

Case Report

Case of Prolonged Viral Shedding: Chronic, Intermittan COVID-19?

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Abstract

COVID-19 is a pandemic that has been affecting the entire world and has caused the death of approximately 2.8 million people. Although the duration of viral shedding varies, an average of 7-10 days is accepted. It is still unclear whether prolonged viral shedding means prolonged contagious period and whether COVID-19 will become chronic or not. This article presents a case with hematological malignancy (lymphoma) with the longest polymerase chain reaction positivity that we could find in the literature (110 days in total).

KEYWORDS: Chronic infection, lymphoma, viral shedding

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INTRODUCTION

Pneumonia cases due to severe acute respiratory syndrome coronavirus 2 (SARS CoV-2), which were first identified in China in December 2019, spread rapidly all over the world. The World Health Organization characterized COVID-19 disease caused by SARS CoV-2 as a pandemic on March 11.¹

The exact diagnostics of the disease is accepted as reverse transcription polymerase chain reaction (RT-PCR) testing positive in nasopharyngeal and/or oropharyngeal swab.² It is thought that the contagiousness of the disease begins in the asymptomatic period and the risk is higher in the early periods when symptoms are observed, and it decreases after 7-10 days. The duration of viral shedding varies and may differ according to age and severity of the underlying disease.³ It has been reported that this duration may be prolonged in patients with hematological malignancies.⁴

Our case is a lymphoma patient who was tested PCR positive for 110 days in total; PCR positive for 60 consecutive days and tested positive after being tested negative for 2 times. We preferred to present this case as it was the case with the longest duration of PCR positivity that we could find in the literature.

CASE PRESENTATION

In this study, 50-year-old male patient presented with fatigue. Physical examination showed a mild splenomegaly (1 cm below left costal margin), and pancytopenia with poor reticulocyte response was observed in laboratory analysis. He was diagnosed with splenic marginal zone lymphoma, with splenic and bone marrow involvement. Remission was achieved after 6 cycles of chemo-immunotherapy (rituximab plus adriamycin, cyclophosphamide, vincristine, and methylprednisolone). Relapse occurred after 1 year with pancytopenia with splenic and bone marrow involvement. Partial remission was achieved with second line chemo-immunotherapy with 6 cycles of rituximab and bendamustine. Due to the indolent nature of the disease (low ki-67 mutation profile), patient was surveyed for 2 years without maintenance. During this period, the patient received supportive treatment with intravenous immunoglobuline (0.4 mg/kg/day every 3 weeks) due to his hypogammaglobulinemia. In the last months of 2019, second relapse was observed and third line chemo-immunotherapy with rituximab-iphosphamide carboplatin and etoposide were commenced.

After the completion of second cycle, the patient was hospitalized with febrile neutropenia and pneumonia in January 2020. Bilateral ground-glass areas were observed on the thorax computed tomography (CT) of the patient (Figure 1). The patient was admitted to the chest diseases clinic with a diagnosis of pneumonia, was given broad-spectrum antibiotherapy, and was discharged on February 7, 2020, after partial clinical and laboratory responses and radiological regression were observed.

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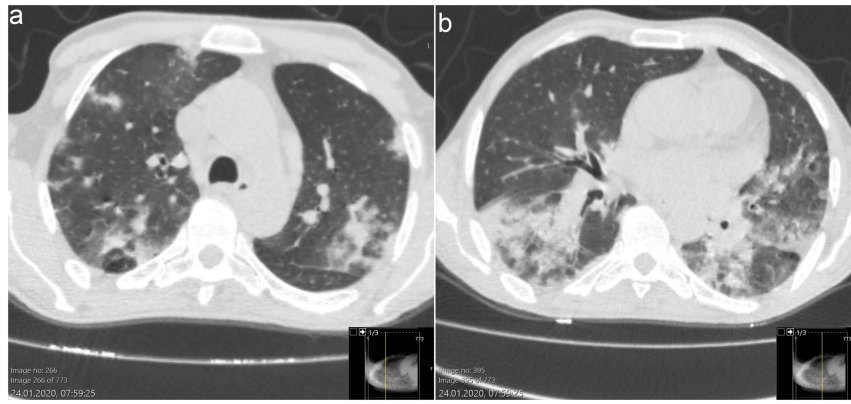


Figure 1. Initial hospitalization CT (January 24, 2020). (a, b) Patchy consolidation fields in the upper lobes of both lungs, more prominent in right lower lobes, and broad consolidation with air bronchogram were observed. CT, computed tomography.

