Case Report

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Can anti-IgE and anti-IL-5 monoclonal antibodies be protective against household transmission of SARS-CoV-2?

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ABSTRACT

Coronavirus disease 2019 (COVID-19) is the general term used for pneumonia caused by acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Keeping the infected individuals in quarantine is very effective in preventing the spread of the disease but isolation and quarantine period increase the risk of household transmission. By December 2020, the rate of household transmission of SARS-CoV-2 has reached up to 85%. Both omalizumab and mepolizumab are used for the treatment of severe persistent asthma. In addition, omalizumab also has an indication for use in chronic urticaria. Both medications have been shown to have some antiviral effects. So, we aimed to discuss potential protective effects of these agents against household transmission of SARS-CoV-2 by reporting six different patients who remained uninfected despite PCR (Polymerase Chain Reaction) (+) SARS-CoV-2 individuals at home and were being treated with monoclonal antibodies.

Keywords: Mepolizumab, omalizumab, SARS-CoV-2

INTRODUCTION

Coronavirus disease 2019 (COVID-19) is the general term used for pneumonia caused by acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and since the first identification of SARS-CoV-2 it has caused one of the greatest pandemics of human history (1). The disease presents with complaints such as high temperature, cough, and sore throat. Infected wild animals and infected humans are the most important sources of transmission (2). Although some vaccines have come into use, there is still no definitive medical treatment for the disease, and handwashing, social distancing, use of masks, and isolation of the infected individuals comprise the most important stages in protection against transmission of the disease (3). Keeping the infected individuals in quarantine is very effective in preventing the spread of the disease but isolation and quarantine period increase the risk of household transmission (4). By December 2020, the rate of household transmission has reached up to 85% (5). Omalizumab is an anti-immunoglobulin (Ig) E and mepolizumab, however, anti-interleukin (IL)-5 antibody. Both medications are used for the treatment of severe persistent asthma in patients with suitable phenotype. In addition, omalizumab also has an indication for use in chronic urticaria. Apart from these effects, both medications have been shown to have some antiviral effects (6). In this case series, we aimed to discuss potential protective effects of these agents against household SARS-CoV-2 transmission in the light of the literature by reporting six different patients who remained uninfected despite PCR (Polymerase Chain Reaction) (+) SARS-CoV-2 individuals at home and were being treated with monoclonal antibodies for chronic urticaria or severe persistent asthma.

CASE

Patient 1: A 37-year-old female patient suffering from severe asthma for five years had been using omalizumab at a dose of 450 mg/4 weeks/subcutaneous for the last 3 years in addition to her current treatment for asthma (vilanterol/fluticasone 100/25 mcg, 1x1, inh; montelukast 10 mg, 1x1, po). During the pandemic, the patient continued omalizumab treatment. In the prick test of the patient, the patient had sensitivities to grass pollen and house dust mites. The patient was being concomitantly treated for allergic rhinitis and chronic sinusitis (Ketotifen hydrogen 2 mg, 2x1, po; fluticasone propionate 2x1, intranasal). The patient did not admit to the emergency department, was not hospitalized, or given systemic steroids due to symptoms of asthma exacerbations within the last 2 years. The Father of

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the patient whose daughter, husband, and father who was living in the same house were found to be SARS-CoV-2 PCR (+) in December 2020 died of COVID-19. Despite living together with 3 SARS-CoV-2 PCR (+) individuals, the patient had no complaint consistent with COVID-19 and was found to be SARS-CoV-2 PCR (-). Her chest x-ray showed no pathology.

Patient 2: A 35-year-old male patient suffering from severe asthma, chronic rhinosinusitis, and nasal polyps for four years had been using mepolizumab at a dose of 100 mg/4 weeks/sc for the last 10 months in addition to his current treatment for asthma (montelukast 10 mg, po, 1x1; formoterol/fluticasone 12/500 mcg 2x1, inh). During the pandemic, he continued his regular mepolizumab treatment. After mepolizumab, the patient did not admit to the emergency department, was not hospitalized, or given systemic steroids due to symptoms of asthma exacerbations. Despite the fact that his 3 children and wife were found to be SARS-CoV-2 PCR (+) in December 2020, our patient had no complaint. His chest x-ray was normal and he had a negative SARS-CoV-2 PCR test.

