sciendo

ПРИЛОЗИ. Одд. за мед. науки, XXXIX 2–3, 2018
CONTRIBUTIONS. Sec. of Med. Sci., XXXIX 2–3, 2018

МАНУ
MASA

10.2478/prilozi-2018-0041

ISSN 1857-9345
UDC: 616-022.7:579.841]:
616.61-089.843-052

COMMUNITY ACQUIRED LEGIONNAIRE'S DISEASE IN A KIDNEY TRANSPLANT PATIENT

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ABSTRACT

This case report details the clinical picture of a renal transplant recipient infected with community acquired Legionella pneumonia. While it is more commonly associated as a nosocomial infection due to pathogenic organisms in a hospital's water supply, this case serves as a reminder to consider the patient's impaired cellular immune function when trying to diagnose community acquired pneumonia.

Keywords: kidney transplantation, Legionella, Legionnaire's disease, community acquired pneumonia

INTRODUCTION

Legionnaires' disease (LD) is a severe form of atypical pneumonia that can be caused by the bacterium Legionella. Legionella pneumophila (LP) serogroup 1 is the predominant culprit, accounting for approximately 80% of all Legionella infections [1]. However, investigations in the immunocompromised population, including solid organ transplant (SOT) patients, show large variation. In a study performed in Barcelona in 2009, all infections were caused by the serogroup 1 [2] while a larger 15-year retrospective study from the USA showed that non-pneumophila Legionella species account for half of all infections [3]. No large-scale study on species and serogroup incidence in the SOT population has been performed, with data seldom from southeast Europe.

Infections can be caused by the inhalation of aerosolized bacterium that resides in contaminated water sources or from contact with soil and compost. Historically, infections have been traced back to cooling towers, shower heads, air conditioning units, communal water systems and professions that expose one to soil such as gardening [4, 5]. The clinical presentation is severe with 44% of patients requiring treatment in the intensive care unit and mortality rates ranging from 1-10% [6].

While it has been reported that Legionella most commonly occurs within the first three months post-transplantation as a nosocomial infection [7], our patient acquired the infection 1 year after the kidney transplantation. Here, we describe a rare case of community acquired pneumonia (CAP) caused by LD.

CASE REPORT

A 59 year old Croatian male received a kidney transplant from a deceased donor in August of 2015 with basiliximab induction. The patient was discharged on tacrolimus, prednisone and everolimus immunosuppressive therapy and required treatment 4 months later due to deterioration of renal function, right sided pneumonia and deep venous thrombosis of his left leg. At an outpatient checkup in July 2016, the patient was in good health and had normal graft function.

One month later the patient was transferred to our hospital in Croatia from Bosnia after presenting with radiologically verified lobar pneumonia, 39°C fevers, dyspnea and a subjective feeling of tachycardia. The patient's blood pressure was 123/80 mmHg, ECG confirmed the presence of a previously unreported atrial fibrillation with a pulse of 135/min, and auscultation of the lungs revealed diffuse rough inspiratory right-sided crepitations with some expiratory wheezing. Mental and gastrointestinal statuses were unremarkable.

The clinical suspicion of pneumonia prompted us to test hemo-, stool and urine cultures; all results were negative for any possible cause. Sputum testing revealed Proteus mirabilis and Streptococcus viridians, but negative results for acid-fast mycobacterium. An urine antigen test (UAT) for Legionella was positive which was repeated and confirmed by a second positive result 5 days later.

An initial chest x-ray showed immense right-sided confluent infiltrates that extended from the base to the apex with liquid pleural reaction (Figure 1). A CT scan also showed the same right lobe inflammatory infiltrate and parenchymal consolidation, but indicated that there were no signs of parenchymal destruction or granuloma formation (Figure 2). Reactive hilar lymph nodes were visible in the middle and superior mediastinum.

Figure 1. *Lung consolidation is most extensive in the basilar segments of the right lung with extension into the apex*

