LEPTOSPIROSIS PRESENTING WITH FEVER AND PULMONARY HEMORRHAGE
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Abstract: Reports of leptospirosis have recently been increasing in Taiwan. We report a case of leptospirosis with the unusual initial manifestation of pulmonary hemorrhage. The patient presented with cough for 1 week and was admitted. After admission, fever, hemoptysis and severe dyspnea developed suddenly. Chest radiograph showed bilateral diffuse pulmonary infiltrates and he was transferred to the emergency room of our hospital. Oxygen saturation was 86% under room air and respiratory rate was 30 per minute. After admission to the thoracic ward on the third morning, parenteral penicillin and trimethoprim-sulfamethoxazole were given empirically, and a dramatic recovery ensued. Microscopic agglutination test showed an increased titer of 1:6400 against Leptospira interrogans serogroup shermani on the fourth day of hospitalization. Neither jaundice nor renal insufficiency occurred during treatment. Pulmonary hemorrhage may be an under-recognized manifestation of leptospirosis in Taiwanese patients. Leptospirosis should be taken into consideration in the differential diagnosis of pulmonary hemorrhage. Early treatment can lead to cure with reduced morbidity.

Key words: Hemorrhage; Leptospirosis; Lung diseases; Signs and Symptoms; Weil’s syndrome

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Leptospires are aerobic, thin, spiral-shaped bacteria.1 Leptospirosis is the most widespread spirochetal zoonosis in the world, being especially prevalent in the tropical areas.1 Human transmission typically occurs via infected animal urine, either by direct contact or indirect exposure through contaminated water or soil. The ports of entry are usually abraded skin or mucosa.2–5 Most patients are exposed to the bacteria during recreational activities, such as swimming in contaminated water.1,5 Pathogenic leptospires rapidly invade the blood and lymphatic circulation after penetrating the skin or mucous membranes and then spread to all sites in the body.1 After an incubation period ranging from a few days to 4 weeks, Leptospira disseminate to different organs, especially the liver, kidneys, muscles, and lungs.1,5

The pathophysiology associated with leptospirosis is poorly understood. However, vascular injury and hemorrhagic diathesis are the prominent events leading to many clinical manifestations.4 The symptoms can vary from those of subclinical infection and self-limited, anicteric, febrile illness to severe and potentially fatal disease. Weil’s syndrome is the most severe form of the infection; patients with this form present with febrile illness, hemorrhagic diathesis, hepatic dysfunction, and acute renal failure. If not treated, patients die within a short time.1,4 The mortality rate varies from 2% to 14%.2,6

Previously reported cases in Taiwan have all described a presentation of Weil’s syndrome, namely icterohemorrhagic leptospirosis.7,8 In those cases, pulmonary manifestations were common, but leptospirosis with pulmonary hemorrhage as the major presentation has not been reported from Taiwan. We report a case of leptospirosis with an unusual presentation consisting of cough, fever, hemoptysis, and severe dyspnea of sudden onset.

Case Report

This previously healthy 29-year-old man had smoked 2 to 3 packs of cigarettes a day for more than 10 years and participated in recreational activities such as swimming, diving, and catching shrimp and crabs in streams. He often drank stream water.
He was admitted to a local hospital on September 1, 2002 because of a non-productive cough lasting 1 week and fever for 1 day. The initial chest radiograph was negative (Fig. 1). Hemoptysis and shortness of breath developed abruptly during the second night of hospitalization. Chest radiograph revealed bilateral diffuse pulmonary infiltrates (Fig. 2).

The patient was immediately referred to our emergency department with a clinical impression of severe pneumonia. On arrival, vital signs were body temperature 38.8°C, pulse rate 101 beats per minute, blood pressure 117/45 mm Hg, and respiratory rate 30 breaths per minute. He was lucid, cooperative, and not icteric. No skin lesions were observed, and auscultation revealed fine crackles over bilateral lung fields. His abdomen was soft. No myalgia was found. The remainder of the physical examination yielded unremarkable results.

Laboratory data showed white blood cell count 8100 cells/mm³ with 85% polymorphonuclear leukocytes, platelet count 101,000/mm³, hematocrit 21.8%, and mean corpuscular volume 57.8 µm³. Blood chemistry values were as follows: creatine kinase, 22 U/L; albumin, 2.8 g/dL; alanine aminotransferase, 11 U/L; aspartate aminotransferase, 20 U/L; total bilirubin, 0.9 mg/dL; sodium, 143 mmol/L; potassium, 3.1 mmol/L; and creatinine, 1.2 mg/dL. The data revealed normal liver and renal function tests but presence of hypoalbuminemia and hypokalemia. Prothrombin and activated partial thromboplastin times were 13.3 seconds (normal control 11.5 seconds) and 44.1 seconds (normal control 30.9 seconds), respectively. Results of urinalysis were normal. Oxygen saturation was 86% as measured by pulse oximetry with the patient breathing room air. Oxygen was given through a nasal cannula.

The patient was transferred to our thoracic department (within 2 hours) on the morning of the third day of hospitalization. He was given parenteral empiric antibiotic treatment with penicillin G sodium 3,000,000 units every 6 hours and co-trimoxazole (trimethoprim-sulfamethoxazole) 480 mg every 8 hours. After 1 dose of antibiotics, his vital signs improved, with temperature 37.3°C, respiratory rate 28 per minute, pulse rate 70 per minute, and blood pressure 98/50 mm Hg.

