A Case of Macrophage Activation Syndrome in an Elderly Female

Shilpa Singh D.O., Jason Mause M.D., Douglas Lienesch M.D.

Christiana Care, Newark, DE

Introduction

- Macrophage activation syndrome (MAS) is a rare but potentially fatal condition seen in association with certain rheumatologic disorders.
- In this case, we discuss a 74-year-old female with a complex past medical history who presented to the ED with fever and fatigue.

Case

History of Presenting Illness:

•74-year-old female with a past medical history of scleroderma and ANCA-associated vasculitis with pauci-immune glomerulonephritis leading to ESRD on hemodialysis who presented to the ED with fever and fatigue.

Initial Exam

- Vital Signs: Temp 38.7◦C, BP 132/70 mmHg, HR 82 bpm, RR 20 breaths/min, Pulse Ox 100% on Room Air
- Physical exam findings were notable for cachectic appearance with slight confusion, but without any neurologic deficits. No rash or organomegaly.
- WBC 2400, Hgb 7.9, Platelets 212, BMP with notable Crt 3.06 but otherwise unremarkable.

Hospital Course

- The patient was evaluated for infectious, hematologic, and neurologic etiologies.
- CT C/A/P imaging revealed only a known chronic hematoma from prior kidney biopsy and MRI brain was without acute abnormalities.
- Lumbar puncture without significant findings, infectious workup including cultures and viral studies were negative.
- Rheumatologic labs were ordered given patient's pertinent history of autoimmune disease, particularly anti-SCL70 antibodies, which were consistent with her previous history of Scleroderma.
- Lab results were notable for ferritin 11,727 ng/ml, pancytopenia, elevated c-reactive protein at 60.3 mg/L, elevated triglycerides 273 mg/dl, normal haptoglobin and low fibrinogen.
- During her hospitalization, she began to develop progressive altered mental status with rapid decline in cognitive functioning, confusion, and continued febrile episodes.
- In this setting, there were concerns for macrophage activation syndrome.

Treatment Regimen

•The patient was started on high-dose steroids with Solumedrol and daily Anakinra, an IL-1 antagonist.

•Following initiation of treatment, there was notable progressive improvement of fevers, mental status, and lab abnormalities. Ferritin came down to 1047 ng/ml, triglycerides came down to 60 mg/dl.

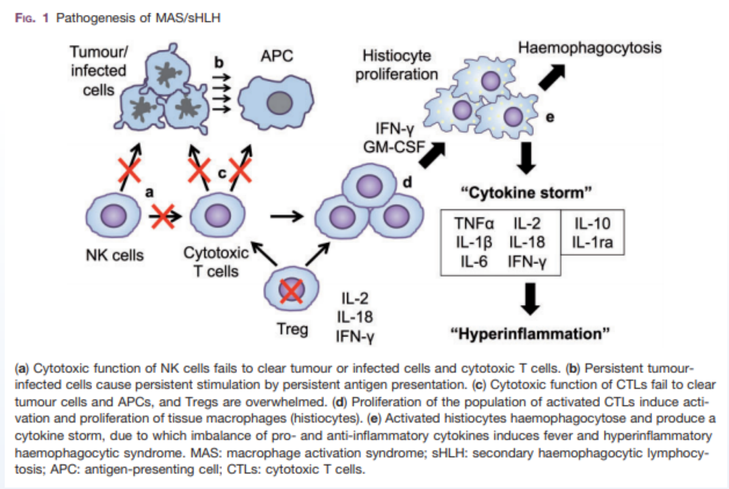
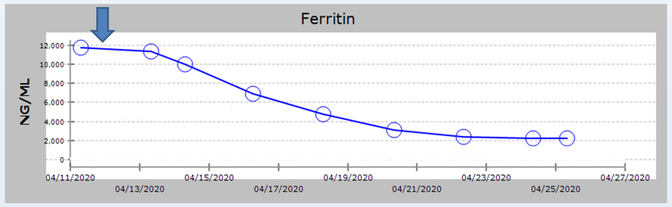


Fig. 1 Pathogenesis of MAS/sHLH

(a) Cytotoxic function of NK cells fails to clear tumour or infected cells and cytotoxic T cells. (b) Persistent tumour-infected cells cause persistent stimulation by persistent antigen presentation. (c) Cytotoxic function of CTLs fail to clear tumour cells and APCs, and Tregs are overwhelmed. (d) Proliferation of the population of activated CTLs induce activation and proliferation of tissue macrophages (histiocytes). (e) Activated histiocytes haemophagocytose and produce a cytokine storm, due to which imbalance of pro- and anti-inflammatory cytokines induces fever and hyperinflammatory haemophagocytic syndrome. MAS: macrophage activation syndrome; sHLH: secondary haemophagocytic lymphocytosis; APC: antigen-presenting cell; CTLs: cytotoxic T cells.

