

COVID-19 in a patient with severe asthma using mepolizumab

Kurtuluş Aksu, M.D., Selma Yesilkaya, M.D., Musa Topel, M.D., Suleyman Turkyilmaz, M.D., Dilek Cuhadar Ercelebi, M.D., Ali Oncul, M.D., Ilkay Koca Kalkan, M.D., and Hale Ates, M.D.

ABSTRACT

Background: There is a lack of information about the course of coronavirus disease 2019 (COVID-19) in patients with severe asthma who were treated with biologics. Some reports indicated that treatment with benralizumab, dupilumab, and omalizumab in patients with severe asthma was not associated with significant adverse effects during COVID-19.

Methods: Asthma itself or the biologic agents used to treat asthma can have a positive effect on the course of COVID-19. There seem not to be any cases that specifically reported the use of mepolizumab in a patient who was infected with COVID.

Results: We reported of a 55-year-old woman with a diagnosis of severe asthma for; 3 years and who was being treated with mepolizumab, with no evidence of loss of asthma control, at the time of contracting COVID-19 and who had been followed up in the allergy clinic. In addition, there are no data on mepolizumab therapy in patients with elevated liver enzyme levels.

Conclusion: With this case, we also reported that no adverse effects were observed during mepolizumab treatment in a patient with elevated liver enzyme levels.

(Allergy Asthma Proc 42:e55–e57, 2021; doi: 10.2500/aap.2021.42.200125)

Although for months, the world has been struggling with the coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), we still do not have clear information about the management of this infection. The rapid spreading of the coronavirus epidemic forced clinicians to make decisions with ambiguous information.¹

In the early stages of the pandemic, we thought that the COVID-19 rate, as well as disease mortality and morbidity, would be higher in patients with the chronic respiratory disease than in the healthy population.^{2–4} However, asthma has not been identified as an important risk factor for COVID-19.^{5,6} These findings support that asthma cannot be considered a risk factor for susceptibility to COVID-19 and that there are unexplained missing links in the pathogenesis. One special population that we do not have any idea about the course of COVID-19 is patients with severe asthma

who are treated with biologics. It was reported that a patient with severe asthma and treated with dupilumab survived COVID-19 without any clinical deterioration.⁷ Different reports also noted that treatment with benralizumab, dupilumab, and omalizumab is not associated with a significant negative impact during active COVID-19 infection in severe asthma.^{8–10} Currently, there are no data available on whether mepolizumab therapy modulates the course of COVID-19 in patients with severe asthma and treated with mepolizumab.

CASE REPORT

A 55-year-old female patient, who was diagnosed with asthma in her thirties, has been followed up in an allergy clinic with a diagnosis of severe asthma for ~3 years. The body mass index of the patient was 28 kg/m². In the spirometric examination, her forced expiratory volume in 1 second (FEV₁) was 440 mL (19% predicted), forced vital capacity was 860 mL (32% predicted), and the FEV₁ to forced vital capacity ratio was 52%. The best FEV₁ detected in her follow-up was 1000 mL (43% predicted). There was no finding in the history of the patient that suggested atopy, and no aeroallergen sensitivity was detected in the allergy tests. Sensitivity to seasonal and perennial aeroallergens, including house-dust mites, animal dander, cockroach, mold spores, and pollens (grass, trees, and weeds), was not detected in the skin-prick test. With the serum specific immunoglobulin E (IgE) measurements, it

From the Division of Immunology and Allergy, Department of Chest Diseases, University of Health Sciences, Atatürk Chest Diseases and Chest Surgery Education and Research Hospital, Ankara, Turkey
No external funding sources reported.

The authors have no conflicts of interest to declare pertaining to this article
Written informed consent was obtained from the patient

Published ahead of print on December 21, 2020

Address correspondence to Kurtuluş Aksu, M.D., Atatürk Göğüs Hastalıkları ve Göğüs Cerrahisi Hastanesi, Göğüs Hastalıkları Anabilim Dalı, Allerji Kliniği, Keçiören, 06280, Ankara, Turkey

E-mail address: kurtulusaksu@yahoo.com

Copyright © 2021, OceanSide Publications, Inc., U.S.A.