Patient 3: A patient who had been using omalizumab due to chronic urticaria for two years got pregnant after initiation of omalizumab treatment and his omalizumab treatment was continued during pregnancy. In addition, the patient, who was on a diet and using insulin glargine 1x24 units/ sc for gestational diabetes mellitus, were using L-thyroxine 75 mcg, po, 1x1 due to Hashimoto's thyroiditis. Although her husband was found to be SARS-CoV-2 PCR (+) at 6 months of pregnancy, the patient who continued her regular omalizumab treatment was found to be SARS-CoV-2 PCR (-) and she had no complaint consistent with COVID-19.

Patient 4: A patient followed-up with allergic asthma for eighteen years had been given 13 doses of omalizumab treatment at a dose of 300 mg/4 weeks/subcutaneous in addition to levocetirizine/montelukast 5/10 mg, 1x1, po and beclomethasone dipropionate/formoterol fumarate 100/6, 2x1, inh for treatment of asthma. Although his parents living in the same house with him were found to be SARS-CoV-2 PCR (+), he had no complaint and was found to have a negative SARS-CoV-2 PCR test.

Patient 5: A 52-year-old female patient who was being followed-up with a diagnosis of asthma for twenty years and had sensitivities to cockroaches and home dust mites was using mepolizumab treatment at a dose of 100 mg/4 weeks/ sc for 9 months in addition to her current treatment for asthma. Although the daughter and husband of the patient who continued to her regular mepolizumab treatment during the pandemic were found to be SARS-CoV-2 PCR (+), she was found to have a negative SARS-CoV-2 PCR test.

Patient 6: A 37-year-old female patient had been followed-up with a diagnosis of chronic urticaria for eight years and had received a total of 30 doses of omalizumab at a dose of 300 mg/4 weeks/ sc due to intermittent recurrences within the last 3 years. The patient who also had obesity in addition to chronic urticaria were using ketotifen 2 mg, po,1x1; montelukast sodium 10 mg, po, 1x1; and Fexofenadine 180 mg/1x1/ po. Despite the fact that her sister and mother living in the same house with her were found to be SARS-CoV-2 PCR (+), no symptoms suggesting COVID-19 were observed and the patient was found to be SARS-CoV-2 PCR (-).

Table 1. The demographic and clinical properties of the patients

	Age	G	Diagnosis	Duration of disease	Monoclonal antibody	Number of injections	SARS-CoV-2 PCR (+) family members	Other treatments	Comorbidities
Patient A	37	F	Severe asthma	5 years	Omalizumab	36	Father, Husband, Daughter	-Vilanterol/ fluticasone 100/25 mcg, 1x1, inh -Montelukast 10 mg, 1x1, po	-Allergic rhinitis -Chronic sinusitis
Patient B	35	M	Severe asthma	4 years	Mepolizumab	10	Wife, Three children	-Montelukast 10 mg, po -Formoterol/fluticasone 12/500 mcg 2x1, inh	-Chronic rhinosinusitis -Nasal polyps
Patient C	29	F	Chronic urticaria	2 years	Omalizumab	7	Husband	-Cetirizine 10 mg, 1x1, po	-Gestational diabetes mellitus -Hashimoto's thyroiditis
Patient D	23	M	Severe asthma	18 years	Omalizumab	13	Mother, Father	-Levocetirizine/ montelukast 5/10 mg, po -Beclomethasone dipropionate/ formoterol fumarate 100/6, 2x1, inh	-None
Patient E	52	F	Severe asthma	20 years	Mepolizumab	9	Daughter Husband	-Montelukast sodium 10 mg, 1x1, po -Formoterol/fluticasone 12/500 mcg 2x1, inh	
Patient F	37	F	Chronic urticaria	8 years	Omalizumab	30	Sister Mother	-Ketotifen 2 mg, 2x1, po -Montelukast sodium 10 mg, 1x1, po	-Obesity

G: gender, SARS-CoV-2 PCR: Acute respiratory syndrome coronavirus 2 Polymerase Chain Reaction

DISCUSSION

COVID-19 has become one of the greatest pandemics of human history since December 2019 when it was first defined and by January 2021, it has led to the death of more than 1.900.000 people (7). One of the most effective ways of preventing the spread of the disease is the prevention of disease transmission to healthy individuals. For this purpose, the use of masks, hand washing, social distancing, and isolation of infected individuals are essential. However, quarantine of the infected individuals increases the risk of household transmission. Therefore, the reduction of household transmission also is of vital importance for the COVID-19 pandemic. Lack of SARS-CoV-2 transmission in all of the patients with different clinical diagnoses receiving a monoclonal antibody despite the presence of SARS-CoV-2 PCR (+) individual(s) in the same house suggests that injections of monoclonal antibodies like omalizumab and mepolizumab may have a protective function against SARS-CoV-2 transmission in these patients due to their some antiviral effects.

