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HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS TRIGGERED BY COVID-19 – A CASE REPORT

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BACKGROUND

Hemophagocytic lymphohistiocytosis (HLH) is a potentially fatal systemic inflammatory disease characterized by cytokine storm. It presents with sudden onset and progression, and it is characterized by cytopenia and hyperferritinemia. Its signs and symptoms include sudden and incessant fever, lymphadenopathy, hepatosplenomegaly and multiple organ failure syndrome. It has two presentations: primary and secondary forms. The secondary may originate from viral, bacterial and/or fungal infections, but also from malignancies and autoimmune diseases. In the disease course, preexisting factors affect the functionality of CD8 T lymphocytes and NK cells, as well as the overactivation of toll-like receptors. Consequently, a state of intense inflammation occurs, which is triggered by a high production of cytokines (especially IL-6). This sequence of events is responsible for the activation of T lymphocytes and macrophages, which generate the cytokine storm. In patients with COVID-19, those factors can cause HLH, with fever, cytopenia, acute respiratory distress syndrome, renal and neurological disorders.

CASE REPORT

A 32-year-old woman was admitted to the emergency room with acute and diffuse abdominal pain associated with hypotension, malaise and icteric syndrome. She had no comorbidities. The patient reported a recent RT-PCR confirmed COVID-19 infection. Volume expansion, antibiotic therapy and use of vasoactive drugs were performed. In laboratorial tests, bicytopenia (normocytic normochromic anemia and thrombocytopenia), renal and hepatic dysfunction were observed, in addition to high ESR/CRP. In the imaging examinations, signs of incipient hepatopathy and splenomegaly appeared. She evolved with mental confusion, high refractory fever, worsening of cytopenia and renal function, disseminated intravascular coagulation, requiring orotracheal intubation, hemodialysis, and fresh frozen plasma transfusion. Serologies for hepatitis B and C, HIV and syphilis were negative. ANA and RF also negative. Investigation for arboviruses and leptospirosis were negative. Seric ferritin 2,850 ng/dL and triglycerides 472 mg/dL. She was transferred to the ICU and diagnosed with HLH secondary to SARS-CoV2 (Table 1). Pulse therapy with methylprednisolone 1 g/day for 3 days was started, and afterwards the patient presented clinical and laboratorial improvement, including discontinuation of vasoactive drugs. Subsequently, a myelogram was performed demonstrating hypercellular bone marrow with megakaryocytic hyperplasia.

CONCLUSION

Hemophagocytic lymphohistiocytosis can be triggered by a number of conditions. The current pandemic has shown several surprises, such as the possibility of triggering secondary HLH. When a COVID-19 patient presents symptoms that mimic rheumatological diseases such as fever, cytopenia and hyperferritinemia, the occurrence of this entity should be considered. The early recognition and diagnosis are fundamental to the prognosis and survival of patients.

Table 1. Scores used for HLH diagnosis.

Clinical and laboratory features of cytokine storm syndrome reported in COVID-19 patients and their relationship to cytokine storm syndrome criteria			
HLH-04 Criteria	HScore	Ferritin: ESR Ratio	COVID-19 Features
Fever	Fever		Yes
Splenomegaly	Splenomegaly		Unknown
	Hepatomegaly		Unknown
Anemia	Anemia		Yes
Thrombocytopenia	Thrombocytopenia		Yes
Neutropenia	Neutropenia		Yes
Hypertriglyceridemia	Hypertriglyceridemia		Unknown
Hypofibrinogenemia	Hypofibrinogenemia		Yes
Hemophagocytosis	Hemophagocytosis		Yes
Low NK cell activity			Unknown
Hyperferritinemia		Hyperferritinemia	Yes
Elevated soluble CD25	Hyperferritinemia		Yes
	Elevated soluble CD25		Unknown, but AST and ALT elevated
	Elevated Serum GGT		
			Some with HIV infection
	Underlying immunosuppression	Falling ESR	
			Unknown

COVID-19: corona virus disease 2019; HLH: hemophagocytic lymphohistiocytosis; ESR: erythrocyte sedimentation rate; ALT: alanine aminotransferase; AST: aspartate aminotransferase; HIV: human immunodeficiency virus; NK: natural killer; GGT: gamma-glutamyl transferase