Mepolizumab as a Potential Protective Factor of COVID-19 Mortality: A Case Report of Chronic Bronchitis and Asthma in an Elderly Patient

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Patient: Male, 75-year-old
Final Diagnosis: COVID-19 pneumonia
Symptoms: Chills • cough • dyspnea • fever
Medication: —
Clinical Procedure: —
Specialty: Infectious Diseases • Microbiology and Virology • Pharmacology and Pharmacy

Objective: Unusual clinical course
Background: Patients with multiple comorbidities who are infected with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) have a higher risk of mortality. However, treatment with mepolizumab may be a key factor in counteracting the risk of these comorbidities. We present a patient who had an uneventful recovery from coronavirus disease 2019 (COVID-19), despite having 5 independent risk factors for severe disease and increased mortality.

Case Report: A 75-year-old man with a long-standing history of asthma, chronic bronchitis, coronary artery disease, and hypertension presented to the Emergency Department in November 2020 with a 4-day history of fever, chills, shortness of breath, cough, and fatigue. Six months prior to this presentation, the patient was hospitalized for severe chronic bronchitis and acute exacerbation of asthma. His medications included mepolizumab, aclidinium, ramipril, diltiazem, aspirin, albuterol sulfate, and micronized budesonide/micronized formoterol fumarate dihydrate. Physical examination was unremarkable, except for cardiopulmonary distress. Laboratory tests showed leucocytosis. His chest X-ray revealed infiltrates and interstitial edema in the lower lung fields. A PCR test for SARS-CoV-2 was positive. COVID-19 pneumonia was diagnosed, and the patient was admitted to the hospital, where he was treated with atecaminophen, amoxicillin, dexamethasone, and supplemental oxygen. The patient remained stable and was discharged from the hospital the following day. He was free of all symptoms after 21 days.

Conclusions: This case of a 75-year-old man who presented with mild COVID-19 supports the findings from other reports of improvement in clinical outcomes for some patients with asthma who received treatment with mepolizumab.

Keywords: Asthma • Bronchitis, Chronic • COVID-19 • IL5 Protein, Human • Mepolizumab • SARS-CoV-2

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Background

The risk of mortality in patients infected with severe acute respiratory syndrome coronavirus-2 (SARS-CoV-2) increases several-fold for those with multiple comorbidities [1]. Some of these comorbidities include chronic bronchitis [2], hypertension [3], and coronary artery disease [4]. However, the risk of mortality due to SARS-CoV-2 is unclear in patients with asthma [5]. Some studies have shown an increased risk [6], whereas others have shown a decreased risk [7]. Moreover, a meta-analysis of 150 studies conducted worldwide did not show conclusive evidence of increased risk for coronavirus disease 2019 (COVID-19) diagnosis, hospitalization, or mortality in patients with asthma [8]. One possible explanation for this unclear evidence is the lack of information regarding medications used by patients [8]. Nevertheless, the decreased risk of mortality observed among asthma patients could be due to treatment with biologics, such as mepolizumab [9].

This report is of a 75-year-old man with several comorbidities, including asthma, chronic bronchitis, hypertension, and coronary artery disease, who was hospitalized for mild COVID-19. The patient had an uneventful recovery despite having these independent risk factors for severe disease and mortality for COVID-19. He was receiving mepolizumab before being infected with SARS-CoV-2. Mepolizumab, which is a humanized anti-interleukin-5 (anti-IL-5) monoclonal antibody, reduces the production and survival of eosinophils and is approved for the treatment of asthma [10,11].

