

Regen-COV-2 Antibody Cocktail Mediated Clearance of SARS-COV-2 in an Immunocompromised Patient

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Coronavirus disease 2019 (COVID-19) affects different people in different ways. Most infected people develop mild to moderate illness and recover without hospitalization. This case report presents a patient who had difficulty eradicating the coronavirus due to being treated with rituximab, which depletes B lymphocytes and therefore disables the production of neutralizing antibodies. The regen-COV-2 antibody cocktail consists of two monoclonal antibodies: casirivimab and imdevimab. This cocktail successfully helped the patient's immune system eradicate the virus without auto specific severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) antibody production. In vitro studies confirm that eradication of the intact the virus. This case report emphasizes the importance of providing external antiviral antibodies regularly, like the regen-COV-2 antibody cocktail, as post- and even pre- SARS-CoV-2 infection prophylaxis in patients treated with rituximab.

COVID-19 infection manifests across a wide range of clinical severity, from a mild upper respiratory tract illness to a diffuse viral pneumonia causing acute respiratory failure [1]. Most infected people develop mild to moderate illness and recover without hospitalization. Rituximab, an anti-CD20 monoclonal antibody, is one of the main

treatments for B-cell malignancies [2]. It acts by depleting normal and pathogenic B cells [3]. Patients treated with rituximab are at a higher risk for prolonged severe forms of COVID-19 [2,3]. In a previous study, we described the use of combined external anti-viral agents like convalescent plasma and remdesivir that successfully helped the patient's immune system eradicate the virus in immunocompromised patient who presented with a persistent SARS-COV-2 infection, without B-cell population recovery [4].

In this case report, we present a successful eradication of persistent SARS-COV-2 infection from a follicular lymphoma patient who had been recently treated with three courses of rituximab. The Regen-COV-2 antibody cocktail, which consists of two monoclonal antibodies, casirivimab, and imdevimab [5], successfully helped the patient's immune system eradicate the virus.

PATIENT DESCRIPTION

A 71-year-old female patient was diagnosed with follicular lymphoma 5 years prior to the COVID-19 infection and diagnosed with lung adenocarcinoma 4 years prior to the COVID-19 infection. She also underwent a left upper lobe resection. The stage of the disease was T3N0 STAGE IIB. The patient became infected with the SARS-COV-2 (defined as day 1) without specific symptoms. Two weeks later, she finished the isolation period without any need for specific treatment or hospitalization. On day 46, she came to the emergency room with general weakness and fever. The reverse transcription polymerase chain reaction (RT-PCR) from a nasopharyngeal sample was positive

for coronavirus. Inflammation markers were elevated. A chest X-ray showed bilateral consolidation. She was admitted to the internal medicine department. The patient was treated as a community acquired pneumonia and given tazocin antibiotics for pneumonia in immunocompromised patients. Throughout the hospitalization period, the patient was hemodynamically stable with normal saturation levels at room air. On day 56, she presented with desaturation (80% at room air), dyspnea, and recurrent fever. Laboratory tests showed an elevation in inflammatory markers.

A repeated SARS-CoV-2 RT-PCR test was positive, without production of SARS-CoV-2 antibodies [Table 1]. Rituximab mediated depletion of B-cells, so the patient could not produce SARS-CoV-2 antibodies. A computed tomography scan showed bilateral ground glass consolidation occupying 50% of the lung volume, with no evidence of pulmonary embolism. Cell cultures confirmed that the patient still had intact live SARS-CoV-2 viruses on day 56 [Table 1], causing concern for a continuous persistent SARS-CoV-2 infection. The patient was therefore, transferred to the COVID-19 department. Initially, she was treated with high-flow noninvasive ventilation. The classic treatment of steroids and remdesivir did not affect the situation of the patient. To achieve virus eradication, the patient received a course of Regen-COV-2 antibody cocktail (600 mg). She improved and was discharged 10 days later.

