A Rare Case of Macrophage Activation Syndrome in a Patient with Behcet's Disease

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Abstract

A 37-year-old male of Pakistani origin with longstanding fever developed orogenital ulcers, skin rash, cellulitis and thrombophlebitis had a positive HLAB51 and was diagnosed with Behcet's disease. During the same hospital stay patient acutely developed pancytopenia, non-remitting fever, a high serum triglycerides and serum ferritin and bone marrow biopsy evidence of Macrophage activation syndrome (MAS), but remained non responsive to intravenous steroids and intolerant to intravenous immunoglobulins (IVIG) and finally succumbed to septic shock.

Keywords: Behcet's Disease, HLAB51, Macrophage Activation Syndrome.

Introduction

Macrophage activation syndrome (MAS) is a life-threatening complication that can occur in the setting of any uncontrolled rheumatic disorder or severe infection.[1] MAS traditionally associated with systemic onset juvenile idiopathic arthritis (S-JIA)[2,3] but its occurrence in the setting of SLE is not uncommon.[4] It is characterized by non-remitting fever, lymphadenopathy and hepatosplenomegaly supported by cytopenias, transaminitis, coagulopathy, hypertriglyceridemia, hyperferritinemia and hypoalbuminemia along with bone marrow evidence of hemophagocytosis.[5] Majority features, however, overlap with those of any patient presenting acutely with sepsis or DIC and it is of paramount importance to suspect MAS in any acutely ill patient in the setting of a rheumatic disorder.

Behcet's disease on the other hand is a pan vasculitis that predominantly affects young males, characterized by mucosal, skin involvement and any organ system involvement and follows a chronic relapsing and remitting course.[6] There are no specific diagnostic tests for Behcet's making it a diagnostic challenge.

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Case Report

Our patient was a 37-year-old, married male of Pakistani origin, an accountant with no history of smoking or illicit drug use. He had a history of intermittent, high -grade fever for nearly one year with no clinical features of autoimmune disorders, chronic infections and malignancy. During the past year the patient was investigated extensively to ascertain the cause of his fever. His complete blood counts were normal, liver function tests were three times above normal limit and of mixed pattern. Screening for Hepatitis A, B, C, HSV, HIV, EBV, brucella and malaria were all negative. CT abdomen showed mild hepatosplenomegaly and lymphadenopathy, liver biopsy done twice showed mixed inflammatory cell infiltrates in portal tract while immunohistochemistry stains did not show any evidence of malignancy. His anti bodies for autoimmune hepatitis were negative and so were ANA, ENA, anti-dsDNA, c-ANCA and p-ANCA with normal

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Submitted: 04th September, 2024 **Received:** 18th September, 2024
Accepted: 26th February, 2025 **Published:** 21st June, 2025

How to Cite This Article: Siddique M, Ahmed NM, Farman S, Abdullah MA, Ahmed A. A Rare Case of Macrophage Activation Syndrome in a Patient with Behcet's Disease. J Case Rep Med Stud Train. 2025;2(1):12-13

serum ceruloplasmin and alfa fetoprotein. CT chest and echocardiography were unremarkable.

Patient was provisionally treated as autoimmune hepatitis and given a trial of oral prednisolone by his attending physician, to which his fever was responsive following which he started taking over-the-counter oral prednisolone upto 40mg/day. Two months into this practice patient presented to us with dysphagia, vomiting and a papulonecrotic rash over the trunk. His upper gastrointestinal endoscopy showed aphthous ulceration along the esophagus with extensive candidiasis while PCR for CMV and HIV infection were again negative. Intravenous acyclovir, fluconazole, hydrocortisone and supportive measures started.

Two weeks into therapy patient developed pancytopenia, excruciatingly painful oral and genital ulcers, his skin rash remained non progressive with interface dermatitis and peri adnexal and peri vascular mixed inflammation on biopsy while his HLAB51 was positive. Solumedrol pulse therapy was given with improvement in cell counts, oral colchicine started. Another week into hospitalization patient developed cellulitis and thrombophlebitis of right arm, dopplers showed a thrombosed right cephalic vein. Antibiotics, oral apremilast and intravenous solumedrol given.