Case Report

A 75-year-old man with a long-standing history of chronic bronchitis, asthma, coronary artery disease, and hypertension presented to the Emergency Department (ED) in a hospital in Vancouver, Canada, in November 2020, with a 4-day history of fever, chills, cough, fatigue, and shortness of breath at rest. Prior to experiencing these symptoms, the patient was moderately active, and his asthma, chronic bronchitis, and coronary artery disease were well controlled. Over the 4-day period, his symptoms became progressively worse, and he was taken to the hospital. Of significance, he was hospitalized 6 months prior to this presentation for severe chronic bronchitis and acute exacerbation of asthma. In addition, he was hospitalized in 2015 for coronary artery disease. The comorbidities were well controlled with medications, and asthma exacerbations were limited to no more than 1 to 2 times per year. He did not smoke cigarettes or drink alcohol. His medications include mepolizumab subcutaneously every 4 weeks, a humanized anti-interleukin-5 (anti-IL-5) monoclonal antibody that reduces the production and survival of eosinophils and is approved for the treatment of asthma [10], aclidinium 400 mcg twice daily, ramipril 10 mg once daily, diltiazem 180 mg once daily, aspirin 81 mg once daily, albuterol sulfate 2 puffs 4 times daily, as needed, and micronized budesonide/micronized formoterol fumarate dihydrate 3 puffs 2 times daily, as needed. Moreover, he was unvaccinated for COVID-19, as the vaccine was unavailable at the time. On arrival at the ED, his vital signs were as follows: blood pressure of 143/100 mm Hg; pulse rate of 115 beats/min; respiratory rate of 20 breaths/min; oxygen saturation of 94% on ambient air; and temperature of 37.8°C. His physical examination was unremarkable, except for cardiopulmonary distress. His body mass index was 24.9 kg/m². A chest X-ray showed infiltrates and was suggestive of interstitial edema in the lower lung fields. In addition, there were increased perihilar vascular markings. Spirometry testing revealed severe obstructive lung disease (FEV₁ 1.25 L [41% predicted]; FVC 3.05 L [79% predicted]; FEV₁/FVC ratio [41% predicted]). Venous blood gas showed the following results: pH of 7.36, pCO₂ of 41 mm Hg, and bicarbonate of 22 mmol/L. An electrocardiogram (ECG) showed sinus tachycardia, with no other abnormalities. The following laboratory values were significant: leukocyte count of 1.89×10⁹ cells/L, monocyte count of 8.1×10⁸ cells/L, immature granulocyte count of 1.1×10⁹ cells/L, and increased band neutrophils. The eosinophil count was <1×10⁴ cells/L. A PCR test (British Columbia Center for Disease Control Laboratory Designed Test-ABI Platform) for SARS-CoV-2 was positive, and COVID-19 pneumonia was subsequently diagnosed. He was admitted to the hospital, where he was treated with acetaminophen 1000 mg 4 times daily, as needed, amoxicillin 500 mg 3 times daily, as needed, dexamethasone 4 mg once daily, and supplemental oxygen via a nasal cannula. A blood culture for bacteremia was negative. His vital signs stabilized overnight, and he was discharged from the hospital the following day, with amoxicillin and dexamethasone prescribed for 10 days. He and his close contacts were placed in quarantine for 14 days. The patient recovered without any events and was free of all symptoms after 21 days from the time of discharge.

Discussion

We present a case of an elderly, male patient who had 5 independent risk factors for increased COVID-19 mortality [4]. The patient had been receiving mepolizumab treatment for asthma before he was infected with SARS-CoV-2. Of particular significance, his case of COVID-19 pneumonia was mild, which suggested that the mepolizumab may have had protective effects on the course of his COVID-19 pneumonia [8]. This patient was diagnosed with COVID-19 in the early phase of the global pandemic [12], when the disease was still relatively unknown and there were no available recommended antivirals [13], no readily available anti-SARS-CoV-2 monoclonal antibodies [14], no approved COVID-19 vaccines [15], and no established therapeutic management guidelines for COVID-19. At first glance, it
may seem counterintuitive that this patient presented with a mild form of COVID-19 pneumonia even though he had several risk factors that increased his likelihood of developing severe disease, intensive care unit (ICU) hospitalization, and mortality [16]. These risk factors included chronic bronchitis [4], hypertension [3], coronary artery disease [4], male sex [17], and older age [18]. Moreover, this patient was at increased risk of ICU admission and death from COVID-19 because of his recent hospitalization for severe asthma [19].

