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Case Report: Refractory Acute Respiratory Distress Syndrome Supported by Extracorporeal Membrane Oxygenation due to Coinfection with *Chlamydia pneumoniae* and Leptospirosis in Reunion Island

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Abstract. Infection with *Leptospira* spp. is common in Réunion, a tropical island in the Indian Ocean. However, respiratory coinfections between strains of *Leptospira* spp. and other microorganisms are rarely described. Here, we describe the first reported case of coinfection between *Leptospira* spp. and *Chlamydia pneumoniae*, responsible for refractory acute respiratory distress syndrome requiring extracorporeal membrane oxygenation with a favorable outcome. In a case of leptospirosis with severe respiratory illness, testing for respiratory coinfection, especially with atypical pathogens, could explain the seriousness of the clinical condition and lead to specific treatment.

INTRODUCTION

Leptospirosis is a common zoonosis in areas where it is endemic and has a relatively high mortality rate. It is caused by a spirochete, *Leptospira* spp., exposure occurring through direct contact with infected animals or through indirect contact of the skin or mucous membranes with contaminated water or soil. Each year, around 100 cases are reported in Réunion. Thirty-one percent of them require hospitalization in the intensive care unit,[1] with a case fatality rate of around 8%.[2] Cases of bacterial coinfection are rare. We describe here the first case of respiratory coinfection with *Chlamydia pneumoniae* in a patient with leptospirosis who developed refractory acute respiratory distress syndrome requiring venovenous extracorporeal membrane oxygenation.

CASE SUMMARY

A 28-year-old patient with no medical history consulted the emergency department in the southern winter (during the month of July) for a deterioration in general health with an influenza-like illness (without cough or sputum), having experienced lower back pain and chills for the previous 4 days. On questioning, he presented a posteriori risk factor for exposure to *Leptospira* spp. (bathing in a freshwater river for 20 minutes). On admission to the emergency department, the patient had a fever of 39°C, blood pressure of 116/55 mmHg, heart rate of 105/minute, respiratory rate of 20/minute, and 96% saturation without oxygen. On clinical examination, he had a tender abdomen with pain on right lumbar palpation. The remainder of the clinical examination was unremarkable (no mucocutaneous jaundice).

A urine test strip was analyzed, and blood and proteins were found. Biology found leukocytes at 13.2 G/L, a hemoglobin level of 11.3 g/dL, a platelet count of 78 G/L, a glomerular filtration rate of 76 mL/minute (creatinine level at 114 µmol/L), and C-reactive protein at 308 mg/L. The hepatic laboratory tests were completely normal (with total bilirubin level at 18 µmol/L, aspartate aminotransferase at 22 U/L, alanine aminotransferase at 32 U/L, alkaline phosphatase at 123 UI/L, and gamma-glutamyl transferase at 21 U/L). The initial diagnosis was acute right pyelonephritis, and antibiotic therapy with ceftriaxone was started after performing blood cultures and a cytobacteriological examination of the urine. Given the current context, a coronavirus disease 2019 PCR was carried out and came back negative. A thoraco-abdominopelvic computed tomography scan was performed with injection of contrast agent. The scan rejected the initial diagnosis of pyelonephritis and found diffuse and extensive parenchymal pulmonary injury with multiple bilateral centrilobular nodules with a tree-in-bud pattern (Figure 1). Five hours after admission to the emergency department, the patient suffered a clinical worsening with respiratory distress requiring orotracheal intubation, mechanical ventilation, and transfer to the intensive care unit. This was marked by clinical intra-alveolar hemorrhage (hemoptysis associated with bilateral alveolar and interstitial opacities on chest X-ray**)** with acute respiratory distress syndrome (PaO2/FiO2 ratio of 60 mmHg). Because of severe hypoxemia, a fiberoptic bronchoscopy with bronchoalveolar lavage was not performed. A transthoracic echocardiogram was performed which was normal (left ventricular ejection fraction, left ventricular filling pressures, and right ventricular function). Anti-infective treatment with cefotaxime, spiramycin, and oseltamivir was initiated after taking microbiological samples (bacteriological examination of bronchial aspiration and plasma PCR for leptospirosis). Six hours after admission to the hospital, faced with a rapidly worsening respiratory state, venovenous extracorporeal membrane oxygenation was used (Simplified Acute Physiology II and Sequential Organ Failure Assessment scores were 54 and 14, respectively). Given the initial severity of symptoms and rapid clinical worsening, a search for respiratory coinfection was carried out. A bronchial aspiration was tested by multiplex PCR (Seegene Allplex™ respiratory panel, Eurobio Ingen, Les Ulis, France) for the following pathogens: influenza, respiratory syncytial virus, adenovirus, enterovirus, parainfluenza, *Human Metapneumovirus*, human bocavirus, rhinovirus, coronavirus (NL63, 229E, and OC43), *C. pneumoniae*, *Mycoplasma pneumoniae*, *Legionella* spp., *Haemophilus influenzae*, *Streptococcus pneumonia*e, and *Bordetella* (*para*) *pertussis.* Pneumococcal and *Legionella* urinary antigen tests were also carried out. Plasma PCR for leptospirosis came