Figure 1: Pathogenesis of MAS/sHLH [1]



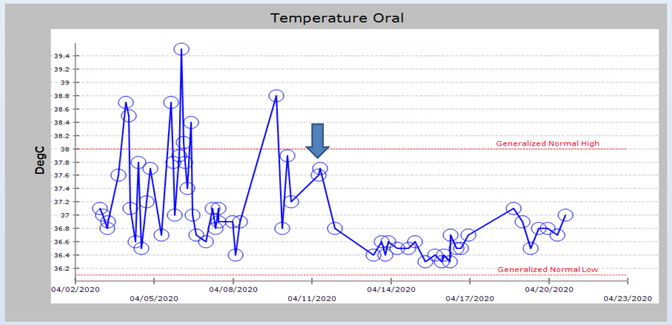


Figure 2: Ferritin and Temperature trend during admission (arrow indicates start of treatment)

Clinical Features of MAS	Laboratory Features of MAS
Non-remitting fevers	Cytopenia
Hepatomegaly	Abnormal liver function test
Splenomegaly	Coagulopathy
Lymphadenopathy	Decreased ESR
Hemorrhages	Hypertriglyceridemia
	Hyponatremia
	Hypoalbuminemia
	Hyperferritinemia

Table 1: Clinical and Lab features of MAS [1]

Discussion

• The importance of the recognition of this relatively uncommon disease is important to ensure the appropriate treatment is started in a timely manner and to prevent further decompensation given its associated severity.

Pathogenesis

•MAS is also known as Secondary Hemophagocytic Lymphohistiocytosis (sHLH), although it is specifically termed Macrophage Activation Syndrome when associated with autoimmunity.

•Historically, MAS has been associated with Adult Onset Still's Disease and systemic juvenile idiopathic arthritis.

•Ebstein-Barr Virus in particular has been shown to be a trigger of MAS.

•MAS results in a cytokine storm leading to systemic inflammation with mental status changes and subsequent lab abnormalities distinct from Adult Onset Still's Disease including alterations in LFTs, Ferritin, LDH, Triglyceride, and d-dimer levels.

Diagnosis and Treatment

- First Line Tx is Corticosteroids- methylprednisolone, prednisolone, or dexamethasone
  - •Additional treatments include cyclosporine, IL-1 Receptor Antagonists (Anakinra), intravenous immunoglobulin (IVIG), cyclophosphamide, plasma exchange.

Prognosis

- Overall mortality is around 41%[1].
- Factors associated with poorer prognosis: substantially elevated serum ferritin level (in fact, a rapid rate of decrease in serum ferritin level by over 50% after treatment portends a lower risk of mortality), older age at onset, increased comorbidities, shock and severe thrombocytopenia at presentation.

Conclusion

• Consider MAS when patient presents with fever, history of autoimmunity, with notable lab abnormalities including elevated triglycerides and ferritin, leukopenia, thrombocytopenia, elevated CRP, with normal to low haptoglobin, fibrinogen, and ESR.

•Start first line treatment with steroids, or IVIG in steroid-refractory MAS. If there are features of established HLH, start Anakinra as a second line treatment. Anakinra has also been shown to be successful when used with steroids alone.

Citations

1. Stuart J Carter, Rachel S Tattersall, Athimalaipet V Ramanan, Macrophage activation syndrome in adults: recent advances in pathophysiology, diagnosis and treatment, *Rheumatology*, Volume 58, Issue 1, January 2019, Pages 5–17, https://doi.org/1 6
2. Lerkvaleekul B, Vilaiyuk S. Macrophage activation syndrome: early diagnosis is key. *Open Access Rheumatol*. 2018;10:117-128. Published 2018 Aug 31. doi:10.2147/OARRR.S151013

ChristianaCare™