

The Sequential Use of Extracorporeal Cytokine Removal Devices in an Adolescent With COVID-19 Receiving Continuous Renal Replacement Therapy

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This case reports on an a 14-year-boy (43 kg) without any respiratory symptoms, who was admitted to a regional hospital with a fever of one day associated with vomiting and breakthrough seizures.

Case presentation

- Known medical history included a de novo G-Protein Subunit Alpha O1 (GNAO1)-mutation with movement disorder, epilepsy, and severe intellectual disability receiving baclofen, tetrabenazine, carbamazepine, and clobazam
- On admission, his temperature was 40.1°C, heart rate 150/min, blood pressure 90/50 mmHg, and desaturation requiring oxygen supplementation
- He exhibited vigorous involuntary movements and developed a status dystonicus
- Blood tests on admission showed a white blood cell count of $9.1 \times 10^9/L$ (neutrophil and lymphocyte count of $7.7 \times 10^9/L$ and $0.9 \times 10^9/L$, respectively), urea 2.9 mmol/L, creatinine 41 $\mu\text{mol/L}$ (baseline creatinine level was 31 $\mu\text{mol/L}$) and creatine kinase (CK) level of 117575 IU/L. Moreover, he was also found to pass brownish-red (myoglobin-positive) urine
- He went on to develop disseminated intravascular coagulation with thrombocytopenia with an abnormal clotting profile (INR 1.7, aPTT >120 s, D-dimer 5072.9 ng/ml and fibrinogen 2.24 g/L)
- The nasopharyngeal swab proved positive for SARS-CoV-2
- He was started on hyperhydration, empirical piperacillin/tazobactam and one dose of remdesivir
- Oral chloral hydrate was used for sedation
- Urine output was maintained at 2–3 ml/kg/hour but the persistent fever and tachycardia continued, as did the excessive movements
- He later developed stage 2 acute kidney injury (AKI) with an estimated glomerular filtration rate (eGFR) of 75 ml/min/1.73 m² and was therefore transferred to the pediatric intensive care unit (PICU) for further management
- His CK level rose sharply to the peak level of 449,100 IU/L with hypernatremia (sodium level of 155 mmol/L) and metabolic acidosis (pH 7.33, bicarbonate level of 13.8, and base excess of –11.8 mmol/L)

- The lactate level was 2.3 mmol/L, troponin-T level was 170 ng/L and the eGFR reduced to 66 ml/min/1.73m²
- He developed abnormal liver function tests with serum levels of alanine aminotransferase (ALAT) 1469 IU/L, aspartate aminotransferase (ASAT) 6577 IU/L, and ammonia 52 µmol/L
- There were also elevated levels of inflammatory markers including ferritin 5842 pmol/L, procalcitonin 13.63 ng/ml, and C-reactive protein (CRP) 130 mg/L
- The clinical diagnosis was multisystem inflammatory syndrome in children (MIS-C) related to SARS-CoV-2 infection triggering status dystonicus and subsequent rhabdomyolysis-associated AKI
- After his transfer to the PICU, his blood pressure dropped to 60/40mmHg and SpO₂ was 90%
- A bedside echocardiogram showed impaired septal motion and mildly impaired left ventricular contractility with fractional shortening of 25%
- He subsequently required intubation for respiratory failure, and a norepinephrine infusion was started at 0.03 µg/kg/min for hemodynamic support
- Multiple sedative medications were used for sedation and control of his dystonia and dyskinesia in addition to his usual medications
- Remdesivir was not continued due to his impaired liver function. Tocilizumab was started later
- He was started on continuous renal replacement therapy (CRRT) due to rhabdomyolysis-associated AKI
- Ten hours after CRRT initiation, a CytoSorb hemoadsorption column was integrated into the CRRT circuit to enhance myoglobin and cytokine removal

Treatment

- CytoSorb was first incorporated into the CRRT circuit for myoglobin and cytokine removal (hour 18 – 40), which was followed by sequential use of Oxiris (hour 40 – 80), followed by another CytoSorb adsorber (hour 85 – 110), giving a total of 100 hours of extracorporeal blood purification [EBP] therapy
- CytoSorb was used in conjunction with CRRT run in high-volume continuous veno-venous hemodiafiltration (HF CVVHDF) mode using the Prismaflex system
- Position of the adsorber: post-CRRT filter

Measurements

- Hemodynamics and catecholamine requirements
- Inflammatory parameters
- Creatine kinase

Results

- Initially, he continued to deteriorate with persistent hypotension requiring escalation of inotropes. However, there were no major complications related to the EBP therapy including hemodynamic compromise

- Cytokine profile revealed a marked reduction of levels of several cytokines including tumor necrosis factor-alpha (TNFα), interleukin (IL)-6, IL-8, and IL-10 after the EBP therapy. His condition improved under both EBP therapies and the serum ferritin, C-reactive protein, and procalcitonin levels also dropped gradually, which correlated well with his clinical progress and the trend of cytokine levels
- The serum levels of CK gradually decreased

Patient Follow-Up

- A dose of intravenous immunoglobulin (IVIG) and dexamethasone were added during therapy
- It was possible to stop all inotropes 4 days after PICU admission
- Extubation was possible on 8th day of PICU admission
- The CRRT doses were gradually reduced, and it was possible to stop CRRT support 8 days after admission
- The clinical course was complicated by secondary *Pseudomonas aeruginosa* pneumonia requiring an additional course of antibiotics for two weeks
- The patient was finally discharged from the PICU to his original hospital one month after admission

Conclusions

- In this case of an adolescent with MIS-C following SARS-CoV-2 infection as well as rhabdomyolysis-associated acute kidney injury, the application of extracorporeal blood purification therapy was associated with pronounced hemodynamic stabilization, as well as a marked reduction in levels of several cytokines and creatine kinase
- It was noted that both pro-inflammatory and anti-inflammatory cytokines were removed, and the removal efficacy varied between different devices. However, the authors note that the two devices (CytoSorb + Oxiris) appeared to complement each other's adsorption capacity
- The authors conclude that this case demonstrates that extracorporeal cytokine removal can be safely applied in children with MIS-C and can be considered as adjunctive therapy in selected patients with critically ill conditions