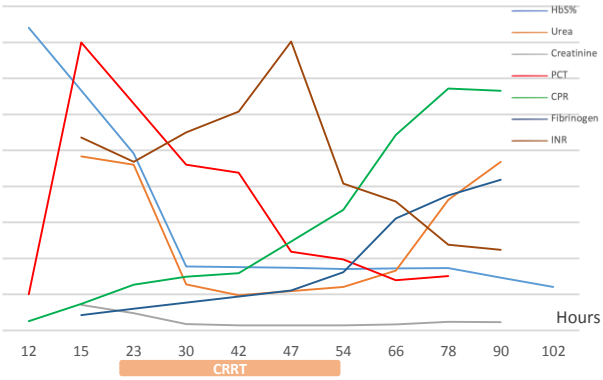
Covid19, Pneumococcus, Sickle Cell Disease and Microangiopathy: a case report of the perfect storm successfully treated by CRRT

Pietro Lonardi[1], Francesca Matarozzo[2], Sergio Grassitelli[3], Bruno Gianoglio[4] and Licia Peruzzi[4]

[1]Postgraduate School of Pediatrics, University of Turin, Italy,
[2] Postgraduate School of Pediatrics, University of Piemonte Orientale, Novara, Italy 3 Intensive Care Unit, Regina Margherita Children's Hospital, Turin, Italy
[4]Pediatric Nephrology Unit, Regina Margherita Children's Hospital, Turin, Italy
Email address: pietro.lonardi@unito.it

CASE REPORT:

A Nigerian 20-months-old girl presented to the ER in critical clinical condition with fever, hypotonia and lethargy. Lab tests showed hypoglycaemia with metabolic acidosis and normocytic anaemia, with normal white blood cell and platelet count. The C-reactive protein (CRP) level was 12.8 mg/L (nv <5 mg/ml), procalcitonin levels were high (50 ng/ml, nv<0.5 ng/ml). The blood smear showed sickled red cells. Thus, she received glucose solution, a dose of ceftriaxone, a red blood cell transfusion and a haemoculture was collected. The child has been tested positive for SARS-CoV-2 nasopharyngeal swab.
In a few hours her clinical conditions rapidly worsened with significant respiratory distress that required mechanical ventilation and admission to ICU. Chest X-ray showed interstitial infiltrates with no consolidation. Sars-Cov-2 was confirmed on BAL.



At re-evaluation her inflammatory markers were skyrocketing (PCT 400ng/ml, PCR 37 mg/dl, WBC 18080/mmc). A therapy with meropenem, vancomycin and immunoglobulins was started.
Laboratory tests showed a severe thrombotic microangiopathy (haemolytic anaemia with dropping Hb and platelet count, undetectable haptoglobin, high LDH levels) with concomitant fulminant hepatic failure. Haemoculture was positive for S. Pneumoniae. Hb electrophoresis showed HbS presence and genetic analysis confirmed the diagnosis of sickle cell disease.
Facing the diagnosis of sepsis and the multifactorial thrombotic microangiopathy secondary to SARS-Cov-2, sepsis and sickling crisis, continuous renal replacement therapy (CRRT) as continuous veno-venous hemodiafiltration was started choosing citrate anticoagulation, due to extremely altered coagulation asset with a Prismax® HF20 device (Qb 70 ml/min, PBP 700 ml/h, Dialysate 1000 ml/h, Replacement 700 ml/h, Calcium compensation Ca 130% for persistent hypocalcemia).
CRRT was performed for 24 hours then the coagulation of the circuit required the circuit substitution with a ST60 and heparin anticoagulation due to the prevailing thrombotic diathesis developed for the sickling crisis.
CRRT was maintained 36 hours and then interrupted with the reverting of the metabolic acidosis, diuresis reprisal and hemodynamic stabilization. Mechanical ventilation was discontinued on day 11th and the child discharged from the ICU after 18 days in improving conditions, normalized renal function and complete resolution of the systemic involvement.

DISCUSSION

Up to date this is one of the most critical paediatric patients admitted to our hospital for Sars-Cov-2 infection. The severe thrombotic microangiopathy had a multifactorial aetiology involving Sars-Cov-2, pneumococcal sepsis and SCD which led to MOF. The particularly severe thrombotic microangiopathy (TMA) observed in our patients is very likely the result of 4 different pathogenetic mechanisms simultaneously involving the endothelium.

THROMBOTIC MICROANGIOPATHY

Endothelitis in patients with COVID 19 has been demonstrated as a consequence of direct endothelial cells infection by virus throughout angiotensin converting enzyme 2 (ACE2) receptor. Viral replication causes inflammatory cell infiltration, endothelial cell apoptosis and microvascular prothrombotic effects.[3]

Endothelium is one of the major protagonists in sepsis. The inflammatory pathways lead to its transition from an anticoagulant state to a procoagulant one by a modification of its surface and increased permeability leading to fluids leakage.[4]

In SCD, red blood cells sickling determines intravascular haemolysis and the release of free haemoglobin which reduces NO bioavailability and induces the expression of adhesion molecules leading to activation of endothelial cells.[2]

BIBLIOGRAPHY
1. Fakhouri F, Zuber J, Frémeaux-Bacchi V, Loirat C. Haemolytic uraemic syndrome. *Lancet*. 2017;390(10095):681-696. doi:10.1016/S0140-6736(17)30062-4
2. Rees DC, Williams TN, Gladwin MT. Sickle-cell disease. *Lancet*. 2010;376(9757):2018-2031. doi:10.1016/S0140-6736(10)61029-X
3. Varga Z, Flammer AJ, Steiger P, et al. Endothelial cell infection and endotheliitis in COVID-19. *Lancet*. 2020;395(10234):1417-1418. doi:10.1016/S0140-6736(20)30937-5
4. Hotchkiss RS, Moldawer LL, Opal SM, Reinhart K, Turnbull IR, Vincent JL. Sepsis and septic shock. *Nat Rev Dis Prim*. 2016;2(June). doi:10.1038/nrdp.2016.45

38th Vicenza Course on AKI&CRRT
a week of virtual meetings
2-6 November 2020