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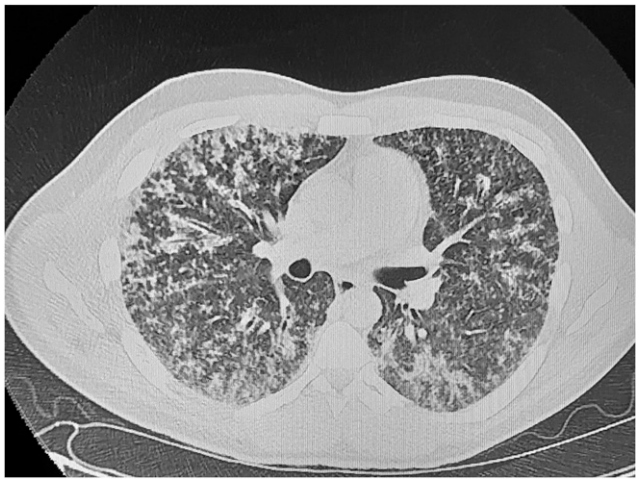

FIGURE 1. Chest computed tomography showed multiple bilateral centrilobular nodules with a tree-in-bud pattern.

back positive on day 2 (with a computed tomography [CT] value of 20.4), and antibiotic therapy was changed to amoxicillin. On day 3, the multiplex respiratory PCR also came back positive for *C. pneumoniae* (with a CT value of 40.8), prompting the introduction of spiramycin treatment for a total duration of 7 days.

On day 1, the patient developed a septic myocarditis, which required 48 hours of treatment with dobutamine. He also presented acute renal failure (with a peak plasma creatinine level of 257 µmol/L on day 3). Renal failure progressed favorably without the need for dialysis (with a plasma creatinine level of 93 µmol/L on day 5). The total bilirubin level increased moderately with a peak of 40 µmol/L on day 3. The patient presented with thrombocytopenia with a nadir platelet count of 43 G/L on day 3. From day 5, the platelet count remained above 100 G/L. The outcome was secondarily favorable under antibiotic treatment, allowing discontinuation of the extracorporeal membrane oxygenation on day 8, discontinuation of mechanical ventilation on day 18, discharge from the intensive care unit on day 25, and discharge from the hospital on day 35.

DISCUSSION

Leptospirosis can be a serious pathology.[1] Coinfections are rare but can worsen prognosis.[3,4]

Patients with severe community-acquired pneumonia are less frequently tested for atypical pathogens such as *C. pneumoniae*,[5] although this is the second most common atypical pathogen responsible for community-acquired pneumonia in certain tropical zones.[6] *Chlamydia pneumoniae* lung disease does not generally require hospitalization, and the outcome is generally favorable, but some respiratory complications can be serious, with a potentially high mortality.[7] This is linked in part to the diagnostic delay and to an unsuitable first-line probabilistic antibiotic therapy.[8] In the tropical island of Réunion, there are no data on the microorganisms responsible for community acquired pneumonia. Leptospirosis is a common zoonosis in Réunion,[2] which is very rarely complicated by respiratory failure requiring extracorporeal membrane oxygenation. Between 2004 and 2017, only eight patients from the thousands of cases of leptospirosis in Réunion Island required respiratory support through extracorporeal membrane oxygenation[9] and one had a 2009 pandemic H1N1 influenza virus coinfection.[10]

It is difficult to ascertain whether *C. pneumoniae* was actually implicated in the disease, rather than occupying an ecological niche in the lung without causing disease. Nevertheless, in clinical practice, it is difficult not to treat the presence of microorganisms as influenza or *C. pneumoniae* in a patient with severe pneumonia. Moreover, it should be noted that these microorganisms are treatable and known to be true pathogens of the upper airways.

These cases illustrate the fact that in the event of severe respiratory impairment in a patient with leptospirosis, associated coinfection should be sought, in particular treatable pathogens such as influenza or *C. pneumoniae*. We believe that all leptospirosis patients with acute respiratory failure should be screened for respiratory coinfection.

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