



Invasive Listeriosis After Severe Acute Respiratory Syndrome Coronavirus-2 (SARS-CoV-2) Infection

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Acute deteriorated consciousness is commonly reported in elderly COVID-19 patients. Secondary bacterial infection is common in critically ill COVID-19 patients. *Listeria monocytogenes* is a gram-positive, facultatively intracellular rod-shaped bacterium ubiquitously distributed in the environment and is an opportunistic and foodborne pathogen. Pregnant women and their newborns, adults aged 65 years or older, and immunocompromised people are more vulnerable to *Listeria*-related invasive disease. A 74-year-old man with severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection with initial presentations of headache and acute disorientation, which was finally diagnosed with *L. monocytogenes* bacteremia and meningitis. Multiplex polymerase chain reaction (Multiplex PCR) assay was used to rapidly diagnose it in the emergency department.

Keywords: *Listeria monocytogenes*, Listeriosis, Multiplex PCR

Introduction

Listeria monocytogenes is a gram-positive, facultatively intracellular rod-shaped bacterium ubiquitously distributed in the environment and is an opportunistic and foodborne pathogen. Pregnant women and their newborns, adults aged 65 years or older, and immunocompromised people are more vulnerable to *Listeria*-related invasive disease. However, *L. monocytogenes* is an uncommon pathogen involved in secondary bacterial infection in patients contracting coronavirus disease 2019 (COVID-19),¹ which may lead to delayed diagnosis. Herein, we present the case of a 74-year-old man with severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) infection with initial presentations of headache and acute disorientation, which was finally diagnosed with *L. monocytogenes* bacteremia and meningitis. Multiplex polymerase chain reaction

(Multiplex PCR) assay was used to rapidly diagnose it. He fully recovered without neurological sequela after receiving appropriate antimicrobial treatment.

Case Report

A seventy-four-year-old male with a medical history of hypertension and dyslipidemia received four SARS-CoV-2 vaccination doses. He was diagnosed with SARS-CoV-2 infection by rapid antigen test, with symptoms of frequent cough five days before admission, and started to take the traditional Chinese medicine formula NRICM101 since then. He later developed vomiting, diarrhea (2–3 times per day), urinary incontinence, decreased appetite, chills, severe headache, and high systolic blood pressure over 200 mmHg at home. In addition, severe headache, mild fever (37.5 °C), acute disorientation with

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slurred speech, and bizarre behavior were noted in the emergency department. The laboratory examination is listed in Table 1. Cerebrospinal fluid (CSF) analyses presented an opening pressure of 24 mmH₂O, a closing pressure of 20 mmH₂O, pleocytosis (white blood cell [WBC]: 323/μL) with a predominance of neutrophils (47%), elevated total protein (333 mg/dL), and increased lactate (10.6 mmol/L) (Table 1), suggesting bacterial meningitis. FilmArray meningitis/encephalitis panel testing (BioFire Diagnostics, LLC) of CSF was positive for *L. monocytogenes*. Blood and CSF cultures also yielded *L. monocytogenes* five days later. The patient later received ampicillin with one week of gentamycin for *L. monocytogenes* bacteremia and meningitis; nirmatrelvir/ritonavir was also administered to treat coexisting COVID-19. His fever subsided, and consciousness recovered to the previous levels on the third day after antimicrobial therapy. He recovered without neurological sequelae.

Discussion

Acute deteriorated consciousness is commonly reported in COVID-19 patients. SARS-CoV-2-associated or SARS-CoV-2-mediated encephalitis is the most common type observed (59.3%), followed by autoimmune encephalitis.^{2,3}

Bacterial or fungal co-infections among COVID-19 patients are not common. Previous studies suggested that about 3%–9% of COVID-19 patients have co-infections.^{1,4-7} Secondary bacterial infection is a notable complication associated with worse outcomes in COVID-19 patients.^{1,8} Listeriosis can result in invasive diseases, especially central nervous system (CNS) infections such as meningitis, meningoencephalitis, rhombencephalitis, or cerebritis. Pregnant women, newborns, adults aged 65 years or older, and immunocompromised patients are considered more vulnerable to Listeriosis. However, few studies have

Table 1. Laboratory results of this case

Variable	Results	Normal values
Blood		
WBC (/μL)	14,800	3,400–9,500
Segment (%)	89.4	40.8–76.6
Lymphocyte (%)	3.8	15.4–47.0
Monocyte (%)	6.4	4.4–11.8
Hb (g/dL)	14.9	13.3–17.2
Platelet (/μL)	152	143–349
Blood culture	<i>Listeria monocytogenes</i>	No growth
CSF		
Pressure (cmH ₂ O)	24	5–20
CSF appearance	Clear	Clear
White cell count (/μL)	323	0–5
Neutrophil (%)	47	0–6
Lymphocyte (%)	30	40–80
Monocyte (%)	19	15–45
Protein (mg/dL)	146	15–45
Glucose (mg/dL)	63	40–70
Glucose CSF: serum ratio	0.41	0.6
Lactate (mmol/L)	10.6	1.1–2.4
Gram stain	Not found	Not found
Culture	<i>Listeria monocytogenes</i>	No growth
FilmArray ^a	<i>Listeria monocytogenes</i>	Not detected

^aBioFire Diagnostics, LLC.

CSF: cerebrospinal fluid; Hb: hemoglobin; WBC: white blood cell.

discussed the relationship between Listeriosis and COVID-19.⁹ Our report highlighted the importance of *Listeria* bacteremia and meningitis in COVID-19 patients.

Innate and adaptive immunity is critical for controlling *L. monocytogenes* infection.¹⁰ The innate immune mechanisms are triggered within minutes to hours after infection. Although they are not microbe specific, they are able to limit the exponential growth of *L. monocytogenes* and may even reduce bacterial dissemination to secondary infection sites. Weak or delayed innate immunity allows *L. monocytogenes* to replicate exponentially for several days and thus is a major determinant of disease severity. SARS-CoV-2 infection induces gut microbiome dysbiosis associated with bacterial translocation into the blood.¹¹ Furthermore, T cell functions are dysregulated and exhausted after acute SARS-CoV-2 infection and gut dysbiosis¹², leading to imbalanced cellular immunity.¹³ Therefore, *L. monocytogenes*, an opportunistic and foodborne pathogen, might more easily invade COVID-19 patients and end up with bacteremia and meningitis.

Timely microbiological diagnosis of CNS infections is challenging due to limited access and time to CNS samples. *L. monocytogenes* is not as common as *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Neisseria meningitidis* in acute bacterial meningitis; therefore, most cases with *L. monocytogenes* meningitis were diagnosed by conventional microbiology cultures. Utilizing the Multiplex PCR assay is associated with a faster turnaround time of CSF testing and increased yield of viral and bacterial organisms. Although not especially technique and labor-intensive or time consuming, conventional processes of microscopy and culture for microbiological analysis of CSF have relatively poor diagnostic accuracy and reliability. In our case, the diagnosis of *L. monocytogenes* meningitis was five days earlier than the conventional microbiologic cultures by using multiplex PCR. Rapid and accurate diagnosis of multiplex PCR indeed shortens the diagnosis time and improves antimicrobial stewardship targeting a reduction in the duration of empiric treatment while enhancing patient outcomes.^{14,15}

In conclusion, secondary bacterial infection is common in critically ill COVID-19 patients. As SARS-CoV-2 infection can lead to an immunocompromised condition, opportunistic pathogens such as *L. monocytogenes* and more severe complications should be considered. High suspicion of *L. monocyto-*

genes invasive disease related to SARS-CoV-2 infection with multiplex PCR is crucial in early detecting this uncommon condition.

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