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Case Report

A Case of COVID-19 and *Legionella* Pneumonia

Antonella Spacone[1]*, Antonietta Esposito[1], Riccardo Di Fonzo[2], Tommaso Spina[2], Adriano Barone[2], Alessandra Di Lorito[2], Antonio Gravino[2], Chiaravaleria Di Giacomo[2], Giacomo Zuccarini[1] and Giustino Parruti[3]

[1]*Respiratory Medicine Unit, Pescara General Hospital, Pescara, Italy*

[2]*Covid-Unit, Pescara General Hospital, Pescara, Italy*

[3]*Infectious Diseases Unit, Pescara General Hospital, Pescara, Italy*

***Corresponding Author:** Antonella Spacone, Respiratory Medicine Unit, Pescara General Hospital, Pescara, Italy.

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Abstract

Background: Coronavirus disease (COVID-19) is a global pandemic infectious disease characterized by an acute respiratory and systemic syndrome, appearing for the first time on December 31, 2019 in China. Since then, the disease rapidly spread and was declared a pandemic by the World Health Organization on March 11, 2020.

Legionella, as a cause of community-acquired pneumonia, is often under-recognized. According to the Centers for Disease Control and Prevention, although 18,000 to 25,000 cases of pneumonia due to *Legionella pneumophila* occur each year, this diagnosis is reported in only 1200 to 1500 cases, due to the nonspecific signs and symptoms of the disease and inadequate testing for *Legionella.* This case report describes a patient who developed bilateral pneumonia due to COVID-19 and *Legionella*.

Case Report: A 56-year-old man presented with fever, cough, gastrointestinal symptoms and myalgia and a diffuse bilateral lung infiltration with ground-glass opacities on chest tomography images. He was first suspected of having COVID-19 pneumonia, but then *Legionella* pneumonia was also diagnosed. The patient promptly received supportive treatment including anti-inflammatory treatment, heparin, and antibiotic therapy with macrolide and rifampicin.

Conclusion: This case underscores the importance of appropriate differential diagnosis during the current COVID-19 pandemic, so that other treatable causes of pneumonia may not be overlooked. In the present case, early diagnosis of co-infection with *Legionella*, which can be fatal if untreated, especially in the elderly, prompted appropriate treatment and led to full clinical resolution. This case study emphasizes the importance of an early and prompt diagnosis of pulmonary coinfections in the current wave of COVID-19 pandemic.

Keywords: *Covid-19; Legionella; Pneumonia*

Introduction

In December 2019, the novel coronavirus 2 (SARS-CoV-2) appeared in China, becoming a global pandemic [1]. SARS-CoV2 is an airborne virus that can spread through small droplets of saliva in a similar manner as cold and influenza [2]. The symptoms of SARS-CoV2 related pneumonia, COVID-19, are remarkably variable among individuals, ranging from asymptomatic interstitial lung disease to severe pneumonia with respiratory failure and possibly multiple organ failure [3]. On binding to epithelial cells in the respiratory tract, SARS-CoV-2 starts replicating and migrating down to the airways and enters alveolar epithelial cells. The rapid replication of SARS-CoV-2 in the

lungs triggers a strong immune response. Cytokine storm causes progression of disease, in particular, acute respiratory distress syndrome and respiratory failure, which is considered the main cause of death in patients with COVID-19 [4,5]. Older patients (aged > 60 years) and those with serious pre-existing diseases have a greater risk of developing acute respiratory distress syndrome and experiencing death [6-8]. The median incubation period is estimated to be 5.1 days, with 97.5% of symptomatic infections becoming evident within 11.5 days [9]. The most common symptoms include fever, cough, fatigue, slight dyspnea, sore throat, headache, conjunctivitis and gastrointestinal symptoms including diarrhea, nausea and vomiting [10-12].

Bacteria of the *Legionella* species are aerobic, gram-negative, intracellular pathogens and can be an important cause of community-acquired and nosocomial pneumonia, the pneumonic form of infection known as Legionnaire's disease [13,14]. Symptoms typically arise 2 to 10 days after airway exposure to the pathogen [13].

The case of *Legionella* pneumonia described in this report became symptomatic 3 days after the patient started working as a dishwasher. *Legionella* bacteria are typically transmitted via inhalation aerosols from contaminated water or soil. Reported sources of infection are diverse and include showers, pools, hot tubs, aquariums, fountains, birthing pools, drinking water systems, air conditioning systems, cooling towers and other water collection systems [13]. In previous reports from Europe and North America, the incidence of pulmonary *Legionella* disease ranged from 2% to 15% of all community-acquired pneumonias, requiring hospitalization in nearly all presenting cases, and being the second cause of admission to the intensive care units among patients with community acquired pneumonia.