Blood tests of the patient showed thrombocytopenia and severe lymphopenia. Biochemical analysis showed stable plasma electrolyte concentrations. Inflammatory parameters, C-reactive protein,

Table 1. SARS-CoV-2 infection status as detected by nasopharynx SARS-CoV-2 PCR tests and viral culture

Days after first positive COVID-19 test	Nasopharynx COVID-19 RT-PCR test cycle threshold	COVID-19 antibodies plasma	Intact virus in viral culture	RT-PCR (COVID-19) from viral culture
1	+	–	Not conducted	Not conducted
44	+ (19)	–	Not conducted	Not conducted
56	+ (19)	–	+	+
62	– (36)	–	–	–

Cell cultures showed intact viruses on day 56. Negative cell culture for the coronavirus was verified on day 62 after the Regen-COV-2 antibody treatment. Viral RNA was extracted from nasopharyngeal samples and RT-PCR was conducted. Results were considered valid only when the cycle threshold value of the reference gene was ≤ 32 . The cytotoxic effect was calculated. Vero E6 cells were cultured in DMEM and infected with the SARS-CoV-2 virus. The cytopathic effect was microscopically determined. To confirm that the cytopathic effect was due to SARS-CoV-2, a real time RT-PCR for the virus was performed on the cell supernatant.

COVID-19 = coronavirus disease 2019, RT-PCR = reverse transcription polymerase chain reaction, SARS-CoV-2 = severe acute respiratory syndrome coronavirus 2

and ferritin were increased after being transferred to the COVID-19 department and decreased a few days after treatment with the Regen-COV-2 antibody cocktail.

SARS-CoV-2 infection and immunity status were tested. RT-PCRs were performed on nasal and throat samples on days 1, 41, 56, and 62 after the first positive corona test was conducted. To confirm that the virus was viable and intact, a viral cytotoxic effect was tested on a VERO cell culture. The results show that the patient had been positive for at least 56 days SARS-CoV-2 without producing SARS-CoV-2 antibodies [Table 1]. The Regen-COV-2 antibody cocktail intervention succeeded in eradicating the virus. Negative SARS-CoV-2 RT-PCR results were initially achieved after the intervention (day 62). A cytotoxic culture assay confirmed the eradication of the virus after this intervention (day 62) [Table 1].

COMMENT

In this case report, we showed a patient treated with rituximab who presented with a persistent SARS-CoV-2 infection. Rituximab creates difficulties in eradicating the coronavirus due to indiscriminate depletion of B cells.

During hospitalization in the COVID-19 department, the patient received a course of the Regen-COV-2 antibody cocktail. This cocktail consists of two monoclonal antibodies: casirivimab and imdevimab [5]. The patient improved under this treatment and on day 62 an RT-PCR assay from a nasopharyngeal swab was negative and no coronavirus antibodies were found. Furthermore, a cell culture test was repeated, with no presence

of live intact viruses. Patients treated with rituximab need passive immunotherapy to eradicate viruses. The supply of these antibodies by convalescent plasma [2,3] or the Regen-COV-2 antibody cocktail is critical for the proper function of the immune system in mediating viral clearance.

Patients taking immunosuppressive drugs like rituximab can experience a suppression of their immune system from a few months to more than a year [3]. Numerous studies have shown that it is difficult for the immune systems of these patient to eradicate the SARS-CoV-2 [2-4]. It should be noted that these patients are at high risk for persistent SARS-CoV-2 infections and complications [2-4], which raises the possibility of long COVID-19 syndrome.

B-cell suppressed patients are not vaccinated because they do not have the antibody-producing B cells. However, once infected, it is very important to help the immune system of these patients in clearing the virus. This function can be accomplished by convalescent plasma [3,4] or products that contain specific antibodies against the virus, like the Regen-COV-2 antibody cocktail [5].

The question remains whether the eradication of the SARS-CoV-2 is long-term after treatment and whether these patients can be infected again because of their inability to produce antibodies against the virus. It might be necessary to provide external antiviral antibodies regularly, like the Regen-COV-2 antibody cocktail, as post-SARS-CoV-2 infection prophylaxis in rituximab treated patients. However, maybe the benefit of the Regen-COV-2 treatment for these patients as

pre-exposure prophylaxis is also important.

CONCLUSIONS

Regen-COV-2 antibody cocktail helped to eradicate SARS-CoV-2 virus in immunocompromised patient treated with rituximab who presented with a persistent SARS-CoV-2 infection.

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