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EDİTÖRE MEKTUP / LETTER TO THE EDITOR

Development of ANCA-associated vasculitis after COVID-19 in a patient with Lynch syndrome and atypical hemolytic uremic syndrome

Lynch sendromu ve atipik hemolitik üremik sendrom ile takipli bir hastada COVID-19 sonrası ANCA ilişkili vaskülit gelişimi

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To the Editor;

COVID-19 disease can be asymptomatic or cause serious clinical conditions affecting various systems[1]. The lung is the most frequently affected organ, but the kidney may be affected commonly. The combination of pulmonary disease and renal failure is not uncommon. Pulmonary Renal Syndrome (PRS) secondary to vasculitis is a clinical presentation associated with diffuse alveolar hemorrhage and acute glomerulonephritis. It is most commonly seen due to anti-neutrophil cytoplasmic antibodies (ANCA) associated vasculitis[2,3]. The treatment of these patients is very difficult because COVID-19 pneumonia can often be confused with these complaints and lead to severe limitations in the immunosuppressive therapy that should be used to treat ANCA-associated vasculitis (AAV).

At the beginning of the epidemic, our knowledge of the relationship between COVID-19 and vasculitic syndromes was limited. It was the first information known that patients receiving immunosuppressive therapy are more susceptible to infection and have a more severe disease course. Later, cases of vasculitis secondary to infection began to be reported. We presented a patient who was followed up with atypical hemolytic uremic syndrome (A-HUS) and Lynch syndrome, who was diagnosed with vasculitis due to newly developed ANCA positivity and alveolar hemorrhage after COVID-19 pneumonia and successfully treated with immunosuppressive therapy.

A 65-year-old male patient with a history of colon cancer, renal cell carcinoma, parotid tumor, and basal cell carcinoma was diagnosed with A-HUS one year ago. After plasma exchange, the need for dialysis was eliminated with 1200 mg/2-week eculizumab treatment. Two months ago, he was hospitalized for increasing dyspnea and hemoptysis. His COVID-19 PCR test was positive. In addition to favipiravir and antibiotic therapy, five sessions of plasmapheresis, immune plasma infusion, and tocilizumab treatment were performed in the intensive care unit because of bilateral patchy opacities and hemoptysis on the chest radiograph. After treatment, his pulmonary findings regressed, but he was discharged with the hemodialyses program, as his renal function was not improved. The patient applied on the 10th day after discharge, complaining of shortness of breath and hemoptysis. On admission to the clinic, the CRP level was 284 mg/L, the erythrocyte sedimentation rate was 105 mm/h, and the chest X-ray revealed patchy bilateral opacities. Plasmapheresis treatment was initiated when findings consistent with alveolar hemorrhage were noted in the thorax tomography. The patient's PCR test was negative two times for the COVID -19; the c-ANCA was positive (+++), and the anti-GBM antibody was negative. Immunosuppressive therapy was initiated. The patient who was found to have AAV was treated with

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six sessions of plasmapheresis, 70 g of IVIG, methylprednisolone (500 mg for three days followed by 1 mg/kg/day), and 500 mg of cyclophosphamide. The patient, whose pulmonary findings regressed, was discharged with maintenance therapy with azathioprine 1.5 mg/kg/day.

One of the most critical problems in treating ANCA-associated vasculitis is distinguishing between an infectious complication caused by immunosuppressive therapy and an exacerbation of the disease. The fear that immunosuppressive therapy for a rheumatic disease may turn into a more mortal disease due to the underlying possible infectious disease puts clinicians in a problematic situation.

So far, Staphylococcus aureus, Streptococcus pneumonia, Haemophilus influenza, Klebsiella pneumonia, Helicobacter pylori, Epstein-Barr, and Hepatitis C are known to cause AAV[4]. COVID -19 may cause severe lung involvement and renal failure. Both its ability to perform PRS with its primary involvement and its ability to cause vasculitis secondarily through de novo ANCA formation makes treatment of the disease very difficult.

Early in the pandemic, the first case was reported in patients with COVID-19 and AAV who received rituximab for granulomatous polyangiitis[5]. Subsequently, data on the increase in disease incidence and more severe disease course in patients receiving immunosuppressive therapy have been repeatedly shared.

The first case of AAV developing after COVID-19 was published by Hussein et al.[6]. In the patient with associated alveolar hemorrhage, plasmapheresis was performed for six sessions, and the subsequent COVID -19 PCR test was positive. A positive COVID-19 test detected after long-term follow-up of the patient suggests that hospital-acquired COVID-19 transmission is more likely than ANCA positivity caused by COVID-19.

The first case of AAV induced after COVID -19 infection was presented with a case in Germany who was followed up for hemoptysis and acute renal failure. The patient was PR3 ANCA positive granulomatous polyangiitis. It was reported that AAV developed concurrently with COVID-19 pneumonia and recovered with immunosuppressive therapy and plasma exchange[7]. In the article by Nupur et al. it was reported that ANCA-positive glomerulonephritis secondary to the development of de novo antibodies occurred after infection in two patients observed for COVID -19. The development of new antibodies was attributed to immune dysregulation due to the cytokine storm caused by COVID -19[8].

The primary dilemma in treating ANCA-associated vasculitis induced by COVID -19 is that the aggressive immunosuppression required for vasculitis may increase the infectious status. Extended-spectrum antibiotic treatment should be initiated immediately. Specific to AAV, remission induction in PRS consists of immunosuppressive combination therapy consisting of prednisolone and cyclophosphamide or rituximab. In critically ill patients with severe pulmonary hemorrhage or renal insufficiency, plasma exchange should also be planned because of mortality and preservation of renal function[9].

Concerns about the administration of immunosuppressive therapy in COVID -19 patients have changed with the RECOVERY and WHOREACT trials. For the first time, a significant reduction in mortality was demonstrated with low-dose dexamethasone (6 mg once daily for ten days or 6 mg until hospital discharge) in patients receiving invasive or noninvasive ventilation supplemental oxygen[10,11].

The dysregulation of the immune system that occurs after infectious diseases such as COVID -19 can lead to newly formed antibodies to severe immune responses and the development of vasculitis. We wanted to remind researchers that additional diagnoses, especially vasculitic syndromes, should be considered in patients with an atypical presentation in the increasing frequency of COVID infection. Our case was treated with plasma exchange in addition to immune plasma infusion because he had an alveolar hemorrhage in the intensive care unit, where he was further treated for COVID-19. We think that the tocilizumab treatment he received to treat COVID temporarily suppressed the vasculitis picture in the patient. Still, the patient developed a recurrence within two weeks because the immunosuppressive therapy was not sufficient to treat the ANCA-associated vasculitis.

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