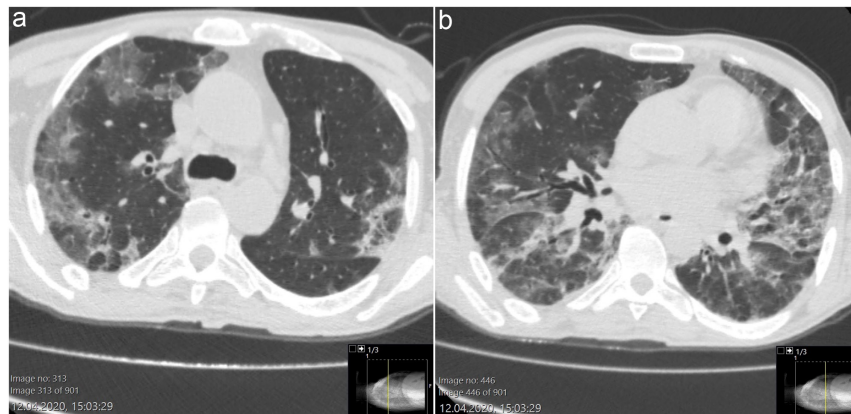


Figure 2. Second hospitalization CT (April 12, 2020) where the patient was diagnosed with COVID-19. (A) Patchy widespread infiltrative fields were observed in the significant peripheral ground-glass density in the upper lobes of both lungs and radiological findings were consistent with COVID-19. (B) In lower lobes, changes in the form of broad sequelae fibroatelectatic band were observed, according to the previous examination (January 24, 2020) regression detected in consolidation areas. CT, computed tomography.

The patient was admitted to the emergency room with respiratory symptoms on April 12, 2020. Thoracic CT findings of the patient were compatible with COVID-19 (Figure 2). The PCR result obtained from the patient was positive. Laboratory examinations showed serum Na: 129 mmol/L, CRP: 3.76 mg/dL, D-dimer: 17.1 mg/L, and albumin: 3.4 g/dL. Other laboratory results were within normal limits. Sputum, blood, and urine cultures were negative. The patient was given hydroxychloroquine (10 days), oseltamivir (5 days), favipiravir (5 days), immune plasma therapy (2 units), and broad spectrum antibiotic treatments. The patient's clinical condition partially improved as a result of the treatments, and the PCR positivity continued for 2 months. The patient, who was hospitalized for 64 days in total, had a negative PCR result at the end of the 60th day, and the patient was discharged from the hospital.

The patient was admitted to the emergency room again in July 2020. The patient had more pronounced respiratory complaints and had a fever. There was consolidation and accompanying ground-glass density on thoracic CT (Figure 3) performed. Polymerase chain reaction test obtained from throat swab was positive. Laboratory examinations showed serum Na: 135 mmol/L, CRP: 12.7 mg/dL, D-Dimer: 0.64 mg/L, and albumin: 3.2 g/dL. *Klebsiella pneumoniae* grew in sputum culture. Broad spectrum antibiotic treatments and 2 units of immune plasma therapy were given to the patient. The patient tested PCR negative after 5 days and radiological regression was observed, and then the patient was discharged on the 16th day. The patient's monthly hematology intra venous immune globulin (IVIG) treatment was continued at the pandemic ward.

MAIN POINTS

- In immunocompromised patients, COVID-19 PCR positivity may be prolonged.
- Recurrent positive and negative results can be observed in COVID-19 PCR results in immunocompromised patients.
- Prolonged PCR positivity in immunocompromised patients may not always indicate active infection. Hence, viroculture should be performed if possible.

