Macrophage activation syndrome in a patient lately diagnosed with malaria

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Introduction: Macrophage activation syndrome (MAS) is a hyperinflammatory condition, potentially fatal, that can be triggered by various autoinflammatory diseases, infections and malignancies.

Report: A 13-year old boy presented with a 4-days history of fever and myalgia. Exams showed anemia, thrombocytopenia, leukopenia and raised CRP. Blood smear was consistent with microcytic anemia. On admission he underwent IVIG infusion and ceftriaxone. His clinical conditions deteriorated with unremitting fever, dyspnoea, hypotension and hepatosplenomegaly. Trilineage cytopenia, high ferritin, increased CRP, decreased ESR, hypofibrinogemia, hypertriglyceridemia and hypoalbuminemia were consistent with the diagnosis of Macrophage Activation Syndrome (MAS)/ Hemophagocytic Lympho-Histiocytosis (HLH). Myeloaspirate showed excessive macrophage activity with hemophagocytosis and no blasts.

2004 Diagnostic criteria for HLH	Index case
Clinical criteria	
Fever	yes
Splenomegaly	yes
Laboratory criteria	
Cytopenia (affecting 2 of 3 cell lines in peripheral blood)	yes
Hemoglobin <9 g/dl	yes
Platelet < 100 x 10 ³ per dl	yes
Neutrophil <1,000 per dl	yes
Fibrinogen <1.5 g/L and/or	
Hyper triglyceridemia (fasting triglyceride >3.0 mmol/l)	yes
Histopathologic criteria	
Hematophagocytosis in bone marrow or spleen or lymph nodes	yes
No evidence of malignancy	yes
Additional criteria	
Low or absent NK activity	no
Ferritin >500 g/L	yes
Soluble CD 25 (i.e. IL2 receptor) 2,400 U/ml	no

Hemocultures, and PCR for bacteria and viruses on blood resulted negative. Genetic risk factors for MAS/fHLH were negative. He was started on high-dose corticosteroids and on etoposide and cyclosporine shortly after, due to poor response. Two doses of anakinra were also given for persisting fever. Due to the scarce improvement, other possible infectious MAS triggers were reconsidered: PCR for malaria resulted positive and his peripheral blood smears confirmed forms *P. falciparum* (parasite index 1%).

He was started on iv artesunate and quinine chlorhydrate with subsequent clinical improvement.

Oral steroids and cyclosporine were gradually tapered in 30 days. He did not have history of recent travels out of Italy.

Conclusion: The association between MAS and malaria has been occasionally described. In our patient, malaria was diagnosed only after the failure of specific treatment for MAS. As many features of malaria and MAS can overlap, clinicians should be alert to investigate both conditions in cases with unremitting fever and pancytopenia.