was treated with antibiotic by local practitioner. Gradually, he developed dyspnea and blood-stained sputum. High-resolution CT thorax showed bilateral high-density shadow involving all lobes on August 6th in other hospital (**Figure 1A**), where he was given cefoselis and hemostatic therapy, but his hemoptysis progressed to massive hemoptysis on August 8th. The patient was sent to emergency department of Xiangya Hospital, Central South University and rechecked CT thorax showed bilateral lung lesions markedly progressed (**Figure 1B**), and bronchial artery embolization was urgently treated due to fatally massive hemoptysis and the patient's hemoptysis temporarily improved a little. One day later, he got admitted in Respiratory Intensive Care Unit of Xiangya Hospital, where he was thoroughly investigated. On admission, he still had severe polypnea and persistent hemoptysis (about 100 ml/day), but without fever. His blood pressure was 133/68 mmHg and his respiratory rate was 30 times/min. Physical examination revealed moist rales and wheezing rales were heard in bilateral lung. He has no obvious jaundice or tenderness of gastrocnemius muscles. Initial arterial blood gas indicated type 1 respiratory failure with high flow oxygen of 15 L/min (pH-7.46, PCO_2 28 mmHg, HCO_3^- 19.9 mmol/l, PO_2 68 mmHg, SaO_2 94%). Routine blood picture showed leukocyte 21 900/cu mm, neutrophilic leukocytosis 20000/cu mm, thrombocytopenia 143000/cu mm and hemoglobin 114 g/L. Liver enzyme aspartate transaminase (AST) and alanine transaminase (ALT) were normal with serum total bilirubin of 17.7 mg/dl and direct bilirubin of 7.8 mg/dl. Routine urine examination and renal parameters were normal. Serum procalcitonin (7.680 ng/ml), Erythrocyte sedimentation rate (67 mm/h) and C-reactive protein (155 mg/L) were significantly elevated respectively. Chloride levels were normal except for elevated triglyceride (3.07 mmol/l). Thrombin time (TT) and activated partial thromboplastin time (APTT) were prolonged (28.98/58.2 s), and D-dimer (1.75 mg/L) and fibrinogen (15 g/L) were elevated.

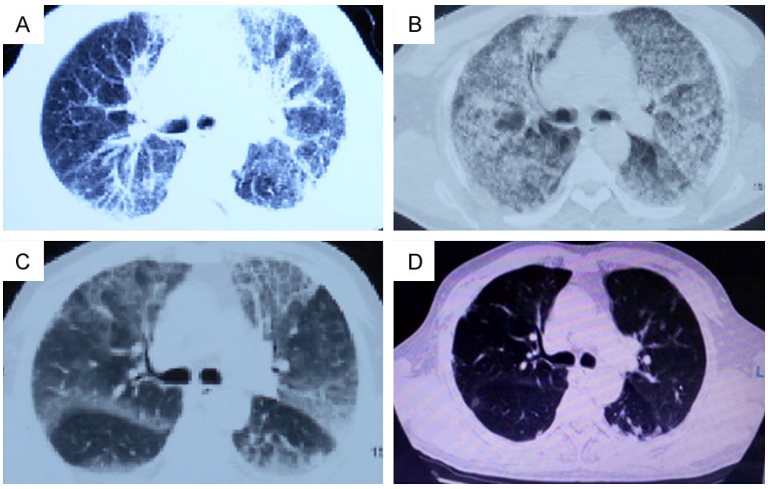

Figure 1. Serial CT thorax scans of a 58-year-old man who presented with fever and hemoptysis, A: CT scan showed high-density opacities involving both lung fields on August 6th, 2015, two days before admission; B: CT scan showed high-density opacities involving both lung fields progressed fast compared with A in just two days; C: CT scan showed diffuse high-density shadow improved significantly after timely and correct treatment of 1 week; D: CT scan showed a near normal image with minimal localized interstitial shadows on the left side at half-month after discharge.

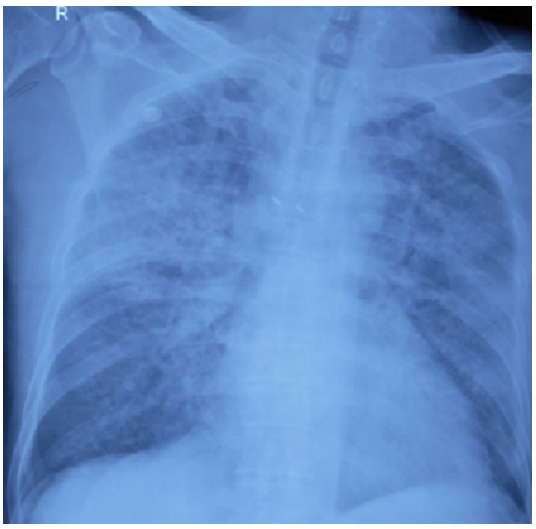

Figure 2. Chest radiograph showed bilateral uniform opacities with middle and upper distribution 2 days after admission.

