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CASE REPORT

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COVID-19 Infection in a Patient with Common Variable Immunodeficiency: Experience with Favipiravir and Intravenous Immunoglobulin

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ABSTRACT

Data regarding COVID-19 infection in patients with common variable immunodeficiency (CVID) are limited. Herein, we present a 28-year-old male patient with CVID admitted for intravenous immunoglobulin (IVIG) replacement with myalgia and a productive cough. A nasopharyngeal swab for the SARS CoV-2 polymerase chain reaction assay was positive. Chest computed tomography was consistent with COVID-19 pneumonia. The patient refused hospitalization and the applicable treatment for COVID-19. Although he was prescribed IVIG, he had a lapse in IVIG replacement due to supply problems. The patient was later brought to the emergency room due to the deterioration of his general condition with dyspnea, tachypnea, shortness of breath, cough, and fever five days after the initial presentation. He was treated with favipiravir and IVIG and had a positive outcome. Results of COVID-19 infection in CVID patients are diverse, possibly due to underlying genetic defects. Although our patient had an increased risk for severe disease due to CVID, a lapse in IVIG replacement, and obesity, he did not require intensive care or intubation. Further studies are needed to determine and develop treatment strategies for COVID-19 infection in patients diagnosed with CVID.

Keywords: COVID-19, common variable immunodeficiency disorders, immunodeficiencies, immunoglobulin, convalescent plasma

INTRODUCTION

COVID-19 disease, caused by the new coronavirus (severe acute respiratory syndrome, SARS-CoV2), spread rapidly to the whole world and has led to the death of more than 2 million people. COVID-19 can lead to variable diseases ranging from asymptomatic disease to life-threatening clinical conditions such as acute respiratory distress syndrome, multi-organ failure, and death, depending on factors such as age, gender, and comorbidities. COVID-19 has a severe course in elderly individuals over the age of 65, in those with comorbid diseases such as hypertension, obesity, cardiovascular disease, and diabetes mellitus, and in immunocompromised individuals (1,2).

Common variable immunodeficiency (CVID) is a group of diseases characterized by hypogammaglobulinemia, recurrent sinopulmonary infections, and inadequate vaccine response (3). Although immunodeficiency is a risk factor for COVID-19, data in the literature are limited. In this case report, we present the clinical course of a patient with CVID and COVID-19 pneumonia treated with favipiravir and intravenous immunoglobulin (IVIG). Patient consent has been obtained to publish this case report.

CASE REPORT

A 28-year-old male patient with CVID for ten years was receiving monthly IVIG replacement treatment. The patient had a history of recurrent upper and lower respiratory infections but had no evidence of bronchiectasis. He had no family history regarding CVID. The last IgG level was 1177 mg/dL, IgM was 25 mg/dL, and IgA was undetectable. Absolute lymphocyte count was previously within normal limits. The patient also had morbid obesity and fatty liver disease.

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During the second peak of COVID-19 spread in Turkey, the patient was admitted to the Immunology outpatient clinic for IVIG replacement therapy. He had a runny nose, mild-to-moderate myalgia, and a productive cough with some white to yellow phlegm on admission. He had no history of fever, chills, headache, chest pain, shortness of breath, loss of appetite, nausea, vomiting, or diarrhea. On physical examination, he appeared well, alert, and oriented with no dyspnea or tachypnea. He was afebrile. The blood pressure was 132/78 mmHg, and the heart rate was 102 beats/minute. Oxygen saturation was 95% on room air. Fine crackles were heard over both lungs. He was subsequently sent to the isolation unit for further evaluation.

The patient had elevated c-reactive protein (42 mg/L) and lactate dehydrogenase levels on initial laboratory examination. The coagulation profile, liver and kidney function tests, and electrolytes were normal. Computed tomography of the chest showed multifocal bilateral scattered patchy ground glass opacities consistent with viral pneumonia (Figure 1, first row). A nasopharyngeal swab for the SARS CoV-2 polymerase chain reaction assay was positive. The patient refused hospitalization and the applicable treatment for COVID-19. He was prescribed IVIG.

