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Case Report
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Fulminant Waterhouse-Friderichsen-Like-Syndrome Caused by COVID-19 Induced Hyperinflammation in an Infant: A Medical Strategy for Complete Regeneration

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Abstract

In this report, a case of a COVID-19-associated life-threatening hyperinflammation with multi-organ failure in an 8-week-old male infant is presented. The patient was successfully treated with cortisone and tocilizumab which led to a full recovery.

Keywords: Infant; COVID-19; SARS-CoV-2; Hyperinflammation; Immunosuppression; Tocilizumab; Waterhouse-Friderichsen

Introduction

This study presents a rare case of a COVID-19-associated life-threatening hyperinflammation with multi-organ failure in an infant and a successful treatment approach which lead to a full recovery.

Case Presentation

An 8-week-old male infant weighting 4.1 kg was transferred to our Pediatric Intensive Care Unit (PICU) from an external ward. Following a spontaneous vaginal delivery at term, the first 8 weeks of the baby's life were uneventful. Four days prior to his admission, the parents developed mild respiratory symptoms such as coughing and rhinorrhea, and both tested positive for SARS-CoV-2 *via* a PCR test. The father was vaccinated twice against SARS-CoV-2; the mother was not vaccinated against the disease due to advice given to her by her gynecologist. When the child presented to the pediatric ward, he had a temperature of 39°C and the parents noted that he had been drinking less milk than usual. The supervising pediatrician noted that the patient was weak and showed clinical signs of sepsis, including low blood pressure, extended capillary refill time, and a grayish skin color. The patient was immediately treated with intravenous fluid therapy and antibiotics (ampicillin and gentamicin). Following treatment, the patient developed respiratory insufficiency and was intubated and mechanically ventilated. The patient was then transferred to our PICU. On arrival, the child presented with a Waterhouse-Friderichsen-like-syndrome with petechiae, hypoperfusion, and ecchymosis all over the body with clinical signs of severe septic shock (Figure 1). The patient presented with arterial hypotension. Therefore, a central line and an arterial catheter were placed, and crystalloid fluid therapy and noradrenaline were administered to increase blood circulation. The SARS-CoV-2 PCR test returned positive with a CT value of 26.6. Blood work showed massively elevated inflammatory parameters (C-Reactive Protein (CRP) 4.85 mg/dl, procalcitonine (PCT) >400 ng/ml, IL-6 >50.000 g/ml), disseminated intravascular coagulation (Quick 31%, aPTT 100s, D-dimer 45000 ng/ml) and bone marrow suppression (leukocytes 1.68/nl, neutrophils 0.71/nl, platelets 17/nl). During the first 18 h of treatment, the patient received a total volume of 2000 ml of intravenous fluids (480 ml/kg). This was due to arterial hypotension and capillary leakage that occurred despite vasopressor administration. Multiple transfusions of erythrocytes, thrombocytes and plasma were also administered. The dosage of vasopressors had to be raised constantly, with noradrenalin reaching 0.6 µg/kg/min and suprarenin 0.2 µg/kg/min, and continual doses of terlipressin were administered which resulted in a blood pressure of only 55/25 mmHg. Echocardiography showed a hyperdynamic systolic function of the left ventricle with kissing walls and a collapsed inferior vena cava due to volume deficiency. A brain sonograph showed normal perfusion and no evidence of pathology (Figure 2). Within 12 h after arrival, an abdominal catheter was placed and a Continuous Peritoneal Dialysis (CPD) was initiated due to complete anuria. Further antibiotics were administered in high doses (ampicillin, cefotaxime, and gentamicin)

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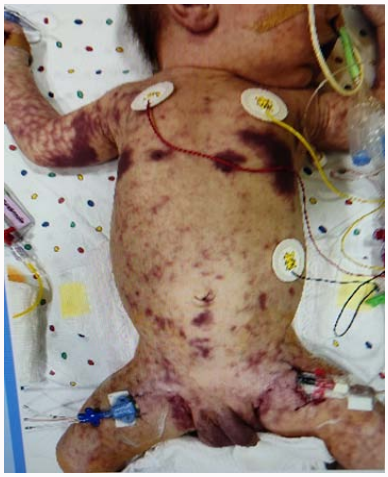

Figure 1: Initial presentation of the patient after insertion of a central line and arterial catheter. Written consent was obtained from the parents.

