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Case Study

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LEPTOSPIROSIS PRESENTING AS ACUTE RESPIRATORY DISTRESS SYNDROME: A RARE PHENOMENON

Ashutosh Tiwari*[1] and Sudha Kansal[2]

[1]Senior Registrar, Medical Intensive Care Unit, Indraprastha Apollo Hospitals, Delhi, India.
[2]Senior Consultant, Critical Care and Pulmonary Medicine, Indraprastha Apollo Hospitals, Delhi, India.

***Corresponding Author: Dr. Ashutosh Tiwari**

Senior Registrar, Medical Intensive Care Unit, Indraprastha Apollo Hospitals, Delhi, India.

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ABSTRACT

Leptospirosis, a self-limiting zoonosis, presents with significant complications and high mortality rates. Although pulmonary symptoms and signs in patients with leptospirosis have been infrequently described, the scenario has changed in recent years, with cases of severe hemoptysis and acute respiratory failure being described. When acute respiratory failure is present, dyspnea, pulmonary edema, and alveolar and interstitial hemorrhages are common clinical-pathological features. Despite considerable knowledge about this disease, questions on its clinical presentation and evolution still need to be addressed. We here report a case of Leptospirosis presenting as acute respiratory distress, which is a rare association or clinical presentation of the disease, yet an extremely crucial one to be highlighted upon.

KEYWORDS: Leptospirosis, a self-limiting zoonosis, presents with significant complications and high mortality rates.

INTRODUCTION

Leptospirosis, a zoonosis caused by Leptospiras, is generally found in tropical and rural regions, but cases have been reported in temperate climates and developed countries.[1] With a worldwide occurrence, leptospirosis is more common in the tropics, where conditions are more favorable for transmission. Humans generally get infected from direct exposure to infected urine of carrier mammals or from soil or water contamination by wild mammals. Additionally, the disease is associated with specific occupational activities such as farming, veterinary medicine, and military training; recreational activities such as swimming; poor living conditions; and seasonal rainfall in the tropics.[2] Although being a self-limiting disease, several severe cases with significant complications and high mortality rates have been reported in the literature.[3] The severe forms of the disease are associated with a case-fatality rate of 5 to more than 40%.[4] The early phase of the disease is generally characterized by fever, chills, headache and severe myalgia. In 5 to 15% of clinical infections, progression to severe multisystemic complications occurs, such as jaundice, renal failure, and bleeding disorders.[3] Although pulmonary symptoms and signs in patients with leptospirosis have been infrequently described, the scenario has changed in recent years, with cases of severe hemoptysis and acute respiratory failure being described.[5-8] When acute respiratory failure is present, dyspnea, pulmonary edema, and alveolar and interstitial hemorrhages are common clinical-pathological features. Despite considerable knowledge about this disease, questions on its clinical presentation and evolution still need to be addressed.[4]

We here report a case of Leptospirosis presenting as acute respiratory distress, which is a rare association or clinical presentation of the disease, yet an extremely crucial one to be highlighted upon.

CASE REPORT

A 32-year-old male patient presented with hemoptysis and acute respiratory distress. He also complained of fever, nausea, vomiting, myalgias, and headache since the past 5 days. His medical history was only significant for acute pancreatitis secondary to alcohol abuse. Physical examination confirmed high body temperature (40.5◦C), normal blood pressure and urine output, and crackles in the lower lobes of both the lungs. Laboratory results were as follows: WBC count, 7.4 × 103/μL; platelets, 97 × 103/μL; hematocrit, 27%; C-reactive protein, 231 mg/L (normal <5 mg/l); urea 54 mg/dl; creatinine, 6.1 mg/dl; aspartate transaminase, 43 U/L (normal <32 U/L); alanine transaminase, 37 U/L (normal <32 U/L); alkaline phosphatase, 112 U/L (normal <104 U/L); and total bilirubin, 15 mg/dL, with a direct component of 5 mg/dL. Arterial blood gas measurements (on mask with reservoir bag 15 l/min oxygen) were as follows: pH, 7.48; PaCO2, 30 mm Hg; PaO2/FiO2 = 52, base excess, −1.5 mmol/L. Admission chest X-ray showed diffuse bilateral infiltrates. An X-ray of the chest

on day 1 demonstrated diffuse alveolar infiltrates (Figure 1), more pronounced in the lower lobes. Urine routine showed multiple RBCs but the cultures were sterile. He received ceftriaxone and levofloxacin. In view of high spikes of fever and macular rashes, he was started on doxycycline as well. The patient had recurrent hemoptysis (300 ml total) that subsided with cold saline lavage, but required intubation for hypoxemia and poor Glassgow coma scale. A ventilatory support with lung protective strategy was instituted (initial settings: assist-control mode, FiO2 = 1, Peep = 12 cm H2O, inspiratory flow 60 l/min, tidal volume 6 ml/kg, mean airway pressure = 27 cm H20). A transoesophageal echocardiography showed a normal left ventricular function with low filling pressures. The patient underwent a bronchoscopy with bronchoalveolar lavage. Bacterial, mycobacterial, viral, and fungal culture findings of the fluid were negative. Significant hemoptysis persisted for 4 days. Injections tranexa, FFP, and Vitamin K were given for control of bleeding. HIV serology was negative. Fever subsided after day 7. CT scan of the chest performed on day 8 showed a marked regression of alveolar infiltrates but the presence of ground-glass opacities (Figure 2).