In their meta-analysis, Parohan et al showed that the pooled risk of mortality for COVID-19 infection for the following independent risk factors was 2.7 for hypertension, 3.7 for cardiovascular disease, 3.5 for chronic obstructive pulmonary disease, 4.5 for age >65 years, and 1.5 for male sex [20]. Interestingly, a nationwide analysis by Guan et al revealed that the hazard ratio of mortality for COVID-19 infection was 2.6 for patients with 2 or more comorbidities when compared with patients without any comorbidities [21]. Thus, we believe that our patient's risk of mortality would have been increased several-fold, given this combination of 5 independent risk factors, all of which have an individual hazard ratio of greater than 1.5 [3]. Moreover, recent evidence revealed that the risk of death is 1113 times higher in a patient infected with SARS-CoV-2 who has 2 of 9 combined comorbidities [22].

However, on closer examination, our patient was receiving medications that may have altered his clinical outcome. The use of corticosteroids [23] and calcium channel blockers [24] in our patient may have produced some beneficial effects. In the RECOVERY trial, it was found that dexamethasone reduced COVID-19 mortality by 2.8% when compared with usual care (age-adjusted rate ratio, 0.83; 95% confidence interval [0.75-0.93]; P<0.001) [25]. Furthermore, the use of angiotensin-converting enzyme (ACE) inhibitors or angiotensin receptor blockers in this patient was most likely of no consequence regarding COVID-19 mortality. ACE inhibitors were thought to be a risk factor for patients with COVID-19 because of their potential to increase ACE-2, the primary SARS-CoV-2 receptor, but the literature does not support such a claim [26-28]. One good candidate that may have affected the disease severity and mortality is mepolizumab, a biologic agent that inhibits IL-5 [11], but its contribution to reducing disease severity and mortality in COVID-19 patients is still unclear.

Mepolizumab, which is a humanized monoclonal antibody indicated for treating refractory eosinophilic asthma, has been suggested to reduce the severity of illness and mortality associated with COVID-19 in patients with asthma [9]. Our case corroborates with evidence from other recent reports of patients with severe asthma who required hospitalization for COVID-19 and showed improvement in clinical outcomes after treatment with mepolizumab [29,30]. In addition, pre-clinical studies provided experimental evidence that eosinophils have potential antiviral activity [31]. However, whether the acquired eosinopenia associated with COVID-19 [32] directly contributed to the disease course has yet to be determined. Furthermore, despite this patient's severe exacerbation of asthma as a result of COVID-19, his eosinophil levels remained within normal ranges, and he was discharged less than 24 h after hospital admission.

It has been hypothesized that SARS-CoV-2 infection activates eosinophils, which then migrate to the lungs and in turn are lysed [33]. This lysis causes phagocyte recruitment, and this process may trigger hyperinflammation and a cytokine storm [34]. However, our patient's eosinophil count was normal, most likely due to suppression by mepolizumab [9]. Thus, we believe that this may have been a contributory mechanism to preventing hyperinflammation and the cytokine storm usually observed in severe cases of COVID-19 [29].

Similar to our patient, several cases have been reported of patients with a history of uncontrolled asthma who had been receiving mepolizumab before SARS-CoV-2 infection [29,35]. Aksu et al reported a case of a 55-year-old woman who had been hospitalized several times because of severe asthma but who recovered well despite COVID-19 [29]. Additionally, a 61-year-old man with hypertension and a 20-year history of eosinophilic asthma who was receiving monthly injection of mepolizumab contracted COVID-19 and recovered without complications [35]. However, unlike our patient, the patients in both of these reported cases [29,35] were treated with favipiravir, an antiviral which has been shown to improve clinical outcomes in COVID-19 patients [36].

