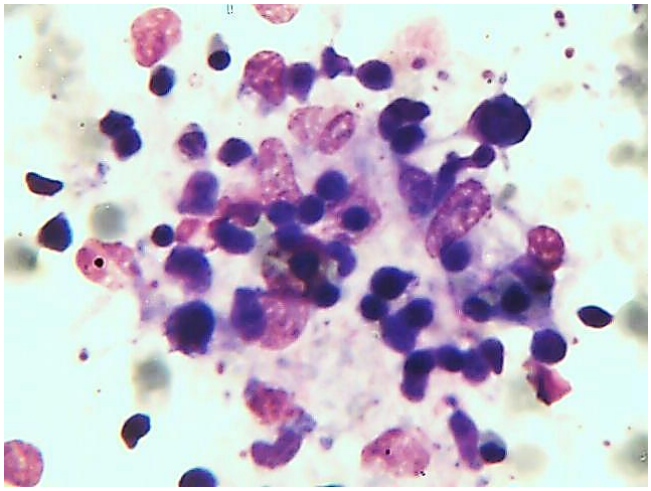

Figure 1: Giemsa ,HP: Hemophagocytosis (Macrophages Engulfing Erythroid Cells)

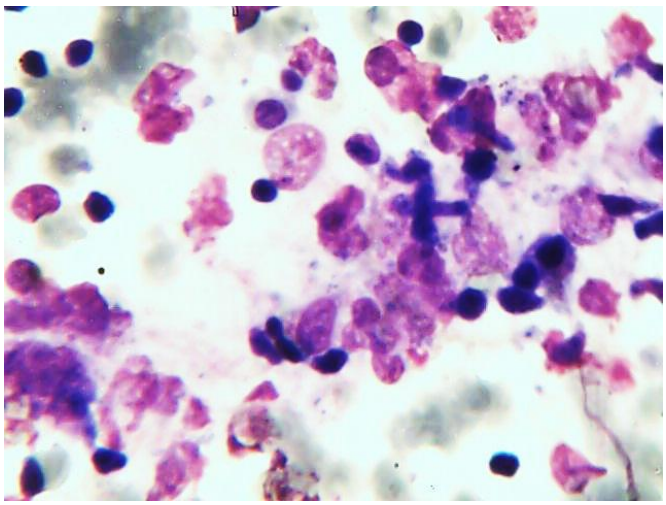

Figure 2: Giemsa ; HP : - Hemophagocytosis)

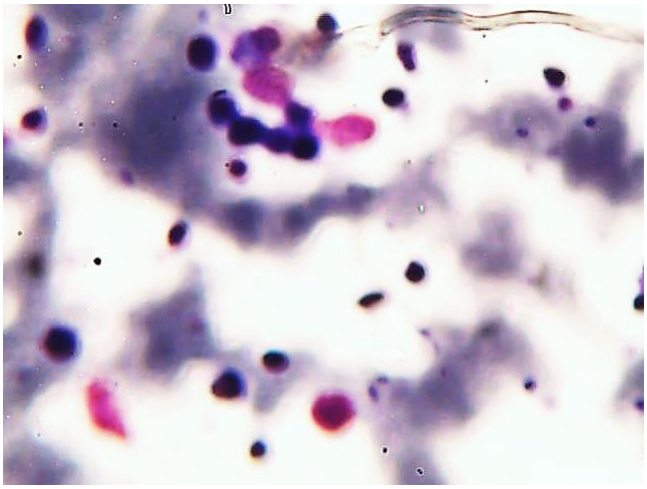

Figure 3: Giemsa , LP: - Macrophage Engulfing Many Erythroid Cells.

