



## CASE REPORT

# COVID-19 in a human T-cell lymphotropic virus type-1 carrier

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## Abstract

This is the first report of COVID-19 in a human T-cell lymphotropic virus type-1 (HTLV-1) carrier. HTLV-1 infection can cause immune dysfunction even in asymptomatic carriers. This case highlights the need for guidance on management of COVID-19-HTLV-1 coinfection, specifically on the appropriate use of corticosteroid treatment while considering secondary infection.

## KEYWORDS

coinfection, COVID-19, human T-cell lymphotropic virus type-1, SARS-CoV-2

## 1 | INTRODUCTION

Coronavirus disease (COVID-19), which is caused by severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2),

has been spreading worldwide. It can cause acute respiratory distress syndrome (ARDS), which has high morbidity and mortality, especially in patients with underlying diseases.<sup>1</sup> However, there is a lack of clinical data on

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COVID-19 in individuals with human T-cell lymphotropic virus 1 type-1 (HTLV-1) infection, and a need for guidance on management of patients with HTLV-1 and COVID-19 coinfection.<sup>2</sup> Herein, we report a fatal case of COVID-19 in a previously undiagnosed HTLV-1 carrier.

## 2 | CASE HISTORY

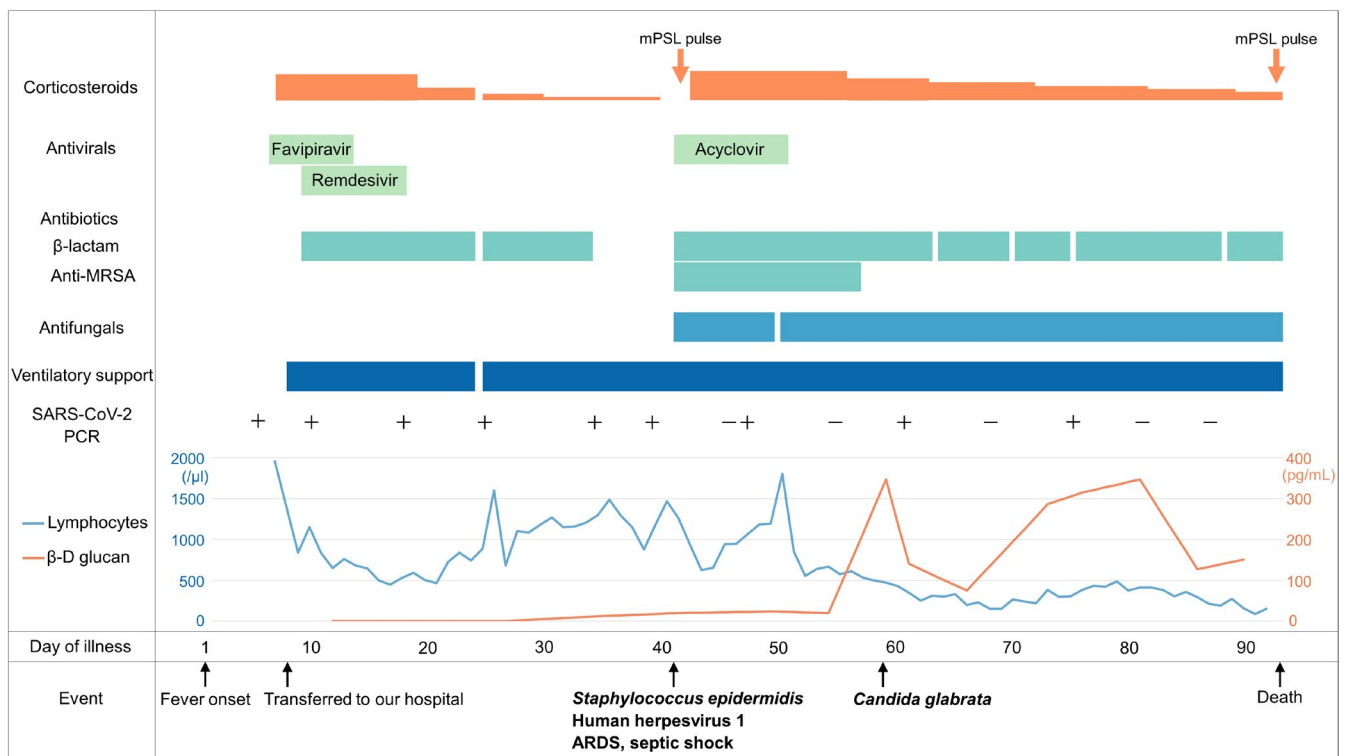
A 73-year-old man with a 20-pack year smoking history presented to the hospital with a 6-day history of fever. His medical history included diabetes, dyslipidemia, and surgery for gallbladder and colon cancer.