Bronchoscopy was performed 2 days after the patient’s shortness of breath improved. Bronchoalveolar lavage was done from the right lower lobe with 200 mL warm saline in 4 aliquots, and 98 mL (49%) of serosanguineous fluid was recovered. Microbiological studies, including tests for bacteria, tuberculosis, fungi, cytomegalovirus, and Pneumocystis carinii were all negative. The lavage fluid contained 63% sideromacrophages, which strongly suggested pulmonary hemorrhage. Results for serum antinuclear antibody and rheumatoid factor were negative. Serological tests for dengue fever, scrub typhus, murine typhus, and Mycoplasma infection were negative. Workup for microcytic anemia suggested beta thalassemia syndrome. Although a urine culture for Leptospira was not obtained, the microscopic agglutination test (MAT) against Leptospira interrogans serogroup shermani indicated an increased titer to 1:64000 on the fourth day of hospitalization.

Fig. 1. Chest radiograph at admission reveals no abnormalities.

Fig. 2. Chest radiograph on the second day of hospitalization shows diffuse infiltrations in the bilateral lungs.
The chest radiograph on the fourth day of hospitalization showed complete resolution of the previous findings (Fig. 3). He was discharged on the fifth day of hospitalization, with a prescription for oral doxycycline 100 mg twice daily for 10 days. He was able to start diving again 1 day after discharge. Two weeks later, a paired serum for MAT showed a 1:800 titer to *Leptospira interrogans* serogroup *shermani*. The screening MAT against *Leptospira* for his 2 pet dogs was negative.

**Discussion**

Pulmonary manifestations are common in patients with leptospirosis, with an incidence ranging from 20-70% in reported series. The most common pulmonary symptoms are cough, hemoptysis, and chest pain. Pulmonary manifestations are primarily hemorrhagic rather than inflammatory reactions. The exact mechanism is unclear at present. Pulmonary involvement can be the presenting or most dramatic feature of leptosporial infection. Therefore, several authors have suggested that leptospirosis should be considered in the differential diagnosis of pulmonary hemorrhage. In a report from the Indian Ocean region, all leptospirosis-related deaths were caused by pulmonary hemorrhage, as confirmed by post-mortem examinations.

Im et al reported that radiographs in 57% of patients showed abnormalities on the third to seventh day after the onset of clinical symptoms. Among the serial chest radiographs of 19 patients with complete resolution, 68% showed resolution in 5-10 days, and 32% showed resolution in 11-15 days. In our patient, the radiographic abnormality appeared suddenly 8 days after the onset of cough. After empiric antibiotics, the radiographic abnormalities in our patient resolved even more rapidly than in the series of Im et al.

Jaundice is the most obvious manifestation of hepatic dysfunction. Other laboratory manifestations include decreased serum albumin level, increased globulin level, and impaired production of vitamin K-dependent clotting factors. Tubular damage and hypoxia secondary to renal ischemia cause renal insufficiency and failure. Azotemia, oliguria, and anuria commonly occur in the second week of the disease. Hypokalemia has been reported. Proteinuria, hyaline or granular casts, hematuria, and pyuria, as demonstrated in urinalysis, have been found in 70-80% of cases.

In our patient, cough, shortness of breath, and pulmonary hemorrhage were the main presenting features. The patient’s liver and renal function tests were normal. These manifestations differ from those previously reported in Taiwanese patients. Possible explanations for this difference include a less virulent pathogen or a milder form of leptospirosis. However, *Leptospira interrogans* serogroup *shermani*, the pathogen in this case, is a frequent causative agent of icterohemorrhagic leptospirosis. Therefore, the virulence of the pathogen is unlikely to have contributed to the uncommon presentation. Furthermore, as mentioned before, the presence of hypoalbuminemia, hypoprothrombinemia, and hypokalemia indicated both hepatic and renal involvement in this patient. Allen et al reported that massive pulmonary hemorrhage can occur early in the clinical course, even before jaundice and renal failure occur. Our patient’s condition may have represented an early stage of classical icterohemorrhagic leptospirosis. It is likely that full blown Weil’s syndrome would have developed if early treatment had not been given.

A recent case report also described the presentation of diffuse alveolar hemorrhage, as in our patient, but with a negative initial chest radiograph. On the third day of admission, elevated creatinine and bilateral patchy infiltrations were found on chest radiograph. If adequate antibiotic treatment had been prescribed immediately on his admission, the clinical course might have been less eventful.

The first report of leptospirosis from Taiwan was published in 1976. However, leptospirosis was not considered a common infectious disease until 2 cases from our hospital were reported in 1997. Awareness of this disease is the most important factor for successful diagnosis and treatment. Without
adequate and early treatment, this treatable disease can be fatal. In Taiwan, leptospirosis is often overlooked. This case demonstrates the need for awareness of pulmonary hemorrhage as an initial presentation of leptospirosis in Taiwanese patients. Furthermore, the clinical course of this case suggests that severe complications of leptospirosis, such as respiratory failure and/or multiple organ dysfunction, can be prevented if appropriate intervention is administered at a very early stage of the disease.

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References