Case Report: Cardiovascular Complications of COVID-19 in Patients With Multiple Sclerosis: A Lesson From Our Experience

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ABSTRACT

Background and Aim: COVID-19 is an emerging threat that could affect the cardiovascular system in the setting of a cytokine storm syndrome. This study examines the cardiac injury associated with COVID-19 in patients with Multiple Sclerosis (MS).

Case Presentation: We analyzed 6 cases of MS in association with COVID-19 who underwent cardiac evaluation during their hospitalization. The mean age of our patients was 36.6 years. Two patients had Secondary Progressive MS (SPMS), one patient had Primary Progressive MS (PPMS), and the rest had Relapsing-Remitting MS (RRMS). Our patients were on both immunomodulatory and immunosuppressive Disease-Modifying Therapies (DMTs). None of our patients had a cardiovascular risk factor or developed cardiovascular complications. Their electrocardiogram, echocardiography, and cardiac enzymes were within normal limits.

Results: Their mean length of hospitalization was 11.8 days. After a month of follow-up, all patients returned to their baseline neurological status except the one with PPMS and moderate COVID-19, who experienced 0.5 points increase in her expanded disability status scale score.

Conclusion: Patients with MS might be at risk of developing severe COVID-19 in which cardiac injury is a crucial complication. There are limited data describing myocarditis associated with COVID-19 in patients with MS. However, our cases revealed no evidence of cardiac injury in patients with MS, even under immunosuppressive DMTs.

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1. Introduction

he first cases of COVID-19 were reported in December 2019 in China. Soon, the disease rapidly spread worldwide. While the typical clinical course of COVID-19 is mainly characterized by respiratory tract symptoms, the cardiovascular system might be the immediate target of COVID-19 [1]. Upon infection with COVID-19, a cascade of inflammatory responses results in vasodilation and increased endothelial permeability leading to pulmonary distress. The increased inflammatory response could stress the cardiovascular system, which is considered one of the leading causes of mortality in critically ill patients with COVID-19 [2, 3].

The patients with Multiple Sclerosis (MS) are a group of interest as they might develop severe complications of COVID-19 regarding the autoimmune nature of MS and the effects of Disease-Modifying Therapies (DMTs) [4]. There are limited data on cardiovascular complications associated with COVID-19 among patients with MS, and we aimed to describe six patients with MS and COVID-19 who underwent cardiologic evaluation during their hospitalization.

2. Case Presentation

The first case was a 34-year-old woman with one week history of fever, cough, and dyspnea presented to the emergency department due to exacerbation of her symptoms. Her past medical history was remarkable for Relapse-Remitting MS (RRMS) since 8 years ago, which was well controlled by Interferon (INF) beta-1a (Rebif) subcutaneously injected three times a week. Her last major relapse occurred 2 years ago. Her baseline Expanded Disability Status Scale (EDSS) score was 1. Her initial vital signs on admission were temperature of 38.0°C, RR of 22, HR of 100, blood pressure of 125/75 mm Hg, and 94% saturation. She was also found to have an EDSS score of 2.

Her chest Computed Tomography (CT) showed patchy ground-glass infiltration in the left lung. The patient was tested for COVID-19 Polymerase Chain Reaction (PCR) of a nasopharyngeal swab which came back positive. The patient underwent standard COVID-19 treatment. The Disease-Modifying Treatment (DMT) continued as it was used as adjuvant therapy in COVID-19. The electrocardiogram revealed normal sinus rhythm, and the echocardiography demonstrated the normal left ventricular size and normal left atrial dimension. Left Ventricular Ejection Fraction (LVEF) was estimated to be 65%. No pericardial effusion or valvular dysfunction was detected.

The patient improved over 5 days and was discharged after 8 days while completely returning to her baseline status. Case number 2 was a 45-year-old female with a history of active Secondary Progressive MS (SPMS) for 21 years, admitted to the emergency department with a three-day history of generalized weakness, shortness of breath, and fever. Her medication was notable for fingolimod 0.5 mg daily since two years ago. Her last major relapse occurred 10 months ago with cerebellar signs. Her previous Magnetic Resonance Imaging (MRI) of the brain and spine was performed 3 months before admission, revealing no evidence of disease activity. Her baseline EDSS score was 2.5. On examination, her vital signs showed a temperature of 37.9°C, Repiration Rate (RR) of 20, Heart Rate (HR) of 94, blood pressure of 135/80 mm Hg, and saturation of 96%. The neurological examination was notable for an EDSS score of 3.

