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Therapeutic Apheresis and Dialysis

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LETTERS TO THE EDITOR

Application of plasmapheresis for Covid-19 patients

Dear Editor,

SARS-CoV-2 is a betacoronavirus similar to severe acute respiratory syndrome (SARS) virus and uses the same receptor as the angiotensin-converting enzyme 2 for cell entry.[1] Coronavirus disease (Covid-19) has become problematic by causing a worldwide outbreak as it is easily spread by respiratory droplet transmission or touching eye, nose or mouth with infected hands. Most of the infections are mild causing no/mild pneumonia but about 5% of infections cause critical situations as respiratory failure, shock and multiorgan dysfunction (MOD).[2] The fatal outcomes of SARS-CoV-2 are associated with an excessive immune response. There are many examples that inflammatory cytokines play a central role for adult respiratory distress syndrome (ARDS) due to SARS infections.[3] Significant amounts of macrophage migration inhibitory factor was found to induce the release of tumor necrosis factor-alpha (TNF-α) and interleukin-8 (IL-8), in the alveoli of ARDS cases.[4] Among these patients infected with SARS virus, a cytokine storm as well as viral replication occurs leading to death. IL-1β, IL-2, IL-10, and IL-12 are important and especially during the later stages of the disease TNF-α and IL-6 become dominant to cause the hypercytokinemia.[3] To alleviate this in Covid-19 patients, there are some currently used investigational therapies, such as RNA polymerase inhibitors like favipiravir to downregulate viral replication and IL-6 pathway inhibitors (tocilizumab, siltuximab, etc.). In this article, we aimed to emphasize that plasma exchange (PEX) therapy, although with a high cost and risk of complications, could be an important therapy and worthwhile to try by removing cytokines and possibly circulating viral RNA's simultaneously.

Plasmapheresis (PEX) is an extracorporeal treatment that selectively removes abnormal substances, most notably larger molecules from the blood. The American Society for Apheresis 2019 guidelines designate sepsis with MOD as category 3 and grade 2B recommendation for PEX (Category 3: optimum role of apheresis therapy is not established; decision making should be individualized. Grade 2B: weak recommendation, moderate-quality evidence).[5] In sepsis with MOD, PEX is considered to improve organ function by clearing inflammatory and antifibrinolytic mediators and replenishing anticoagulant proteins to restore hemostasis.[6] In addition PEX can be used to remove viral RNA that induces hypercytokinemia. There is a report supporting the benefit of double filtration plasmapheresis (DFPP) to reduce viral RNA for hepatitis C virus (HCV) with the reason that HCV particles are huge enough (approximate diameter of 55-60 nm) to pass the membrane so they can be eliminated; this is beneficial for downregulating viral load, even among patients who relapsed following previous interferon-beta induction therapy.[7] Similarly SARS-CoV-2 has a diameter of 60-140 nm, also large enough to be eliminated with DFPP. This is the main rationale for performing PEX therapy for critical patients with severe lung injury unresponsive to adjunctive treatments. Similar to DFPP, during the H7N9 outbreak, some blood purification modules such as PEX, plasma absorption and/or hemo/plasma filtration have been used with success for cytokine/chemokine clearance.[8,9] Recently, the United States Food and Drug Administration has approved the use of investigational device exemption for Toraymyxin in the treatment of Covid-19 patients suffering from septic shock.[10]

As a conclusion, the Covid-19 outbreak has become an important cause of mortality within a couple of months. Some novel therapies are emerging, but most of them remain still investigational without randomized clinical trials (RCTs). There is as risk of novel mutations that render the disease resistant to most of the therapies including antiviral drugs. That would decrease the spectrum of drugs available. PEX can be considered as a salvage or adjunctive treatment with the rationale of clearing out the related cytokine storm and possibly viral burden. There is an unmet need of more RCTs to decide the benefits and to specify the place of PEX in Covid-19 treatment.

CONFLICT OF INTEREST

The authors declare no potential conflict of interest.

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Good response to cryofiltration in a patient with cryoglobulinemic vasculitis complicated with systemic lupus erythematosus

Dear Editor,

Cryoglobulinemic vasculitis is a rare systemic vasculitis in which typical manifestations are arthralgia, purpura in lower limbs, peripheral neuropathy, and proliferative glomerulonephritis. Cryoglobulinemic vasculitis is associated with life-threatening conditions such as rapidly progressive renal failure. Predisposing conditions include hepatitis C virus (HCV) infection, lymphoproliferative disorders, or autoimmune disease including systemic lupus erythematosus (SLE).

A 75-year-old women suffered from arthralgia, lower limb purpura, fever, Raynaud's phenomenon, and leg edema. She was also found to have urinary protein, pancytopenia, positive for anti-nuclear antibody, double-stranded DNA antibody, and rheumatoid factor, hypocomplementemia, and cryoglobulin 6 years ago. Skin biopsy on the lesion of her right leg revealed necrotizing vasculitis. She was diagnosed with SLE according to the American College of Rheumatology Revised Criteria for the Classification of SLE and mixed cryoglobulinemic vasculitis according to the preliminary classification criteria for the cryoglobulinemic vasculitis based on her clinical symptoms and laboratory findings. She was treated with prednisolone (PSL) 20 mg/day and tacrolimus (TAC) 2 mg/day. Her symptoms and laboratory findings improved. We maintained the target TAC blood trough concentration of 5 ng/mL. However, her lower limb purpura and leg edema got worse, serum C3 level decreased from 72 mg/dL to 55 mg/dL and urinary protein increased (0.8-2.0 g/day) as tapering dosage of PSL 10 mg/day, then she was admitted to our hospital. She had fever, lower limb purpura, and pitting edema in