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Use of Monoclonal Antibodies Therapy for Treatment of Mild to Moderate COVID-19 in 4 Patients with Rheumatologic Disorders

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Background: The use of monoclonal antibodies therapy (MAT) in early mild to moderate Coronavirus disease 2019 (COVID-19) has gained importance in recent times. However, there is limited information on the safety and efficacy of MAT in treating COVID-19 in patients with underlying rheumatologic diseases. Patients with rheumatologic diseases are usually on long-term corticosteroids and immunosuppressive therapy, which increases their risk for progressing to more severe forms of COVID-19. We report a case series of 4 patients with rheumatologic diseases who were treated with MAT for COVID-19.





Material/Methods: A retrospective observational study was conducted in our institution on patients with underlying rheumatologic disorders who received MAT as per the EUA protocol of the FDA.

Results: Two of the 4 patients were on immunosuppressive therapy at the time of receiving MAT. They recovered from COVID-19 without any adverse outcomes. No flare of underlying rheumatologic disease was noted.

Conclusions: MAT was observed to be a safe and effective therapy in 4 patients with rheumatological illnesses and COVID-19 treated at our hospital.

Keywords: **Arthritis, Rheumatoid • Casirivimab • Imdevimab • Lupus Erythematosus, Systemic • Psoriasis • Sjogren's Syndrome**

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Background

The COVID-19 pandemic caused by severe acute respiratory distress syndrome coronavirus 2 (SARS-CoV2) was first detected in December 2019, then rapidly spread throughout the world [1]. The virus enters the host's cells via the angiotensin-converting enzyme receptor 2 (ACE-R2) and initiates a T cell response leading to a release of high levels of cytokines [2-6]. Patients infected with SARS-CoV-2 can present with a wide range of symptoms from asymptomatic or mild to severe acute respiratory distress syndrome (ARDS) and multiorgan failure.

SARS-CoV-2 infection in patients with rheumatologic disorders is an area of special interest due to a potential higher risk in these patients to progress to severe forms of the disease considering the chronic immunosuppressive state because of corticosteroids and other medications used to treat their underlying disease [7,8]. Moreover, some reports have suggested that COVID-19 infection can induce disease flares in patients with an established or new-onset rheumatologic disease [9-11]. Reports on the prognosis of COVID-19 infection in patients with rheumatologic disorders have been conflicting. While some studies have shown higher rates of complications, increase of flare rate, or death in this population [12-17], others have suggested that the disease progression and complication rates are similar in patients with underlying rheumatologic diseases compared to the general population [18-24].

The use of MAT including bamlanivimab, casirivimab-imdevimab, and bamlanivimab-etesevimab in the management of mild to moderate COVID-19 in patients with high risk for disease progression due to underlying comorbidities has shown promising results in the outpatient setting [25-27]. As a community hospital serving a low-income neighborhood in the Bronx with a high prevalence of disease comorbidities, we have had a positive experience with the use MAT in several patients who successfully recovered from SARS-CoV-2 infection. The efficacy and safety of these antibodies have not been fully assessed in patients with rheumatologic diseases; therefore, we report the outcome of 4 patients with distinct rheumatologic conditions who were treated with MAT for COVID-19 at our center.

Material and Methods

A retrospective observational study was conducted from November 27, 2020 to March 17, 2021 at BronxCare Health System. The study was approved by the Institutional Review Board (IRB) at BronxCare Health System (IRB # 01 14 21 16).

Adult patients (≥ 18 years of age) diagnosed with mild to moderate COVID-19 based on National Institutes of Health (NIH) guidelines were offered MAT [28,29]. Patients who had

associated rheumatologic test results were included in the study. COVID-19 was diagnosed using the real-time reverse transcriptase polymerase chain reaction (RT-PCR) of SARS-CoV-2 in nasopharyngeal swabs from the study population. The inclusion and exclusion criteria were based on emergency use authorization (EUA) guidelines issued by the Food and Drug Administration (FDA) during the study period for bamlanivimab (700 mg) or casirivimab-imdevimab (1200 mg-1200 mg). Patients were clinically monitored during the drug administration in an ambulatory setting and were observed for at least 1 h after infusion. They were then followed up by phone/telehealth visits until the COVID-19 symptoms resolved. On resolution of symptoms, patients were followed up in ambulatory clinics to evaluate for any adverse events or flare of underlying rheumatological diseases.

Data pertaining to demographics, comorbidities, and medications were abstracted from electronic medical records. All patients were followed up via telehealth or clinic visits.

Results

Case 1: A Patient with Psoriasis

A 41-year-old White woman presented to our outpatient clinic with worsening fatigue, body aches, sore throat, ageusia, and anosmia that started 7 days prior to presentation. She had a positive nasopharyngeal COVID-19 polymerase chain reaction (PCR) test result, which was performed 6 days prior to presentation. Her medical history was significant for well-controlled psoriasis diagnosed at age 28 and managed with topical steroids and emollients. Moreover, she had hypothyroidism, polycystic ovarian syndrome, obesity (body mass index [BMI] 37.6) depression, anxiety, and chronic venous insufficiency. Due to her presentation of symptoms for less than 10 days and risk factor including BMI over 35, she was offered bamlanivimab. She agreed to treatment and tolerated infusion without any complications.