Her chest CT showed diffuse ground-glass opacities in both lungs. Blood work was significant for leukocytosis (White Blood Cell (WBC) 11100/ with 5% lymphocyte). COVID-19 PCR detected the virus. The electrocardiogram showed a normal sinus rhythm. Moreover, echocardiography demonstrated normal left ventricular and atrial size. LVEF was estimated to be 55%, and mild Mitral Regurgitation (MR) was detected. There was no evidence of pericardial effusion. Pulmonary Arterial Pressure (PAP) was 15 mm Hg.

The patient underwent standard COVID-19 treatment. Regarding lymphopenia and active infection, fingolimod was discontinued, and the patient was planned to switch to high dose INF beta-1a. The patient's condition improved over 10 days, and was discharged after 14 days. Her follow-up examination was notable for significant recovery within six weeks without rebound of fingolimod cessation.

Case number 3 was a 41-year-old smoker man who presented to the hospital with a 5-day history of progressive dyspnea and cough. His past medical history was remarkable for RRMS since 12 years ago. The patient was on dimethyl fumarate (240 mg twice a day) for 6 years. His last major relapse occurred 3 years ago, and his baseline EDDS score was estimated to be 2. On physical examination, the patient was febrile and tachypneic.

His chest CT and nasopharyngeal swab PCR were compatible with COVID-19. His laboratory findings were significant for leukocytosis (WBC 19700/ with

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10% lymph). The standard treatment for COVID-19 was instituted. The DMT was discontinued, and INF betala was started for the patient. The electrocardiogram showed no abnormality. Echocardiography parameters were all normal, with an EF of 60%.

The patient's condition improved within a week, and he was discharged after 10 days. The patient returned to his baseline neurological status within 5 weeks while on INF beta-1a (subcutaneous injection three times a week).

Case number 4 was a 22-year-old woman with a history of RRMS for 3 years who presented to the hospital with fever and generalized weakness. She was treated with INF beta-1a (CinnoVex: intramuscular injection weekly) since the beginning of the disease without evidence of clinical and para-clinical activity within this period.

On examination, her vital signs were within normal except for low-grade fever and low saturation (90% on room air and 95% by nasal oxygenation). The neurological examination was unremarkable.

Her chest CT showed mild ground-glass opacities in both lungs. Blood work was considerable for leukocytosis (WBC 11500/ with 6% lymph) with elevated Erythrocyte Sedementation Rate (ESR) to 45 mL and C-reactive protein to 38 mg/dL. COVID-19 PCR confirmed the diagnosis. The patient was treated with appropriate treatment and non-invasive oxygenation. Additionally, her DMT continued as usual.

Cardiac evaluation, including electrocardiogram and echocardiography, were within normal. The patient's condition improved over 3 days, and was discharged on day 6. At the patient's request, she underwent a brain MRI which was negative for disease activity. In addition, at one-month follow-up, the patient was neurologically stable.

Case number 5 was a 37-year-old man who presented to the hospital with a 5-day history of severe chills and fever. His past medical history was notable for active SPMS since 13 years ago. He was on rituximab (1 g intravenous every six months) since three years ago, infused 5 months before admission.

On examination, the vital signs revealed a temperature of 38.0°C, RR of 20, HR of 100, blood pressure of 110/75 mm Hg, and saturation of 92%. He was also found to have an EDSS score of 3.5.

His chest CT and laboratory findings were all in favor of COVID-19. The patient was under medical treatment leading to significant recovery over 10 days. Cardiac examination showed normal sinus rhythm, normal left ventricular and atrial size without evidence of valvular dysfunction or pericardial effusion. LVEF and PAP were found to be 55% and 12 mm Hg, respectively. The patient was discharged after 14 days while he was completely back to his baseline.

Case number 6 was a 41-year-old woman with 7 years history of Primary Progressive MS (PPMS) who presented to the emergency department following upper respiratory symptoms. Her medical history was notable for ocrelizumab (600 mg intravenous every 6 months), infused three months before admission.

On examination, she was febrile with low saturation (88% on room air and 92% by nasal oxygenation). The EDSS score was estimated to be 4, which was 0.5 points higher than her baseline EDSS.

