ASTHMA ALLERGY IMMUNOLOGY
ASTIM ALLERJİ İMMÜNOLOJİ

doi: 10.21911/aai.574
Asthma Allergy Immunol 2020;18: Supplement:1, 23-26

CASE REPORT

Received: 17.09.2020 • Accepted: 12.10.2020
Online Published: 11/11/2020

SARS-CoV-2 in a Patient with Persistent Asthma Taking Omalizumab: The First Case in Turkey

Emel ATAYIK, Gökhan AYTEKİN

Depatment of Adult Allergy and Immunology, Konya City Hospital, Konya, Turkey

Corresponding Author: Emel ATAYIK ✉ emelakinci@yahoo.com

ABSTRACT

Since the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) was first reported in Wuhan, China, it has been one of the largest pandemics in the history which has been aggressively spreading all over the world and affected more than 6 percent of world's population. In SARS-CoV-2 pandemics, patients with severe asthma require particular attention due to not only the underlying airway disease, but also immunomodulatory treatments used. Although it is known that viruses infecting the respiratory mucosa are risk factors for asthma attacks and that viral infections at early stage of the life are risk factors for development of asthma, and patients with a chronic disease have been declared as the risk group for severe SARS-CoV-2 infection by The Centers for Disease Control and Prevention (CDC), some studies reported that ratio of patients with asthma is relatively lower among the patients hospitalized for SARS-CoV-2. This suggests that treatments used for asthma may be protective against SARS-CoV-2. In addition, our knowledge regarding effect of omalizumab on mortality and morbidity in patients with asthma using omalizumab in SARS-CoV-2 infection is limited. In this case report, through reporting this first case of accompanying SARS-CoV-2 case in a patient with severe persistent asthma using omalizumab from Turkey, we aimed to discuss potential effects of omalizumab treatment on accompanying SARS-CoV-2 pneumonia in these patients.

Keywords: SARS-CoV-2, omalizumab, severe asthma

INTRODUCTION

Since first reported in Wuhan, China, in December 2019, severe respiratory syndrome coronavirus 2 (SARS-CoV-2) has spread rapidly around the world and has become one of the largest pandemics in history, affecting approximately 6% of the global population (1, 2).

Severe asthma patients must take extra care in the SARS CoV-2 pandemic, not only because of the underlying airway disease but also because of the immunomodulator treatments used. Although viral infections at an early stage of life are known to be a risk for the development of asthma, and viral infection of the respiratory mucosa is known to be a risk for asthma attacks, and the Centre for Disease Control and Prevention (CDC) has announced that patients with an underlying chronic disease are a high-risk group for SARS-CoV-2 infection, some studies have reported that very few asthma patients have been hospitalised because of SARS-CoV-2 infection (3, 4). This suggests that the drugs used in the treatment of asthma could be protective against SARS-CoV-2. Moreover, there is limited information about the effect of omalizumab on morbidity and mortality in asthma patients with SARS-CoV-2 infection who are using omalizumab (2,5).

The case presented here is the first case in Turkey of a SARS-CoV-2 patient with severe persistent asthma who was taking omalizumab treatment, with the aim of discussing the potential effect of omalizumab treatment for SARS-CoV-2 pneumonia in these patients.

CASE

A 74-year old female, who was being followed up in our clinic, presented on 15 March 2020 with the complaints

ORCID Emel ATAYIK / 0000-0002-7011-7752, Gökhan AYTEKİN / 0000-0002-9089-5914

of headache and widespread muscle pain that had been ongoing for 3 days, and subsequent loss of appetite. The patient had been taking omalizumab 450 mg/2 weeks for 2 years for a diagnosis of severe persistent allergic asthma, and the asthma was under control. At the time of presentation, complaints of a dry cough and fever were present, and from the history it was learned that the patient's daughter with whom she lived was under treatment for COVID-19 and was PCR (+). Other than hypertension, the patient had no additional disease, and was hospitalised with an initial diagnosis of COVID-19. The general condition of the patient was fair, with full consciousness, mild tachypnea, respiration 24/min, O_2 saturation of 94% and temperature of 38.1°C. The respiratory system examination revealed bilateral expiratory rhonchi. The blood tests showed pancytopenia with elevated C-reactive protein (CRP) and acute phase reactants (Table I). Thorax computed tomography (CT) images were compatible with COVID-19 pneumonia and infiltrations with frosted glass density in multiple bilateral lobes and segments were observed (Figure 1). The nasopharyngeal swab was reported as positive for COVID-19 with the polymerase chain reaction (PCR) test.

