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Pathology

EXPLORING THE SPECTRUM OF HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS: A CASE SERIES.

Dr Sakshi Anekar — Post graduate student in Department of Pathology , KAHER's Jawaharlal Nehru Medical College, Belagavi.

Dr. Vijayalaxmi Dhorigol — Head of Department of Pathology. KAHER's Jawaharlal Nehru Medical College, Belagavi.

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INTRODUCTION-

Hemophagocytic lymphohistiocytosis (HLH) is a rare yet life-threatening condition characterized by an overwhelming inflammatory response driven by excessive immune system activation. While HLH is typically associated with pediatric populations, it can also present in adults, albeit less frequently. Adult-onset HLH is increasingly recognized in clinical practice, with cases often triggered by underlying conditions such as infections, malignancies, or autoimmune diseases. The incidence of adult HLH is estimated to range between 1 and 2 cases per million individuals annually, though this number may be underreported due to diagnostic challenges and variable presentation. Early identification and prompt treatment are crucial, as untreated HLH carries a high risk of mortality. The clinical picture often includes persistent fever, cytopenias, hepatosplenomegaly, and elevated levels of inflammatory markers such as ferritin and soluble interleukin-2 receptor. A multidisciplinary approach is essential to improve outcomes in adult patients diagnosed with this complex syndrome. [1]

CASE DETAILS-

A total of 4 adult HLH cases were studied, all fulfilling the WHO 2004 criteria for HLH diagnosis. The male-to-female ratio was 3:1. Common clinical features included fever and pancytopenia in all patients. Hepatosplenomegaly was observed in one patient, while lymphadenopathy and skin rashes were present in two cases. Increased serum ferritin levels were recorded in three patients. Bone marrow aspiration and trephine biopsy performed in all four cases showed evidence of hemophagocytosis.

Individually, one 38-year-old female presented with pancytopenia, fever, and hepatosplenomegaly, with bone marrow findings showing normoblastic hypercellular marrow with hemophagocytosis. A 23-year-old male exhibited normocytic normochromic anemia with thrombocytopenia, splenomegaly, and increased serum ferritin levels, suspected of having dengue. His bone marrow was normocellular with normoblastic features and evidence of hemophagocytosis. Another patient, a 37-year-old male, showed pancytopenia, cervical lymph node swelling, and elevated serum ferritin levels, with hypercellular normoblastic marrow revealing hemophagocytosis. Lastly, a 42-year-old male presented with pancytopenia, right inguinal lymph node swelling, and skin rashes, and his bone marrow revealed hypercellular normoblastic features with hemophagocytosis. The prognosis in adult cases was observed to be poorer compared to pediatric cases in this study. A multidisciplinary approach is essential to improve outcomes in adult patients diagnosed with this complex syndrome.

Table – Summary of the 4 adult cases of HLH studied.

Patients.	Age / Sex	Peripheral smear Report	Bone Marrow Report	Clinical Findings
Case 1	38 year Female	Pancytopenia	Normoblastic Hypercellular marrow with haemophagocytosis.	Fever, Hepatosplenomegaly.
Case 2	23 year Male	Normocytic Normochromic Anemia with Thrombocytopenia	Normocellular Normoblastic Marrow with Haemophagocytosis.	Fever, Splenomegaly, Increased serum Ferritin levels, Dengue?
Case 3	37 year Male	Pancytopenia	Normoblastic Hypercellular Marrow with evidence of hemophagocytosis.	Fever, Swelling of cervical Lymph node, Increased serum ferritin
Case 4	42 year old Male	Pancytopenia	Normoblastic Hypercellular marrow with hemophagocytosis.	Fever, Right inguinal lymph node swelling, Skin rashes

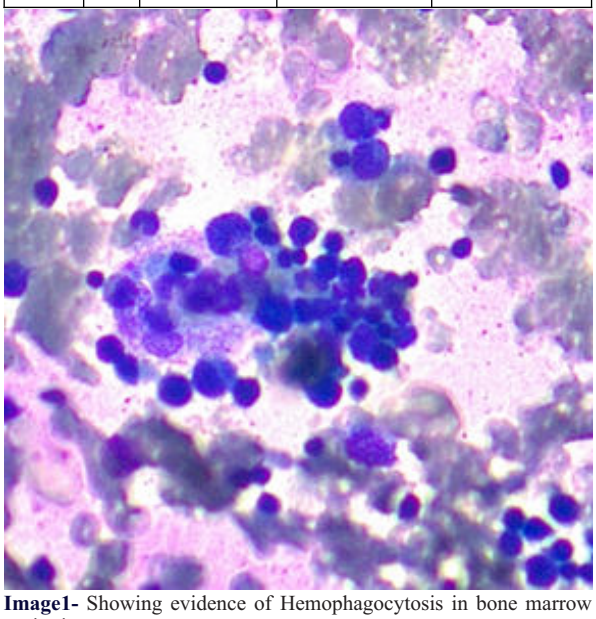

Image1- Showing evidence of Hemophagocytosis in bone marrow aspiration.