Four weeks into hospital admission although the patient remained conscious and alert, he developed unremitting high-grade fever and his pancytopenia recurred, with no evidence of hemolysis while serum triglycerides and ferritin were markedly raised. Patient was treated for MAS, confirmed on bone marrow biopsy which also showed growth of methicillin resistant staphylococcus aureus (MRSA). His PCR for CMV now came out positive, his CD4 count was 200 while repeat PCR for HIV was negative. Antibiotics and anti- viral therapy were further modified, I/V solumedrol continued, cyclosporine started but the patient developed septic shock. IV immunoglobulins were given but our patient was intolerant to them. Anakinra was in plan but not locally available. After six weeks of hospitalization patient went into cardiac arrest and succumbed to sepsis and DIC.

Discussion

MAS is a rare complication of uncontrolled autoimmune disorders, severe infections and malignancies which if left untreated has a mortality as high as 20-53%. To our knowledge this is the first case of MAS in a patient with Behcet's disease. The clinical features of MAS are non-specific and overlap with those of severe sepsis and DIC while its management is a completely different entity.[7] It is thus of prime importance to suspect, and test for MAS in any acutely ill patient.[8] Our patient had a nonspecific disease course delaying diagnosis, eventually developed clinical features of Behcet's and over days became critically ill. The diagnosis of MAS was made early and treatment started but intolerance to IVIGs and non-availability of anakinra remained a major limitation to his management.[9] The catapulting event in his case however was CMV infection rather than Behcet's disease itself which remained localized to mucocutaneous and vascular involvement. Owing to ongoing infections including MRSA and CMV, intravenous steroids, the mainstay of therapy of MAS became a two-edged sword.

Conflict of Interest: None.

Funding: None.

References

1. Grom AA, Alexei A. Macrophage activation syndrome, a review of diagnosis, treatment, and prognosis. Rheumatologist. 2012; 4: 22–30.
2. Ravelli A, Magni-Manzoni S, Pistorio A, et al. Preliminary diagnostic guidelines for macrophage activation syndrome complicating systemic juvenile idiopathic arthritis. J Pediatr. 2005; 146(5): 598–604. doi: https://doi.org/10.1016/j.jpeds.2004.12.016.
3. Shimizu M. Macrophage activation syndrome in systemic juvenile idiopathic arthritis. Immunol Med. 2021; 44(4): 237–45. doi: https://doi.org/10.1080/25785826.2021.1912893.
4. Amoura Z. 02 Macrophage activation syndrome in SLE. Lupus Science & Medicine. 2019; 6(Suppl 2): doi: https://doi.org/10.1136/lupus-2019-la.5.
5. Ravelli A, Minoia F, Davì S, et al. 2016 Classification Criteria for Macrophage Activation Syndrome Complicating Systemic Juvenile Idiopathic Arthritis: A European League Against Rheumatism/American College of Rheumatology/Paediatric Rheumatology International Trials Organisation Collaborative Initiative. Ann Rheum Dis. 2016; 75(3): 481–9. doi: https://doi.org/10.1136/annrheumdis-2015-208982.
6. Kiafar M, Faezi ST, Kasaeian A, et al. Diagnosis of Behçet's disease: clinical characteristics, diagnostic criteria, and differential diagnoses. BMC Rheumatol. 2021; 5(1): 2. doi: https://doi.org/10.1186/s41927-020-00172-1.
7. La Rosée P, Horne A, Hines M, et al. Recommendations for the management of hemophagocytic lymphohistiocytosis in adults. Blood. 2019; 133(23): 2465–77. doi: https://doi.org/10.1182/blood.2018894618.
8. Lerkvaleekul B, Vilaiyuk S. Macrophage activation syndrome: early diagnosis is key. Open Access Rheumatol. 2018; 10: 117–28. doi: https://doi.org/10.2147/oarrr.s151013.
9. Wampler Muskardin TL. Intravenous Anakinra for Macrophage Activation Syndrome May Hold Lessons for Treatment of Cytokine Storm in the Setting of Coronavirus Disease 2019. ACR Open Rheumatol. 2020; 2(5): 283–85. doi: https://doi.org/10.1002/acr2.11140.