The patient was assessed on days 1, 3 and 10 after infusion. She had a noticeable improvement of symptoms on day 1 with almost complete resolution of myalgia, ageusia, and anosmia by day 10 after treatment. No flare-up of psoriasis was noted after bamlanivimab administration.

Case 2: A Patient with Systemic Lupus Erythematosus

A 63-year-old Hispanic woman presented to our outpatient testing center for a screening nasopharyngeal COVID-19 test prior to an elective upper gastrointestinal endoscopy. She was asymptomatic at the time of testing, but the PCR test was positive. She developed anosmia, ageusia, fatigue, subjective

Table 1. Description of each patient's presenting symptoms, current therapy, follow-up period, and adverse events.

Case	Underlying rheumatological disease	Current Medications	Presenting symptoms	Infusion administered	Adverse events during infusion	Follow-up duration	Adverse events during follow-up period
1	Psoriasis	Levothyroxine Vitamin B12 Ibuprofen	Fatigue, body aches, sore throat, ageusia and anosmia	Bamlanivimab	None	73 days	None
2	Systemic lupus erythematosus	Omeprazole Nifedipine Amlodipine Denosumab Mycophenolate Calcium Vitamin D Duloxetine Losartan Pioglitazone Simvastatin Metformin Pancreatic enzymes	Anosmia, ageusia, fatigue, subjective fever and cough	Bamlanivimab	None	87 days	None
3	Sjogren syndrome and Raynaud disease	Aspirin Metoprolol Olmesartan Vitamin E Magnesium	Anosmia, ageusia, fatigue, subjective fever and cough	Casirivimab-imdevimab	None	111 days	None
4	Psoriatic arthritis	Ixekizumab Dulaglutide Paroxetine Amlodipine Benazepril	Myalgia, subjective fever, cough, sore throat, and anosmia	Casirivimab-imdevimab	None	45 days	None

fever, and cough 1 day after testing. One week after onset of symptoms, she was seen at the outpatient clinic for worsening cough and fatigue.

The patient's medical history included systemic lupus erythematosus (SLE) diagnosed at age 48 when she developed malar rash, arthritis, anemia, leukopenia, and positive antinuclear antibodies (ANA) and anti-double stranded DNA antibody (dsDNA). She was initially treated with hydroxychloroquine, azathioprine, and sulfasalazine. At age 49 she experienced a lupus flare with cutaneous vasculitis, which was treated with mycophenolate and prednisone. At the time of her COVID-19 illness, she was being treated with mycophenolate. In addition, she had a history of hypertension, diabetes type II, osteoporosis, and chronic pancreatitis.

Due to her risk factors, comorbidities, and time-frame of symptoms, she was offered treatment with bamlanivimab. The infusion was uneventful and she tolerated it well. She was assessed on days 2, 3, and 6 after treatment. She had a

progressive improvement of symptoms and resolution of myalgia and subjective fevers as early as day 2 after infusion. On day 3 she reported improvement of her mood and no more feeling of sadness, and by day 6 she had improvement of anosmia and ageusia. There was no evidence of a lupus flare after bamlanivimab infusion.

Case 3: A Patient with Sjogren Syndrome and Raynaud Disease

A 71-year-old Hispanic woman presented to our outpatient clinic with fever, cough, diarrhea, and generalized pain for the past 7 days. She had a positive SARS-CoV-2 PCR test performed 2 days prior to the current presentation. She had a history of Sjogren syndrome diagnosed in 2010 when she presented with sicca symptoms and Raynaud disease. She received conservative symptomatic management for her autoimmune disease. She also had hypertension, obesity, atrial fibrillation treated with ablation, vertigo, dyslipidemia, and multiple past abdominal surgeries for episodes of diverticulitis and peritonitis.

The patient was eligible for monoclonal antibody infusion and she received casirivimab and imdevimab. She tolerated the infusion well. Patient was assessed on days 1 and 4 after treatment and noted to have resolution of fever on day 1. On day 4 after infusion she reported resolution of diarrhea and body aches. She had occasional persistent cough and loss of appetite. She did not experience any exacerbation of her Sjogren syndrome or Raynaud disease symptoms.

Case 4: A Patient with Psoriatic Arthritis

A 65-year-old Hispanic woman presented to our outpatient clinic with worsening myalgia, subjective fever, cough, sore throat, and anosmia for the past 6 days (Table 1). She had a positive SARS-CoV-2 PCR test performed 5 days prior to the current visit. She was diagnosed with psoriatic arthritis in 2000 and initially treated with methotrexate, and then she underwent multiple biologic therapies including etanercept, adalimumab, apremilast, ustekinumab, secukinumab, and certolizumab, but all were withdrawn due to inadequate response or adverse effects. At the time of her COVID-19 illness she had been using ixekizumab for the past 2 months. She had experienced improvement of her psoriatic arthritis on this, and the last dose was administered 9 days prior to presentation. In addition, she had hypertension, diabetes type II, rosacea, aortic stenosis, gastroesophageal reflux disease, multiple strokes, asthma, and fatty liver with advanced fibrosis.

