

A Case of Fulminant *Fusobacterium necrophorum* Bacteremia Secondary to Non-severe COVID-19

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Abstract

The Omicron variant of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) is more infectious than the previous variants but less severe; more patients are being followed up without hospitalization. Identification of patients with severe disease symptoms as early as possible and prompt initiation of treatment are crucial. A case of a 19-year-old man with mild COVID-19 is described in this report. He died of a secondary infection with *Fusobacterium necrophorum* bacteremia and a progressive hemorrhagic disorder. The diagnosis was made based on the clinical course and needle necropsy results. In non-severe COVID-19 patients, rapid deterioration of the disease symptoms requiring emergency treatment should lead to suspicion of additional fatal infections with similar clinical symptoms.

Categories: Emergency Medicine, Infectious Disease
Keywords: secondary infection, coronavirus, sars-cov-2, bacterial infection, omicron variant, fusobacterium necrophorum, covid-19

Introduction

The clinical symptoms of COVID-19 differ among the variants [1]. While previous variants of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), such as the delta variant, are characterized by shortness of breath, runny nose, and fever, the Omicron variant of SARS-CoV-2 is characterized by upper respiratory tract symptoms such as sore throat and a lower risk of critical illness [1]. Patients with mild COVID-19 who do not require supplemental oxygen therapy are generally treated at home. Some risk factors for severe disease that have been reported so far include older age, diabetes mellitus, and an immunocompromised host.

We report an unusual case of a mildly ill COVID-19 patient, without a high risk of serious illness, who died soon after admission due to a *Fusobacterium necrophorum* infection. This experience suggests that even for patients with mild COVID-19 without risk factors, there is a need to remain alert for additional serious bacterial infections, and prompt intervention should be initiated before their condition worsens.

Case Presentation

A 19-year-old man was diagnosed with COVID-19 by a reverse transcription-polymerase chain reaction (RT-PCR) test for SARS-CoV-2, a day after the onset of fever. He had no past medical history of illness and had already been administered two doses of the Pfizer-BioNTech COVID-19 vaccine (BNT162b2). He was followed up at home because of a mild illness with no risk of progressing to severe COVID-19. However, his clinical symptoms gradually deteriorated, with a sore throat, fever (with a body temperature of over 40°C), and chills. Five days after onset, he presented with impaired consciousness and was transferred to a nearby acute-care hospital. He was intubated, and norepinephrine was administered owing to severely impaired consciousness and hypotension. A whole-body computed tomography (CT) scan at the hospital revealed neither any signs of pneumonia nor any other findings as the source of the fever. The patient was transferred to our tertiary care center because intensive care was required.

On arriving at our hospital, a physical examination revealed a consciousness disturbance with a Glasgow Coma Scale (GCS) of E1VTM4. The heart rate was 180 beats per minute, and the blood pressure was 94/69 mmHg under continuous infusion of 0.1 µg/kg/min of norepinephrine. Initial blood examination revealed severe inflammation, acute kidney injury (AKI), and severe coagulopathy. Arterial blood gas analysis revealed metabolic acidosis (Table 1).

| Variables | Results | Normal range |
|------------------------------|---------|---------------|
| Arterial blood gas analysis* | | |
| pH | 7.296 | 7.380 ~ 7.460 |

