Hemophagocytic lymphohistiocytosis with concurrent malarial infection

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DESCRIPTION

A 24-year-old man with no significant medical history was presented to our emergency department with 5 days of fever with chills, rigors and abdominal pain. He had recently travelled to the Southern part of India. Physical examination showed a temperature of 101.2°F, conjunctival pallor, left upper quadrant abdominal tenderness and moderate splenomegaly. Complete blood count revealed haemoglobin: 9.0 g/dL (normal: 12–16 g/dL), white cell count (WBC): 2600/cu mm (normal: 4000–11 000/cumm) and platelets: 80 000/cu mm (normal: 15 000–4 50 000/cu mm). Liver function test was remarkable for direct hyperbilirubinemia of 3 mg/dL (normal: 0–0.3 mg/dL). Peripheral smear examination showed *Plasmodium falciparum* with a parasite density estimated to be 5 for every 100 WBCs on a thick peripheral smear. Severe malaria was confirmed and the patient started on a treatment with intravenous artesunate. After initiation of treatment, although his fever resolved, pancytopenia continued to worsen and the patient developed confusion, generalised petechiae, ecchymosis and spontaneous gum bleeding. Ferritin was elevated at 6463 ng/mL (normal:24–336 ng/mL) and triglyceride at 282 mg/dL levels (normal: <150 mg/dL). An emergent bone marrow biopsy was performed, which revealed numerous hemophagocytes along with malarial gametocytes (figure 1). Satisfying six out of eight criteria as per hemophagocytic lymphohistiocytosis (HLH) 2004 guidelines, hemophagocytic lymphohistiocytosis was diagnosed and the patient was started on intravenous dexamethasone 10 mg/m^2 as per HLH-94 protocol.[1 2] Etoposide was not initiated due to hepatic impairment. His blood cultures were negative and serological tests for Epstein-Barr virus (EBV), HIV, herpes simplex virus, hepatitis B and E, Lyme disease, and cytomegalovirus (CMV) were also negative. He did not have any family history of HLH. The patient clinically improved after initiation of steroids and was transitioned to oral proguanil–atovaquone malaria completion therapy. He was discharged on day 10 on oral prednisone with dose tapered over 8 weeks as per protocol. On continued follow-up as outpatient after 2 weeks, it showed reduction in ferritin to 723 ng/mL, normal blood counts and no parasitemia. There was no relapse of the disease.

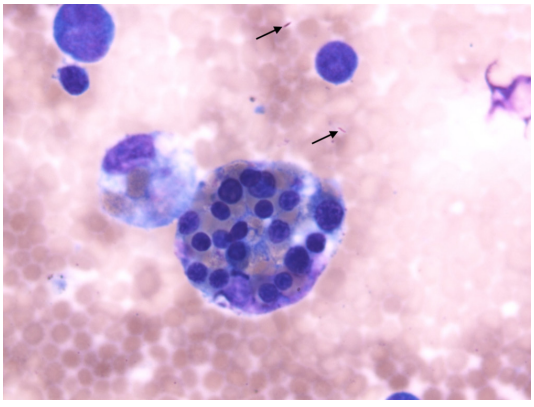

Figure 1 Bone marrow biopsy histology showing hemophagocytes with malarial gametocytes (shown with arrows).

Learning points

- Hemophagocytic lymphohistiocytosis(HLH) is a rare immunological condition, characterised by widespread activation of the inflammatory system, mononuclear phagocytic system in the bone marrow and reticuloendothelial system. Primary HLH is caused by a genetic mutation while secondary HLH occurs in patients without a family history of mutations, in whom an evident triggering factor results in the disease.
- Common triggers for secondary HLH are viral infections (like EBV, CMV, HHV 8, dengue, HIV), bacterial infections (like *Salmonella typhi*, *Mycobacterium tuberculosis*), parasitic infections like malaria (both Vivax and Falciparum),[3] malignancies (especially T-cell lymphomas), and other lymphoproliferative disorders and auto immune conditions including systemic lupus erythematosus, rheumatoid arthritis, Sjogren syndromeand dermatomyositis.
- Untreated HLH has a 90% mortality rate and persistence of pancytopenia, despite the treatment of malaria, should raise suspicion of HLH. Diagnosis is made with bone marrow biopsy and it is usually responsive to steroids.

Contributors DS was involved in the patient care and planning of manuscript. SS involved in the retrieval of images. SSA was involved

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in the preparation of manuscript and patient care. AJ was involved in the preparation and editing of manuscript.

Competing interests None declared.

Patient consent Obtained.

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