The patient was eligible for anti-COVID-19 monoclonal antibody infusion and she received casirivimab and imdevimab. She tolerated the infusion well, with no adverse effects. She was assessed on days 1 and 7 after treatment and reported improvement of cough on day 1. By day 7, she had partial improvement of anosmia, ageusia, and myalgia. She did not experience any flare of her psoriatic arthritis or skin lesions.

Discussion

The present case series reports our successful experience with use of MAb in the treatment of patients with COVID-19 and underlying rheumatological disorders. Our patients had various rheumatological conditions, including systemic lupus erythematosus, psoriasis, Raynaud disease, Sjogren syndrome, and psoriatic arthritis. At the time of MAT treatment, 2 of our patients were also using concomitant immunosuppressive therapy including topical steroids, mycophenolate, or ixekizumab. All 4 patients tolerated the MAT treatment and had a positive response to the therapy.

While most cases of COVID-19 present with milder flu-like illness, critical cases can rapidly progress to septic shock and multiorgan failure. Proinflammatory cytokines and dysregulated immune response play a central role in this inflammatory

cascade of COVID-19 induced severe infection [30]. Similarly, autoimmune conditions are also characterized by the presence of a dysregulated immune system, leading to inflammatory reactions and end-organ damage [31]. Autoantibody production is another key feature of autoimmune disorders and has been shown to occur in COVID-19 patients. Pascolini and colleagues presented data from 33 consecutive patients with COVID-19 and showed the presence of autoantibodies, including antinuclear antibody, anticytoplasmic neutrophil antibodies, and antiphospholipid antibodies in 45% of these patients [32]. Other studies have also reported similar findings in COVID-19 patients [33,34]. These observations suggest similarities between pathogenic pathways of COVID-19 and autoimmune disorders.

Medications that have been used to treat rheumatological condition have been frequently used in COVID-19. Steroids, a cornerstone therapeutic choice in several rheumatological conditions, were among the earliest drugs to show a survival benefit in patients treated for COVID-19 [35]. Tocilizumab, which is an anti-interleukin-6 receptor monoclonal antibody and is used in the treatment of rheumatoid arthritis, giant cell arteritis, and systemic sclerosis, has been shown to improve outcomes in patients with COVID-19 [34,35]. Despite the similarities in pathogenesis and disease management, COVID-19 infection in patients with underlying autoimmune conditions poses many challenges. An observational multicenter study of 1641 patients with autoimmune system disorders showed significantly higher prevalence of COVID-19 in these patients compared to the general population [14]. This increased prevalence could be attributed to the susceptibility of the immunocompromised patients to infectious agents. Studies have also reported new onset as well as exacerbation of underlying rheumatologic conditions after COVID-19 infection [15,38]. Possible mechanisms that have been attributed to development of autoimmunity after SARS-CoV-2 infection include molecular mimicry due to cross-reacting epitopes, as well as cytotoxicity due to migration of the virus-specific CD 8+ T-cells into the tissues and viral persistence, leading to viral antigen driven immune injury [38]. These concerns further highlight the importance of treating COVID-19 illness, especially early in the illness.

Bamlanivimab plus etesevimeb or casirivimab plus imdevimab are the recombinant MAb that are currently approved by the FDA under emergency use authorization (EUA) [28,29]. This EUA recommends the use of MAT for the treatment of mild to moderate COVID-19 in patients who are at high risk of developing severe infection within 10 days of symptoms onset.

Bamlanivimab targets the receptor-binding domain (RBD) of SARS-CoV-2 S protein. Etesevimeb binds to an overlapping epitope in RBD of S protein, whereas casirivimab and imdevimab bind to non-overlapping epitopes in RBD of SARS-CoV-2 SP protein [25-27]. In this case series, we share our experience of successful treatment

of early, mild COVID-19 illness with COVID-19-specific MAT in patients with underlying rheumatologic conditions and at higher risk for progressing to severe forms of the disease.

Our case series has some limitations. First, we have only presented data on 4 patients, which is a very small sample size. Second, while our case series does report successful outcomes after MAT use in patients with rheumatological conditions, it does not prove the therapy is beneficial, as we did not have a placebo-controlled group. Our study suggests that COVID-19-specific MAT is safe when used in patients with autoimmune

disorders, including those already receiving immunosuppressive agents at the time of MAT. In addition, we have not observed any flares of their disease after monoclonal antibodies infusion.

Conclusions

In our case series of patients with underlying rheumatological conditions, we report successful treatment of COVID-19 with MAT. Further studies are recommended to validate our study findings.

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