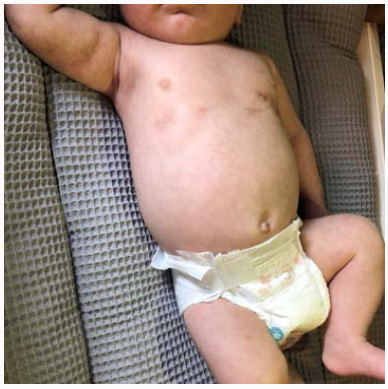

Figure 2: Presentation of the patient after discharge from the hospital.

along with hydrocortisone. There was still significant respiratory insufficiency which meant that high ventilation pressures and FiO_2 of 0.8 were needed for oxygenation of the patient. The situation was worsened by the additional occurrence of repetitive pulmonary hemorrhage. In addition to that a series of seizures occurred that were treated with levetiracetam. Multiple blood cultures were run pre- and post-antibiotic administration to determine the cause of the severe sepsis. Additionally, urine and ascites cultures and microbiological samples were sent for pathology testing. These tests showed no evidence of bacteria. Furthermore, a search PCR for eukaryotic DNA in the blood did not find any evidence of a bacterial infection. After 16 h of treatment, the patient was still unstable despite the maximum permissible doses of medications. The patient remained in poor clinical condition and laboratory results showed ongoing severe inflammation with PCT and IL-6 over the upper cutoff and positive SARS-CoV-2 PCR result with no proof of bacterial infection. As a final control of the symptoms, blocking of the inflammation was attempted. Therefore, dexamethasone (20 mg/m^2) and tocilizumab (12 mg/kg) were administered. Five hours after initiating anti-inflammatory medications, there was a rapid improvement in the patient's condition. The rate of intravenous fluids was decreased; medicinal circulatory support was rapidly decreased and was ceased after a further 8 h. The blood work showed a rapid decrease in the inflammatory parameters (Figure 3, 4), and the hematologic and coagulatoric situation stabilized within days (Figure 5). The

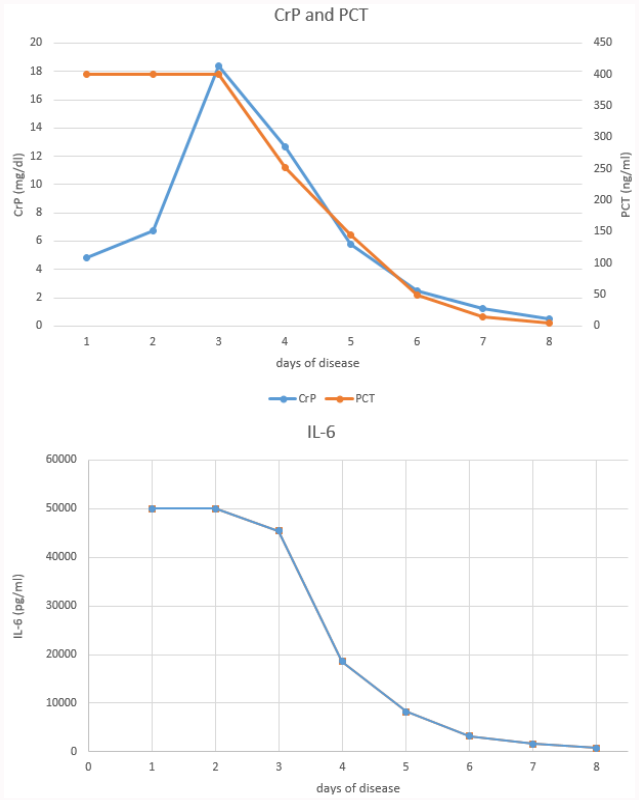

Figure 3 and 4: Inflammation parameters CrP, PCT, and IL-6 over time.

