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Case report,

Acute Focal Myocarditis Secondary to Severe Legionella Infection: A Case Report and Review of the Literature

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Abstract:

Legionnaire's disease (LD) is a severe form of atypical pneumonia caused by any species of Legionella. LD can rarely involve the heart and present as myocarditis, pericarditis, or endocarditis. We report a case of focal myocarditis secondary to Legionella. A 49-year-old male was admitted to the hospital for shortness of breath and found to have Legionella pneumonia. An echocardiogram was done because of elevated troponin and shortness of breath, which revealed the new onset of systolic heart failure and focal hypokinesis. The patient received a total of 10 days of levofloxacin 750 mg, and he was discharged home with a cardiology follow-up. This case highlights that Legionella infection should be suspected in patients with unexplained myocardial damage/inflammation.

Keywords: Legionella myocarditis**,** Legionnaires disease, elevated troponin, heart failure with reduced ejection fraction

Introduction:

Legionnaires' disease (LD) is a severe lung infection caused by the Legionella species of bacteria. It is estimated that 90% of patients require hospitalization and 10% die [1]. The term Legionellosis syndrome includes Legionnaires' disease, Pontiac fever, and extrapulmonary forms [1]. Legionella pneumophila is the most common pathogen causing Legionella infections among the different Legionella species, with serogroup 1 being the most common [2]. Extrapulmonary legionnaires are rare and can include interstitial nephritis, myositis, endocarditis, pericarditis, and myocarditis [3]. Cardiac involvement is usually secondary to pulmonary infiltration only a few days after the onset of pulmonary symptoms, but myocarditis may be the only manifestation indicative of LD [4]. It is recommended that a diagnosis of Legionella should be considered when there is myocarditis causing an arrhythmia, even in the absence of pulmonary involvement [4]. In this report, we present a rare case of Legionella-induced focal myocarditis and new onset of heart failure with reduced ejection fraction.

Case Description:

A 49-year-old male with a medical history of mild asthma and hypertension presented to the emergency room with a one-week history of shortness of breath, fatigue and lower extremity weakness. On presentation, the patient's vital signs were as follows: blood pressure: 135/91 mmHg; heart rate: 117 beats/minute; temperature: 98.1 °F; SPo2: 100 percent on room air; and respiratory rate: 23 breaths/minute. Physical examination was remarkable for sinus tachycardia with a heart rate

in the 110s. The laboratory findings are summarized in Table 1. Hepatitis B, Hepatitis C, and HIV screening were negative.

Table 1: Laboratory workup on admission

Test	Results	Reference Range
White Blood Count	6.67	5.00 - 11.00 x10E3/uL
Hemoglobin	14 .1	12.0 - 15.0 G/DL
Platelet	126	150 - 400 x10E3/uL
Sodium	123	135 - 145 mmol/L
Potassium	4.7	3.5 - 5.2 mmol/L
Phosphorus	5.0	2.4 - 4.7 mg/dL
Magnesium	1.8	1.5 - 2.5 mg/dL
Creatinine	5.01	0.5 - 1.1 mg/dl
Blood Urea Nitrogen	62	6 - 23 mg/dl
Anion Gap	21	4-14 mmol/L
Uric acid	14.9	4.0-8.5 mg/dl
Troponin	0.43	<0.031 mg/dl
Aspartate aminotransferase	368	1 - 35 U/L
Alanine aminotransferase	169	1 - 45 U/L
Alkaline phosphatase	52	38 - 126 U/L
Bilirubin Direct	2.4	0.0 - 0.8 mg/dL
Bilirubin Total	3.6	0.1 - 1.2 mg/dL
Total Creatine Kinase	3394	0-195 IUnits/L
Lactate dehydrogenase	1624	0 - 240 IUnits/L
Thyroid stimulating hormone	0.39	0.40 - 4.20 uIU/mL

An electrocardiogram (ECG) revealed sinus tachycardia with a heart rate of 113 beats/minute; otherwise, ECG was unremarkable. Chest x-ray revealed left upper lobe consolidation (Figure 1).

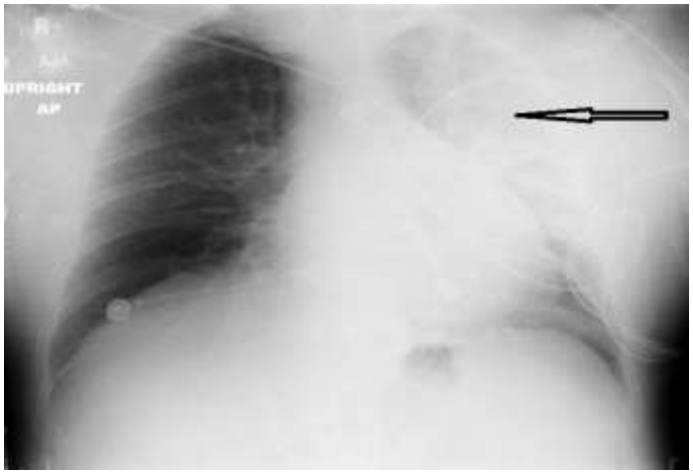

Figure 1: Xray of the chest revealed left upper lobe consolidation (arrow)