The patient was later referred to the emergency room due to the deterioration of his general condition, with dyspnea, tachypnea, shortness of breath, cough, and fever five days after the initial presentation. He could not receive IVIG due to supply problems in the area. On physical examination, he had dyspnea and tachypnea, with shortness of breath. He was febrile (38.4 °C). The blood pressure was 142/82 mmHg, and the heart rate was 136 beats/minute. Oxygen saturation was 84% on room air. The patient was supplemented with nasal oxygen; oxygen saturation was 98% under 6 liters/minute oxygen. A repeat laboratory examination showed an increased c-reactive protein (87 mg/L), lactate dehydrogenase, and ferritin (218 μg/L) levels. Repeat computed tomography of the chest revealed progression in the infiltrations (Figure 1, second row).

He was subsequently hospitalized and treated with 60 g (500 mg/kg) IVIG and favipiravir (1600 mg on day 1, 600 mg on days 2-5, twice daily). Ceftriaxone (2 gr/day) and clarithromycin (500 mg twice daily) were started for suspected concomitant bacterial pneumonia. Acetylsalicylate (100 mg daily), enoxaparin (8000 U, twice daily), and N-acetyl cysteine (600 mg twice daily) were added to the treatment. During follow-up, the dyspnea, tachypnea, and shortness of breath resolved with oxygen

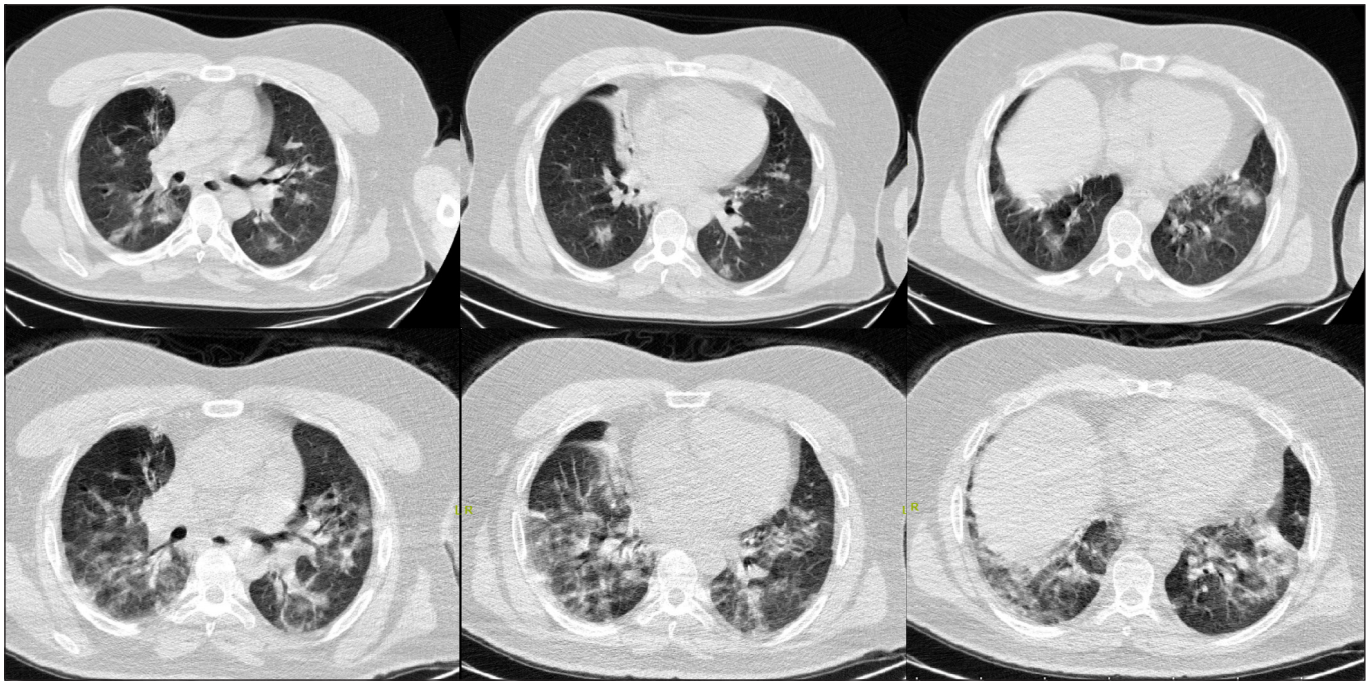

Figure 1. Chest computed tomography findings on initial admission (first row) and on hospitalization (second row).