Treatment for the patient was initiated with hydroxychloroquine (2x200 mg, po), favipiravir (3x 400 mg, po, 5 days), anticoagulant (enoxaparin 1x0.6 ml, sc), slow-release Beta-2 agonist (formoterol 12 mcg 2x1, inhalation), inhaler steroid (budesonide 2x800 mcg, inhalation), and ipratropium bromide (4x100 mcg, inhalation). The patient experienced no additional complaints during follow-up and the nasopharyngeal swab test result was negative for COVID-19 on the 5th day and 14th day of treatment. Following a 14-day quarantine period, the patient was evaluated at the clinic again. The general condition of the patient was good, respiration 16/min, and temperature 36.1°C. The respiratory system examination showed no pathology other than bilateral long expirium. The omalizumab treatment of 450 mg/2 weeks was continued. A significant improvement was observed in the blood tests. Early radiological pathology follow up was not present.

DISCUSSION

In the SARS-COV-2 pandemic, which has affected the whole world as one of the largest pandemics in history, virus-related pulmonary complications in particular are responsible for morbidity and mortality. The nasal and pharyngeal mucosa is the first region of SARS-CoV-2 infection, and just as in other SARS virus infections, SARS-CoV-2 attacks nasal mucosa and respiratory tract submucosal mast cells. Activated mast cells contribute to inflammatory damage by expressing various pro-inflammatory cytokines such as IL-1, IL-6, and IL-33 (1).

Although the CDC declared that individuals with an underlying chronic disease constitute a high-risk group for SARS-CoV-2 infection, there are limited data available about patients with asthma, and some studies

Table I: Serum blood test results of the patient during follow up.

	17.09.19	02.07.20	07.07.20	20.07.20
White blood cells (10^9/L)	6.61	3.83	3.77	5.91
Lymphocytes (10^9/L)	2.19	1.40	1.19	1.40
Monocyte (10^9/L)	0.57	0.37	0.29	0.51
Eosinophils (10^9/L)	0.3	0.02	0	0.02
Lymphocytes, %	27.9	36.4	31.5	20.6
Monocytes, %	8.1	9.8	7.8	8.5
Eosinophils, %	4.2	0.6	0.1	0.3
IgG (g/L)	12.1			18.8
IgM (g/L)	1.2			0.63
IgA (g/L)	2.1			3.3
IgE (IU/mL)	574			3250
CRP	3.5	43.9	77	25
	4.07.20	6.07.20	9.07.20	18.07.20
Real time COVID-19 PCR	(+)	(+)	(-)	(-)

COVID-19: Coronavirus Disease 2019, **Ig:** Immunoglobulin, **CRP:** C-reactive protein.

