

Use of CytoSorb in a patient with severe ARDS following COVID-19 infection

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This case reports on a 51-year-old male patient with a history of transient ischemic attack (TIA) and hypertension, who was admitted to the Emergency Department of the Navarra Hospital Complex in context of the COVID-19 outbreak.

Case presentation:

- In the ten days before admission he complained of fever and dry cough, but without shortness of breath
- On admission, his vital signs were stable with a peripheral oxygen saturation (SpO₂) of 93% on ambient air and a respiratory rate of 23/min
- His nasopharyngeal swab RT-PCR test for SARS-CoV-2 was positive and he was subsequently started on treatment with hydroxychloroquine plus azithromycin
- Blood analysis revealed lymphopenia (800/μl) as well as elevated markers (ferritin 1758 μg/L, CRP 119 mg/L, LDH 397U/L and D-Dimer 2433ng/ml) pointing towards an ongoing SARS-CoV-2 infection
- Chest X-ray showed discrete peripheral opacity in the bottom right lobe
- Over the next 24-48 hours he developed dyspnea and hypoxia with progressing need for supplemental oxygen followed by transfer to the ICU
- The patient was initially put on High Nasal Oxygen Flow (HFNO) with 50 liters per min (lpm) to achieve an SpO₂ >92%
- Furthermore, he was treated with methylprednisolone (125 mg bolus for three days, 60 mg for two days and 30 mg for one day) as well as tocilizumab (600 mg and 400 mg in 24 hours)
- A chest X-ray confirmed diffuse bilateral opacities while blood analysis showed progression of the previously altered parameters (lymphopenia, C-Reactive Protein (CRP) 284 mg/L and ferritin 4070 μg/L)
- After 36 hours on HFNO, his pulmonary function worsened, so he was intubated and ventilated mechanically. After intubation he was diagnosed with moderate to severe acute respiratory distress syndrome (ARDS)
- Protective ventilation with moderate PEEP levels (10-12 cm H₂O), tidal volume of 7ml/Predicted Body Weight (PBW), prone positioning, deep sedation and analgesia, and neuromuscular blockade was initiated resulting in adequate respiratory mechanics (plateau pressure <27 cm H₂O and driving pressure <14 cm H₂O) within the first 72 hours of mechanical ventilation
- On day 4 of mechanical ventilation, he was switched to light sedation and assisted modes of respiratory support
- On day 6 of ICU admission, there was progressive impairment of respiratory function with refractory hypoxemia (PaO₂/FiO₂ of 80 mmHg in prone position, moderate PEEP 12 cm H₂O and no recruitability), moderate hypercapnia (PaCO₂ 60 mmHg) and radiological deterioration with bilateral consolidations in his lungs

- Despite being afebrile and COVID-19-relevant laboratory markers having had already decreased (CRP 91 mg/L, ferritin 1648 µg/L, D-dimer 5627 ng/ml), IL-6 plasma concentrations were markedly increased compared to levels measured after previous tocilizumab/steroid treatment (IL-6 increase from 261 pg/ml to 6994 pg/ml within 48 hours)
- Furthermore, he exhibited hemodynamic instability with norepinephrine requirements of 0.15 µg/kg/min
- A thoracic CT scan was performed confirming the suspected diagnosis of progression to the consolidation phase of COVID-19 pneumonia with severe ARDS in the context of a cytokine storm-induced lung injury
- At that time, the patient met the criteria for Extracorporeal Membrane Oxygenation (ECMO) support with the following parameters: PaO₂/FiO₂ <80 mmHg, Murray Score 3.3, prone position, moderate PEEP and no recruitability, moderate hypercapnia, Pplateau 27-30 cm H₂O and a driving pressure of 15-16 cm H₂O
- However, due to logistical reasons ECMO was not started. Based on a pathophysiological rationale regarding present systemic hyperinflammation the decision was made to initiate CytoSorb blood purification treatment together with continuous renal replacement therapy (CRRT), although there was no strict indication for renal replacement as kidney function was impaired but still sufficient

Treatment

- Two consecutive treatments with CytoSorb were performed for a total treatment duration of 60 hours (1st treatment 24 hours, 2nd treatment 36 hours)
- CytoSorb was used in conjunction with CRRT (Prismaflex, Gambro) run in CVVHDF mode
- Anticoagulation: Citrate
- Blood flow rate: 180 ml/min
- CytoSorb adsorber position: post-hemofilter

Measurements

- Hemodynamics
- Fluid balance
- Metabolic status
- Lung function
- Laboratory parameters

Results

- Treatment resulted in a steady and rapid hemodynamic stabilization accompanied by a decrease in catecholamine requirements. Norepinephrine administration was completely stopped at the end of the 2nd CytoSorb treatment cycle
- Fluid balance could be kept well under control (cumulative/day: first day +1L, second day -2.2L and third day -1.4L)
- The patient did not develop hyperlactatemia nor metabolic acidosis at any time
- During hemoadsorption treatment there was a progressive improvement of oxygenation (PaO₂/FiO₂ from 71 mmHg before treatment to 180 mmHg after completion), ventilation (correction of hypercapnia) and respiratory mechanics such as an increase in compliance of the respiratory system (from 35 ml/cm H₂O before treatment to 44 ml/cm H₂O post-treatment) and a decrease

in driving pressures (16 cm H₂O before treatment, 14 cm H₂O post-treatment). After completion of CytoSorb therapy, the patient was in a supine position, with only a moderate PEEP required while his PaO₂/FiO₂ was 250 mmHg

- Laboratory parameters improved as follows: IL-6 decreased from 4987 pg/ml before to 607 pg/ml after 60 hours of treatment, CRP decreased from 91 mg/l at start to 41 mg/l at the end of treatment, ferritin levels decreased from 1648 µg/ml pre-treatment to 802 µg/ml post-treatment, D-dimers reduced from 4546 ng/l at the beginning to 2459 ng/l after 60 hours of treatment

Patient Follow-Up

- After cessation of hemoadsorption therapy, the clinical course was favorable leading to an regression of lung injury, allowing the patient to be weaned off mechanical ventilation after a prolonged course (31 days)
- On day 36, he was discharged from the ICU with good respiratory function (no need for supplementary oxygen) and motor recovery

Conclusions

- In this patient with severe ARDS following COVID-19 the combined use of CRRT + CytoSorb treatment was associated with hemodynamic stabilization and a concomitant reduction in norepinephrine dosages, control of the inflammatory response as well as improvement in organ functions (lungs, kidneys)
- The decision to initiate CytoSorb + CRRT was based on the assumption that the deterioration was attributed to a "rebound effect" after the initial anti-inflammatory treatment for cytokine storm with 6 days of methylprednisolone and 2 doses of tocilizumab, as well as the continuous viral shedding in the context of a persistent dysregulated inflammatory response, resulting in the progression of lung damage to the consolidative phase of ARDS. Moreover, there are recent findings on the importance of a local dysregulated inflammatory response in the lung that promotes progression of the disease. It is also considered a prognostic marker of fatal outcome in critically COVID-19 patients
- CytoSorb was easy to use in connection with CRRT and no adverse events were observed during or after the treatment