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Case Report

Successful Treatment With Monoclonal Antibodies In One Apds Patient With Prolonged Sars-Cov-2 Infection Not Responsive To Previous Lines Of Treatment.

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Abstract

Remdesivir and SARS-CoV-2-neutralizing monoclonal antibodies were among the several treatment medications used to treat a patient with activated PI3K-kinase delta syndrome (APDS) and a persistent, asymptomatic SARS-CoV-2 infection. Seven days after the delivery of the monoclonal antibody and 105 days after the first positive swab, we saw the virus's elimination. All analyzed samples had wild type SARS-CoV-2 viral results at genotyping. This instance demonstrates the good tolerability and effectiveness of monoclonal antibodies in lowering viral shedding in chronic illnesses that are resistant to other therapies.

Keywords : *SARS-CoV-2, COVID19, IEI, activated PI3K delta syndrome (APDS), monoclonal antibody, remdesivir, long-lasting infection, APDS.*

INTRODUCTION

The underlying illness and comorbidities have an impact on the course of COVID-19 in patients with an inborn error of immunity (IEI). A dysregulated immune response is the primary cause of complications such as thrombosis, cardiac involvement, and respiratory failure (1–9). Overall, the establishment of SARS-CoV-2 variants in immunocompromised patients is linked to persistent infections (10). We report the case of a 25-year-old man with activated PI3K-kinase delta syndrome (APDS) who developed a persistent, asymptomatic SARS-CoV-2 infection that was initially treated with remdesivir. After receiving SARS-CoV-2-neutralizing monoclonal antibodies, the patient's viral load was eventually cleared.

CASE DESCRIPTION

Diagnostic Assessment And Therapeutic Intervention

At the age of sixteen, the patient was diagnosed with APDS (mutation E1021K in PI3KCD). He experienced three episodes of pericarditis, lymphadenopathy, a persistent EBV infection, recurrent otitis and sino-pulmonary infections, and hemolytic anemia since he was a young child. He has received treatment since birth, including respiratory therapy, endovenous immunoglobulin (Igev) replacement therapy, and cycles of rituximab, steroids, and antibiotics. His diffuse large B lymphoma (DLBCL) was completely remitted after receiving treatment in 2016 with rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone (R-CHOP). He was diagnosed in June 2020 with a pulmonary atypical mycobacterial infection and relapsed DLBCL, which were verified by molecular analysis (PCR and probe hybridization) on a specimen of bronchoalveolar lavage fluid.

He had a triple-drug anti-mycobacterial regimen consisting of azithromycin, rifampicin, and ethambutol for a year until June 2021, as well as rituximab, ibrutinib, and bendamustine until December 2020 (11). An antigenic test conducted on a nasal swab (NS) as a SARS-CoV-2 screening necessary for routine investigations came out positive a few days after contact with a positive family member on January 15, 2021. On January

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18, 2021, RT-PCR on an NS verified the positive. On February 20, a CT scan of the thorax showed a sub-pleural pulmonary consolidation without any symptoms. The cultures on nasopharyngeal aspirates and blood came back negative, and the RT-PCR on the NS was still positive for SARS-CoV-2. Igev and piperacillin-tazobactam were used to treat him.

In an effort to achieve viral clearance, the patients were given a COVID-19-vaccinated plasma infusion made by a single donor who had just received a SARS-CoV-2 vaccination and had an electrochemiluminescence-measured anti-S abs level of 916 U/ml (12). Regretfully, the infusion was stopped after a short while due to an adverse event that included fever, a generalized skin rash, and dyspnea. Pulmonary consolidation was virtually completely remitted, according to the CT scan done on April 10. On April 23, NS received treatment with SARS-CoV-2-neutralizing monoclonal antibodies REGEN-COV (casirivimab and imdevimab), which were effective and well tolerated given the maintenance of a high virus load in NS.

Discussion

Frequent and severe infections are common in patients with IEIs. Some authors have examined the progression of SARS-CoV-2 infection in patients with IEIs (1–9) and their reaction to vaccination (13–15) in recent months using extensive multinational cohort studies. Younger patients with IEIs are more likely than the general population to be admitted to the intensive care unit (ICU), and the majority of patients with IEIs experience a moderate illness but may exhibit persistent viral replication. Furthermore, the prognosis is poorer for patients with IEIs and immunodeficiency who also have immunological dysregulation (1, 2, 6, 8). Innate mistakes of TLR3 and the IRF-7-dependent pathway, which cause low serum type I IFNs, are more prevalent in previously healthy individuals with severe COVID-19, according to a multicenter research (16).

A hyperactivation of the PI3K-AKTmTOR pathway is a characteristic of APDS. These patients exhibit immune dysregulation symptoms (cytopenia, arthritis, colitis, and lymphoproliferation) with a high risk for lymphoma (19, 20), recurrent sinopulmonary and chronic herpes virus infections, and occasionally persistent granulomatous skin lesions linked to BCG vaccination (18, 19). Despite having reduced cytotoxic activity against viruses like EBV, these individuals have been shown to have high plasmatic levels of INFg (23) and high expression and secretion of INFg by CD8+ (21), CD4+ T, and Tfh T cells (22).

The prolonged infection and perhaps the moderate symptomatology linked to it could have been caused by a variety of circumstances, including the recent chemotherapy and the complex IEI phenotype. Even when given far from the onset of the infection, SARS-CoV-2-neutralizing monoclonal antibodies have demonstrated efficacy in achieving viral clearance. The current example emphasizes the potential advantages of REGN-COV as a treatment for APDS patients with chronic SARS-CoV-2 infection, with the disclaimer that further in vitro and in vivo research is required to determine therapeutic efficacy against novel variations. Remarkably, Takashita et al. just shown in vitro the possible effectiveness of REGEN-COV against the Omicron BA.2 variant that is presently in circulation (30). To evaluate the effectiveness of these medications, their appropriate dosage, and their use in conjunction with other antiviral treatments, more research on larger patient cohorts is required.

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