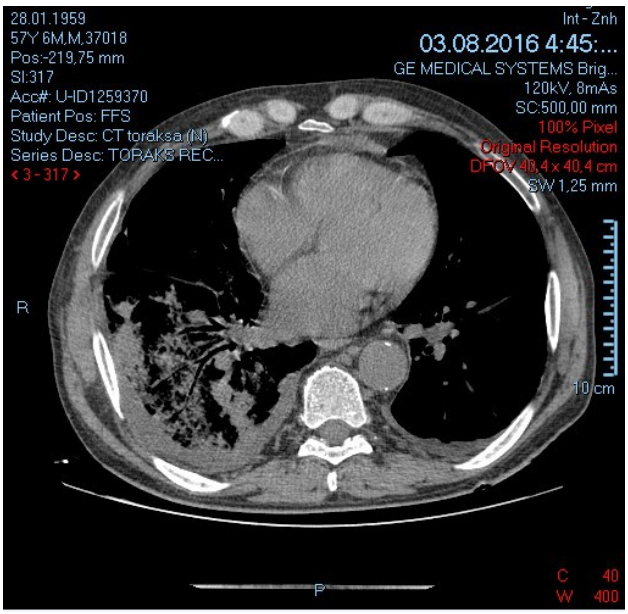

Figure 2. *Air bronchograms can be clearly appreciated amidst the consolidative changes*

Laboratory testing revealed a CRP of 181.6 mg/L, 81.6 % neutrophil count with a normal leukocyte count of $4.06x10^9$/L. The urea and creatinine levels rose to 29.4 mmol/L and 237 μmol/L, respectively. In concordance with the prototypical effects of Legionella, the Na+ levels decreased to 129 mmol/L, K+ to 3.0 mmol/L, total bilirubin to 24 μmol/L, alkaline phosphatase to 194 U/L, GGT to 110 U/L, AST to 112 U/L, and ALT to 144 U/L. The levels of tacrolimus were slightly supra-therapeutic; however the levels of warfarin reached toxic levels with an APTV of 64.9 seconds.

The patient was admitted to the ICU, the warfarin coagulopathy was corrected with 2 doses of fresh frozen plasma, parenteral crystalloid hydration was administered and a combination of piperacillin/tazobactam (for 17 days) and azithromycin (for 5 days) was given. After receiving positive Legionella urine antigen results, the broad antibiotic therapy was switched to levofloxacin. After 6 days of antibiotic treatment, the patient returned to a stable respiratory status as confirmed by a repeated chest x-ray. Laboratory follow-up showed excellent therapeutic response along with decline of inflammatory parameters and serum creatinine values. Moreover, the patient reverted to normal cardiac sinus rhythm.

DISCUSSION

Legionella pneumophila invades alveolar macrophages and replicates intracellularly, requiring a Th1 cell-mediated immune response to sterilize the pathogen. Solid organ transplants require strong immunosuppressive therapy that cripples the host immune response and thus, they are a well-documented risk factor for acquiring LD [8]. LD has been described multiple times in literature as a nosocomial infection in solid organ transplant recipients resulting from a hospital water source, but has rarely been reported as a cause of CAP in KTR [8, 9]. KTR should receive fluoroquinolone therapy instead of macrolides and rifampin to avoid drug-drug interactions with calcineurin inhibitors [10].

Our patient was traveling to Bosnia and had not been admitted as an inpatient for over seven months. Relying on the 2-10 day incubation period is one method to determine the source of infection, however, there have been instances when a patient's oropharynx has been colonized by LP and infected much later [11]. It is more common to contract LD over the warmer summer months when contact with infected water sources and soil is maximized. Additionally, the patient possessed multiple independent risk factors for infection, including: age of 50 years, chronic respiratory disease, diabetes mellitus, end-stage renal disease, compromised cellular immunity and history of recent travel [12, 13].

While LD is characterized by patchy or nodular infiltrates in immunocompetent patient radiographs, it has been commonly reported that renal transplant recipients present with cavitations; which did not match the consolidation seen in our case [10]. Therefore, Legionella spp., like other causes of 'atypical' pneumonia, cannot be confirmed or excluded by distinct radiographic patterns.

The diagnosis of LD can be difficult as the bacterium does not grow on standard microbiology media, and are usually not detected by blood culture, gram stain or culture of sputum. Potentially obscuring and delaying correct diagnoses are the increased rates of false negative results on the UAT in immunocompromised patients [14]. An additional concern is that the UAT for Legionella is sensitive only for L. pneumophila serogroup 1. Taking into account that around 16.3% of infections in the general population are caused by non-serogroup 1 bacteria [1] and up to half of infections in SOT transplant patients [3], clinical suspicion of LD must persist even in cases of negative UAT. Another disadvantage is the test's inability to diagnose relapse or reinfection due to persistence of antigen excretion. Thereby, any patients presenting with symptoms of altered mental status, pneumonia, low Na levels and disturbances in the GI system should be additionally investigated by a bronchoalveolar lavage or serum PCR.

