NOSOCOMIAL *LEGIONELLA* SEPTICEMIA IN PATIENT WITH SYSTEMIC LUPUS ERYTHEMATOSUS: A CASE REPORT AND LITERATURE REVIEW

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Abstract. *Legionella pneumophila* is an important cause of community and hospital acquired pneumonia in immunocompromised patients, but bacteremia caused by this organism is rarely reported. We report here a case of ventilator associated pneumonia caused by *Legionella pneumophila* in a lupus nephritis patient treated with systemic corticosteroids. The patient was treated with intravenous tigecycline initially and then intravenous levofloxacin for a total course of 14 days. The potable water system was investigated but no evidence of contamination was found.

Keywords: *Legionella pneumophila*, ventilator associated pneumonia, lupus nephritis patient

INTRODUCTION

Legionella pneumophila can cause community and nosocomial acquired pneumonia in immunocompromised patients, especially those with defective cell-mediated immunity (Arinuma *et al*, 2015). The diagnosis of *Legionella* infection is difficult because it cannot be isolated by routine laboratory methods (Rihs *et al*, 1985; Scola *et al*, 2004). Most cases of legionellosis can be diagnosed by antigen detection or by molecular identification (Scola *et al*, 2004). As a result, positive blood cultures for legionella are rare. We report here a case of blood culture proven *Legionella pneumophila* pneumonia with *Legionella* septicemia in a patient with systemic lupus erythematosus receiving corticosteroid therapy.

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CASE REPORT

A 25-year-old woman with a history of systemic lupus erythematosus (SLE) was admitted to our hospital for management of her SLE. She had been diagnosed with SLE 5 years previously and was taking prednisolone 5 mg every other day. Two weeks prior to admission, she developed progressive edema, microscopic hematuria, nephrotic range proteinuria and azotemia. She was diagnosed with active lupus nephritis and had been treated with prednisolone 40 mg daily and azathioprine 100 mg daily. After two-week treatment, she was not better and her renal function had progressively declined; she was diagnosed as having rapidly progressive glomerulonephritis.

She was admitted and started on methylprednisolone 500 mg daily for

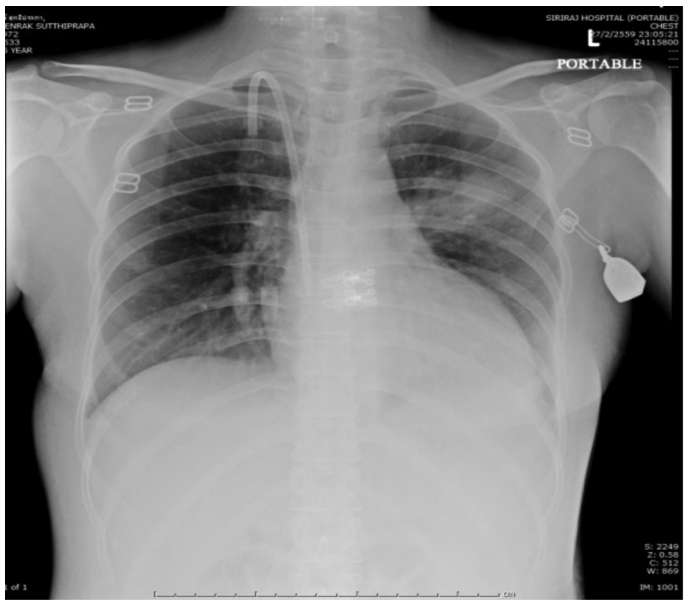

Fig 1–Chest radiography reveals alveolar infiltration in the left upper lung field.