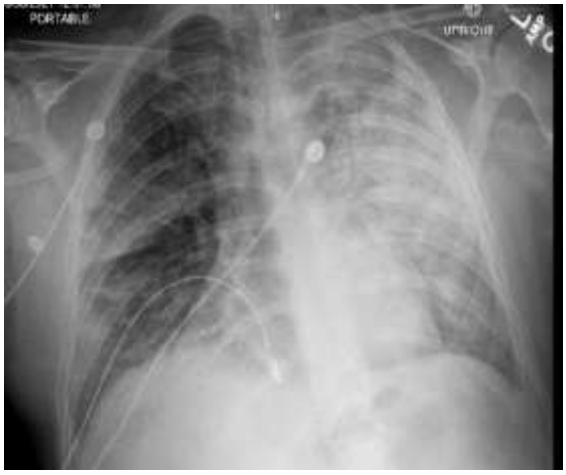

Figure 2: Repeat X-ray of the chest revealed patchy ground-glass interstitial infiltrates

Given hyponatremia, shortness of breath, left upper lobe consolidation, and elevated liver function test, Legionella pneumonia was suspected, and the patient was started on intravenous (IV) azithromycin 500 mg once daily. A urine Legionella antigen test was ordered. On day two of the hospitalization, the patient was confused, with worsening shortness of breath, an upward trending creatinine, and worsening anion gap metabolic acidosis. The repeat chest X-ray revealed patchy bilateral airspace and ground-glass opacities (Figure 2). CT chest with contrast showed patchy ground-glass interstitial infiltrates (Figure 3). The patient was placed on bilevel positive airway pressure (BIPAP) for worsening shortness of breath and transferred to the medical

intensive care unit (MICU). The patient was started on urgent dialysis because of worsening high anion gap metabolic acidosis and symptomatic volume overload.

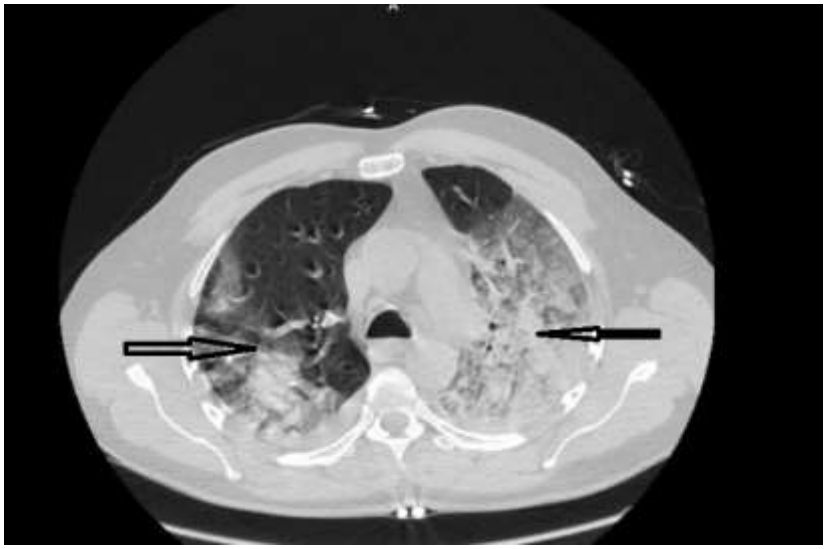

Figure 3: Computed tomography of the chest with contrast revealed bilateral patchy ground-glass interstitial infiltrates (arrow)

On day two, the patient's urine Legionella antigen came back positive. Despite IV azithromycin, the patient's dyspnea continued to worsen, prompting a transition to IV levofloxacin as recommended by the infectious disease team. The patient was also started on IV methylprednisolone 1 mg/kg for severe Legionella infection. An echocardiogram was obtained in light of his symptoms and elevated troponins, revealing an ejection fraction of 20 to 25% with dyskinesia of the mid to distal inferolateral regions.

Cardiology was consulted for the new onset of cardiomyopathy and systolic heart failure. COVID-19 PCR was obtained to rule out COVID-19 induced myocarditis, which was negative. The myocarditis was attributed to a Legionella infection based on the clinical presentation, elevated troponins, and echocardiogram findings. The patient was started on carvedilol 3.125 mg twice daily and, after four days in the MICU, was moved to the cardiac unit. The patient received a total of 3 dialysis sessions during his 12 days of hospital stay. His respiratory distress was improved throughout the hospital course, and he maintained SPO2 above 90% on room air. The patient received a total of 10 days of levofloxacin 750 mg, and he was discharged home on a regimen that included carvedilol, hydralazine, and isosorbide mononitrate. Outpatient plans included cardiology and nephrology follow-up with ischemic workup pending improvement in renal function.

