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Florence Nightingale

Case Report

Infections that may be missed during the COVID-19 pandemic, legionella pneumophila infection: A case report

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ABSTRACT

During pandemics, certain uncommon diseases might manifest within vulnerable populations. An example is *Legionella* spp, an aerobic, gram-negative pathogen that can thrive intracellularly. This microorganism holds significance for public health, being responsible for both pneumonia acquired in community settings and healthcare settings. Among *Legionella* cases, *Legionella* pneumophila accounts for about 90% of them. When observing coronavirus disease 2019 (COVID-19) patients in the intensive care unit, it's crucial to consider *Legionella* as a possible alternative diagnosis due to its similar clinical manifestations. In this case report, we aim to highlight a 43-year-old male patient, previously without any chronic conditions, who was initially diagnosed with COVID-19 but later identified to have *Legionella pneumonia*, presenting with symptoms including confusion, dysarthria, weakness, pain, and respiratory failure upon hospital admission.

Keywords: COVID-19, *Legionella* infection, pandemic, pneumonia.

The coronavirus SARS-CoV-2 is responsible for causing the disease known as coronavirus disease 2019 (COVID-19). The World Health Organization declared the COVID-19 pandemic in March 2020. COVID-19 typically presents with fever and various respiratory symptoms that are non-specific, leading to the need to consider other diseases in the differential diagnosis.[1,2] *Legionella bacteria*, which can be transmitted sporadically or through outbreaks, is a significant cause of pneumonia.[1-3] During a pandemic, the increased workload may result in the possibility of overlooking rare diseases, leading to potential delays in diagnosis and appropriate treatment.[2]

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This case report highlights the significance of considering differential diagnosis in COVID-19 by presenting a patient with *Legionella* pneumophila infection initially managed as a COVID-19 case.

CASE REPORT

A 43-year-old male who had any chronic disease before had been admitted to the hospital with complaints of confusion, dysarthria, weakness, and dyspnea. On laboratory tests, as serum sodium level was low (Na: 120 mmol/L) with detection of ground glass opacities on thorax computed tomography (CT) scan as shown in Figure 1a-d and Table 1, he had COVID-19 diagnosis. On magnetic resonance imaging of the brain, there was no pathological finding as shown in Figure 1e, f. He was internalized to COVID-19 intensive care unit (ICU) with severe hyponatremia and mild hypoxia.

He has been a worker at decontamination and air conditioning systems and he had stayed and worked at a hotel for seven days three weeks ago. He had contact with a COVID-19 patient at his work. He had diarrhea, nausea,