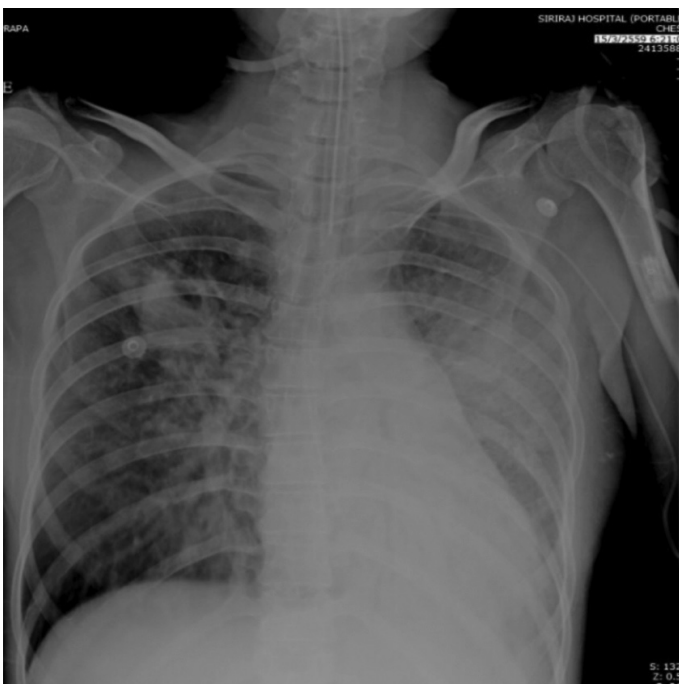

Fig 2–Chest radiography reveals increase infiltration in the left upper lung field and a newly detected consolidation in the right middle lung field.

three consecutive days, followed by prednisolone 50 mg daily. Ten days after admission, she developed high fever and respiratory distress. On physical examination she had a temperature of 39°C, a blood pressure of 70/40 mmHg, a pulse rate of 120 per minute and a respiratory rate of 30/min. Chest auscultation revealed fine crepitations in her left upper lung field. Chest radiography showed consolidation of the left upper lung (Fig1). She was diagnosed with having hospital acquired pneumonia, respiratory failure and septic shock. She was intubated and transferred to a respiratory care unit for hemodynamic monitoring, ventilator support and continuous renal replacement therapy. She also received extracorporeal membrane oxygenation due to profound circulatory failure. At that time, intravenous meropenem was given for empirical therapy. A complete blood count revealed a hemoglobin of 8.8 g/dl, a hematocrit of 26.5%, a MCV of 93.4 fl, a white blood cell count of 52,530/mm^3 with 56.8% neutrophils, 8.7% lymphocytes, 7.4% promyelocytes, 4.9% myelocytes, 13.6% metamyelocytes and 3.7% bands.; her platelet count was 173,000/mm^3, her blood urea nitrogen and creatinine were 72.2 and 2.09 mg/dl, respectively.

Despite 10 days of meropenem, she continued to deteriorate. Chest radiography

showed an increasing infiltrate in the left upper lung field and a new consolidation in the right middle lung field (Fig 2). Sputum cultures before empirical antibiotic treatment revealed *Acinetobacter baumannii* susceptible to colistin and tigecycline. Her antibiotics was then changed to colistin and tigecycline combined. After the change, her fever and respiratory symptoms improved. A blood culture which had been taken previously revealed scanty, thin colonies of gram-negative bacilli on chocolate blood agar. Subculture on Buffered Charcoal Yeast Extract (BCYE) revealed round colonies with iridescent blue sheen and a mottled surface after 72 hours of incubation under aerobic conditions. This was confirmed to be *L. pneumophila* by mass spectrometry (MALDITOF). A sputum culture plated on BCYE agar was negative. 16s ribosomal sequencing of the sputum was positive for *L. pneumophila*. These results confirmed the diagnoses of *Legionella* pneumonia and septicemia. The antibiotic was changed from tigecycline to intravenous levofloxacin to give a total treatment course of 14 days. The water supply system in the respiratory care unit was examined for *Legionella* by culture but the results were all negative. The patient was discharged in stable condition. Although the source of legionellosis could not be identified in this patient, nosocomial legionellosis was the most likely diagnosis because the disease had occurred after 10 days of hospitalization.

DISCUSSION

Legionella species causes community acquired and nosocomial infections, with the most common type being pneumonia. The most common pathogenic serotypes of *L. pneumophila* are 1, 4 and 6 (Koch *et al*, 1997). Commonly reported non-pneumophila species are *L. micdadei* (Koch *et al*, 1997) and *L. longbeachae* (Kümpers *et al*, 2008). *Legionella* infection usually occurs in immunocompromised patients with chronic lung disease and a history of smoking; other associated factors include cell mediated immune defects, such as from the use of corticosteroid and biological agents (Arinuma *et al*, 2015). Solid organ transplant recipients are also at higher risk for acquiring *Legionella* infection, especially heart transplant recipients (Sabria and Yu, 2002).

Clinical manifestations of *Legionella* pneumonia resemble pneumonia caused by other typical pathogens, such as *S. pneumoniae* (Jespersen *et al*, 2010). However extrapulmonary symptoms are more prominent in *Legionella* pneumonia (Kümpers *et al*, 2008). Other manifestations include electrolyte imbalances, such as hyponatremia, hypophosphatemia and relative bradycardia (Jespersen *et al*, 2010). Chest radiographic findings are indistinguishable from other common causes of bacterial pneumonia, such as unilateral alveolar infiltrations or occasionally multilobar infiltration (Kümpers *et al*, 2008).