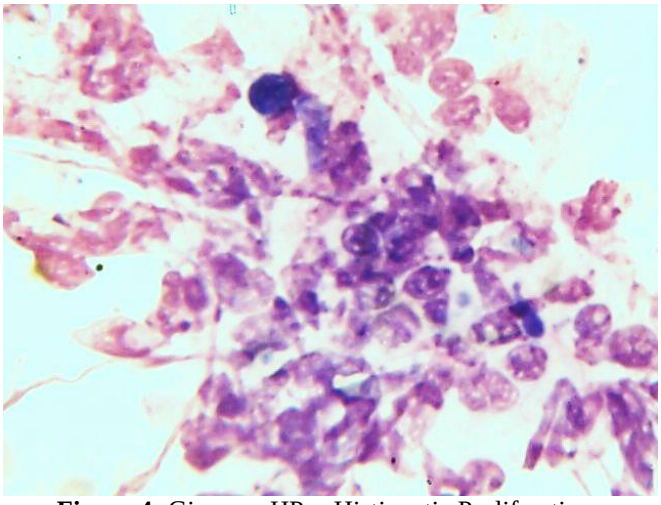

Figure 4: Giemsa ; HP: - Histiocytic Proliferation

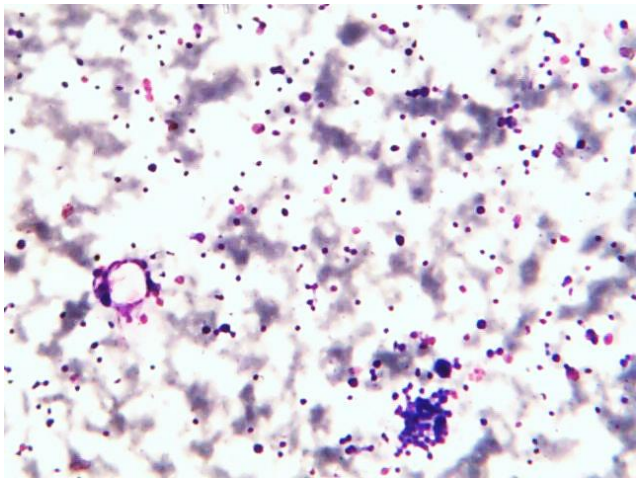

Figure 5: Giemsa ; LP :- Lympho-Histiocytic Proliferation

3. Discussion

Hemophagocyticlymphohistiocytosis (HLH) is a rare life threatening disease of the immune systemcharacterised by proliferation of activated T lymphocytes and macrophages which are morphologically benign. It has 2 types Primary/Familial HLH & Secondary HLH[1]

The current (2008) diagnostic criteria for FAMILIAL HLH[3,4,5]

1. A molecular diagnosis consistent with HLH. These include the identification of pathologic mutations of PRF1, UNC13D, or STX11.

OR

2. Fulfillment of five out of the eight criteria below:
   a) Fever (>100.4 degrees F)
   b) Splenomegaly
   c) Cytopenias affecting at least two of three lineages in the peripheral blood:
      - Haemoglobin<9 g/100 ml (in infants <4 weeks: haemoglobin<10 g/100 ml)
      - Platelets $<100\times10^9$/L
      - Neutrophils $<1\times10^9$/L

d) Hypertriglyceridemia (fasting, greater than or equal to 265 mg/100 ml) and/or hypofibrinogenemia (≤ 150 mg/100 ml)
e) Ferritin ≥ 500 ng/ml
f) Haemophagocytosis in the bone marrow, spleen or lymph nodes
g) Low or absent natural killer cell activity
h) Soluble CD25 (soluble IL-2 receptor) >2400 U/ml.

In addition, in the case of familial HLH, no evidence of malignancy should be apparent.

A 26 days boy presented with hepatosplenomegaly, lymphadenopathy, Jaundice and light hairs.There was history of sibling death with similar complaints. All the typical clinical features of HPS were present in this case. There was no evidence of Malignancy or any Viral, bacterial & fungal infections ruling out Secondary HLH. The common age of HPS is between 5-8 months but in this case Neonate was affected making it a Rare case presentation[6]

Clinical signs and laboratory abnormalities associated with HPS[5]

Clinical sign	% of patient affected
Fever	60-100
Splenomegaly*	35-100
Hepatomegaly	39-97
Lymphadenopathy	17-52
Rash	3-65
Neurologic signs	7-47

Laboratory abnormality	
Anemia*	89-100
Thrombocytopenia*	82-100
Neutropenia*	58-87
Hypertriglyceridemia*	59-100
Hypofibrinogenemia*	19-85
Hyperbilirubinemia	74 19

The various studies on HLH gave the following conclusion which was very well correlated in this case report[5].The B.M. aspirate shows good number of hypercellular B.M. fragments. LymphoHistiocytic proliferation is very prominent. Erythroid cells, lymphocytes & Platelets are Phagocytosed by histiocytes. No Giant granules noted ruling out CHS.

The Diagnosis was confirmed by Molecular testing which showed Mutation in PRF1gene.So this case falls under FHS type [6]

Differential Diagnosis

Secondary HLHMacrophage-activation syndrome or other primary immuno deficiencies that present with hemophagocyticlymphohistiocytosis, such as X-linked lympho proliferative disease. Autoimmune lympho proliferative syndrome.[7]

The diagnosis of acquired or secondary HLH is usually made in association with infection by viruses, bacteria, fungi or parasites or in association with lymphoma, autoimmune disease, or metabolic disease.

A major differential of HLH is Griscellisyndrome (type 2) which have mutations in RAB27A . This is a rare (less than 100 reported cases) autosomal recessive disorder characterized by partial albinism, hepatosplenomegaly, pancytopenia, hepatitis, immunologic abnormalities, and lymphohistiocytosis. Most cases have been diagnosed between 4 months and 7 years of age.

4. Conclusion

Familial HPS is avery rare entity. There is a considerable overlap of clinical & pathological findings of Familial HPS & Secondary HPS,Griscelli syndrome& Macrophage activation syndromes possessing a great diagnostic challenge.
The very rare nature of the disease & its grave prognosis merits its Reporting.

5. Funding: No funding sources

6. Conflict of interest: None declared

7. Ethical approval: Not required

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