The patient was admitted to the emergency room again with diarrhea and general condition disorder in August 2020 and was admitted to the pandemic ward. There were bilateral ground-glass areas in CT scan performed for additional check (Figure 4). Polymerase chain reaction test conducted for COVID-19 was positive again. Laboratory examinations showed serum Na: 130 mmol/L, CRP: 7.59 mg/dL, D-dimer: 0.52 mg/L, and albumin: 2.3 g/dL. Sputum, blood, and urine cultures were negative. Metronidazole and favipiravir together with prednol 40 mg iv were administered to the

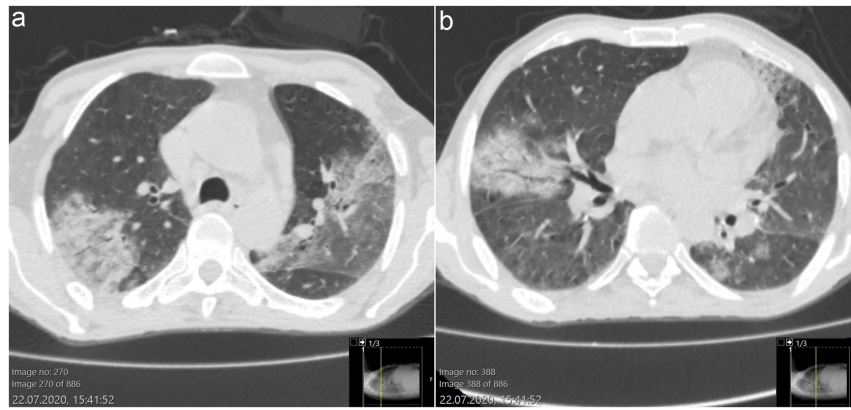


Figure 3. CT of the third hospitalization of the patient (July 22, 2020). (a, b) In the thorax CT examination, infiltration fields in diffuse ground-glass density were observed, and an increase in infiltration areas was observed compared to the May 2020 examination. CT, computed tomography.

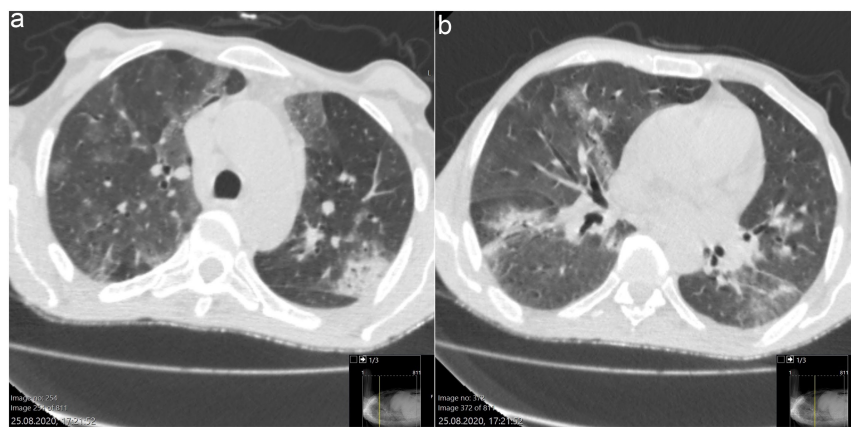


Figure 4. CT of the fourth hospitalization of the patient (August 25, 2020). (a, b) In the thoracic CT performed for additional check, infiltration areas in ground-glass density showing a newly developed broad peripheral weighted distribution pattern were observed and COVID-19 pneumonia findings were evaluated as progression. CT, computed tomography.

patient for 5 days. On this admission, IVIG treatment, which was arranged by the hematology, was continued. When the patient continued to have diarrhea under the current treatments, the COVID-19 PCR in stool was detected to be positive. Since the patient had high fever (38.5°C), newly formed lobar pneumonia was observed on the chest radiograph, and a septic condition was developed, the patient was taken to the intensive care unit. The patient who continued to get supportive treatments in the intensive care unit died on the 41st

day of the third hospitalization and the 178th day of the date when the PCR had been tested positive for the first time (the treatments that the patient received and the clinic are presented in Figure 5).

DISCUSSION

In studies investigating factors associated with prolonged viral shedding, factors such as male gender, period between the hospital admission and the onset of symptoms, and high

