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Macrophage Activation Syndrome: Report of Two Clinical Cases in the Biological Hematology Department of Avicenna Military Hospital, Marrakech

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Abstract

Macrophage activation syndrome (MAS) is a rare but serious immunological emergency often associated with chronic inflammatory diseases. It represents a secondary form of hemophagocytic lymphohistiocytosis (HLH) and is characterized by uncontrolled immune system activation. We report here two clinical cases identified within a biological hematology laboratory, illustrating the varied presentations, diagnostic challenges, biological features, and multidisciplinary management of MAS.

Keywords: Macrophagic activation syndrome; biological hematology; immune response; cytokine storm; hemophagocytic syndrome.

Introduction:

Macrophage activation syndrome (MAS) is a serious complication of autoimmune or inflammatory diseases such as systemic lupus erythematosus (SLE) and systemic juvenile idiopathic arthritis (sJIA) [1]. It results from massive activation of macrophages and cytotoxic T lymphocytes, causing an excessive release of pro-inflammatory cytokines (IL-1, IL-6, IFN-γ, TNF-α) which leads to multiorgan failure [2]. The typical clinical picture includes prolonged fever, hepatosplenomegaly, cytopenias, coagulopathy, hyperferritinemia, and hemophagocytosis. Early recognition is essential to reduce mortality, which may reach 20–40% without timely treatment.

Materials and Methods:

We studied two patients hospitalized between January 2023 and December 2023 for systemic symptoms associated with significant hematological abnormalities. The initial warning signs were identified by the biological hematology lab through detection of cytopenias, hypertriglyceridemia, hyperferritinemia, and low fibrinogen. HLH-2004 criteria were applied [3]. Tests included: CBC, blood smear, ferritin, triglycerides, fibrinogen, liver enzymes, LDH, infectious and immunological screening, and bone marrow aspiration. Clinical evolution, treatment response, and follow-up data were collected.

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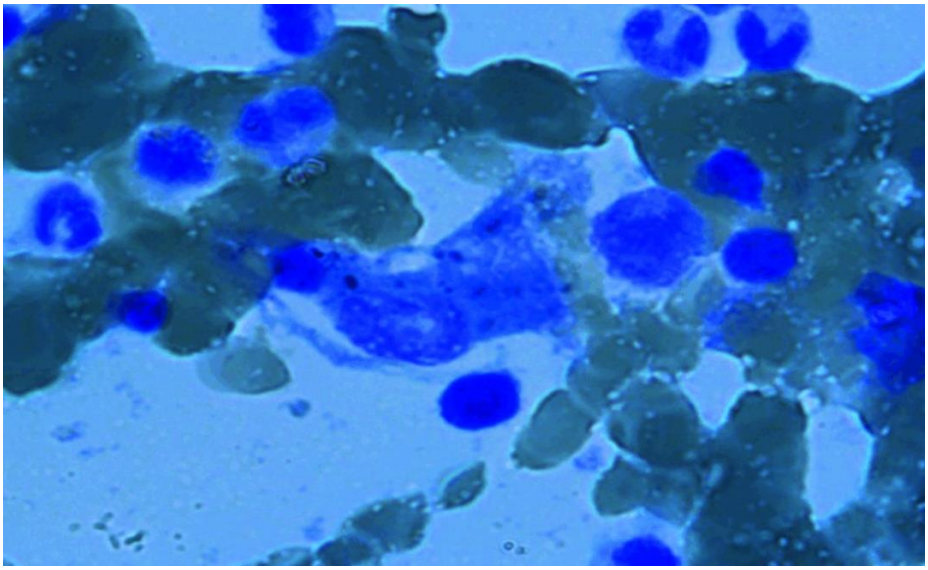
Results:

Case1:

A 13-year-old girl with a two-year history of systemic lupus erythematosus treated with hydroxychloroquine and low-dose corticosteroids was referred for persistent fever, intense fatigue, abdominal pain, and petechiae. Laboratory tests revealed normocytic anemia (Hb 8.1 g/dL), thrombocytopenia (39,000/mm³), leukopenia (3,000/mm³), ferritin at 11,600 ng/mL, triglycerides at 3.0 mmol/L, and fibrinogen at 1.0 g/L. Liver function showed elevated transaminases (AST: 82 IU/L; ALT: 70 IU/L). MRI showed homogeneous hepatosplenomegaly. Bone marrow aspiration revealed typical hemophagocytosis. Treatment included methylprednisolone boluses (1 g/day x 3 days), prednisone (1 mg/kg/day), and cyclosporine A (3 mg/kg/day), leading to rapid clinical improvement and biological normalization within one week. At 3 months, she was in stable remission.



