



## Haemophagocytic Lymphohistiocytosis – A Case Report

Authors

**Indu Choudhary<sup>1</sup>, Roshan Choudhary<sup>2</sup>**

<sup>1,2</sup>Residents, Department of Pathology, Dr. S.N. Medical College, Jodhpur

Email: [docindudbest@gmail.com](mailto:docindudbest@gmail.com)

### Abstract

*Haemophagocytic lymphohistiocytosis (HLH) is a life threatening but benign condition of severe hyper inflammation caused by the uncontrolled proliferation of activated lymphocytes and histiocytes secreting high amounts of inflammatory cytokines. The hallmark of the disease is low or absent NK cells and CD8+ T lymphocytes cytotoxicity. There are two forms of syndrome –Familial hemophagocytic lymphohistiocytosis (FHL) of infants is a rare autosomal recessive disorder demonstrating mutations in perforin gene in 30-50% cases and other reactive hemophagocytic syndrome (RHS) at any age. Epstein-Barr virus, the pathogen that most commonly triggers infection associated HPS (IA-HPS). HLH is fatal if left untreated. We report a case of HLH in an 8 year old male child who presented in paediatric outdoor with complains of high grade fever ( $>103^{\circ}\text{C}$ ), pancytopenia, hepatosplenomegaly along with rashes over face and scalp. Biochemical investigations show very high serum ferritin level i.e. 2830 $\mu\text{g/l}$ , hypertriglyceridaemia and hypofibrinogenamia. Bone Marrow aspirate and biopsy examination revealed all hematopoietic components with prominence of histiocytes and evidence of hemophagocytosis.*

**Keywords:** Hemophagocytic lymphohistiocytosis, Reactive.

### Introduction

Haemophagocytic lymphohistiocytosis (HLH) is a clinical syndrome characterised by uncontrolled proliferation of activated lymphocytes and histiocytes in the bone marrow, liver and spleen. The hallmark of disease is low or absent NK cell and CD8+ T lymphocytes cytotoxicity. The diagnosis of HLH is frequently delayed or made at autopsy because no genetic or biologic marker has been identified. HLH is not a malignancy. Incidence is reported to be 1.2 cases per million persons per year. It most frequently affects infants from birth to 18 months but is also observed in children and adults of all ages. HLH can occur as familial or sporadic disorder and can be triggered

by a variety of events that disrupt immune hemostasis.

### Case Report

A case of 8 years old male child was referred to department of pathology Dr. S.N. Medical College, Jodhpur for bone marrow aspiration examination. Child presented with clinical picture of likely sepsis having high grade fever since 10 days ( $>103^{\circ}\text{F}$ ), hepatomegaly  $>3\text{cm}$  below costal margin, malaise, anorexia associated with weight loss, jaundice,, splenomegaly, multiple erythematous rashes on face and scalp.

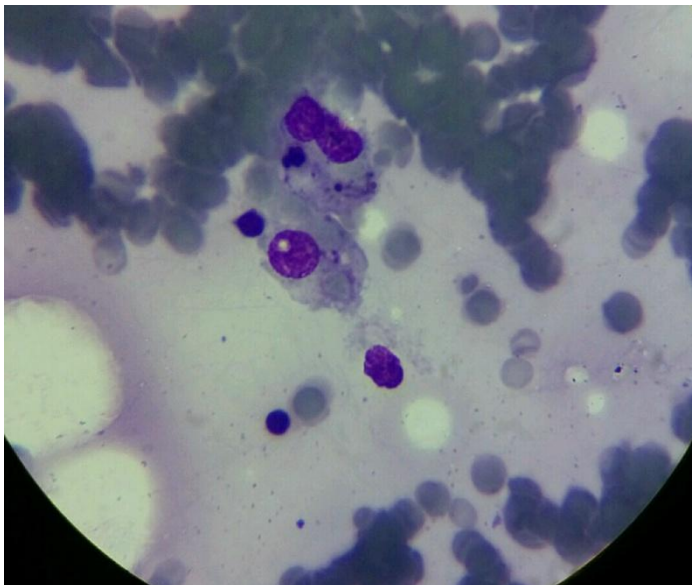
Patient had no relevant familial history neither any evidence of malignancy.