supplementation. The fever resolved on day five, and the patient remained hypoxemic for 12 days. He received supplemental oxygen, up to 10 lt/minute. On day 15, the c-reactive protein and ferritin levels returned to normal. Two separate nasopharyngeal swabs for the SARS CoV-2 polymerase chain reaction assay were negative. The patient was clinically stable, and he only had a nonproductive cough with no need for oxygen supplementation, and was discharged from the hospital. He continued to receive IVIG and acetylsalicylate (100 mg daily) plus enoxaparin (6000 U once daily) for one month as per institutional policy.

DISCUSSION

The COVID-19 pandemic continues to spread rapidly around the world and threatens particularly the susceptible patient population's health. Immunodeficiency such as CVID poses an increased risk for SARS COV-2 as in other infectious diseases. Herein, we presented the clinical course of a patient with CVID and COVID-19 pneumonia treated with favipiravir and intravenous immunoglobulin. Although the patient had an increased risk for severe disease due to CVID, a lapse in IVIG replacement, and obesity, he did not require intensive care.

There are several case reports and two case series in the current literature regarding CVID patients infected with COVID-19. Quinti et al. reported five patients with CVID infected with COVID-19; three patients required intensive care admission and one patient died, whereas the other two patients with agammaglobulinemia had milder symptoms and shorter course (3). In another case series of ten patients reported by Cohen et al., nine had mild to moderate disease, and none had severe respiratory disease or COVID-19 pneumonia. Only seven patients were receiving IVIG replacement, and those who did not receive IVIG also recovered. Therefore, the severity of the infection in the cohort was possibly mild, and these patients are stated to be at standard risk for severe disease (4). Mullur et al. reported a fatal case of COVID-19 in a patient with CVID and obesity, similar to our case, despite high dose IVIG, remdesivir, broad-spectrum antibiotics, and convalescent plasma, possibly due to a lapse in immunoglobulin replacement (5). Although our patient had a lapse in IVIG replacement for several days, he did not have an unfavorable outcome. In other case reports, both Fill et al. and Aljaberi and Wishah reported cases of COVID-19 in patients with CVID treated with hydroxychloroquine and IVIG, resulting in a positive outcome (2,6). Van Damme et al. reported a severe case of COVID-19 in a patient with CVID treated with antibiotics, hydroxychloroquine, and convalescent plasma. The patient required intensive care, intubation, and extracorporeal membrane oxygenation (7). It could be said that patients with CVID infected with COVID-19 have diverse clinical presentations and outcomes, possibly due to underlying genetic defects.

The pathophysiology of COVID-19 infection is complex and involves a hyperactivation of macrophages resulting in a cytokine storm resulting in severe pulmonary and systemic findings (6). In patients with CVID, immunomodulation by either IVIG or convalescent plasma could be beneficial to prevent dysregulated reactions. Therefore, IVIG could be beneficial in treating COVID-19 via its anti-inflammatory effects (8). It was previously suggested early administration of IVIG could be beneficial in a positive outcome and modulate the disease activity either by immunosuppression or cross-reactive antibodies (6). Similarly, convalescent plasma could also benefit patients with CVID as a targeted therapy option (7). Although there are concerns regarding the safety and efficacy of convalescent plasma, current literature suggests it is safe, but the effectiveness still needs to be established (9). Further studies are needed in patients with CVID infected with COVID-19 to establish the effect of convalescent plasma in this unique passive immunization setting.

In our country, we used favipiravir in treating our patient as recommended by the COVID-19 national diagnosis and treatment guidelines, which resulted in a positive outcome. It is crucial to carefully question the possible symptoms of COVID-19 at each visit of CVID patients; early diagnosis and treatment with laboratory and imaging methods are essential in terms of the disease's course. Further studies are needed to determine and develop treatment strategies for COVID-19 infection in patients diagnosed with CVID.

Acknowledgements

None

Ethical Statement

Both written and oral patient consent have been obtained.

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