G/GM tests were positive. Immune globulin was elevated (4370 IU/L). PPD skin reaction, acid-fast *bacilli* of sputum and bronchoalveolar lavage (BAL) and tuberculosis antibody test were negative and other laboratory tests of blood were not abnormal. His abdominal ultrasonography was normal. Chest X-ray revealed bilateral non-homogenous opacities in both middle and upper lung zone (**Figure 2**). Fiber optic bronchoscope still caught sight of active bleeding of left upper lower lobe (**Figure 3**). Thorough history was taken revealing that patient did farm work in the fields a few days before onset of the disease. CT scans and clinical manifestations indicated that pulmonary hemorrhage progressed fast. Treatment with hemostatic drugs and bronchial artery embolization had not very satisfactory hemostatic effect. An experienced old professor suspected of rare severe leptospirosis with extensive alveolar hemorrhage. Two consecutive microscopic agglutination assays test (MAT) of *Leptospira* serovars revealed antibody titres against L. icterochaemorrhagic serogroup were 1:1600 and 1:3200 (cut-off: 1:100). Intravenous piperacillin-tazobactam and proper supportive therapy then started immediately. Within 24 h, hemoptysis improved markedly. Both lung lesions were improved markedly after 1 week by rechecking CT thorax (**Figure 1C**). The patient recovered smoothly and discharged soon. After half month, he attended outpatient department with complete recovery (**Figure 1D**).

Discussion

Leptospirosis is a zoonosis caused by a pathogenic Leptospira species of spirochaetes, which is prevalent in many tropical countries and regions with abundant rainfall, rats and rice fields. The infection is often caused by direct or indirect exposure to urine with pathogenic leptospires from infected reservoir host animals. The high risk population is farm workers, ranchers, field agricultural workers, plumbers, sewer workers, sanitation workers and so on. Incubation period of leptospirosis is about 7 to 10 days. There are two biphasic phases, the septicemic phase and immune phase, in leptospiral infection. The septicemic phase lasts for 4 to 7 days, which mainly presents nonspecific symptoms of fever, chills and body ache. The immune phase follows, which presents endothelial cell damage affecting multi-organs such as liver, kidneys, heart, lungs and meninges.

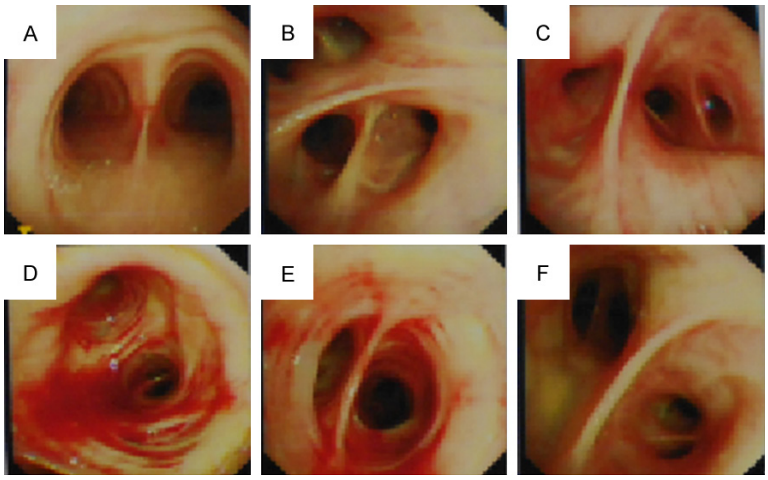

Figure 3. Fiber-optic bronchoscope showed active bleeding of left upper lower lobe after admission to RICU from **Figure 1D**, **1E**.

