Case Presentation

Convalescent plasma therapy in aHUS patient with SARS-CoV-2 infection

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Summary

Endotheliosis, thrombotic microangiopathy and complement system over activation have been described as pathologic features of tissue damage in the setting of coronavirus disease. Interestingly, complement-mediated cell injury is also a typical feature of atypical Hemolytic Uremic Syndrome. Indeed, a growing body of literature has described a higher risk of microangiopathy recurrence, in aHUS patients who test positive for SARS-CoV-2. The correct clinical and therapeutic management patients with a history of HUS and SARS-CoV-2 infection is not well established.

We report a case of SARS-CoV-2 infection in an aHUS patient who did not develop a recurrence of the disease and that was successfully treated with convalescent immune plasma therapy.

Introduction

Endotheliosis has been described as a pathologic feature of organ damage in the setting of coronavirus disease 2019 (SARS-CoV-2) [1]. The involvement of complement system in the endothelial cell damage and in the pathogenesis of SARS-CoV-2 disease has also been highlighted. Complement mediated endothelial-cell activation and injury, is a hallmark of atypical Hemolytic Uremic Syndrome (aHUS) [2]. On this premise, patients with aHUS history who test positive for SARS-CoV-2 have a higher risk of microangiopathy recurrence. We report the second case of SARS-CoV-2 infection in a patient with a history of aHUS who did not develop microangiopathy and was successfully treated with convalescent immune plasma therapy.

Statement of ethics

Written informed consent was obtained from the patient for publication of this case report and any accompanying images. The study did not require a formal approval from the ethics committee according to the Italian law since it was performed as a retrospective description of a clinical case in the context of normal clinical routines (art.1, leg. decree 211/2003). However, it was performed according to the guidelines of the Declaration of Helsinki. Data were previously anonymized, according to the requirements set by Italian Data protection Code (leg. Decree 196/2003).
an efficient respiratory profile with normal blood gas analysis results (pH: 7.44, pCO2: 36 mmHg, pO2: 77 mmHg, P02/FiO2 = 376). Inflammatory markers were moderately increased (C-reactive protein 23.4 mg/L, D-dimer 235 μg/L and interleukin-6 50.6 pg/ml), showing a clinically mild form of SARS-CoV-2. Since the admission, the patient received azithromycin 500 mg per os (once daily for 2 weeks), i.v. dexamethasone (6 mg once per day for 16 days followed by a fast tapering) and s.c. enoxoparin (4000 UI/daily for 50 days).

During the following two weeks, her clinical condition progressively worsened, as she presented dry cough, shortness of breath, and a substantial decrease in Oxygen Saturation down to 89%. The respiratory failure required Venturi masks (FiO2 60%), followed by Continuous Positive Airway Pressure (CPAP) with maximization of FiO2 (100%) and of Positive End Expiratory Pressure (PEEP) (10 cmH2O). Laboratory tests showed a severe increase of inflammatory markers (Figure 1A). Chest X-ray revealed signs of polysegmental bilateral viral pneumonia with multiple ground glass opacity areas (Figure 2A).

At the onset of respiratory symptoms, Ceftriaxone 2 g i.v. (once daily for 16 days) was added to prevent bacterial co-infection. Despite such treatment, the clinical worsening required intensive care unit (ICU) support. Therefore, we decided to start a rescue therapy with three doses of fresh frozen plasma (250 ml for each dose) obtained from a SARS-CoV-2 convalescent patient, according to the Tsunami Protocol. After the second plasma infusion, blood gas analysis revealed an improvement of PO2/FiO2 ratio: from 84, at the beginning of the therapy, to 224 on the 3rd day of plasma administration without other ventilation change. The PO2-FiO2 ratio showed a slightly decrease between the 10th - 20th of November corresponding to a gradually ventilator weaning and the recovery of the spontaneous breathing.

Chest X-ray performed just one day after the last plasma administration, showed a slight reduction of the ground glass opacity areas at the mid-apical level of left lung. 48 hours after the completed immune plasma infusion cycle, the patient returned to our Unit given the respiratory and overall clinical improvement. Inflammatory markers showed a significant decrease after the plasma infusion and a durable change until the end of November when the patient developed a bacterial infection of the central venous catheter (Staphylococcus Epidermidis was detected in blood cultures). Therefore, the central venous catheter for hemodialysis was removed and daptomycin (7 mg/Kg every 48 h) was administered for 10 days with a complete clinical recovery.

During the first week after the end of plasma therapy a slightly decrease in platelet and hemoglobin was observed, associated with a reduction of C3 and C4, without signs of hemolysis (LDH: 288 UI/L, no schistocytes in the blood smear, bilirubin 0.44 mg/dl); therefore aHUS recurrence was excluded.

Inflammatory markers improved and the chest X-ray showed a resolution of SARS-CoV-2 pneumonia (Figure 2C). Hence, 55 days after the SARS-CoV-2 diagnosis, she was discharged.

Discussion

Hyperimmune Plasma (HP) has been successfully used in several viral epidemics such as SARS, MERS, and Ebola [3]. Given this evidence, HP has also been administered to some SARS-CoV-2 patients. The World Health Organization (WHO) allowed the CP treatment for «serious diseases for which there
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To HUS recurrence and the critically worsening respiratory function, we decided to administer HP as rescue therapy. Our patient had a good response to the HP treatment, which also showed a favorable safety profile. Moreover, she had no HUS recurrence, maybe because HP may reduce the viral replication.

In conclusion, our observation, although limited to a single patient, shows that HP can be considered as rescue therapy in patients with moderate-severe SARS-CoV-2 infection and aHUS history, and does not increase the risk of microangiopathy recurrence.

Author Contributions: E.D. Stea wrote the manuscript with support from F. Pesce. V. Pronzo collected the data and designed the figures. All authors provided critical feedback and helped shape the analysis and manuscript. L. Gesualdo supervised the project. Finally, all the authors define the therapy and the medical care of the patient during the job in the Nephrology COVID Unit of Bari.

Data availability statement: All data generated during this study are included in this article. Further enquiries can be directed to the corresponding author.

Disclosure: the authors declare no conflict of interest.

References


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