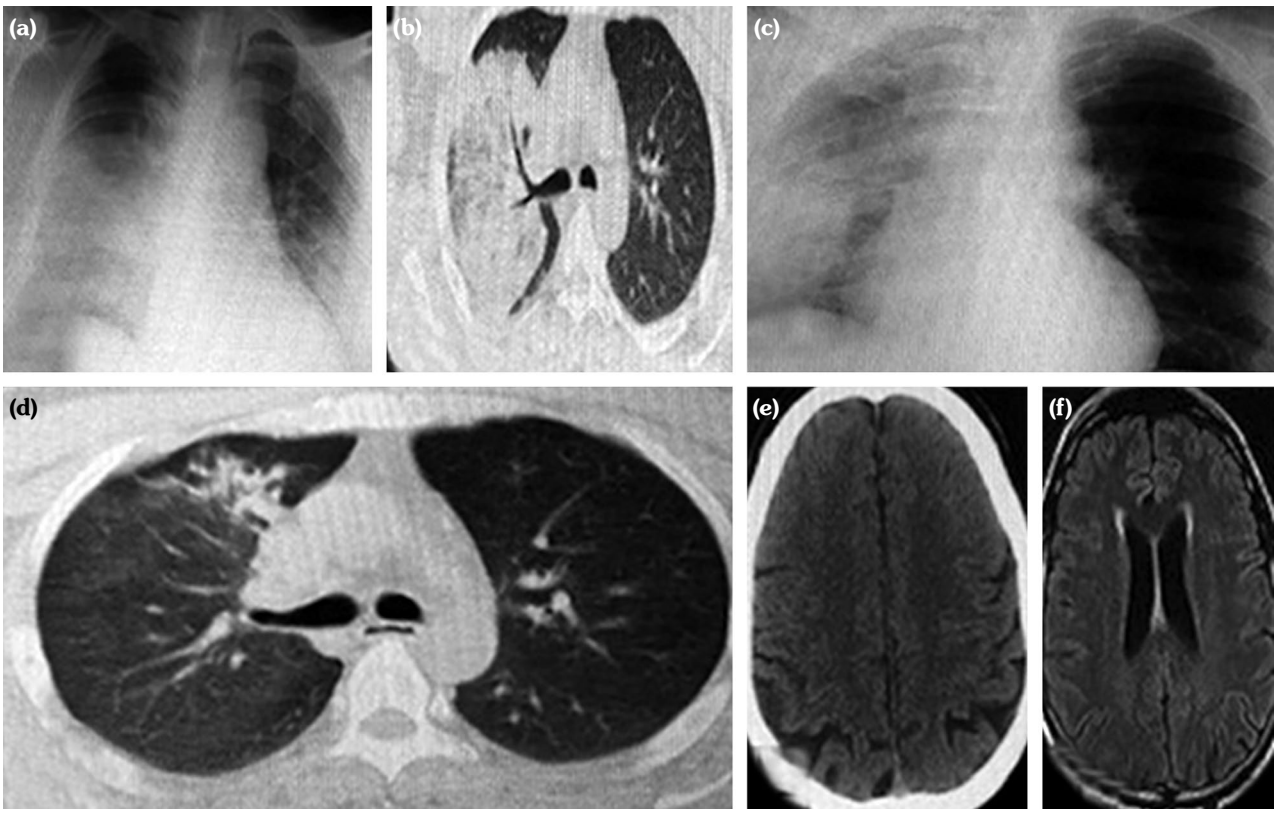

Figure 1. (a-d) Ground glass opacities on X-ray and thorax computed tomography. **(e, f)** Normal magnetic resonance imaging of the patient's brain.

weakness, and headache during the week. Then neurological symptoms like confusion, dysarthria, and walking difficulty developed. He is a smoker (4 pockets/day/22 years) and drinks alcohol (22 years). He had two doses of the BioNTech vaccine (last 3.5 months ago).

At physical examination; confusion, tremor in both hands, and muscle weakness in the lower extremities were detected. He was stabile hemodynamically, with 5L/min O_2 mask SPO_2: %95, respiratory rate: 22/min, blood pressure: 135/78 mmHg and heart rate: 85 beats/min. Saline infusion, empiric intravenous (IV) moxifloxacin 400 mg/day, and other symptomatic treatments were started after getting the cultures. COVID-19 polymerase chain reaction (PCR) test was negative at two tests one day apart. At the same time, we suspected Legionnaires' disease (LD) due to the history, clinical findings, and negative PCR tests. For LD diagnosis; blood, urine, and, sputum samples were collected. *Legionella pneumophila* serogroup-1 (Sg-1) antigen was positive in the urine sample as shown in Table 2. The other tests resulted after 12 days (Table 1). We also used moxifloxacin for LD treatment. During the follow-up serum sodium level: 130 mmol/L; dysarthria, tremors, and weakness got better. After four days in ICU, his all pathological neurologic findings were resolved completely. He got SPO_2 %95 at room air. He externalized from ICU to a normal service room and after six days, he was discharged from the hospital.

DISCUSSION

We presented a case who had an LD diagnosis at the time of COVID-19 peak on February 2022. Some rare diseases can appear in risk groups during the pandemic. Due to increased workload, they can be overlooked.

Legionella bacteria are aerobic, Gram-negative, and intracellular pathogens and are