In the present case report we describe the clinical and laboratory features of this uncommon pulmonary co-infection, necessitating an appropriate diagnostic management for prompt identification and management.

Case Report

A 56-years-old non-smoking male without any underlying pneumological or autoimmune disorder presented with fever, cough, gastrointestinal symptoms and myalgia. Symptoms appeared 1 week before admission to the hospital. Upon examination in the Emergency room, neurological examination was unremarkable. His throat was slightly red without exudates, lung auscultation was clear and abdomen was soft and non- tender. The patient reported no recent travel or contact with a confirmed or suspected case of COVID-19. His temperature was 38.4°C, heart rate 110 bpm and blood pressure 120/80 mmHg; oxygen saturation (SpO_2) 90% on ambient air, with 24 breaths/min. Arterial blood gas analysis revealed: PaO_2 58 mmHg, $PaCO_2$ 30 mmHg, pH 7.46, serum bicarbonate concentration 22 mmol/L. Oxygen-therapy was delivered by nasal cannula at 5 L/min to maintain an SpO_2 of 94%.

Laboratory tests showed mild hyponatremia (132 mEq/L, normal range: 135 - 145 mEq/L); mild leukocytosis, with white blood cell count 12,700/mm^3, normal range: 4,000 - 10,000/mm^3; neutrophil cell count 8,820/mm^3, normal range: 1,800 - 7,500/mm^3; C-reactive protein 202.1 mg/L, normal range: < 10 mg/L; procalcitonin 0.25 ng/mL, LDH 371 U/L, alanine aminotransferase 117 U/L, aspartate aminotransferase 94 U/L, D dimer 1.27 mg/L, normal values < 0.50. An enhanced high-resolution CT scan was performed, showing bilateral ground glass opacities (Figure 1). Both ultrasonography of the abdomen and echocardiography were normal.