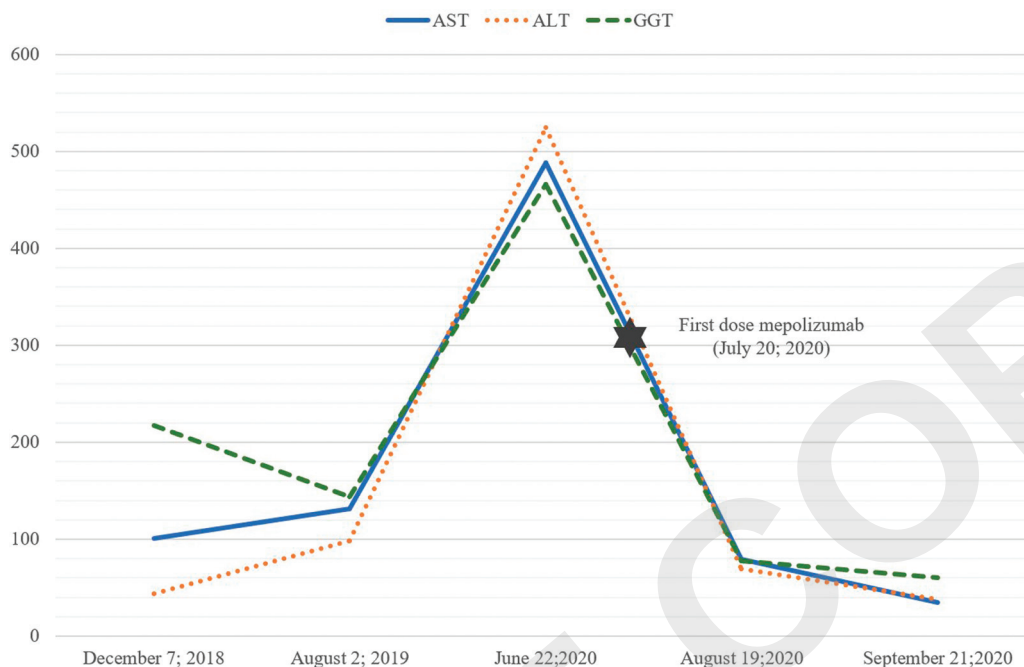


Figure 1. The course of the patient's liver enzyme values. The values are given in IU/L. AST = aspartate aminotransferase; ALT = alanine transaminase; GGT = gamma-glutamyl transferase.

was observed that the patient did not have perennial aero-allergen sensitivity to cockroach, mites, cat and dog epithelium, and molds (deemed sensitive if IgE $\geq$ 0.35 kU/L). The total IgE level was 11.3 IU/mL.

She was regularly using high-dose inhaled corticosteroid and long-acting β -agonist in a combination form of 200 μ g of fluticasone furoate and 25 μ g of vilanterol once daily, inhaled tiotropium, oral theophylline, and oral montelukast. Despite this treatment, the patient had frequent use of systemic corticosteroids and, moreover, had been hospitalized for asthma exacerbation six times in the past year. The patient's Asthma Control Test (ACT) score was 14, and the absolute eosinophil count in her peripheral blood was 540/ μ L. In the biochemical examinations performed in the first evaluation of the patient, alanine transaminase, aspartate aminotransferase, and gamma-glutamyl transferase values were found to be high, whereas bilirubin values were normal (Fig. 1). The enzyme levels remained high during her follow-up. In the examinations performed for the etiology elevated liver enzymes in the patient, no pathology was observed except hepatosteatosis in the abdominal ultrasonography. The autoantibody values of the patient were normal, and hepatitis B virus surface antigen, antibody against hepatitis C virus, and antibody against human immunodeficiency virus evaluations were negative. When considering that mepolizumab treatment would be beneficial for asthma control, the patient consulted with gastroenterology specialist.

On notification by the gastroenterology clinic that mepolizumab could be started with liver enzyme monitoring, the first dose of 100 mg subcutaneous

mepolizumab was administered to the patient on July 20, 2020. After initiation of the mepolizumab treatment, the patient continued the high-dose inhaled corticosteroid and long-acting β -agonist combination, inhaled tiotropium, oral theophylline, and oral montelukast, which she had been using regularly. A significant improvement in the patient's dyspnea and an increase in the ACT score to 21 were observed within the month after the first administration dose. In addition, surprisingly, a decrease in liver enzymes was observed in the follow-up (Fig. 1). The second dose of mepolizumab was administered on August 19, 2020.

In her follow-up, on September 9, 2020, the patient developed weakness, headache, and joint pain. SARS-CoV-2 infection has been confirmed by reverse real-time polymerase chain reaction in the combined nasal-throat swab sample. Favipiravir treatment was initiated and continued for 5 days. During this period, there was no increase in the patient's shortness of breath and no worsening of the ACT score. The treatment of the patient was completed on an outpatient basis without any problems. No additional problem was observed in the follow-up of the patient. The result of a SARS-CoV-2 polymerase chain reaction test checked on September 21, 2020, was negative. Hepatic enzymes were also found to be within normal limits. The third dose of mepolizumab was administered to the patient on September 21, 2020.