Although mepolizumab is not recommended during the early period of SARS-CoV-2 infection when the virus is replicating and there is limited inflammation [34], our patient had already been receiving treatment with mepolizumab before he was infected with SARS-CoV-2. Moreover, SARS-CoV-2 is not more common in asthma patients treated with biologics such as mepolizumab, nor does mepolizumab seem to be associated with adverse outcomes in patients with severe asthma [37]. The association between lung eosinophils and SARS-CoV-2, particularly regarding the role of IL-5 antagonists in providing therapeutic benefits, needs to be investigated further.

Conclusions

This case of a 75-year-old man with several comorbidities who presented with mild COVID-19 supports the findings from other reports of improvement in clinical outcomes for some patients with asthma who received treatment with mepolizumab. In addition, the beneficial role of dexamethasone in recovery of this patient needs to be considered.
References:

1. Kompaniyets L, Pennington AF, Goodman AB, et al. Underlying medical conditions and severe illness among 540,667 adults hospitalized with COVID-19, March 2020–March 2021. Prev Chronic Dis. 2021;18:210123

2. Chen D, Zhang S, Feng Y, et al. Decreased eosinophil counts and elevated lactate dehydrogenase predict severe COVID-19 in patients with underlying chronic airway diseases. Postgrad Med J. 2021 [Online ahead of print]

3. Chen J, Liu Y, Qin J, et al. Hypertension as an independent risk factor for severity and mortality in patients with COVID-19: A retrospective study. Postgrad Med J. 2022;98(1161):515-22

4. Gu T, Chu Q, Yu Z, et al. History of coronary heart disease increased the mortality rate of patients with COVID-19: a nested case-control study. BMJ Open. 2020;10(9):e038976

5. Hartmann-Boyece J, Gunnell J, Drake J, et al. Asthma and COVID-19: Review of evidence on risks and management considerations. BMJ Evid-Based Med. 2021;26(4):195

6. Choi YJ, Park JY, Lee HS, et al. Effect of asthma and asthma medication on the prognosis of patients with COVID-19. Eur Respir J. 2021;57(3):2002226

7. Ferastaroaru D, Hudes G, Jerschow E, et al. Eosinophilia in asthma patients is protective against severe COVID-19 illness. J Allergy Clin Immunol. 2021;9(3):1152-62.e3

8. Terry PD, Eric Heidel R, Dhand R. Asthma in adult patients with COVID-19. Prevalence and risk of severe disease. Am J Respir Crit Care Med. 2021;203(7):893-905

9. Adir Y, Humbert M, Saliba W. COVID-19 risk and outcomes in adult asthmatiic patients treated with biologics or systemic corticosteroids: Nationwide real-world evidence. J Allergy Clin Immunol. 2021;148(2):361-67.e13

10. Keating G. Mepolizumab: First global approval. Drugs. 2015;75(18):2163-69

11. Ferastraoaru D, Hudes G, Jerschow E, et al. Eosinophilia in asthma patients is protective against severe COVID-19 illness. J Allergy Clin Immunol. 2021;9(3):1152-62.e3

12. Polisena J, Ospina M, Sanni O, et al. Public health measures to reduce the risk of SARS-CoV-2 transmission in Canada during the early days of the COVID-19 pandemic: A scoping review. BMJ Open. 2021;11(3):e046177

13. Stasi C, Fallani S, Voller F, Silvestri C. Treatment for COVID-19: An overview. Eur J Pharmacol. 2020;889:173644

14. Chen P, Nirula A, Heller B, et al. SARS-CoV-2 neutralizing antibody LY-CoV555 in outpatients with COVID-19. N Engl J Med. 2021;384(3):229-37

15. Labm VN. BNT162b2 mRNA COVID-19 vaccine: First approval. Drugs. 2021;81(4):495-501

16. Kim L, Garg S, O’Halloran A, et al. Risk factors for Intensive Care Unit admission and in-hospital mortality among hospitalized adults identified through the US coronavirus disease 2019 (COVID-19)-Associated Hospitalization Surveillance Network (COVID-NET). Clin Infect Dis. 2021;72(9):e206-14