Bone marrow aspirate and biopsy examination revealed hypocellularity with suppression of erythropoiesis and myelopoiesis. Megakaryocytes were normal.

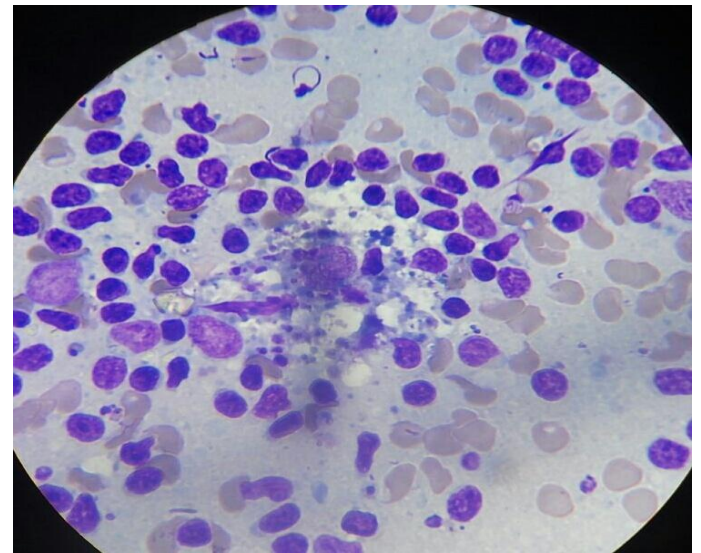
Marrow macrophages were markedly increased and many of them demonstrated phagocytosis of platelets, WBCs and RBCs.

#### Investigation

- Peripheral blood smear revealed pancytopenia especially anaemia Hb – 8.5g/dl, neutropenia and thrombocytopenia. Serum ferritin initially was 2830 $\mu$ g/l which reduced to 1050 $\mu$ g/l after initial treatment paralleling the course of the disease.
- Coagulation profile PT, aPTT, D-dimer was normal except fibrin (1.2gm/l) which was mildly reduced.
- Serum triglycerides were raised (4.5mmol/l).
- Serum bilirubin 3mg/dl
- viral testing positive for EBV
- Soluble CD25 raised 2580U/ml.
- Rest other findings like CT/MRI brain all were normal.



**Figure 1** - Bone marrow aspirate showing macrophage with phagocytised neutrophil



**Figure 2** - Bone marrow aspirate

#### Discussion

On the basis of clinical, biochemical and other relevant investigations our case goes in favour of probable viral origin. Ideally the diagnosis of HLH is based upon fulfilling the published diagnostic criteria used in the HLH 2004 trial.

As HLH mimics septic shock and acute liver failure should be differentiated by early testing for serum ferritin and soluble CD25.

There is overstimulation of immune system, excessive antigen presentation excess of T cell proliferation with infiltration of various organs CNS, Liver, Spleen and Lymph node, resulting in excess of cytokines formation like TNF alpha, INFG, IL-1 and GM-CSF leading to various manifestations.

The first reported case of HLH was described in 1952 by Farquhar and Claireaux who called the disease Familial hemophagocytic reticulosis.

there are Two forms of syndrome - Familial hemophagocytic Lymphohistiocytosis (FHL) of infants is a rare autosomal recessive disorder demonstrating mutations in perforin gene in 30-50% cases, other mutations associated are FHL 1, FHL2 FHL3 FHL4 AND FHL5. The other form reactive hemophagocytic syndrome (RHS) occurring at any age. Epstein-Barr virus, the pathogen that most commonly triggers Infection associated HPS (IA-HPS).

Rapid diagnosis and early therapy can be pivotal.

**Conclusion**

Patients presenting with clinical picture of likely sepsis, i.e. fever, splenomegaly, cytopenias and coagulopathy should be investigated and diagnosis of HLH should be considered especially in child who deteriorates despite maximal therapy.

**References**

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