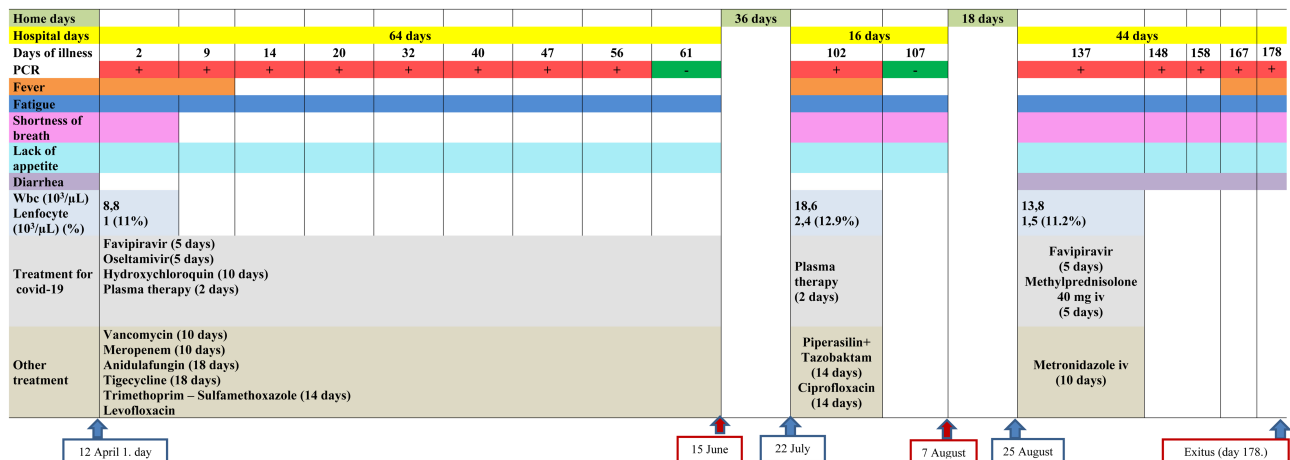


Figure 5. Hospitalization day and treatment.

fever at the time of admission were found to be significant in multivariate analysis.^{5,6} Although it is controversial whether prolonged viral RNA detection means prolonged contagion, it is thought to be essential in terms of patient's isolation and discharge from the hospital.⁷

The first reported case of prolonged viral shedding in the literature was a female patient in China with 60 days of viral shedding.⁸ Later, another case that persisted for 72 days in China was presented.⁹ In a 9-year-old case with autism in Italy, 82 days of viral shedding was reported.¹⁰

It has been reported that COVID-19 progresses more seriously in patients with hematological malignancies and that PCR positivity may persist.¹¹ When our case applied on April 12, according to CT scan of the patient, COVID-19 was suspected and the PCR was tested positive. However, when the patient was evaluated with old CTs, similar findings were observed in January, even though COVID-19 cases were not reported in our country yet. From April 12, when the disease was first confirmed to the date of the patient's death, the patient's complaints continued, even if they recessed from time to time. For the patient with the underlying diagnosis of Non-Hodgkin lymphoma, the PCR was not tested negative for the first 2 months, and on the 60th day, a negative result was reported. The patient, who tested positive again 36 days later, tested negative 5 days after the administration of plasma. Eighteen days later, the PCR was again detected positive. Similar to our case, a case was reported in our country, PCR positivity in a patient with lymphoma continued on day 40 and 3 days after the patient was given immune plasma, the patient's fever reduced. Polymerase chain reaction positivity decreased in quantitative measurements, but PCR was still tested to be positive on day 74.¹²

Although there were periods when our case was intermittent PCR negative, the positivity was detected to be 110 days in total, and it is the case in which the longest viral shedding was observed that we could find in the literature. Although the patient tested negative after immune plasma treatment, the patient tested positive again after a short time. Although the possibility of recurrence/relapse could not be eliminated in our case, the patient was isolated and not allowed to be in contact with anyone other than the patient's spouse since April 12. Unfortunately, for technical reasons, viral culture could not be performed, and it is not clear whether this viral shedding will actually cause contamination. It is not known whether COVID-19 will become chronic, especially in immunosuppressed patients, like viral hepatitis. On the occasion of this case, we have found it appropriate to present the idea of chronic COVID-19 for discussion.

Informed Consent: Written informed consent was obtained from the patient's wife.

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Resources – B.S.K., E.Ç.E., M.D.; Materials – B.S.K., İ.Y., E.Ç.E., T.E.M., C.E., D.K., M.D.; Data Collection and/or Processing – B.S.K., T.E.M., C.E., D.K.; Analysis and/or Interpretation – B.S.K., İ.Y., E.Ç.E., T.E.M., C.E., D.K.; Literature Search – B.S.K., İ.Y., E.Ç.E., T.E.M.; Writing Manuscript – B.S.K., İ.Y., E.Ç.E., M.D.; Critical Review – B.S.K., İ.Y., E.Ç.E., M.D., T.E.M., C.E., D.K.

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