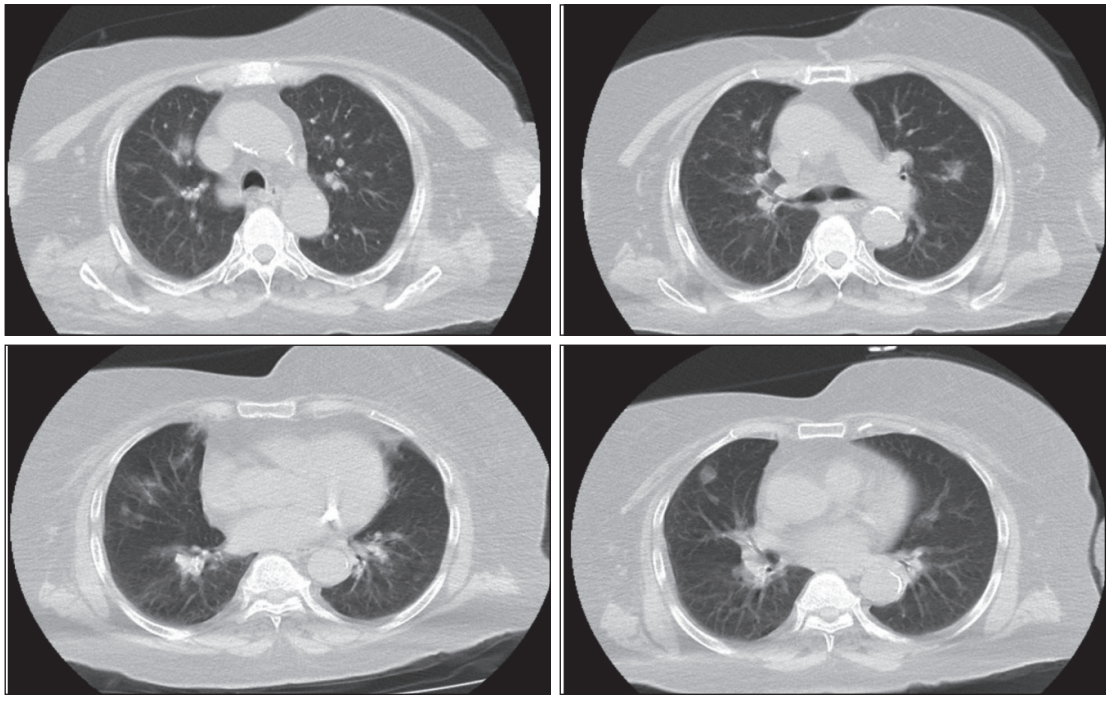

Figure 1: Thorax CT images of the patient.

have even reported a relatively low rate of asthma patients hospitalised because of SARS-CoV-2 (3,4). This has been attributed to the use of immunomodulator agents and/or the down-regulation of angiotensin-converting enzyme-2 (ACE2) mediating the cellular intake of SARS-CoV-2 (6). This suggests that the treatments used for asthma could be protective against SARS-CoV-2.

IgE plays a central role in the pathogenesis of several allergic diseases, primarily asthma (7), and omalizumab is a humanised recombinant IgG1 monoclonal antibody that binds to IgE antibodies with high affinity (8,9). Omalizumab decreases IgE and IgE-related reactions and high affinity FcεRI receptors on mast cells (1). In addition, omalizumab treatment of paediatric asthma patients has been shown to reduce the duration of rhinovirus infection, the spread of rhinovirus, and the risk of rhinovirus infection (10). Furthermore, omalizumab has been shown to have antiviral efficacy by down-regulating high-affinity IgE receptors on the plasmacytoid dentritic cell surface (11). In the Inner-City Anti-IgE Therapy for Asthma and the PROSE (Preventative Omalizumab or Step-up Therapy for Severe Fall Exacerbations) studies, the reduction in viral exacerbations in asthma patients treated with omalizumab was explained with this mechanism (10, 12).

Omalizumab reduces the expression of TLR7, which is a receptor that detects viruses and triggers natural immunity (13). In a rat experimental model, omalizumab small peptide segment (OMZ-SPT) has been shown to reduce the IL-6, IL-1β and TNF-α synthesis in the bronchiolar lavage, the periostin level, and acute pulmonary damage associated with lipopolysaccharides (14). The interferon-related antiviral efficacy of plasma dentritic cells associated with rhinovirus and influenza-induced PBMC is increased by omalizumab (11). There are also studies in the literature showing that omalizumab caused an increase in other immunoglobulin levels and this effect could be used when necessary in patients with immune deficiency (15). With one year of omalizumab treatment in the current case, an increase in IgG, IgM and IgA levels was observed compared to the pre-treatment period. This suggests that omalizumab treatment could have a role in protection against SARS-CoV-2 infection.