Pathogenesis of leptospirosis pulmonary hemorrhage is poorly understood, which may be associated with deposition of complement and immunoglobulin on the alveolar surface [1]. Most leptospirosis causes wild symptoms and shows spontaneous recovery without any specific therapy, but in a substantial number of cases multiple organs could be involved, which would lead to high fatality rate. The combination of jaundice and renal failure, known as Weil's disease firstly described in 1886 [2], remains one of the most clinically recognizable forms of leptospirosis. Patients typically present clinical manifestation with sudden onset of fever, chills, myalgia and headache. Muscle pain and tenderness are common and characteristically involve the calves and lower back. Most severe leptospirosis cases are characterized by dysfunction of multiple organs. Severe pulmonary hemorrhagic leptospirosis (SPHL), presenting massive pulmonary hemorrhage instead of the classic Weil' disease, emerged in recently years is very rare and severe form of leptospira infection [3], which is not often suspected. We successfully managed a rare case of leptospirosis involving isolated lung with massive alveolar hemorrhage. SPHL is an ominous complication of leptospirosis associated with fatality rates >50% [4]. SPHL may develop ARDS with even higher mortality rates. To our best knowledge, this patient with rarely extensive alveolar hemorrhage was first reported case treated with bronchial artery embolization due to fatally massive hemoptysis under indefinite diagnosis, though the hemostatic effect was not very satisfactory. Fortunately, we made a quick and accurate diagnosis and insured the patient to receive timely treatment.

Leptospirosis may be diagnosed with direct detection of the organism or its body fluid or tissues by isolation of leptospires or indirect detection of serological specific antibody levels [5, 6]. The microscopic agglutination test (MAT) is the cornerstone of serologic diagnosis of leptospires with high sensitivity and detection of group specific antibodies, and it is less sensitive in early phase of disease. Positive results are defined as a four-fold increase in antibody titer, a single titer exceeding 1:200 or series titers exceeding 1:100 [7]. Severe pulmonary hemorrhage may be identified by fiber optic bronchoscope and collecting bronchoalveolar lavage fluid. Meanwhile, Chest radiographs show bilateral nonhomogenous infiltrates. The high-resolution tomography scans may show ground-glass opacities, airspace nodules, consolidations and "crazy-paving" patterns [8].

In management, there is controversy regarding the best therapeutic management of leptospirosis. Early initiation of antibiotics, doxycycline, penicillin and third-generation cephalosporins are the preferred antibiotics, which can prevent the progression of severe leptospirosis. However, a Cochrane systematic review failed to provide sufficient evidences and clear guidelines for use of antibiotics [9]. More interestingly, a recent review showed that the benefit of antibiotic therapy for severe leptospirosis remains unclear and the choice of penicillin, doxycycline, or cephalosporin did not affect mortality rates neither nor the duration of fever [10]. We should cautiously prevent asphyxia caused by massive hemoptysis in severe leptospirosis with extensive hemorrhage. Timely initiation of NIV (BiPAP) with high concentration of inspired oxygen or mechanical ventilation with positive end-expiratory pressure should be done with severe pulmonary leptospirosis with respiratory failure. Extracorporeal membrane oxygenator (ECMO) has been used in ARDS cases of leptospirosis [11].

Immunomodulation may be used in severe leptospirosis. Case series analyses have supported use of glucocorticoids in leptospiral pulmonary hemorrhage and show corticosteroids reduce mortality and change outcome significantly when used early in the management of pulmonary leptospirosis [12, 13]. However, a systematic review suggests no sufficient evidence that high dose corticosteroids are effective in severe leptospirosis, and well-designed randomized clinical trials are needed [14]. Dursun et al shows plasma exchange may be beneficial to selected patients unresponsive to conventional therapy [15]. Trivedi et al shows that plasma exchange with cyclophosphamide improved survival in patients of pulmonary alveolar hemorrhage due to leptospirosis, which indicates that immune mechanisms play a key role in the pathogenesis of the disease [16]. A single bonus of recombinant activated factor VII (rVIIa) has been successfully used for treatment of diffuse alveolar hemorrhage secondary to leptospirosis [17]. Furthermore, inhaled nitric oxide and hemofiltration has been used for treatment of pulmonary hemorrhage caused by leptospirosis [18].

In conclusion, a rarely isolated pulmonary hemorrhage in the absence of jaundice and renal dysfunction is often misdiagnosed or diagnosed with delay. We should keep highly suspicious of severe lung involvement presenting diffuse alveolar hemorrhage and progressing quickly with acute febrile illness and severe respiratory symptoms in high risk population who contacted with infected animals, water or soil either directly or in directly. Early diagnosis and management with oxygenation, antibiotic, and proper supportive therapy can prevent complications and mortality.

Disclosure of conflict of interest

None.

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