Table 1. The laboratory parameters of the patient

	Admission to the ICU	1st day	2nd day	3rd day	6th day	10th day
Serum sodium (Na) (mmol/L)	120	130	140	136	130	136
Serum calcium (Ca) (mg/dL)	7.96	8.04	7.45	8.35	9.63	9.80
Potassium (mmol\L)	4.14	4.48	3.36	4.0	6.0	5.48
Chlorine (Cl) (mmol\L)	83.2	90.6	99.4	94	98	96.7
Bilirubin (total) (mg\dL)	0.571	0.504	0.356	0.351	0.30	0.035
CRP (mg\L)	327.18	297	239	127	18	3.97
Procalcitonin (ng/mL)	0.43	0.49	0.32	0.10	0.12	0.07
Glucose (mg/dL)	179.6	285	276	374	568	340
Aspartate transminase (U\L)	94.7	87.6	35.2	23.4	26.3	18
Alanine aminotransferase (U\L)	46.4	48.8	40.1	35.8	78.5	59.1
Blood urea (mg/dL)	32.0	32.2	61	70	66.8	65.8
Creatinine (mg/dL)	1.07	0.91	0.90	0.92	0.86	1.08
Troponin I (ng/mL)	0.100	0.100	0.100	0.100	0.100	0.100
Creatine kinase (U\L)	1471	-	238	18	-	-
Lactate dehydrogenase (U\L)	337	184	-	-	-	-
D-dimer (ng/mL)	887	735	424	131	-	-
Ferritin (ng/mL)	>2000	5815	>2000	2183	>2000	1717
Hemogram						
WBC (10^9/L)	9.66	7.21	9.09	10.11	11.49	14.01
HGB (g/dL)	14.2	14.1	13.7	14	15.8	16.7
PLT (10^3/uL)	265	256	329	421	699	463
LY (10^9/L)	1.25	0.50	0.63	0.78	1.78	3.97
INR	1.10	1.09	1.12	1.08	-	-
Blood Gas						
pH	7.492	7.35	7.45	7.48	7.42	7.43
pCO_2 (mmHg)	31.2	34.9	39.6	41.7	34.8	37.6
pO_2 (mmHg)	40.1	78	82	80	81	64.1
sO_2 (%)	76.8	94.6	96	94	95	90.5
HCO_3 (mmol/L)	25.2	20.0	26.5	29.3	24	24.6
Base (Ecf)	0.6	-5.6	2.4	7	-0.9	0.2
Lactate (mmol/L)	21	2.6	1.6	3.0	2.8	2.5
COVID-19 PCR	Negative	Negative				

ICU: Intensive care unit; CRP: C-reactive protein; WBC: White blood cell; HGB: Hemoglobin PLT: Platelet; LY: Lenfosit; INR: International normalized ratio; PCR: Polymerase chain reaction.

important causes of community-acquired and hospital-acquired pneumonia.[1] *Legionella pneumophila* is responsible for 90% of legionellosis cases.[1,4,5] *Legionella* infections can be transmitted sporadically or as epidemics. Transmission to humans is typically via inhalation from contaminated water or soil.[2]

Legionella spp. have been reported to be detected in the water systems of facilities such as hotels and hospitals that are not maintained.[1,3] *Legionella* spp. the incubation period is in the range of 2-14 days.[6] *Legionella* spp. often cause LD and Pontiac fever.[1,6] Legionnaires' disease refers to pneumonia involving the lower respiratory tract and progressing mildly.[6,7] Pontiac fever, on the other hand, is an acute, self-limiting febrile illness that is usually seen during epidemics.[7] While *Legionella* species

Table 2. The methods and the test results

Method	Sample type	Sampling date	Laboratory acceptance date of the sample	Result date	Result
Legionella pneumophila serogroup-1	Urine	17.02.2022	21.02.2022	21.02.2022	Positive
Legionella pneumophila IgM (IFA)	Serum	17.02.2022	21.02.2022	28.02.2022	Positive
Legionella pneumophila (culture)	Sputum	17.02.2022	21.02.2022	02.03.2022	No reproduction

IFA: Indirect fluorescent antibody.

can cause serious illness in people with risk factors.[1] Risk factors for LD; elderly (especially ≥50 years old), smokers, those with chronic lung disease (chronic obstructive pulmonary disease, emphysema, etc.), immunocompromised patients (cancer, diabetes, kidney failure, etc.), and those using immunosuppressive drugs.[1,2,6,8]

During the COVID-19 pandemic, many hotels and dormitories around the world were closed. With the decrease of the COVID-19 pandemic, the risk of exposure to *Legionella* spp. has increased with the re-use of the water that has been stored in unused water systems.[7,9,10] *Legionella pneumonia* accounts for 3-8% of all pneumonia cases.[1,4,11] In a case report, they detected *Legionella* and SARS-CoV-2 as a co-infection.[1] Co-infection by these two microorganisms is very rare.