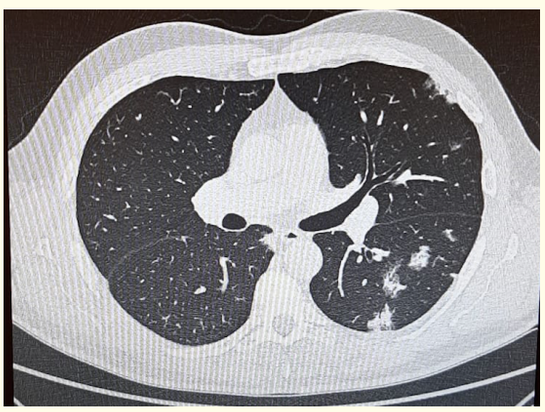

Figure 1a

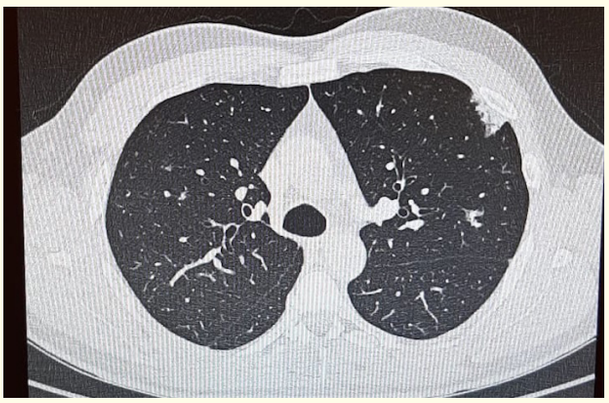

Figure 1b

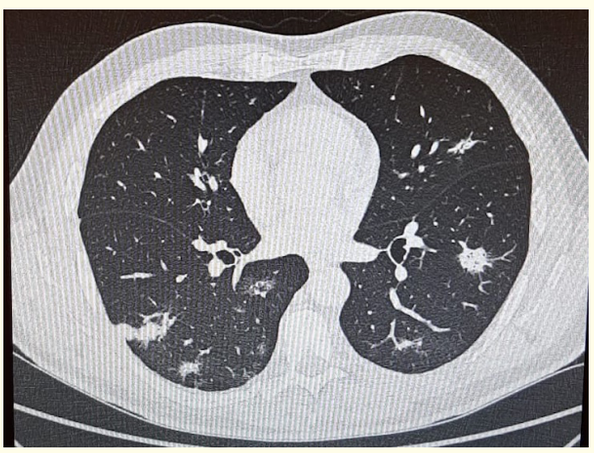

Figure 1c

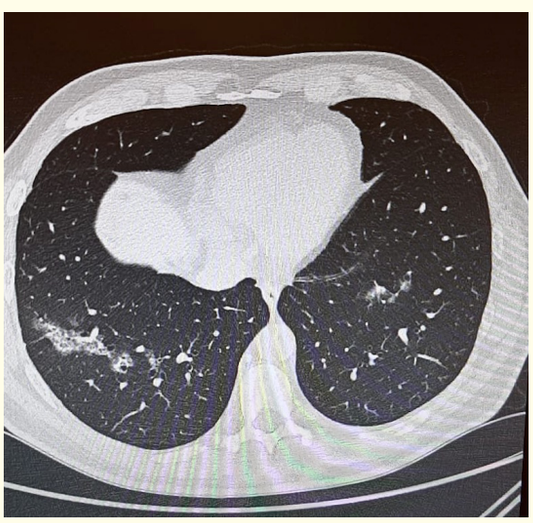

Figure 1d

Figure 1: *Images of HRCT in acute SARS2 and Legionella.*

SARS-CoV-2 RT-PCR on a nasopharyngeal swab tested positive, while blood cultures, as well molecular tests for Influenza viruses and RSV were negative. A urine antigen test for *Legionella* pneumophila type1 was performed as part of our screening procedure for COVID patients and turned out to be positive. Treatment with steroids, low-molecular weight heparin (enoxaparin 6,000 U/daily), azithromycin 500 mg ev/daily and rifampin 600 mg ev /daily was started. Notification of *Legionella* pneumonia was reported to epidemiological surveillance services both at the regional and district levels.

The patient was discharged in good clinical conditions after 10 days, with indication to continue oral rifampicin (600 mg/daily) and azithromycin (500 mg/daily) for 10 additional days. A control CT scan after 1 month showed a complete resolution of lung opacities.

Discussion

Bacterial co-pathogens are commonly identified in viral respiratory infections and are important causes of morbidity and mortality [15-18]. Reports on other coronaviruses estimated that 11% of patients had bacterial co-infections. These were mostly secondary infections in SARS-CoV-1 patient series, with only anecdotal evidence in Middle East Respiratory Syndrome (MERS) patients [16,17,19,20]. At variance, during the 2009 A(H1N1) influenza pandemic, bacterial co-infections was reported in up to 30% of critically ill patients and in 12% of hospitalized patients who did not require ICU admission [18-20]. The principal bacterial co-pathogens were *Staphylococcus aureus* and *Streptococcus pneumoniae* [20]. In a recent review, co-infections were reported in 3.5 - 14.3% of patients with SARS-CoV-2 [21]. The most common organisms reported were *Mycoplasma* species, *Haemophilus influenzae* and *Pseudomonas aeruginosa*. Given that our knowledge of the pathophysiology of SARSCoV-2 is evolving, the pathogenesis of bacterial co-infection is likely partially understood.

In influenza, it is postulated that viral damage of epithelial cells in the lower airway, coupled with mucociliary dysfunction, facilitates the binding of pathogenic bacteria aspirated from the nasopharynx to alveolar surfaces, allowing a bacterial co-infection to be established, in its turn causing further damage by inhibiting the repair and regeneration of the epithelial tract [22].

This case report describes a co-infection of SARS-CoV-2 with *Legionella*. Remarkably, procalcitonin was not elevated, suggesting that it should not be the only parameter to be used to decide further microbiological tests to rule out bacterial co-infections. Molecular testing for seasonal respiratory viruses and search for urinary antigens of S. pneumoniae and *Legionella* pneumophila, in parallel with blood cultures, may be useful to ease early diagnosis of bacterial coinfections thus helping both sparing of useless antibiotic prescriptions and directing appropriate antibiotic therapy [23-24].

Conclusion

Current guidelines do not indicate universal screenings for bacterial co-infections in COVID-19 patients. Radiological patterns of COVID-19 pneumonia, however, may be often indistinguishable from those of bacterial and co-infection pneumonias. In the absence of appropriate microbiological work-up, the frequency of bacterial co-infections will remain ill-defined.

Clinicians should be aware of the possible association of COVID-19 pneumonia with other bacterial causes, to avoid misdiagnoses and delay of appropriate and life-saving antibiotic therapy.

Conflict of Interests

All authors declare that they have no competing interests.

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