| | | |
|--|-------------------|--------------|
| PaO ₂ (mmHg) | 117 | 74.0 ~ 108.0 |
| PaCO ₂ (mmHg) | 38.5 | 32.0 ~ 46.0 |
| HCO ₃ (mmol/L) | 18.2 | 21.0 ~ 29.0 |
| Base excess (mmol/L) | -7.3 | -2.0 ~ 2.0 |
| Lactate (mmol/L) | 7.4 | 0.4 ~ 1.6 |
| Complete blood cell count | | |
| White blood cell count ($\times 10^3/\mu\text{L}$) | 8.0 | 3.3 ~ 8.6 |
| Red blood cell count ($\times 10^6/\mu\text{L}$) | 4.07 | 4.35 ~ 5.55 |
| Hemoglobin (g/dL) | 12.8 | 13.7 ~ 16.8 |
| Hematocrit (%) | 37.2 | 40.0 ~ 50.0 |
| Platelet count ($\times 10^4/\mu\text{L}$) | 0.9 | 15.8 ~ 34.8 |
| Blood biochemistry | | |
| Total bilirubin (mg/dl) | 0.92 | 0.2 ~ 1.2 |
| AST (U/L) | 702 | 8 ~ 30 |
| ALT (U/L) | 262 | 5 ~ 35 |
| LD (U/L) | 2170 | 100 ~ 225 |
| ALP (U/L) | 127 | 38 ~ 113 |
| Total protein (g/dL) | 5.5 | 6.5 ~ 8.2 |
| Albumin (g/dL) | 2.6 | 3.8 ~ 5.2 |
| BUN (mg/dL) | 29 | 8 ~ 20 |
| Creatine (mg/dL) | 2.42 | 0.61 ~ 1.13 |
| Sodium (mmol/L) | 140 | 135 ~ 147 |
| Potassium (mmol/L) | 2.9 | 3.5 ~ 5.0 |
| Chlorine (mmol/L) | 102 | 98 ~ 108 |
| Procalcitonin (ng/mL) | > 100 | < 0.05 |
| C-reactive protein (mg/dL) | 13.3 | < 0.3 |
| Blood coagulation | | |
| Prothrombin time activity assay (%) | below sensitivity | 80 ~ 127 |
| Activated partial thromboplastin time (sec) | 133.7 | 24.0 ~ 32.0 |
| Fibrinogen (mg/dL) | < 30 | 180 ~ 400 |
| Immunological tests | | |
| Heparin-induced thrombocytopenia antibody (U/mL) | < 0.6 | < 1.0 |
| Direct coombs test | negative | negative |
| ADAMTS13 | negative | negative |
| C ₃ (mg/dL) | 99 | 65 ~ 135 |
| C ₄ (mg/dL) | 39 | 13 ~ 35 |

TABLE 1: Laboratory findings at admission to the ICU

Abbreviations: ICU: intensive care unit; WBC: white blood cell count; RBC: red blood cell count; Hb: hemoglobin; Hct: hemocytocrit; Plt: platelet count; T-

Bil: total bilirubin; AST: aspartate aminotransferase; ALT: alanine aminotransferase; LDH: lactate dehydrogenase; ALP: alkaline phosphatase; TP: total protein; ALB: albumin; BUN: blood urea nitrogen; CRP: C-reactive protein; APTT: activated partial thromboplastin time; PT: prothrombin time; ADAMTS-13: disintegrin-like metalloprotease with thrombospondin type 1 motif 13

* Blood gas analysis was performed under the following conditions of invasive mechanical ventilation: pressure-controlled assist/control (AC/PC) mode (FiO₂, 0.5; positive end-expiratory pressure [PEEP], 5 cmH₂O; inspiratory pressure above PEEP [PC], 12 cmH₂O; ventilator respiratory rate, 15 breaths/min)

The patient was initially diagnosed with severe COVID-19 and disseminated intravascular coagulation (DIC). The sequential organ failure assessment score was 13 (respiration: one, coagulation: four, liver: 0, cardiovascular: three, central nervous system: three, renal: two). The DIC score established by the Japanese Association for Acute Medicine [2]-the criteria established for the diagnosis of DIC-was nine points. The patient presented with refractory nasal hemorrhage due to severe coagulopathy, and hemostasis was finally achieved 12 hours after admission with cauterization by an otolaryngologist and a massive blood transfusion. Cefazolin was administered after these procedures.

After these treatments, an additional CT scan of the head was performed, which revealed diffuse cerebral edema and intracranial hemorrhage in the brainstem extending to the fourth ventricle (Figure 1).

