Case Report

Eosinophilic granulomatosis with polyangiitis after COVID-19: A case report

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\textbf{ABSTRACT}

COVID-19 can damage the endothelial cells of every organ in the body and lead to vasculopathy and vasculitis. It has been shown that various types of vasculitis could be a new manifestation of COVID-19. Eosinophilic granulomatosis with polyangiitis (EGPA) is a rare systemic necrotizing vasculitis that affects small vessels. Here we report our experience with a 42-year-old man with a 3-weeks history of fever of unknown origin after two months from COVID-19 recovery presented with loss of appetite, loss of weight, and paresthesia in his lower extremities. After required evaluations including nerve biopsy, EGPA was diagnosed for him.

1. Introduction

Since December 2019, severe acute respiratory syndrome—coronavirus 2 (SARS-CoV 2) which leads to coronavirus disease (COVID-19) has spread throughout the world and has caused many deaths in all countries. Symptoms like fever, dyspnea, cough, malaise, myalgia and arthralgia, anosmia, and ageusia are common in COVID-19 [1–3]. SARS-CoV-2 enters the cells through angiotensin-converting enzyme 2 (ACE2) receptors which are expressed on the smooth muscles of the arterial and venous walls in every organ of the body and explain the possibility of multisystem involvement in COVID-19 [4]. SARS-CoV-2 proteins displayed similarities with the human protein on a comparative peptidome analysis and can destroy self-peptides tolerance, and lead to autoimmunity [5]. Some of the autoimmune disorders such as kawasaki disease and Guillain-Barré syndrome (GBS) have been described as a consequence of post-COVID-19 autoimmune complications [6,7].

EGPA or Churg-Strauss syndrome is an antineutrophil cytoplasmic antibody (ANCA)-associated (AAV) small-vessel vasculitis. Microscopic polyangiitis and granulomatosis with polyangiitis are other forms of AAV. EGPA has 3 phases: a prodromic phase including asthma and rhino-sinusitis, an eosinophilic phase characterized by peripheral eosinophilia and organ involvement, and a vasculitic phase with clinical presentations of small-vessel vasculitis [8]. COVID-19 can mimic the symptoms of EGPA and vice versa. Here, we report a 42-year-old man who presented with a fever of unknown origin (FUO) after COVID-19 recovery, and EGPA was diagnosed after evaluations.
2. Case presentation

A 42-year-old man with a 3-weeks history of FUO, loss of appetite extremities, loss of weight, weakness, and paresthesia in his lower. He had no complaints of vertigo, headache, or gastrointestinal and respiratory symptoms. He also said that he had purple palpable papules on both his legs which disappeared before the time of examination. He had a recent history of sinusitis. He had no history of drug consumption, infectious diseases, malignancies, and rheumatologic diseases except he recovered from mild COVID-19, two months ago. He did not receive medication or oxygen for Covid-19. We did a complete examination of the patient and no finding was detected. Hematology, serology and biochemistry tests were performed and these abnormal findings were detected: white blood count (WBC) = $14.8 \times 10^3/mm^3$ (Normal = $4.5-11.0 \times 10^3/mm^3$), Hemoglobin (HB) = 10.2 g/dL (Normal = 13.2–16.6 g/dL), Hematocrit = 32.6% (Normal = 38.3–48.6), mean corpuscular volume (MCV) = 73.3 fl (Normal = 80–100 fl), Platelet (Plt) = 484 $\times 10^3/mm^3$ ($140–400 \times 10^3/mm^3$), sedimentation rate (ESR) = 38 mm/hr (Normal = 1–13 mm/hr), C-reactive protein (CRP) = 98 mg/L (Normal = Less than 10 mg/L), Albumin = 2.5 g/dL (Normal = 3.4–5.4 g/dL). Liver function tests were normal. Hepatitis B surface antigen and antibody (HBsAg/HBsAb), Hepatitis B core antibody (HbcAb), HIV antibody, Wright, and 2ME wright were negative. Due to lower limb weakness and normal CPK (47 U/L), EMG/NCS was performed for the patient, which was diagnosed with mononeuritis multiplex based on the results of the sural nerve biopsy and EMG/NCS. Then, according to the pattern of mononeuritis multiplex and the history of sinusitis, and suspicion of vasculitis, Anti-Myeloperoxidase antibody (Anti-MPO) or P-ANCA), Rheumatoid factor (RF) was performed. The finding indicated that positive results for Anti-MPO = 8.5 IU/ml (Normal = Less than 0.5 IU/ml) and RF = 64 IU/ml (Normal = 0–20 IU/ml). Also, a nerve biopsy was performed which showed vasculitis. According to the results of nerve biopsy, mononeuritis multiplex, positive Anti-MPO, and history of sinusitis, the patient was diagnosed with EPGA, and methylprednisolone, and Rituximab, were prescribed for him. Then the patient was discharged in good condition. During the patient’s follow-up, the patient’s paresthesia and mononeuritis multiplex completely improved.