Pathological analysis was suggestive of typical lesions of bronchiolitis obliterans with organizing fibroblastic polyps in bronchioles, alveolar ducts, and alveoli, but without inflammatory cells. The patient received prednisolone (1 mg/kg) from day 10. Due to rapid improvement of his respiratory condition, he was extubated on day 15. The initial serology for leptospirosis was negative, the second determination three weeks after was clearly positive (MAT positive at 1:3200 for *Leptospiro icterohaemorrhagiae).*

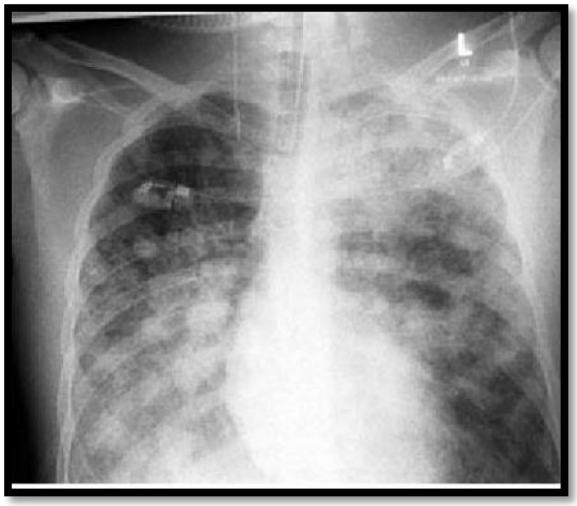

Figure 1: Bilateral diffuse infiltrate in the chest X ray.

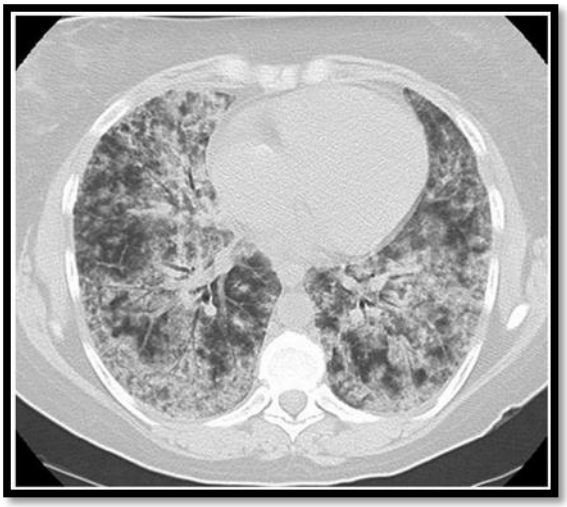

Figure 2: CT scan showing dense consolidation om dependent areas with ground glass attenuation.

DISCUSSION

Leptospirosis, an infectious disease earlier confined to the rural settings, is now being reported to spread to the urban centers,[4] with cases being described even in developed and temperate climate countries.[4.9-11] Simultaneously, in the recent years, there has been a rise in the number of reports of severe leptospirosis associated with hemorrhagic pneumonitis (pulmonary hemorrhage and acute respiratory distress) and a high fatality rate.[12-14]

In the present case report, the absence of hepatic and renal involvement led to a delayed diagnosis of leptospirosis. Generally, hepatic and renal involvement are the first to raise a suspicion toward the disease and severe forms of leptospirosis present major hemorrhagic complications and are usually associated with jaundice and renal impairment (icteric leptospirosis). However, pulmonary symptoms have also been reported in the literature. In a cohort of 26 Spanish patients, 7 patients presented hemoptysis and 3 patients had an acute respiratory distress syndrome, but always associated with a multi organ failure.[15,16] Our case report once again highlights that acute respiratory distress syndrome can be the manifestation of the disease, even in the absence of significant renal or hepatic involvement. An acute respiratory distress syndrome requiring mechanical ventilation is associated with a mortality rate as high as 30 to 60%.[17] Platelet transfusions and desmopressin therapy prove to be effective in massive pulmonary hemorrhage in patients with severe leptospirosis.[18] A recent publication mentions the interest of cyclophosphamide in patients with leptospiral pulmonary alveolar hemorrhage: out of the 33 patients treated with cyclophosphamide, 22 (66.7%) survived; while in the control group, out of 32 patients, 3 (9.4%) survived. The hypothesis is that an exacerbated immune response of the host plays an important role in its pathogenesis.[19]

A study conducted by Vandroux D et al. reported that the prognosis of leptospirosis-related acute respiratory distress syndrome was better in patients with leptospirosis than in other causes of the syndrome.[20] A plausible explanation can be the singular pathophysiology of respiratory involvement associated with leptospirosis respiratory. A direct effect of bacterial inoculums is often considered the underlying mechanism.[21] Additionally, an unidentified bacterial toxin or an indirect effect mediated by host response may also be blamed for the pathogenesis. In humans, leptospirosis associated respiratory involvement differs from other causes of pulmonary hemorrhage, with linear depositions of immunoglobulins and complement on the alveolar surfaces.[22] Lung endothelial cells have been suggested as targets for the lung involvement in leptospirosis through the activation of toll-like receptor 2 or the complement system, which stimulates the release of cytokines, leading to the activation of adhesion molecules: vascular cell adhesion molecule,[23] soluble E-selectin, and soluble intercellular adhesion molecule 1.[24] Moreover, research indicates a potential role of different cytokines and enzyme expressions in blood leucocytes in the severity of the disease and occurrence of bleeding. Two subphenotypes of acute respiratory distress syndrome have been identified,[25] and the higher plasma levels of inflammatory biomarkers including interleukin-8 characterize the second phenotype. Despite its probable immunological mechanism, interleukin-8 is not elevated in leptospirosis.[26,27] Therefore, the mechanisms of the leptospirosis-associated acute respiratory syndrome seem specific and further studies are needed to decipher the role of innate immunity in the severity of the disease.

CONCLUSION

Leptospirosis can induce serious but transient acute respiratory distress syndrome, which might be the only presenting feature in certain cases of disease. Although the pathophysiology of leptospirosis-related acute respiratory distress syndrome is not well understood, its prognosis is better than other causes.

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