Case2:

An 8-year-old boy followed for systemic juvenile idiopathic arthritis was hospitalized for fever >39°C, rash, apathy, and headaches. Lab results: Hb 7.7 g/dL, WBC 2,500/mm³, platelets 34,000/mm³, ferritin 16,800 ng/mL, triglycerides 4.0 mmol/L, fibrinogen 0.8 g/L. CSF was normal. Bone marrow aspiration showed diffuse hemophagocytosis. He was treated with corticosteroids (methylprednisolone 30 mg/kg/day for 3 days), intravenous immunoglobulins (2 g/kg), followed by etoposide (150 mg/m²) according to HLH-94 protocol [7]. By day 4, neurological condition had stabilized and labs improved by day 6. At 6 months, he was in complete remission on cyclosporine.

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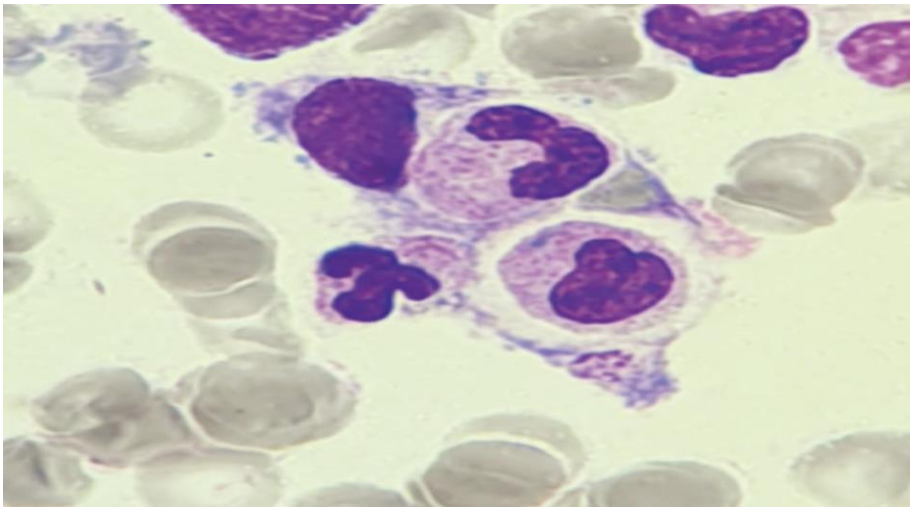

Discussion:

MAS is a severe clinical condition often underdiagnosed due to its polymorphic presentation and overlap with acute inflammatory or infectious diseases. In both reported cases, diagnosis was made in the biological hematology lab, highlighting the key role of biologists in early detection. Patients were followed for SLE and sJIA—two conditions known to be associated with MAS.

Diagnosis relies on HLH-2004 criteria, initially developed for primary HLH but still relevant in clinical practice [3]. Both patients met at least six criteria, supporting a high-probability diagnosis. Among these, **extremely high ferritin levels (>10,000 ng/mL)** are particularly suggestive, although not specific [4,5]. Several studies have shown that ferritin is a sensitive MAS indicator, often correlating with severity.

Other typical biological abnormalities were also present: **pancytopenia**, **hypertriglyceridemia**, **hypofibrinogenemia**, and moderate liver cytolysis [6]. These findings, along with **documented hemophagocytosis**, confirmed the diagnosis in both cases. Hemophagocytosis is not pathognomonic and may be absent in some cases, but when present in a cytokine storm context, it strongly supports the diagnosis.
Therapeutically, **rapid treatment initiation** is key to prognosis. High-dose corticosteroids are first-line and often lead to quick improvement as seen here. In moderate to severe forms, combining with immunosuppressants like cyclosporine A is recommended. In the pediatric case, **IVIg and etoposide** were used due to initial neurological involvement, in line with HLH-94 and expert guidelines (Histiocyte Society, ACR) [7].

Targeted biologic therapies, though not yet systematic, offer promising new options. Drugs like **anakinra (anti-IL-1)**, **tocilizumab (anti-IL-6)** or **ruxolitinib (JAK inhibitor)** are increasingly used in refractory cases, especially with autoinflammatory diseases. These agents

specifically target cytokine storm mediators and often have better safety profiles than classic immunosuppressants [8,9].

Regarding prognosis, current data report **20–40% mortality** without rapid treatment. Our two cases evolved favorably due to early and appropriate intervention. However, relapse risk remains, especially with underlying disease flares or viral infections. Long-term follow-up is essential, with regular monitoring (ferritin, CBC, liver tests) and a multidisciplinary team including biologists, internists, hematologists, pediatricians, and intensivists.

Finally, these cases emphasize the **major diagnostic value of biological hematology laboratories**, often the first to detect MAS warning signs. Enhanced vigilance should be maintained, especially in labs serving at-risk populations (autoimmune patients, pediatrics, hemato-oncology), to initiate early clinical management.

Conclusion: MAS is a serious hematologic emergency, with diagnosis largely dependent on biological hematology findings. Early recognition of biological and clinical signs, combined with rapid and tailored therapy, is essential for improving outcomes. Multidisciplinary collaboration among hematologists, internists, biologists, and intensivists is indispensable.

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