Omalizumab is a monoclonal antibody used for the treatment of antihistamine-refractory chronic urticaria and for treatment of severe asthma in atopic individuals with sensitivity to perennial allergens (8, 9). Mepolizumab, however, is an anti-IL-5 monoclonal antibody approved to be used for the treatment of eosinophilic severe asthma (10). In addition to their currently defined effects, both treatment agents have been shown to have some antiviral effects. Although The Centers for Disease Control and Prevention (CDC) defines the patients with severe asthma as a risk group for COVID-19 infection, previous studies have revealed that the prevalence of patients with asthma among patients hospitalized due to COVID-19 is lower compared to the normal population and that prevalence of asthma is relatively lower among the patients who died of COVID-19. Despite the presence of some contrary studies (11-13), patients with asthma are therefore considered not to be at high risk for SARS-CoV-2 infection (14). As the most important reasons for this situation, reduction of expression of ACE2 (angiotensin-converting enzyme 2) on the respiratory epithelial surface by inhaled steroids used for the treatment of asthma and immunomodulatory effects of the monoclonal antibodies used for treatment have been proposed (15). Gill et al. (16) reported that omalizumab exhibits an antiviral effect by down-regulating high-affinity IgE receptors on the surface of plasmacytoid dendritic cells and by reducing viral antigen presentation by dendritic cells. In addition, omalizumab enhances the interferon-mediated antiviral effectiveness of dendritic cells. In another study, Cardet et al. (17) demonstrated that omalizumab reduces TLR (Toll-like receptor)-7 expression, inhibiting triggering of natural immunity against viral antigens. There also are studies reporting that omalizumab may lead to an increase in levels of immunoglobulins other than IgE and that this situation may be beneficial for immune reconstruction in immunodeficient patients (18). Mepolizumab, however, has been shown to influence the innate and adaptive immune systems via eosinophils (19). Eosinophils also function as antigen-presenting cells in the respiratory tract, and processing and then the presentation of viral antigens by eosinophils leads to the secretion of various eosinophil-mediated cytokines and chemokines, stimulation of CD8+ T cells, and release of nitric oxide (20-22). Furthermore, increased eosinophilic activity and eosinophil-induced cytokines may also cause lung injury. The eosinophil-reducing effect of mepolizumab in tissues and plasma may reduce pulmonary epithelial injury by reducing eosinophil-induced cytokines and chemokines. Oroojalian et al. (23) demonstrated that mepolizumab binds CD147 receptor in respiratory epithelial cells, inhibiting the influx of SARS-CoV-2 virus into the target cell. Sabogal et al. (23) however, showed that mepolizumab increases local B lymphocyte and macrophage counts but reduces neutrophil count and their activation(24)(23)(24). Again, in the same study, mepolizumab was reported to cause an increase in systemic natural killer (NK) (CD3-CD19-CD56+) count, which has an antiviral effectiveness. Furthermore, mepolizumab increases secretory IgA levels and exhibits an antiviral effect also by reducing tryptase levels in the bronchoalveolar lavage fluid. Thusly, these antiviral effects of both omalizumab and mepolizumab may be protective against SARS-CoV-2 transmission and these agents may have prevented SARS-CoV-2 transmission despite the increased risk of household transmission in patients included in our case series who were receiving monoclonal antibody treatment.

CONCLUSION

Household transmission of SARS-CoV-2 is an important route of transmission. Although it is obvious that more extensive studies are needed in order to determine routes of household transmission and to reduce and/or prevent these determining factors, it should be considered that monoclonal antibodies like omalizumab and mepolizumab can make a significant contribution to the prevention of household transmission of SARS-CoV-2 with some antiviral effect and these effects should not be neglected.

ETHICAL DECLARATIONS

Ethics Committee Approval: Ethics committee approval of this study was received from KTO Karatay University Medical School Non-Pharmaceutical and Medical Device Research Ethics Committee (Date: 09/02/2021, Decision No: 2021/021). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

Informed Consent: All patients signed the free and informed consent form.

Referee Evaluation Process: Externally peer-reviewed.
Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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