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HEMOPHAGOCYTIC LYMPHOHISTOCYTOSIS: A CASE REPORT

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Abstract

Background: Hemophagocytic lymphohistiocytosis (HLH) or hemophagocytic syndrome is a rare, life-threatening hyperinflammatory syndrome characterized by excessive, overactive, and abnormal immune activation. It can be either primary (genetic) or secondary to infections, malignancies, or autoimmune diseases. Early diagnosis and treatment are crucial but often challenging due to the nonspecific clinical presentation.

Case presentation: We report a case of 22 a 22-year-old male who presented with persistent fever, hepatosplenomegaly, cytopenias, and elevated ferritin levels. Laboratory findings revealed hypertriglyceridemia, elevated liver enzymes, and high serum ferritin, raising suspicion for HLH. Bone marrow biopsy confirmed hemophagocytosis. The patient was managed with dexamethasone and etoposide according to the HLH protocol, with clinical improvement observed within 12 weeks.

Conclusion: This case highlights the importance of early recognition of HLH and the use of HLH diagnostic criteria for timely treatment. Due to its rapid progression and high mortality, clinicians should maintain a high index of suspicion for HLH in patients with unexplained systemic inflammatory symptoms and cytopenias.

Keywords: Hemophagocytic-lymphohistocytosis ،hemophagocytic syndrome، macrophage activation syndrome.

Introduction

Hemophagocytic lymphohistiocytosis (HLH) or hemophagocytic syndrome is a rare, life-threatening hyperinflammatory syndrome characterized by excessive, overactive, and abnormal immune activation [1]. It can be either primary (genetic) or secondary to infections, malignancies, or autoimmune diseases. In HLH, the immune system reacts to a stimulus (most often an infection), but this response is both ineffective and abnormal. This ineffective and abnormal response leads to a variety of signs and symptoms, which, if left untreated, can potentially become life-threatening[2]. Early diagnosis and treatment are crucial but often challenging due to the nonspecific clinical presentation[3].

The pathophysiology of HLH involves impaired clearance of activated immune cells, leading to persistent macrophage activation, hemophagocytosis, and a cytokine storm, ultimately resulting in multi-organ failure[4]. Diagnostic criteria were established by the HLH-2004 trial**,** which include a combination of clinical, laboratory, and histopathological findings such as fever, Splenomegaly, cytopenias, hypertriglyceridemia, hyperferritinemia, and demonstration of hemophagocytosis in tissues[5]. Although pediatric HLH is more frequently linked to genetic causes, adult-onset HLH is often secondary, with Epstein-Barr virus (EBV**),** lymphomas, and autoimmune diseases such as systemic lupus erythematosus being common precipitants[6,7]. Early recognition and prompt initiation of immunosuppressive therapy, often following the HLH-94 or HLH-2004 treatment protocols (including corticosteroids, etoposide, and cyclosporine), are crucial to improving outcomes, though prognosis remains guarded[8]. In adults, tailored dosing (e.g., lower or less frequent etoposide) is often recommended due to comorbidities and toxicity concerns; however, the HScore developed by Fardet et al. (2004) is widely used in adult practice.

Case report

A twenty-two-year-old male patient from Takhar province, who works as a shepherd, was admitted to Ali Abad Teaching Hospital with complaints of epistaxis and an abdominal mass. He had been experiencing an abdominal mass and a feeling of fullness for the past two months, which had been progressively increasing. In the last few days, he also developed fever, epistaxis, and early satiety. Over the past few days, he had been admitted to various clinics and hospitals but was discharged after a short period.

Upon admission to Ali Abad Teaching Hospital, his vital signs were as follows: blood pressure (BP) 90/50 mmHg, heart rate (HR) 99 beats per minute, and temperature 38.5°C. With physical examination, we found petechiae on his lower extremities, as well as splenomegaly and hepatomegaly. Blood tests revealed the following: complete blood count (CBC) showed pancytopenia, and the peripheral smear confirmed pancytopenia with no abnormal cells. Triglyceride level was 250 mg/dL, and the viral markers were negative. Liver function tests were relatively abnormal. Serum ferritin level was greater than 500 mcg/L, and the lymph node biopsy indicated histiocytosis.

Most conditions that present with similar clinical symptoms were excluded by using the HLH-2004 diagnostic criteria or HSscore. Conditions like tuberculosis, leishmaniasis, drug reactions, autoimmune lymphoproliferative syndrome, thrombotic thrombocytopenic purpura, and

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hemolytic uremic syndrome may fulfill many criteria and should be excluded. The diagnosis was established through the recognition of distinctive symptoms, a comprehensive patient history, an extensive clinical assessment, and a range of specialized tests.