Symptoms and signs such as fever, headache, confusion, and shortness of breath are seen in COVID-19 and *Legionella* spp. Similarly, in both diseases, systemic diseases such as old age, diabetes, and chronic lung diseases are individual risk factors.[1,7] The incubation period of *Legionella* spp. is longer than the incubation period of SARS-CoV-2.[2,6] Thus determining the source of *Legionella* spp. may be more difficult than the source of COVID-19 disease.[6]

This case was at a peak period of the COVID-19 pandemic, had contact with a COVID-19 patient, and symptoms and findings like high ferritin, D-dimer, and serum lactate dehydrogenase. In addition to high laboratory tests such as C-reactive protein, white blood cell, procalcitonin, and low lymphocyte count, as there is no specific and specific definitive test and radiological image for COVID-19; It is undoubtedly acceptable to be evaluated as a COVID-19 patient.[13,14] In addition to the job of the case (being a water decontamination worker), staying in hotels that returned to full capacity, his travels during this period, bilateral ground-glass opacities in the lungs as well as more consolidated areas in the right lung in the thorax CT, less frequent infiltrations in the left lung are other factors in the differential diagnosis. It also paved the way for the consideration of diseases. The COVID-19 PCR two test results, which were examined from the nasopharynx swab sample taken with an interval of 24 hours, were negative. Due to the absence of a typical COVID-19 radiological lung image and the risk factors; LD was suspected in this case. The laboratory tests and radiological images mentioned are not specific to *Legionella pneumonia*, but can be seen in many clinical pictures.[1,15]

Patients followed up with suspected COVID-19 disease should be evaluated considering their symptoms, clinical findings, history of the case, and risk factors in case of suspected LD. If LD is suspected, laboratory tests used for diagnosis should be applied. In this case, samples taken from respiratory secretion, blood, and urine are studied in the laboratory. Detection of specific antigen in urine for *Legionella pneumophila* Sg-1 or antibody against *Legionella pneumophila* Sg-1 in specific single or double serum [(indirect fluorescence with a double serum sample antibody (IFA) or enzyme-linked immunosorbent assay (ELISA)] a significant increase in titers in IFA or ELISA gives definite results.[7] Searching for positivity of *Legionella* antigen in the urine is the most frequently used diagnostic method and its sensitivity is 70% and the specificity is 99%.[6,7,16-18] This test becomes positive in serotypes.[1] It should be kept in mind that other pathogenic *Legionella* spp. were not detected in this urinary antigen test.[6] The diagnosis was made by detecting a specific antigen in the

urine for *Legionella pneumophila* Sg-1 after an average of one hour in the urine sample and after about one week in the patient's blood serum sample, in the sputum culture no growth was detected. According to the results of the research conducted by the local public health directorate, it is thought that the case LD was caught in the hotel where he stayed, most likely after a trip he made about two weeks ago. In this way, the Directorate of Public Health has taken the necessary measures for public health for this LD source.

Although the use of empirical antibiotics in mild to moderate COVID-19 patients reaches 70%, there is not enough evidence to show that it is beneficial.[1,20] Beta-lactam antibiotic group drugs, which are generally used as the first choice in the treatment of bacterial pneumonia, do not affect *Legionella pneumonia*. Macrolides and new-generation quinolones are effective in the treatment of *Legionella*.[1,10,21] In this case, in addition to oxygen support, IV moxifloxacin, and other symptomatic treatments were given for 10 days. The patient was discharged home with full recovery after being treated in the hospital for 10 days.

In studies, in Europe between 2006 and 2010, the annual incidence of LD was 1/100,000 and the mortality rate was 6.6% and the mortality rate was 25-40% in *Legionella pneumonia*.[1,7,12,13,19]

In our country Cesur et al.[23] presented an LD case who had *Legionella* antigen positivity in the urine. They suspected *Legionella pneumophila* in the patient who applied to the emergency department with high fever and dyspnea. COVID-19 PCR was negative. The patient was discharged home after ceftriaxone and levofloxacin treatment.

In conclusion, LD should be considered in the differential diagnosis of critically ill COVID-19 patients admitted to the ICU, as well as other diseases that cause a similar clinical picture. The patient's anamnesis, clinical symptoms, test results, and imaging examinations should be thoroughly examined; We believe that early diagnosis and initiation of treatment by performing rapid and reliable tests in suspicion of LD will be an important step to reduce the mortality in the ICU, as well as to prevent unnecessary health expenditures and inappropriate antibacterial drug use.

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Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Analyzed and interpreted the patient data, performed the physical examination, and was a major contributor in writing the manuscript: M.K.; Major contributor in writing and reading and correcting any misspellings in the manuscript: K.S.K.; Major contributor in writing the manuscript: A.O.; Major contributor in writing the manuscript: E.G.; All authors read and approved the final manuscript.

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