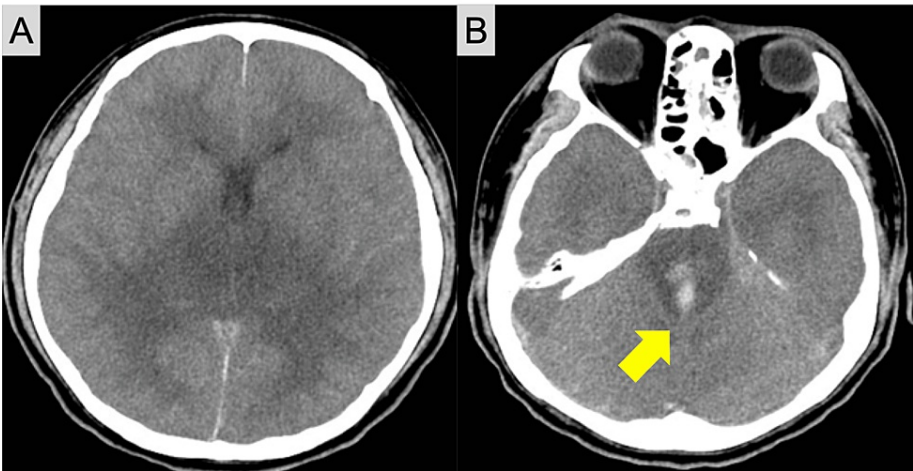


FIGURE 1: Head computed tomography (CT) scan after the resuscitation

The findings of the head CT scan after the resuscitation demonstrated diffuse cerebral edema (A) and intracranial hemorrhage (arrow) in the brain stem, which expanded to the fourth ventricle (B).

The patient died of increased intracranial pressure due to a brain hemorrhage, two days after admission. The two initial sets of blood bacterial cultures were found to be positive for *F. necrophorum*.

Post-mortem needle biopsies of the kidney, lung, and bone marrow revealed glomerular neutrophils, interstitial neutrophils in the alveolar septum, and hypercellular bone marrow, respectively (Figure 2).

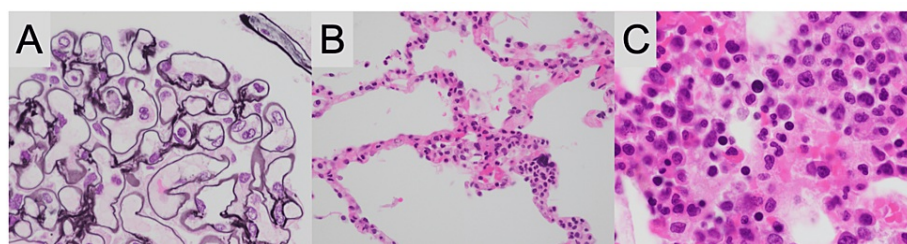


FIGURE 2: Histopathological images of needle necropsies of the kidney (A), lung (B), and bone marrow (C)

(A) A few neutrophils within renal glomerular capillaries with no convincing feature of thrombotic angiopathy, such as thromboendothelial swelling (periodic acid-methenamine silver stain, $\times 1,000$); (B) thickened pulmonary alveolar septa with neutrophils, suggesting septic pneumonitis (hematoxylin-eosin stain, $\times 400$); (C) hypercellular bone marrow without a feature of hemophagocytic syndrome (hematoxylin-eosin stain, $\times 1,000$)

There were no convincing features of thrombotic angiopathy or hemophagocytic syndrome. Considering the clinical course and the needle necropsy results, the patient was finally diagnosed with DIC and septic shock due to *F. necrophorum* bacteremia secondary to COVID-19.

Discussion

This case provides us with an important message: when non-severe COVID-19 patients without any risk factors present with rapid deterioration of the disease symptoms requiring emergency treatment, suspicion must be raised for additional fatal infections that are associated with COVID-19 infection, exemplified by mucormycosis and pulmonary aspergillosis [3,4].

According to a survey by the National Institute of Infectious Diseases in Japan, 96.6% of COVID-19 cases in Japan during February 2022 were caused by the Omicron variant; the present case occurred during this period [5]. The Omicron variant is highly infectious but less symptomatic [1]. In Japan, non-severe COVID-19 patients with SpO₂ >96% are generally not recommended for hospitalization but rather are advised to receive home care to reduce the occupancy of hospital beds, which are needed for more critical patients. The clinical characteristics of the Omicron variant require an appropriate support system to identify patients with non-severe COVID-19 developing severe conditions and a manifest direction to hospitalize severe patients without delay.

Fever and sore throat are closely associated with upper airway infection caused by flu viruses, Group A Streptococcus, and *F. necrophorum* [6]. Among them, *F. necrophorum* infection is more common in healthy young adults, especially males, and is endemic to the mid-pharynx, the gastrointestinal tract, or the vagina; some cases are asymptomatic, but fever is the most common clinical manifestation (39%), followed by a sore throat (13.6%) [7]. Severe complications have also been reported in 38% of *Fusobacterium* bacteremia: thrombosis (18%), abscess (16%), and Lemierre syndrome (10%) [7]. Lemierre syndrome has been in focus again in recent times as a fatal disease because of the trend of avoiding prescribing antibiotics for mild laryngitis [8]. The present reported mortality rates are 5%-11% [7,9,10]. In this case, too, there was a high suspicion of Lemierre syndrome; however, the diagnosis was not made.

