Hyperinflammation Meets Autoimmunity: Acute Hemophagocytic Syndrome as an Initial Manifestation of Lupus – A Report of Three Cases

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Introduction

Macrophage Activation Syndrome (MAS) is a rare but severe hyperinflammatory condition driven by immune dysregulation. While MAS is often secondary to infections or malignancies, its presentation as an inaugural manifestation of systemic lupus erythematosus (SLE) is exceptionally rare, posing significant diagnostic and therapeutic challenges.

Observation

Characteristics	Case 1	Case 2	Case 3
Age / Sex	25 years / Female	31 years / Female (Postpartum Day 5)	40 years / Female
Reason for Admission	Febrile pancytopenia with tumoral syndrome	Fever, hepatosplenomegaly, and bicytopenia	General condition deterioration and hepatomegaly
Clinical Findings	General deterioration , Hepatosplenomegaly , Lupus-specific skin lesions, inflammatory arthralgia	Fever, hepatosplenomegaly	Lower limb edema, hepatomegaly, inflammatory polyarthralgia
Laboratory Results	Pancytopenia, hyperferritinemia, hypofibrinogenemia, hepatic cytolysis, proteinuria with hematuria	Severe anemia, thrombocytopenia, hyperferritinemia, hepatic cytolysis, proteinuria (2 g/24 h)	Pancytopenia, hyperferritinemia, hypofibrinogenemia, renal dysfunction, proteinuria (6.25 g/24 h)
Immunology	Positive ANA, anti-DNA, anti-Sm, anti-SSA antibodies, complement consumption Coombs +	Positive ANA, anti-DNA antibodies, complement consumption	Positive ANA, anti-DNA, anti-Sm, anti-SSA, anti-SSB antibodies, complement consumption
Bone Marrow Aspiration	Confirmed hemophagocytosis	Confirmed hemophagocytosis	Confirmed hemophagocytosis
HLH-2004 Criteria	≥ 5 criteria met	≥ 6 criteria met	≥ 5 criteria met
H-Score / MAS Probability	203 / 88–91%	228 / 96–98%	204 / 88–93%
SLE (ACR/EULAR 2019 Score)	38 / 10	16 / 10	31 / 10
Treatment	Methylprednisolone pulses, oral corticosteroids, IV immunoglobulins,MMF hydroxychloroquine	Methylprednisolone pulses, oral corticosteroids,MMF , hydroxychloroquine	Methylprednisolone pulses, oral corticosteroids, cyclophosphamide
Outcome	Clinical improvement	Clinical improvement	Death due to massive pulmonary embolism

Discussion

Macrophage Activation Syndrome (MAS) is a rare but severe complication of systemic lupus erythematosus (SLE), and in some cases, it may represent the initial manifestation of the disease. In our series, MAS was the revealing feature of SLE in all three patients, who presented with fever, cytopenias, a marked inflammatory response, hepatic and renal involvement, and high disease activity.These findings are consistent with the meta-analysis by Wang et al. (2024), which reviewed 86 cases of SLE-associated MAS. Their study emphasized that more than half of the cases were inaugural and frequently associated with high disease activity, hypocomplementemia, and multiorgan involvement. Despite advances in management, the mortality rate remains substantial in cases with delayed diagnosis.In our experience, early recognition based on HLH-2004 criteria and immunological markers enabled the prompt initiation of immunosuppressive therapy. Two patients showed favorable outcomes following methylprednisolone pulses, high-dose oral corticosteroids, and additional immunosuppressive agents. Unfortunately, the third patient died from a thromboembolic event, highlighting the potentially life-threatening nature of MAS in the context of SLE.

Conclusion

These cases underscore the importance of recognizing MAS as a rare but severe inaugural presentation of SLE. Early diagnosis and prompt therapeutic intervention are essential to improving outcomes in this life-threatening condition

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