## 3 | DIAGNOSIS, INVESTIGATIONS, AND TREATMENT

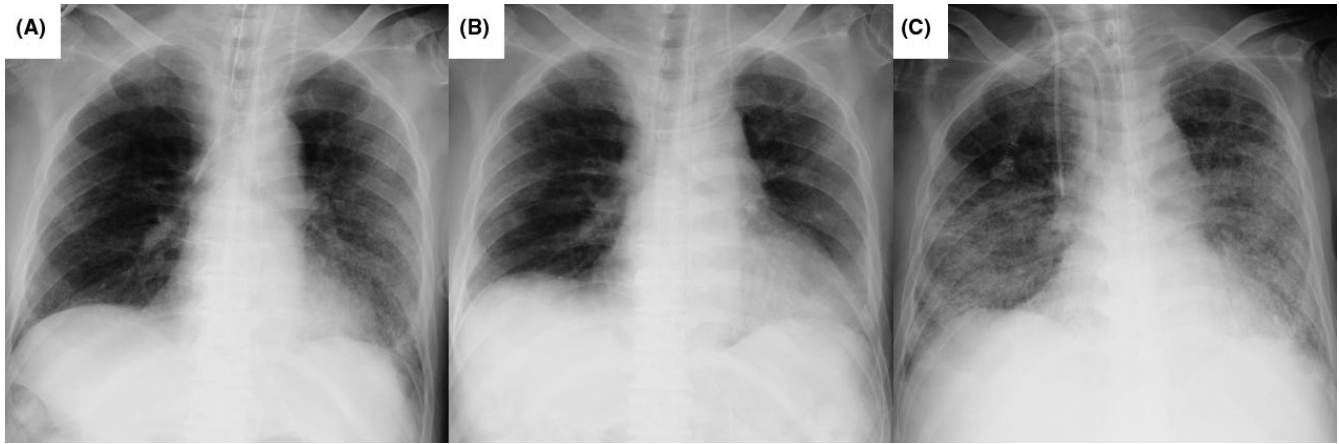
On physical examination, his vital signs were as following: blood pressure 124/78 mmHg, respiratory rate 23 breaths per minute, peripheral oxygen saturation (SpO<sub>2</sub>) 94% (in room air), and the body temperature 37.0°C. Chest computed tomography (CT) showed bilateral subpleural ground-glass opacities. A nasopharyngeal specimen tested positive for SARS-CoV-2 infection using real-time reverse transcriptase-polymerase chain reaction. Laboratory tests showed an elevated C-reactive

protein (CRP) (4.27 mg/dl; upper limit of normal, 0.3 mg/dl), while other laboratory test results were normal. He was initiated a compassionate administration of favipiravir (1,800 mg twice daily, followed by 800 mg twice daily) and ciclesonide inhalation. He was transferred to our hospital on Day 8 after symptom onset due to progressive respiratory failure. His vital signs were pulse rate 67 beats per minute, blood pressure 145/73 mm Hg, respiratory rate 29 breaths per min, SpO<sub>2</sub> 96% (on 5 L/min oxygen), and the body temperature 36.9°C. He was admitted to the intensive care unit (ICU) and mechanically ventilated on the same day due to further worsening of respiratory failure.

The patient's clinical course is summarized in Figure 1. Chest X-ray (Figure 2A) and CT on admission showed marked radiographic worsening with bilateral subpleural ground-glass opacities. His laboratory test results showed lymphopenia (840 cells/ $\mu$ l) and slightly elevated CRP and ferritin levels, but his D-dimer level was normal. Screening tests for infectious diseases revealed HTLV antibodies on chemiluminescent immunoassay. The results of a line immunoassay and PCR for the HTLV-1 provirus were positive, confirming this diagnosis of asymptomatic HTLV-1 infection. He was treated with dexamethasone (6 mg daily), remdesivir (200 mg daily followed by 100 mg daily), and intravenous meropenem (1 g three times a day). His respiratory condition and radiographic imaging



**FIGURE 1** Clinical course of the patient. mPSL, methylprednisolone; MRSA, methicillin-resistant *Staphylococcus aureus*; ARDS, acute respiratory distress syndrome



**FIGURE 2** (A) Chest X-ray taken on admission in our hospital (illness Day 9) showing bilateral ground-glass opacities. (B) Chest X-ray taken immediately after extubation (illness Day 24) showing improvement of chest infiltrations. (C) Chest X-ray taken on illness Day 92 showing bilateral consolidation and ground-glass opacities

were improved (Figure 2B), and he was extubated after two weeks of mechanical ventilation.