Furthermore, considering the significance of a timely diagnosis, knowledge of local epidemiology is of crucial benefit in reducing the morbidity and mortality of LD in KTR. Our main goal is to emphasize the importance of adequate counselling for prevention of exposure and raising awareness of the possibilities of infection among the high risk populations, as well as to show that due to variability of presentation, disease acquisition, possible non-reliability of tests and the lack of adequate epidemiologic data, it can be difficult to either make or exclude a diagnosis of LD.

REFERENCES

1. Helbig JH, Bernander S, Castellani Pastoris M, et al. Pan-European study on culture-proven Legionnaires' disease: Distribution of Legionella pneumophila serogroups and monoclonal subgroups. Eur J Clin Microbiol Infect Dis. 2002; 21(10): 710–6.
2. Gudiol C, Garcia-Vidal C, Fernández-Sabé N, et al. Clinical features and outcomes of Legionnaires' disease in solid organ transplant recipients. Transpl Infect Dis. 2009; 11(1): 78–82.

3. Sivagnanam S, Podczervinski S, Butler-Wu SM, et al. Legionnaires' disease in transplant recipients: A 15-year retrospective study in a tertiary referral center. Transpl Infect Dis. 2017; 19(5): 1–8.
4. Yu VL, Plouffe JF, Pastoris MC, et al. Distribution of Legionella Species and Serogroups Isolated by Culture in Patients with Sporadic Community-Acquired Legionellosis: An International Collaborative Survey. J Infect Dis [Internet]. 2002; 186(1): 127–8.
5. Pedro-Botet ML, Stout JE, Yu VL. Legionnaires' disease contracted from patient homes: The coming of the third plague? Eur J Clin Microbiol Infect Dis. 2002; 21(10): 699–705.
6. Kathleen L. Dooling M, Karrie-Ann Toews M, et al. Active Bacterial Core Surveillance for Legionellosis — United States, 2011–2013. Morb Mortal Wkly Rep. 2015; 64(42): 1186–205.
7. Jernigan D, Sanders L, Waites K, Brookings E, Benson R, Pappas P. Pulmonary Infection Due to Legionella-Cincinnatiensis in Renal-Transplant Recipients - 2 Cases and Implications for Laboratory Diagnosis. Clin Infect Dis. 1994; 18(3): 385–9.
8. Kümpers P, Tiede A, Kirschner P, Girke J, Ganser A, Peest D. Legionnaires' disease in immunocompromised patients: A case report of Legionella longbeachae pneumonia and review of the literature. J Med Microbiol. 2008; 57(3): 384–7.
9. Lück PC, Schneider T, Wagner J, et al. Community-acquired Legionnaires' disease caused by Legionella pneumophila serogroup 10 linked to the private home. J Med Microbiol. 2008; 57(2): 240–3.
10. Fraser TG, Zembower TR, Lynch P, et al. Cavitary Legionella pneumonia in a liver transplant recipient. Transpl Infect Dis. 2004; 6(2): 77–80.
11. Marrie TJ, Bezanson G, Haldane DJ, Burbridge S. Colonisation of the respiratory tract with Legionella pneumophila for 63 days before the onset of pneumonia. J Infect. 1992; 24(1): 81-6.
12. Den Boer JW, Yzerman EPF, Schellekens J, et al. Large outbreak of Legionnaires' disease at a flower show, the Netherlands (vol 8, pg 37, 2002). Emerg Infect Dis. 2002; 8(2): 180.
13. Burillo A, Pedro-Botet ML, Bouza E. Microbiology and Epidemiology of Legionnaire's Disease. Infect Dis Clin North Am. 2017; 31(1): 7–27.
14. Kashuba ADM, Ballow CH. Legionella urinary antigen testing: Potential impact on diagnosis and antibiotic therapy. Diagn Microbiol Infect Dis. 1996; 24(3): 129–39.

Резиме

ЛЕГИОНЕРСКА БОЛЕСТ СТЕКНАТА ВО ЗАЕДНИЦА КАЈ ПАЦИЕНТ СО ПРЕСАДЕН БУБРЕГ

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Овој приказ на случај дава детали за клиничката слика на примач на пресаден бубрег инфициран со Legionella pneumonia добиена од заедницата. Иако почесто се поврзува со нозокомијалната инфекција, поради патогените организми во водоснабдувањето на болницата, овој случај служи како потсетник за да се разгледа оштетената клеточна имунолошка функција на пациентот кога се прави обид да се дијагностицира пневмонија стекната во заедницата.

Клучни зборови: трансплантација на бубрег, Legionella, легионерска болест, пневмонија стекната во заедницата