Guidelines have been released outlining the criteria required for diagnosing HLH. A clinical diagnosis of HLH is established if more than five of the following symptoms are observed: fever, splenomegaly, anemia, leukopenia, thrombocytopenia (or pancytopenia), hypertriglyceridemia, and

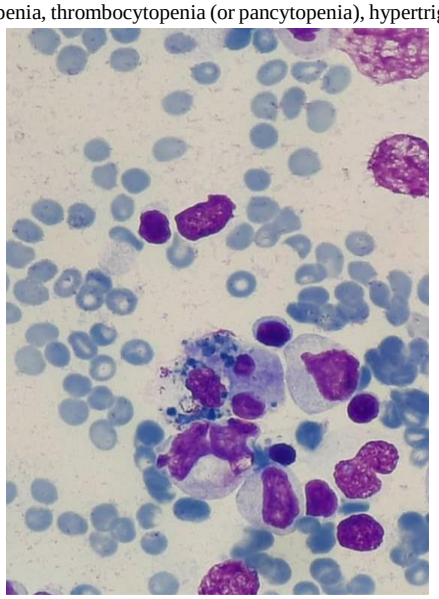

Fig 1 A: Light microscopic images of the bone marrow aspirate smear slides demonstrated trilineage hemopoiesis with the presence of an increase in haemophagocytic histiocytosis. Smear prepared by A. Masih Haidari

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In Afghanistan, where infections such as tuberculosis (TB) and visceral leishmaniosis remain endemic, secondary HLH should be considered early in young adults with persistent fever, cytopenias, organomegaly, hyperferritinemia, coagulopathy, and liver dysfunction that are disproportionate to the apparent infection burden. Early recognition and protocolized treatment are crucial to reduce mortality[11].

Furthermore, its manifestations and symptoms are indescribable. There are no descriptive diagnostic criteria, so it is often misdiagnosed or treated as other diseases. Therefore, its prevalence is low worldwide, and it is classified among rare diseases [12, 13].

However, before diagnosis this disease differential diagnosis included Digeorge syndrome (the patient did not have chromosome deletion, congenital defects, or congenital heart disease, kawaski disease (the patient did not exhibit widespread inflammation of the skin vessels or enlarged lymph nodes in the neck, nor redness of the eyes), tuberculosis (evidence for tuberculosis was negative), leishmaniasis, (there was no evidence of it), drug allergies (there was no history of any specific medication), and liver disease (liver function tests did not indicated any initial liver damage.

Differential diagnosis was conducted, and all these diseases were ruled out based on clinical findings and other evidence.

Conclusion

Due to its nonspecific and non-descriptive manifestations, HLH can often be overlooked in diagnosis or mistakenly considered as another disease. Reporting this case will aid in the diagnosis of this condition in the future, helping to prevent misdiagnosis and allowing patients to receive timely diagnosis and urgent treatment.

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elevated ferritin levels. Additionally, bone marrow findings indicate cell destruction by macrophages and reduced activity of natural killer cells (Figure 1A and B)[10].

Due to the nonspecific nature of the symptoms associated with hemophagocytic lymphohistiocytosis, this young patient experienced a lengthy illness and was hospitalized multiple times before receiving a diagnosis.

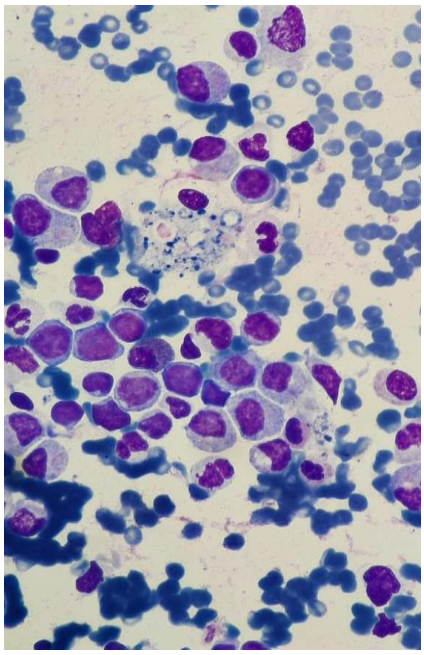

Fig 1 B: Light microscopic images of the bone marrow aspirate smear slides demonstrated trilineage hemopoiesis with the presence of an increase in haemophagocytic histiocytosis. Smear prepared by A. Masih Haidari.

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