However, he developed recurrent respiratory failure with radiographic worsening and was reintubated on Day 24 after symptom onset. He was treated with intravenous piperacillin/tazobactam (4.5 g four times a day) for suspected bacterial pneumonia. The dexamethasone was switched to prednisolone (10 mg daily), followed by tapering and discontinuation; however, his condition did not improve significantly. He developed a septic shock and severe ARDS due to a catheter-related *Staphylococcus epidermidis* bloodstream infection 41 days after symptom onset. Laboratory tests showed an elevated  $\beta$ -D glucan level (19.7 pg/ml; upper limit of normal, 11 pg/ml). He also developed mouth ulcers, and human herpesvirus 1 was detected in a nasopharyngeal swab by metagenomic next-generation sequencing. Therefore, we started intravenous administration of piperacillin/tazobactam (4.5 g four times a day), vancomycin (targeting trough concentrations of 15 to 20 mg/L), sulfamethoxazole-trimethoprim (3 g three times a day for 21 days), and acyclovir (500 mg three times a day for 10 days). We also restarted corticosteroids to treat ARDS, septic shock, and possible recurrence of COVID-19-related inflammation. Although his clinical condition was gradually improved, laboratory tests showed a sudden elevation of his  $\beta$ -D glucan level (347.2 pg/ml) on Day 59 after symptom onset. *Candida glabrata* was cultured from gastric juice and stool specimens. Although blood cultures were negative, he was diagnosed with invasive candidiasis which we attributed to the use of corticosteroids, broad-spectrum antibiotics, and vascular devices, as well as to a prolonged ICU stay. He was treated with intravenous micafungin (150 mg daily) and amphotericin B (300 mg daily), and his  $\beta$ -D glucan levels were transiently decreased; however, his clinical condition and chest infiltrations gradually worsened (Figure 2C).

#### 4 | OUTCOME

He eventually died 93 days after symptom onset due to uncontrollable infections.

#### 5 | DISCUSSION

We describe a fatal case of COVID-19 in an HTLV-1 carrier. Despite receiving intensive care, including invasive ventilatory support, antibiotics, antifungals, antivirals, and corticosteroids, the patient died of multiple secondary infections. Although previous studies have found that the risk factors for false-positive HTLV-1 results include cross-reactivity of severe acute respiratory syndrome coronavirus 1 infection,<sup>3,4</sup> the patient was confirmed to have HTLV-1 infection by both antibody and PCR tests. To the best of our knowledge, this is the first case report of COVID-19 in an HTLV-1 carrier.

Although HTLV-1 can cause several fatal diseases such as adult T-cell leukemia (ATL) and HTLV-1-associated myelopathy/tropical spastic paraparesis, the majority of infected individuals remain asymptomatic throughout their lives.<sup>5</sup> Importantly, HTLV-1 infection can cause immune dysfunction even in asymptomatic carriers.<sup>5,6</sup> Infection of CD4+ T cells by HTLV-1 might reduce CD4+ T-cell function, and expression of HTLV-1 regulatory proteins inhibits pathogen sensing.<sup>5,7</sup> COVID-19 can cause a decrease in CD4+ T and CD8+ T cells<sup>8</sup> and be a risk factor for fungal infections and reactivation of herpesvirus infection, including cytomegalovirus infection.<sup>9,10</sup> In our patient, possible immune dysfunction by HTLV-1 and SARS-CoV-2 coinfection could be a factor in multiple secondary infections. There is only one previous case report of COVID-19 in a patient with HTLV-1 infection, in which the patient

with ATL recovered without developing secondary infections.<sup>11</sup> However, the reasons for our patient developing a more severe disease than that developed by the patient with ATL are unclear because of the differences in patient backgrounds. The patient with ATL developed COVID-19 while undergoing chemotherapy and was also treated with corticosteroids. Therefore, further accumulation of cases is required to better understand the clinical features of COVID-19 in patients with HTLV-1 infection.

In the present case, the patient had a relatively good response to the initial steroid treatment and relapsed after its discontinuation, which motivated us to continue steroids while tapering. However, long-term corticosteroid therapy in patients with severe COVID-19 may increase the risk of invasive fungal infection.<sup>12,13</sup> Therefore, it is needed to optimize corticosteroid treatment for COVID-19, especially in immunocompromised patients such as HTLV-1 carriers.

In conclusion, this report describes a fatal case of COVID-19 in an HTLV-1 carrier. This case highlights the need for the accumulation of similar cases and guidance on how to prevent and manage secondary infection in patients with COVID-19-HTLV-1 coinfection. Clinicians should bear in mind that long-term steroid use may contribute to an increased risk of secondary infection in such patients.

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#### CONFLICT OF INTEREST

All authors declare that they have no competing interests.

#### AUTHOR CONTRIBUTIONS

TE involved in study design, data collection, and manuscript preparation. TS involved in study design and manuscript preparation. HH, SA, YA, TN, YN, NT, and AU collected the data. All authors participated in revising the manuscript critically and approved the final manuscript.

#### ETHICAL APPROVAL

Patient gave written informed consent to publish this case report and related evidence.

#### CONSENT


Local ethical guidelines state no need of ethical approval for a case report.

#### DATA AVAILABILITY STATEMENT

Data sharing was not applicable to this article as no datasets were generated or analyzed during the current study.

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