The diagnosis of *F. necrophorum* was delayed till the end because the symptoms of SARS-CoV-2 (Omicron variant) infection are almost the same as those for *F. necrophorum*. A throat swab was not sent for culture sensitivity. COVID-19 medication was not administered; only antipyretics were administered. Therefore, the administration of appropriate antibiotics was delayed. Careful diagnosis is necessary so as not to miss lethal bacterial infections that overlap with COVID-19 symptoms, as was the case in this report.

Conclusions

Here, we report a fatal case of severe *F. necrophorum* infection secondary to mild COVID-19. Our case emphasizes the importance of diagnosing overlapping severe bacterial infections with similar clinical symptoms as COVID-19 during the treatment of patients with COVID-19, even though the patient may not have any risk factors. This would help in the initiation of prompt intervention before the patient's condition deteriorates.

Additional Information

Disclosures

Human subjects: Consent was obtained or waived by all participants in this study. **Conflicts of interest:** In compliance with the ICMJE uniform disclosure form, all authors declare the following: **Payment/services**

info: All authors have declared that no financial support was received from any organization for the submitted work. **Financial relationships:** All authors have declared that they have no financial relationships at present or within the previous three years with any organizations that might have an interest in the submitted work. **Other relationships:** All authors have declared that there are no other relationships or activities that could appear to have influenced the submitted work.

References

1. Menni C, Valdes AM, Polidori L, et al.: Symptom prevalence, duration, and risk of hospital admission in individuals infected with SARS-CoV-2 during periods of omicron and delta variant dominance: a prospective observational study from the ZOE COVID Study. *Lancet*. 2022, 399:1618-24. [10.1016/S0140-6736\(22\)00327-0](https://doi.org/10.1016/S0140-6736(22)00327-0)
2. Gando S, Iba T, Eguchi Y, et al.: A multicenter, prospective validation of disseminated intravascular coagulation diagnostic criteria for critically ill patients: comparing current criteria. *Crit Care Med*. 2006, 34:625-31. [10.1097/01.ccm.0000202209.42491.38](https://doi.org/10.1097/01.ccm.0000202209.42491.38)
3. Lai CC, Yu WL: COVID-19 associated with pulmonary aspergillosis: a literature review. *J Microbiol Immunol Infect*. 2021, 54:46-53. [10.1016/j.jmii.2020.09.004](https://doi.org/10.1016/j.jmii.2020.09.004)
4. Raut A, Huy NT: Rising incidence of mucormycosis in patients with COVID-19: another challenge for India amidst the second wave?. *Lancet Respir Med*. 2021, 9:e77. [10.1016/S2213-2600\(21\)00265-4](https://doi.org/10.1016/S2213-2600(21)00265-4)
5. NIID, Japan: detection status by strain by novel coronavirus genome surveillance. (2022). Accessed: December 28, 2022: <https://www.mhlw.go.jp/content/10900000/000910353.pdf>.
6. Weber R: Pharyngitis. *Prim Care*. 2014, 41:91-8. [10.1016/j.pop.2013.10.010](https://doi.org/10.1016/j.pop.2013.10.010)
7. Almohaya AM, Almutairy TS, Alqahtani A, Binkhamis K, Almajid FM: *Fusobacterium* bloodstream infections: a literature review and hospital-based case series. *Anaerobe*. 2020, 62:102165. [10.1016/j.anaerobe.2020.102165](https://doi.org/10.1016/j.anaerobe.2020.102165)
8. Afra K, Laupland K, Leal J, Lloyd T, Gregson D: Incidence, risk factors, and outcomes of *Fusobacterium* species bacteremia. *BMC Infect Dis*. 2013, 13:264. [10.1186/1471-2334-13-264](https://doi.org/10.1186/1471-2334-13-264)
9. Karkos PD, Asrani S, Karkos CD, Leong SC, Theochari EG, Alexopoulou TD, Assimakopoulos AD: Lemierre's syndrome: a systematic review. *Laryngoscope*. 2009, 119:1552-9. [10.1002/lary.20542](https://doi.org/10.1002/lary.20542)
10. Ramirez S, Hild TG, Rudolph CN, et al.: Increased diagnosis of Lemierre syndrome and other *Fusobacterium necrophorum* infections at a Children's hospital. *Pediatrics*. 2003, 112:e380. [10.1542/peds.112.5.e380](https://doi.org/10.1542/peds.112.5.e380)