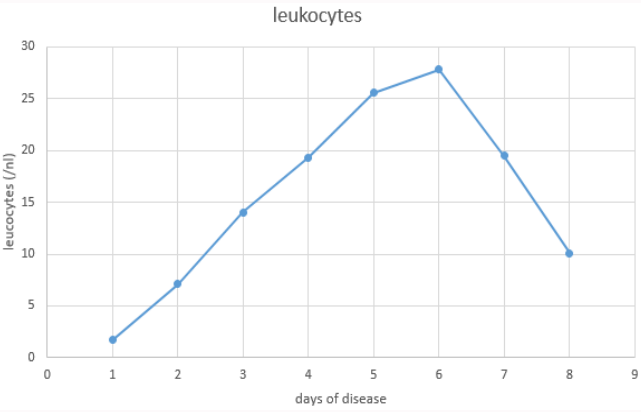

Figure 5: Leukocyte levels over time.

mechanical ventilation was de-escalated quickly, and the patient was successfully extubated 7 days after intubation. He received high flow support for an additional 2 days. The spontaneous diuresis improved rapidly, and the CPD was ceased 7 days after treatment. In the following days, the patient's condition continually improved. Spontaneous enteral feeding was established, and there were no further clinical signs of neurological problems. On day 15, a follow-up Electroencephalography (EEG) was performed which showed physiological activity and no evidence of hypersynchronous activity. On the same day, a cerebral Magnet Resonance Imaging (cMRI) was undertaken that showed several disseminated parenchymal and cortical micro bleedings but no evidence of hypoxic brain damage or inflammatory changes in the brain parenchyma. The patient was transferred to the intermediate care ward after 9 days of treatment in the PICU. He was discharged from the hospital after 16 days of

treatment.

Discussion

In the initial stages of this case, a severe bacterial sepsis was assumed. However, no bacteria could be found in the microbiological screenings as would be expected in a life-threatening bacterial sepsis. Nonetheless, the patient was treated with broad-spectrum antibiotics which produced no effect. In summary, it is thought that the cause of the Waterhouse-Friderichsen-like-syndrome with multi-organ failure was most likely a COVID-19 associated dysregulation of the immune response with extensive systemic hyperinflammation, the so called "cytokine storm" [1]. In adult patients these reactions can be seen in serious cases that begin with respiratory symptoms and lead to a severe Acute Respiratory Distress Syndrome (ARDS) [2]. Clinical deterioration is often rapid, and in a large proportion of cases the severeness of the disease is caused by systemic hyperinflammation. These dysregulations of the immunologic response may benefit from immunomodulation, with significant positive results [3-6]. Pediatricians tend to see hyperinflammation weeks after SARS-CoV-2 infection, and it is even occasionally seen in asymptomatic patients. Most of these patients are severely ill and, in some cases, require intensive care. During the COVID-19 pandemic, a disease in children called Multisystem Inflammatory Syndrome (MIS-C) was discovered [7,8]. Patients with MIS-C present with a variety of symptoms including high fever, abdominal pain, mucocutaneous irritation, and circulatory disorder, and are usually within the age range of 3-8 years. The treatment includes prednisolone, IVIG or, in some cases, anakinra [8-12]. This type of hyperinflammation is very rare, even in patients presenting with MIS-C as a result of COVID-19 disease. While numerous trials recommending immunomodulatory therapies for COVID-19 in adults have been published, there is no such guidance provided for children. Therefore, immunomodulatory therapy in children can only be considered on a case-by-case basis [13]. Systemic corticosteroids such as dexamethasone repress pro-inflammatory gene transcription and inhibit cytokine production and are therefore effective in treating many diseases with underlying inflammatory conditions [14,15]. The multicenter Randomized Evaluation of COVID-19 Therapy (RECOVERY) showed a reduction in 28-day mortality in adult patients treated with dexamethasone [16]. In contrast, IL-6 plays an important role in the COVID-19 cytokine storm and elevated levels are predictive of a fatal outcome [6,17]. Tocilizumab as an IL-6 receptor monoclonal antibody has been proposed to treat adult patients in critical condition [18]. This case showed that the acute hyper-reaction of the immune system to the SARS-CoV-2 infection and the resulting cytokine storm led to severe multi-organ failure that almost resulted in death. The treatment of dexamethasone and tocilizumab that was administered to reduce hyperinflammation produced a rapid change in the patient's clinical presentation and lead to the patient making a full recovery. The patient was neurologically unharmed with only cerebral micro bleedings and there was no evidence of hypoxic brain damage in the brain parenchyma.