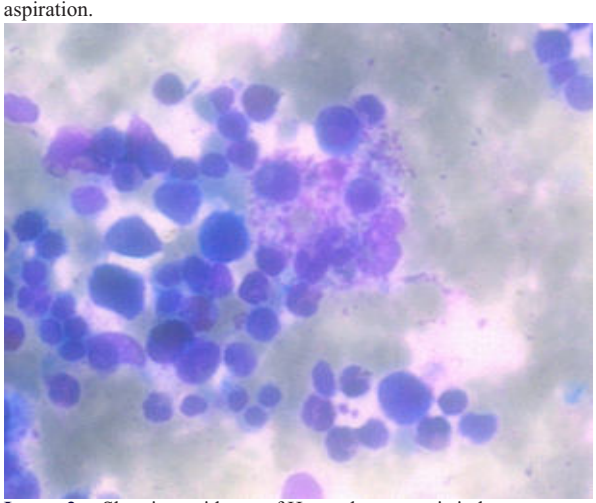

Image 2 - Showing evidence of Hemophagocytosis in bone marrow aspiration.

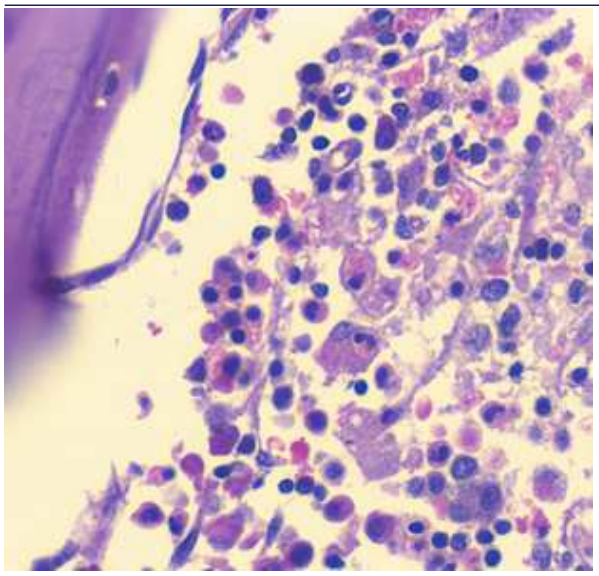

Image 3- Evidence of Hemophagocytosis in bone marrow trephine biopsy.

DISCUSSION –

The findings of this study are consistent with previous literature indicating that HLH in adults is often associated with underlying conditions such as infections, malignancies, or autoimmune diseases [2]. Fever and cytopenias were prominent features in all cases, aligning with the common clinical presentation of HLH [3]. Elevated serum ferritin levels, observed in three of the four cases, are a significant marker for HLH diagnosis and correlate with disease severity [4]. Ferritin levels exceeding 10,000 µg/L have been considered a hallmark indicator of HLH and are strongly linked to increased mortality risk [5]. Bone marrow aspiration revealing hemophagocytosis was present in all cases, reinforcing the importance of this diagnostic tool in suspected HLH cases [6]. However, it is important to note that hemophagocytosis alone is not pathognomonic and must be interpreted in conjunction with clinical findings [7].

The presence of lymphadenopathy and skin rashes in some patients mirrors earlier studies showing that these features are more commonly seen in HLH triggered by underlying malignancies or autoimmune conditions [8]. This aligns with reports suggesting that HLH secondary to lymphoma or systemic lupus erythematosus is frequently accompanied by lymph node involvement and cutaneous manifestations [9]. The 23-year-old male in this study was diagnosed with suspected dengue, a viral infection known to precipitate HLH, as seen in previous studies identifying dengue-induced HLH as a growing concern in endemic regions [10].

The poorer prognosis observed in adult cases compared to pediatric patients is well-documented in literature, highlighting the need for early diagnosis and aggressive treatment strategies [11]. Adult patients often present with multi-organ dysfunction at the time of diagnosis, which further complicates management and contributes to increased mortality rates [12]. Effective treatment often involves a combination of immunosuppressive therapy and addressing the underlying trigger, but emerging therapies such as ruxolitinib and emapalumab have shown promising results in refractory cases [13]. Continuous monitoring of inflammatory markers such as ferritin, triglycerides, and soluble CD25 levels is critical for assessing treatment response and guiding therapeutic decisions [14].

CONCLUSION-

This study highlights the clinical features, diagnostic findings, and outcomes in four adult patients diagnosed with HLH. The data emphasizes the need for heightened clinical suspicion, especially in patients presenting with persistent fever, cytopenias, and elevated inflammatory markers. Prompt diagnosis through bone marrow examination and serum ferritin assessment is crucial in improving outcomes. Given the poorer prognosis observed in adult HLH cases, early initiation of appropriate treatment remains vital. Additionally, the complex and varied presentations of HLH require a multidisciplinary approach for optimal management. Further research involving larger cohorts is needed to better understand the epidemiology, clinical patterns, and prognostic factors in adult HLH patients.

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