DISCUSSION

Herein we present a female patient who had COVID-19 while receiving mepolizumab treatment for

underlying severe asthma. The fact that COVID-19 did not progress and the underlying asthma did not worsen in the presented patient suggested that respiratory diseases or the biologic agents used in the treatment of respiratory diseases may have had protective effects on the course of COVID-19. Other cases in the literature that reported a mild course of COVID-19 in patients with severe asthma treated with biologic drugs strengthen the possibility of the existence of mechanisms that we do not yet know that asthma or drugs used in asthma positively affect the course of COVID-19.^{7–10} In addition, according to the latest reports, favipiravir is encouraging, with a small but significant improvement in clinical recovery time in patients with COVID-19 who are symptomatic and have mild-to-moderate disease. In the presented case, the fact that favipiravir treatment was initiated as soon as COVID-19 was diagnosed may have contributed to the reduction of the duration of mild disease.¹¹ Until the results of randomized controlled studies conducted on the effect of antiviral agents on the course of COVID-19 are available, it does not seem possible to know the accuracy of these assumptions.

Another point of interest is the course of the patient's liver enzymes during treatment with mepolizumab. Although the reduction in liver enzyme levels began before mepolizumab was given, her liver enzymes were still significantly elevated when mepolizumab treatment was initiated. This was concerning because there were no data about the use of mepolizumab in patients with elevated liver enzymes. As far as we know, this was the first case that reported mepolizumab treatment initiated in a patient with elevated liver enzymes. The patient did not have any problems. Moreover, after mepolizumab treatment, her liver enzyme levels returned to normal without any additional treatment and did not increase again in the follow-up. However, no specific reason that explains the decrease in liver enzymes has been determined. The patient, in the meantime, did not experience any changes in body mass index or a new clinical condition. Achieving asthma control and preventing exacerbations with mepolizumab treatment may have restored liver enzyme elevation in the patient by improving the oxygenation of the patient or preventing the adverse effects of drugs used during asthma exacerbations. The main weakness of the report is that the measurements were not compared between the presented patient with asthma and controls.

CONCLUSION

The presented report described a woman with asthma and with elevated liver enzyme levels who benefited from mepolizumab. This patient with severe asthma on mepolizumab treatment developed COVID-19 and did well. Possible factors such as a mild course of COVID-19 in patients with asthma or a positive effect of mepolizumab on the course of COVID-19 can only be clarified by increasing our knowledge of COVID-19 in patients with asthma. Additional reports on the safe use of mepolizumab in patients with high liver enzyme levels, as in the presented case report, will increase our treatment options in this asthma population.

REFERENCES

1. Bellanti JA. The role of the allergist/immunologist in the COVID-19 pandemic: a Janus-faced presentation. *Allergy Asthma Proc.* 2020; 41:397–412.
2. Halpin DMG, Faner R, Sibila O, et al. Do chronic respiratory diseases or their treatment affect the risk of SARS-CoV-2 infection? *Lancet Respir Med.* 2020; 8:436–438.
3. Novel Coronavirus Pneumonia Emergency Response Epidemiology Team. Vital surveillances: the epidemiological characteristics of an outbreak of 2019 novel coronavirus diseases (COVID-19) — China, 2020. *China CDC Weekly.* Available online at <http://weekly.chinacdc.cn/en/article/doi/10.46234/ccdcw2020.032>; accessed May 17, 2020.
4. Joshi AY, Mullakary RM, Iyer VN. Successful treatment of coronavirus disease 2019 in a patient with asthma. *Allergy Asthma Proc.* 2020; 41:296–300.
5. Li X, Xu S, Yu M, et al. Risk factors for severity and mortality in adult COVID-19 in patients in Wuhan. *J Allergy Clin Immunol.* 2020; 146:110–118.
6. Caminati M, Lombardi C, Micheletto C, et al. Asthmatic patients in COVID-19 outbreak: few cases despite many cases. *J Allergy Clin Immunol.* 2020; 146:541–542.
7. Förster-Ruhrmann U, Szczepek AJ, Bachert C, et al. COVID-19 in a patient with severe chronic rhinosinusitis with nasal polyps during therapy with dupilumab. *J Allergy Clin Immunol.* 2020; 146:218–220.e2.
8. Lommatzsch M, Stoll P, Virchow JC. COVID-19 in a patient with severe asthma treated with omalizumab. *Allergy.* 2020; 75:2705–2708.
9. García-Moguel I, Díaz Campos R, Alonso Charterina S, et al. COVID-19, severe asthma, and biologics. *Ann Allergy Asthma Immunol.* 2020; 125:357–359.e1.
10. Bhalla A, Mukherjee M, Radford K, et al. Dupilumab, severe asthma airway responses, and SARS-CoV-2 serology. *Allergy.* 2020 Aug 6:10.1111/all.14534.
11. Agrawal U, Raju R, Udwadia ZF. Favipiravir: a new and emerging antiviral option in COVID-19. *Med J Armed Forces India.* 2020; 76:370–376. □

Copyright of Allergy & Asthma Proceedings is the property of OceanSide Publications Inc. and its content may not be copied or emailed to multiple sites or posted to a listserv without the copyright holder's express written permission. However, users may print, download, or email articles for individual use.