Discussion:

LD is a community-acquired or nosocomial respiratory infection that can clinically mimic other causes of bacterial pneumonia [5]. Legionella spp. are widely distributed in water distribution systems; the temperature at 50°C is a favorable element for their multiplication [6]. The clinical picture of LD is not specific. It can range from mild disease to severe pneumonia requiring hospital admission [6]. After an incubation period of 2 to 14 days, patients present with fever (the most common symptom), general malaise, myalgia, headache, asthenia and anorexia. However, fever may be masked in immunocompromised patients [6]. In half of the cases, a purulent expectorant cough and pleuritic chest pain can be seen [6]. Note that gastrointestinal and neurological manifestations reinforce the diagnosis of LD [6]. Abnormal laboratory findings can be detected as hyponatremia, leukocytosis, increased erythrocyte sedimentation rate (ESR), elevated C - reactive protein (CRP) and elevated creatine kinase [6]. Although there are no pathognomonic radiological

signs of LD, a patchy, unilobar infiltrate that progresses to lung tissue consolidation is the most common pattern reported [7]. Chronic lung disease, smoking, glucocorticoid treatment and hematological cancers are all risk factors [6]. Because it is quick and inexpensive, the urine soluble antigen test is the first-line diagnostic of choice [6,8]. In addition, it has high sensitivity (70-100%) and specificity (95-100%) [8]. However, it is only sensitive for L. pneumophila serogroup 1 [8]. The culture of the sample from the lower respiratory tract is the method of choice [6].

While extrapulmonary manifestations are rare, the myocardium is the most affected site in cardiac manifestations [9]. Myocarditis can be challenging to diagnose in current clinical practice due to polymorphic symptomatology and clinical signs ranging from asymptomatic presentation to sudden cardiac death from ventricular fibrillation [10]. According to the Working Group on Myocardial and Pericardial Diseases of the European Society of Cardiology (ESC), clinical suspicion of myocarditis is based on the following criteria: a) clinical presentation (chest pain, new or worsening dyspnea, etc.), b) electrocardiographic evidence may show non-specific ST-segment changes, T-wave inversions and ST-segment elevations imitating acute myocardial ischemia, c) laboratory findings (serum cardiac biomarkers, specifically troponin I and troponin T, can be elevated in cases of myocarditis and help to confirm the diagnosis, but lack sensitivity), d) imaging findings may show segmental wall motion abnormalities (although echocardiographic findings are highly dependent on both the manner and timing of a patient's presentation). Cardiac magnetic resonance (CMR) results include the coexistence of T1- and T2-related criteria indicating myocardial inflammation [11]. In addition to identifying myocardial damage, excluding obstructive coronary artery disease is crucial in diagnosing myocarditis, especially when the clinical presentation mimics an acute coronary syndrome [11]. However, a definitive diagnosis of myocarditis may require endomyocardial biopsy (EMB), which is the gold standard and also allows an etiological diagnosis [11].

Cardiac symptoms usually appear after the onset of pulmonary symptoms [4]. The course of myocarditis is variable, ranging from a mild form to overt heart failure [4]. As for echocardiographic signs, left ventricular dysfunction is usually found [4]. It is important to mention that myocarditis may be the sole manifestation of L. pneumophila infection [3,4]. Diagnosis is usually based on clinical and laboratory findings such as hyponatremia, leukocytosis, transaminitis, and elevated ESR and CRP. An endomyocardial biopsy is only used in unusual cases where other tests are not diagnostic [2,4]. In a literature review done in 2017, it was found that ten patients had positive Legionella urine antigens, with eight having reduced left ventricular ejection fraction on echocardiogram; only two cases in which the final diagnosis was based on cardiac biopsy [12].

Because of their bactericidal effect, intracellular penetration potential and broad-spectrum activity against all Legionella species, macrolides and fluoroquinolones are preferred antibiotics for LD [13]. Interestingly, when levofloxacin and azithromycin were compared in cohort studies, there was little change in mortality rates [13]. Some authors, however, propose using these two antibiotics in combination in cases of severe LD and extrapulmonary organ involvement [4,12]. The duration of treatment is generally 7 to 10 days, with the possibility of extension in certain situations such as immunosuppression [12]. In the majority of patients with LD presenting with heart failure, left ventricular dysfunction is reversible when the patient's conditions are adequately treated [4]. However, partial improvement or fatal complication has been observed in some cases [4].

Conclusion:

It is important to consider the diagnosis of myocarditis secondary to Legionella with or without pneumonia, especially in high-risk patients. Clinicians should also be aware of the presence of the spread of infection to other organs, even if the patient is asymptomatic. Treatment should be initiated as soon as possible for a favorable prognosis. Further randomized trials are required to evaluate the efficacy of anti-Legionella antibiotics

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