CONCLUSION

In conclusion, the current data suggest that allergic asthma patients are at lower risk of severe SARS-CoV-2 infection because of the inhaled corticosteroids and/or the monoclonal antibody treatment used for asthma. To draw a more definitive conclusion, there is a need for further studies to review the interaction of monoclonal antibodies such as omalizumab with chronic pulmonary diseases such

as asthma. Nevertheless, omalizumab may be a promising new treatment agent for protection against the pulmonary damage associated with SARS-CoV-2. The case presented in this paper can be considered of value as the first SARS-CoV-2 case in Turkey using omalizumab because of severe persistent allergic asthma. The relatively mild clinical course of SARS-CoV-2 and the outcomes seen in this patient support the hypothesis that omalizumab could be protective against SARS-CoV-2 infection in patients with asthma.

REFERENCES

1. Abdelmaksoud A, Goldust M, Vestita M. Omalizumab and COVID-19 treatment: Could it help? Dermatol Ther 2020:e13792.
2. Çelebioğlu E. Asthma and COVID-19. Asthma Allergy Immunol 2020;18(1):56-7.
3. Docherty AB, Harrison EM, Green CA, Hardwick HE, Pius R, Norman L, et al. Features of 20 133 UK patients in hospital with covid-19 using the ISARIC WHO Clinical Characterisation Protocol: Prospective observational cohort study. BMJ 2020;369:m1985.
4. Zhang JJ, Dong X, Cao YY, Yuan YD, Yang YB, Yan YQ, et al. Clinical characteristics of 140 patients infected with SARS-CoV-2 in Wuhan, China. Allergy 2020;75(7):1730-41.
5. Lommatzsch M, Stoll P, Virchow JC. COVID-19 in a patient with severe asthma treated with Omalizumab. Allergy 2020 (Epub ahead of print).
6. Peters MC, Sajuthi S, Deford P, Christenson S, Rios CL, Montgomery MT, et al. COVID-19-related genes in sputum cells in asthma. relationship to demographic features and corticosteroids. Am J Respir Crit Care Med 2020;202(1):83-90.
7. Corry DB, Kheradmand F. Induction and regulation of the IgE response. Nature 1999;402(6760 Suppl):B18-23.
8. Presta LG, Lahr SJ, Shields RL, Porter JP, Gorman CM, Fendly BM, et al. Humanization of an antibody directed against IgE. J Immunol 1993;151(5):2623-32.
9. Fick RB Jr. Anti-IgE as novel therapy for the treatment of asthma. Curr Opin Pulm Med 1999;5(1):76-80.
10. Esquivel A, Busse WW, Calatroni A, Togias AG, Grindle KG, Bochkov YA, et al. Effects of omalizumab on rhinovirus infections, illnesses, and exacerbations of asthma. Am J Respir Crit Care Med 2017;196(8):985-92.
11. Gill MA, Liu AH, Calatroni A, Krouse RZ, Shao B, Schiltz A, et al. Enhanced plasmacytoid dendritic cell antiviral responses after omalizumab. J Allergy Clin Immunol 2018;141(5):1735-43.e9.
12. Busse WW, Morgan WJ, Gergen PJ, Mitchell HE, Gern JE, Liu AH, et al. Randomized trial of omalizumab (anti-IgE) for asthma in inner-city children. N Engl J Med 2011;364(11):1005-15.
13. Cardet JC, Casale TB. New insights into the utility of omalizumab. J Allergy Clin Immunol 2019;143(3):923-6.e1.
14. Wang T, Hou W, Fu Z. Preventative effect of OMZ-SPT on lipopolysaccharide-induced acute lung injury and inflammation via nuclear factor-kappa B signaling in mice. Biochem Biophys Res Commun 2017;485(2):284-9.
15. Cildag S, Senturk T. The effect of omalizumab treatment on IgE and other immunoglobulin levels in patients with chronic spontaneous urticaria and its association with treatment response. Postepy Dermatol Alergol 2018;35(5):516-9.