3. Discussion

The classic definition of FUO to was stated by Petersdorf and Beeson: “fever higher than 38.3 °C (100.9 °F) on several occasions, persisting without a diagnosis for at least 3 weeks despite at least 1 week’s investigation in hospital” [9]. There are 5 underlined etiologies of FUO: infection, neoplasia, (such as rheumatologic or connective tissue diseases), miscellaneous diseases, and an undiagnosed illness. Our patient had 3 weeks of fever, so we performed the required evaluations and ruled out infectious diseases and malignancies. According to the mononeuritis multiplex, skin lesions, sinuses imaging findings, leukocytoclastic vasculitis in the nerve biopsy, RF, and P-ANCA positive results, we considered rheumatologic diseases, EPGA, for the patient.

Endothelial cells’ function is a key point to regulate inflammatory processes including cell adhesion, and coagulation through anti-inflammatory and anti-coagulation factors such as nitric oxide (NO), prostacyclin (PGI2), endothelin, tissue plasminogen activator (tPA), intercellular adhesion molecule (ICAM)-1, etc. SARS-CoV-2 entry within the vascular endothelial cell leads to cellular apoptosis and a decrease in the anti-thrombotic and anti-inflammatory activity of the endothelium [10,11]. Viral inclusions and inflammatory cells accumulate within the endothelial cells of the organs. ACE2 and the transmembrane protease serine 2 (TMPRSS-2) help SARS-Cov-2 to attach and enter endothelial cells. Clot formation, diffuse lymphocytic aggregation, and apoptotic bodies in vessels were also seen in the autopsies of COVID-19 patients [11].

Urticular vasculitis has been reported in a 64-year-old woman after one month of COVID-19 recovery. Her symptoms were muscle weakness, malaise, anorexia, and new-onset generalized skin rashes. The cutaneous biopsy demonstrated dermal edema and features of leukocytoclastic vasculitis and urticarial vasculitis were diagnosed [12]. There is a report of a 29-year-old man with purple palpable papules, and blisters on his abdomen, buttocks, and both lower legs. He also has muscular pain in his legs and abdominal pain with diarrhea. He recovered from COVID-19 one month before the appearance of skin lesions. The lesions were leukocytoclastic vasculitis and SARS-CoV-2 PCR was positive in the skin biopsy [13]. Another Leucocytoclastic vasculitis case, was an 83-year-old woman with a history of hypertension, transient ischemic attack (TIA), atrial fibrillation, chronic renal disease presented with purple palpable papules, and seroelastic blisters on both legs after one month of from COVID-19 recovery. The authors suggested interleukin (IL)-6 levels may play an important role in vasculitis which is increased in COVID-19 [14].

SARS-CoV-2 antigens may trigger the antibodies and antigen-antibody complex formation that target the endothelium and leads to the leucocytoclastic vasculitis appearance in pathology assessment. However, there is no strong evidence about the role of SARS-CoV-2 in the pathophysiology of vasculitis. EGPA and COVID-19 share common symptoms and some EGPA patients mimic COVID-19 features, which makes it challenging to distinguish them from each other [15]. So far, there is no report of EGPA after COVID-19 recovery and our report is the first one.

In summary, vascular endothelial damage in COVID-19 lowers the normal regulatory function of the cells. Also, viral-triggered autoantibody synthesis causes antigen-antibody complex deposition in the vessels and leads to vasculitis. Before diagnosing COVID-19-related vasculitis, we should evaluate any medication use, history of rheumatologic diseases, and infections. Our patient had not had any of these underlying conditions, so the vasculitis could be considered a complication of COVID-19 after recovery from the disease.

4. Conclusion

We shared our experience with a 42-year-old male with EGPA after COVID-19 recovery. COVID-19 can cause endothelial injury through inflammatory processes. Although there are many reports of occurring vasculitis as a new COVID-19 manifestation, there are a few reports of vasculitis after COVID-19 recovery. So far, it has not been demonstrated an exact relationship between COVID-19 and
the pathophysiology of vasculitis.

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**Ethical approval**

Informed consent was obtained from the patient, and it is available upon request.

**Author contribution**

S.K drafted the manuscript, F.A and S.R conducted the medical examinations and collected the required data, and A.L designed the study and drafted the manuscript. All authors read and approved the final version of the manuscript.

**Declaration of competing interest**

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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