The mortality rate of nosocomial legionellosis has been reported to be 33-46% (Jespersen *et al*, 2010). Case reports of *Legionella* septicemia are rare and have a high mortality rate. Rihs *et al* (1985) reported 6 cases of culture proven bacteremic legionellosis, all severe and all died. *Legionella* septicemia cases are usually categorized in two types: infective endocarditis and bacteremic pneumonia (Patel *et al*, 2005; Jespersen *et al*, 2010). *Legionella* is a recognized cause of blood culture negative prosthetic valve infective endocarditis (PVE) in immunosuppressed patients (Park *et al*, 1994). Patel *et al* (2005) reported

5 cases of hemoculture proven *Legionella* PVE, half were caused by *L. pneumophila*. The clinical course of these 5 cases were subacute to chronic and emboli were rare. In those cases, the prognosis was generally favorable although most needed valve replacement. However native valve infective endocarditis (NVE) due to *Legionella* is rare. Samuel *et al (* 2011) reported the first case of *L. pneumophila* NVE in a 42 year-old woman who had received corticosteroid treatment for hypersensitivity pneumonitis. The clinical course of that case was severe and included septic shock and acute respiratory distress syndrome. However, she responsed well to intravenous antibiotic treatment and did not need valve replacement.

Lai *et al* (2010) reported a case of hospital acquired pneumonia (HAP) with bacteremia caused by *L. pneumophila* from Taiwan in an elderly patient with ITP who received steroid treatment; the clinical setting was similar to our patient. That patient was successfully treated with intravenous ceftazidime and clindamycin initially, followed by ciprofloxacin for 14 days. Our case suggests *Legionella* infection should be considered in patients who are seriously ill, elderly or immunocompromised due to receiving, corticosteroids or immunosuppressant agents. In the case of a HAP which does not response to betalactam antibiotics, *Legionella* should be considered (Kümpers *et al*, 2008).

The gold standard to diagnose *Legionella* infection is culture on BCYE agar (Rihs *et al*, 1985). Blood cultures have only a 10-30% sensitivity for detecting *Legionella* (Rihs *et al*, 1985); therefore, in suspected cases it is important to perform daily blind subcultures on BCYE agar plates. This process requires 2-7 days to complete (Rihs *et al*, 1985). Other advanced diagnostic tools consist of checking a urine antigen for *L. pneumophila* serogroup 1; this has a sensitivity of up to 70% or by checking direct PCR of the urine, bronchoalveolar lavage fluid and serum, which has a sensitivity of 80-90% (Rihs *et al*, 1985; Scola *et al,* 2004).

First line antimicrobial therapy for *Legionella* infection includes new generation macrolides and respiratory fluoroquinolones (FQ) (Sabrià *et al,* 2005). Alternative treatment drugs for *Legionella* include tetracycline, doxycycline and trimethoprim-sulfamethoxazole (Yu, 2009). A few studies reported patients who received fluoroquinolones had a shorter time to fever defervescence and a more rapid restoration to well-being compared to macrolides (Sabrià *et al,* 2005; Pedro-Botet and Yu, 2006). Some experts recommended the combination of fluoroquinolones and azithromycins for patient who are severely ill or have extrapulmonary manifestations (Yu, 2009). The recommended duration of treatment is 7-10 days in non-severe cases with expeditiously response to treatment (Yu, 2009), but in severe cases and in immunocompromised hosts, the duration of treatment should be extended to 21 days (Pedro-Botet and Yu, 2006; Yu, 2009).

Tigecycline has also been reported to be effective in treating *Legionella* (Pedro-Botet *et al,* 2009; Valve *et al,* 2010). One *in vitro* study reported tigecycline has comparable intracellular killing compared to fluoroquinolones and macrolides (Bopp *et al,* 2011). Tigecycline was given in our patient to treat extended drug resistant *A. baumannii* resulting in partial improvement. However, tigecycline is only approved for complicated skin and soft tissue infections, complicated intraabdominal infections and community acquired bacterial pneumonia, so treating *Legionella* bacteremia with tigecycline may

lead to unfavorable outcome and should be avoided (FDA, 2016). From this reason, our patient was changed to levofloxacin for 14 days.

In conclusion, we report here a case of nosocomial *Legionella* pneumonia and bacteremia in an immunocompromised patient who had been diagnosed with blood culture and successfully treated with levofloxacin.

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