References

1. Mehta P, McAuley DF, Brown M, Sanchez E, Tattersall RS, Manson JJ. COVID-19: Consider cytokine storm syndromes and immunosuppression. The Lancet. 2020;395(10229):1033-4.
2. McGonagle D, Sharif K, O'Regan A, Bridgewood C. The Role of cytokines including Interleukin-6 in COVID-19 induced pneumonia and macrophage activation syndrome-like disease. Autoimmun Rev. 2020;19(6):102537.
3. Kluge S. S3_German guidelines for the therapy of patients with COVID-19_2022-03.
4. STAKOB. Information on the detection, diagnosis and therapy of patients with COVID-19.
5. Kim JS, Lee JY, Yang JW. Immunopathogenesis and treatment of cytokine storm in COVID-19. Theranostics. 2021;11(1):316-29.
6. Diorio C, Henrickson SE, Vella LA. Multisystem inflammatory syndrome in children and COVID-19 are distinct presentations of SARS-CoV-2. J Clin Invest. 2020;130(11):5967-75.
7. Sai BVK, Kumar H, Arun Babu T, Chaitra R, Satapathy D, Kalidoss VK. Clinical spectrum of Multisystem Inflammatory Syndrome in Children (MIS-C) associated with COVID-19 infection. Indian J Pediatr. 2022;89(4):418.
8. Patel JM. Multisystem Inflammatory Syndrome in Children (MIS-C). Current allergy asthma Rep. 2022;22(5):53-60.
9. Yilmaz Ciftdogan D, Ekemen Keles Y, Cetin BS. COVID-19 associated multisystemic inflammatory syndrome in 614 children with and without overlap with Kawasaki disease-Turk MIS-C study group. Eur J Pediatr. 2022;181(5):2031-43.
10. Bassiri H, Canna SW. IL-1 receptor antagonist, MIS-C, and the peculiar autoimmunity of SARS-CoV-2. Lancet Rheumatol. 2022;4(5):e305-e307.
11. Wessels PA, Bingler MA. A comparison of Kawasaki disease and multisystem inflammatory syndrome in children. Prog Pediatr Cardiol. 2022;65:101516.
12. Roarty C, Waterfield T. Review and future directions for PIMS-TS (MIS-C). Arch Dis Child. 2022;archdischild-2021-323143.
13. Dulek DE, Fuhlbrigge RC, Tribble AC. Multidisciplinary guidance regarding the use of immunomodulatory therapies for acute coronavirus disease 2019 in pediatric patients. J Pediatric Infect Dis Soc. 2020;9(6):716-37.
14. Batu ED, Özen S. Implications of COVID-19 in pediatric rheumatology. Rheumatol Int. 2020;40(8):1193-213.
15. Feldstein LR, Rose EB, Horwitz SM. Multisystem inflammatory syndrome in U.S. children and adolescents. N Engl J Med. 2020;383(4):334-46.
16. RECOVERY Collaborative Group. Convalescent plasma in patients admitted to hospital with COVID-19 (RECOVERY): A randomised controlled, open-label, platform trial. Lancet. 2021;397(10289):2049-59.
17. Zhao M. Cytokine storm and immunomodulatory therapy in COVID-19: Role of chloroquine and anti-IL-6 monoclonal antibodies. Int J Antimicrob Agents. 2020;55(6):105982.
18. Somers EC, Eschenauer GA, Troost JP. Tocilizumab for treatment of mechanically ventilated patients with COVID-19. Clin Infect Dis. 2021;73(2):e445-e454.