Her chest CT revealed diffuse ground-glass opacity in her left lung. The laboratory examination was notable for leukocytosis (WBC 14600/ with 7% lymph). The patient underwent non-invasive oxygenation and standard treatment for COVID-19. The cardiac evaluation was normal. The patient did not develop cardiac complications within hospitalization and was discharged on day 19 with an EDSS of 4. She gradually returned to her baseline status after a month.

3. Discussion

We reported six cases of MS in association with CO-VID-19, who underwent cardiac evaluation during their hospitalization. The mean age of our patients was 36.6 years. Two patients had SPMS, one patient PPMS, and three patients RRMS. The mean course of the disease was estimated to be 10.6 years. Our patients were on both immunomodulatory and immunosuppressive DMTs. The DMTs were discontinued due to lymphopenia and active infection. None of our patients had a cardiovascular risk factor or developed cardiovascular complications during hospitalization. Five patients had mild COVID-19. The one with moderate COVID-19 did not need invasive oxygenation. The mean length of the hospitalization was 11.8 days. After a month of followup, all patients returned to their baseline neurological status except one with PPMS and moderate COVID-19, who developed a 0.5 point progression of EDSS score.

Since the first case report of cardiac manifestation of COVID-19 [5], much has been learned about different cardiac manifestations of COVID-19, including myo-

cardial injury, myocarditis, acute myocardial infarction, heart failure, dysrhythmias, and venous thromboembolic events [2]. It was recognized early during the outbreak of COVID-19 that more than 20% of patients with CO-VID-19 had some degrees of cardiac injury, which was mainly evident in patients with hypertension. Moreover, observational data have shown that myocardial injury is a strong independent predictor of adverse outcomes [6]. The primary mechanism of cardiac injury is assumed to be a cytokine storm leading to leukocyte adhesion to endothelial cells overlying pre-existing atheroma, further contributing to plaque disruption and acute cardiac injury. The systemic inflammation could also increase vascular stress at the level of the coronary arteries resulting in myocardial infarction. Other contributing factors are poorly understood, including pro-thrombotic inflammatory sequelae from viral infections and global ischemia related to multi-organ failure, respiratory distress, and associated hemodynamic and metabolic abnormalities [7-9].

On the other hand, patients with MS are a group of interest among clinicians as they are at higher risk for developing complications of COVID-19, as both the autoimmune nature of the disease and immunosuppressive DMTs increase the risk of infection. More importantly, some DMTs may have implications on the future of the SARS-CoV-2 vaccine [10, 11]. However, the published data highlighted the benign course of COVID-19 among patients with MS, which was consistent with the general population. Notably, there are limited data on cardiac injury associated with COVID-19 in patients with MS. Trpkov et al. first reported a 62-year-old woman with PPMS who developed acute myocarditis associated with COVID-19 in the setting of a cytokine storm syndrome and ST-elevation myocardial infarction with LVEF of 24%. The patient was treated with a recombinant interleukin-1 receptor antagonist leading to marked clinical and para-clinical improvement [12]. Similarly, Erika Faircloth et al. reported a 60-year-old man with MS who developed acute myocarditis associated with CO-VID-19. Treatment with norepinephrine, vasopressin, dobutamine, broad-spectrum antibiotics, methylprednisolone, heparin, furosemide, and tocilizumab resulted in his clinical improvement [13].

A unique aspect of our work is the para-clinical assessment to screen the cardiac injury in the course of CO-VID-19. Similar to previous reports, our patients had a benign course of COVID-19, and no cardiac complications occurred during hospitalization. Given the increasing cases of COVID-19 worldwide, understanding the cardiovascular manifestations of COVID-19 in patients with MS, a group of particular attention, is a crucial concern. Although our data cannot preclude cardiac complications of COVID-19 in patients with MS, it suggests less concern in approaching these patients.

4. Conclusion

While patients with MS seem to be at higher risk of developing a severe form of COVID-19, which might be complicated with cardiac injury, our case reports did not reveal a higher incidence of cardiovascular complications in patients with MS, even in those under immunosuppressive DMTs.

Ethical Considerations

Compliance with ethical guidelines

All ethical principles are considered in this article. The participants were informed about the purpose of the research and its implementation stages. They were also assured about the confidentiality of their information. They were free to leave the study whenever they wished, and if desired, the research results would be available to them.

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Authors' contributions

All authors equally contributed to preparing this article.

Conflict of interest

The authors declared no conflict of interest.

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