## COVID-19 in an Allergic Bronchopulmonary Aspergillosis Patient: A Case Report

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In Coronavirus Disease 2019 (COVID-19), it is yet unclear how the course of the disease progresses, especially in patients with chronic lung diseases, such as asthma and allergic bronchopulmonary aspergillosis (ABPA).<sup>1,2</sup> In this case report, we present a patient who was followed up with the diagnosis of ABPA in our Pediatric Allergy and Immunology outpatient clinic to discuss the patient's management and prognosis after the diagnosis of SARS-CoV-2 infection.

A 16-year-old male was brought to our clinic with complaints of cough, runny nose, and fever. The patient, who had been followed up in our clinic with the diagnosis of ABPA for the last 4 years,3 was regularly receiving anti-IgE analog omalizumab (monthly, 300 mg) treatment besides inhaled corticosteroid+long-acting  $\beta$ -agonist combination. In his past medical history, there was nothing significant. There was no known history of COVID-19 and consanguinity in his family. On physical examination, he looked pale, body temperature was 38°C, heart rate was 110/min, blood pressure was measured as 100/60 mmHg, and respiratory rate was 25 per minute. Respiratory system examination of the patient revealed prolonged expiration, mild wheezing, and localized crepitation. In the laboratory tests, leukocyte count was 12 100/µL, neutrophil 7.760/µL, lymphocyte 2.420/µL, eosinophil 743/µL, hemoglobin 13.4 g/dL, hematocrit 42.4%, thrombocyte number 318 000/µL, erythrocyte sedimentation rate 14 mm/h, C-reactive protein (CRP): 50 mg/L, ferritin 60 ng/mL, D-dimer: 100 ng/mL, and total IgE was 3.130 kU/L. Routine biochemistry values were within normal limits. Our patient's asthma control test (ACT) decreased from 25 to 19 after the last visit. Moderate obstructive and restrictive findings were present in the spirometry of the patient as predicted values before (during admission)/after 10 days of COVID-19 treatment, respectively, FEV1 60/79%, FVC 55/73%, FEV1/FVC 107/107, PEF 58/74%, FEF2575 57/82%. Posteroanterior chest radiography and contrast-enhanced thorax computed tomography (CT) showed diffuse tubular, partly cystic, bronchiectasis, especially in upper zones of both lungs and peribronchial thickening accompanying with acinar infiltrative changes. Thoracic CT examination did not show any findings typical for SARS-CoV-2 infection. There was not any deterioration or significant difference in the patient's chest radiography and tomography findings compared with the earlier ones (Figure 1A and B). The polymerase chain reaction test taken from the patient for SARS-CoV-2 infection was positive. Ceftriaxone (100 mg/kg/day), favipiravir (1600 mg ×2/1 day and 600 mg ×2/4 days), dexamethasone (6 mg/day/5 days), and salbutamol nebulization (6 × 5 mg/day) treatments were initiated and the treatment was completed in 10 days. The CRP value became negative and previous spirometry findings improved after COVID-19 treatment. His response to COVID-19 treatment was adequate. During COVID-19 therapy, he did not have any complications due to the disease, and his disease course was uncomplicated. The patient was discharged with improvement on the 10th day of hospitalization and called for outpatient follow-up. Since our patient was brought to us during the therapy interval, we did not need to apply monthly omalizumab during SARS-CoV-2 infection. After he recovered from COVID-19, we continued his regular omalizumab therapy because he did not have a severe and/or complicated SARS-CoV-2 infection.

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Figure 1. a, b. No significant change before (a) and after (b) the COVID-19 treatment in thorax CT.

There are two points to be addressed in our patient. First, according to our literature review, there has not been any report describing the effect and course of SARS-CoV-2 infection in an ABPA patient. There has been a case report of uncommon presentation of ABPA development (without SARS-CoV-2 infection) in a previously healthy male during mandatory lockdown (isolation) in Italy, who decided to live in the basement of his house due to the COVID-19 pandemic.4 Second, the effect of omalizumab therapy on COVD-19 disease in an ABPA patient. Although it is not probable to make big implications concerning omalizumab use in ABPA from a distinct case, the experience with omalizumab from other chronic lung diseases such as asthma is better to be discussed. Severe asthma patients utilizing biologic therapy such as omalizumab shown by Eger et al.5 to be related with a more severe progress of COVID-19 compared to the general population. This was thought to be a result of co-morbidities, the severity of asthmatic respiratory tract inflammation, the utilization of biologics, or a combination of these. However, there was not any reported experience of SARS-CoV-2 infection and omalizumab use in ABPA, such as in our patient, in the literature.

In contrast to Eger et al.'s report, Omalizumab treatment has been speculated to protect from severe forms of COVID-19 by means of enhancing anti-viral immunity. The use of omalizumab in vivo reinstated interferon-alpha (IFN- $\alpha$ ) signaling in plasmacytoid dendritic cells to such respiratory viruses via omalizumab-downregulated  $\mathsf{Fc}\epsilon\mathsf{Rl}\alpha$  expression on the cell surface.<sup>6-8</sup> Moreover, omalizumab was also shown to have inhibitory effects on inflammatory cells, such as neutrophils, in chronic urticaria.9 There are also literature data stating that omalizumab lessens inflammation by hindering proinflammatory cytokines and affects mast cells, hampering the discharge of inflammatory agents, for example, proteases.<sup>10</sup> In Preventative Omalizumab or Step-up Therapy for Severe Fall Exacerbations (PROSE) study, omalizumab therapy was able to decline rhinovirus infection duration, viral clearance, and illness frequency.<sup>2,6,7</sup> Since the reasons mentioned above, our patient may have mild signs and symptoms of COVID-19 disease and overcome it without any complications. Also, World Allergy Organization (WAO), multinational Allergic Rhinitis and its Impact on Asthma (ARIA) groups, and the European Academy of Allergy and Clinical Immunology (EAACI) recommend continuing as usual in patients without suspected infection or proven SARS-CoV-2 infection by weighing the benefits and risks individually.<sup>11,12</sup> We did not hesitate to continue omalizumab therapy, in our patient, because he did not have a severe and/or complicated SARS-CoV-2 infection and recovered rapidly.

In conclusion, this patient showed us that ABPA patients experiencing SARS-CoV-2 infection could probably overcome COVID-19 disease without any significant consequences. However, the course and prognosis of COVID-19 in ABPA patients, especially using omalizumab, is not yet satisfactorily known.

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