17. Ramos-Rincon JM, Buonaiuto V, Ricci M, et al. Clinical characteristics and risk factors for mortality in very old patients hospitalized with COVID-19 in Spain. J Gerontol Biol Sci Med Sci. 2021;76(3):e28-37

18. O’Driscoll M, Ribiero Dos Santos G, Wang L, et al. Age-specific mortality and immunity patterns of SARS-CoV-2. Nature. 2021;590(7844):140-45

19. Shi T, Pan J, Vasiliev E, et al. Risk of serious COVID-19 outcomes among adults with asthma in Scotland: A national incident cohort study. Lancet Respir Med. 2022;10(4):347-54

20. Parohan M, Yaghoubi S, Seraji A, et al. Risk factors for mortality in patients with Coronavirus disease 2019 (COVID-19) infection: A systematic review and meta-analysis of observational studies. Aging Male. 2020;23(5):1416-24

21. Guan WJ, Liang WH, Zhao Y, et al. Comorbidity and its impact on 1590 patients with COVID-19 in China: A nationwide analysis. Eur Respir J. 2020;55(5):2000547

22. Antos A, Kwong ML, Balmoroz T, et al. Unusually high risks of COVID-19 mortality with age-related comorbidities: An adjusted meta-analysis method to improve the risk assessment of mortality using the comorbid mortality data. Infect Dis Rep. 2021;13(3):700-11

23. Van Paassen J, Vos JS, Hoekstra EM, et al. Corticosteroid use in COVID-19 patients: A systematic review and meta-analysis on clinical outcomes. Crit Care. 2020;24(1):696

24. Crespi B, Alcock J. Conflicts over calcium and the treatment of COVID-19. Evol Med Public Health. 2021;149-56

25. Horby P, Lim WS, Emberson JR, et al. Dexamethasone in hospitalized patients with COVID-19. N Engl J Med. 2021;384:693-704

26. Najafi N, Davoudi A, Izadyar H, et al. The effect of ACE inhibitors and ARBs on outcomes in hospitalized patients with COVID-19. Ir J Med Sci. 2022 [Online ahead of print]

27. Sharma R, Kumar A, Majed J, et al. Drugs acting on the renin-angiotensin-aldosterone system (RAAS) and deaths of COVID-19 patients: A systematic review and meta-analysis of observational studies. Egypt Heart J. 2022;74:64

28. Aksu K, Yesilka S, Topel M, et al. COVID-19 in a patient with severe asthma using mepolizumab. Allergy Asthma Proc. 2021;42(2):55-57

29. Atayáik E, Aytekin G. First SARS-CoV-2 infection in patients with severe asthma patients treated with mepolizumab. Respir Case Rep. 2021;10(2):73-77

30. Liu J, Chen J, Wang J, et al. Eosinophilic asthma: A single center real life experience. Tuberk Toraks. 2022;70(3):231-41

31. Lindsay AW, Schwartz JT, Rothenberg ME. Mechanisms of allergic diseases: Eosinophil responses during COVID-19 infections and coronavirus vaccination. J Allergy Clin Immunol. 2020;146(1):1-7

32. Tanni F, Akker E, Zaman MM, et al. Eosinopenia and COVID-19. J Am Osteopath Assoc. 2020;120(8):504-8

33. Bohrer AC, Castro E, Tocheny CE, et al. Rapid GPR183-mediated recruitment of eosinophils to the lung after SARS-CoV-2 infection. Cell 2022;70(3):e238-45

34. Corsetti E, Amor P, Pestelli E, et al. Favorable course of COVID-19 in patients using omalizumab for chronic spontaneous urticaria. J Allergy Clin Immunol Pract. 2022;10(10):2588-95