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A case of Acute Myeloid Leukemia presenting as Hemophagocytic Lymphohistiocytosis

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ABSTRACT:
Hemophagocytic syndrome also called as Hemophagocytic lympho histiocytosis is an uncommon, life-threatening, hyperinflammatory syndrome causing pancytopenia. It is an important cause of fever with pancytopenia and multiorgan failure. Patients with acute myeloid leukemia are prone to develop hemophagocytic lymphohistiocytosis because of an impaired immune response and a high susceptibility to severe infections. We present a case of acute myeloid leukemia presenting as HLH.

Keywords: Hemophagocytic lympho histiocytosis, acute myeloid leukemia, hyperferritinemiahypercytokinemia, hypertriglyceridemia

I. INTRODUCTION

Pancytopenia is an important clinical and hematological entity in which all three major formed elements of blood (red blood cells, white blood cells and platelets) are decreased in number. Pancytopenia could be a result of decreased production of the cells or increased destruction. Anyone presenting with pancytopenia requires a thorough evaluation to identify the underlying etiology.1Hemophagocytic lymphohistiocytosis can be diagnosed in up to 10% of patients with acute myeloid leukemia undergoing intensive chemotherapy and is associated with early mortality. Fever, very high ferritin levels and marrow hemophagocytosis represent the cornerstone of the diagnosis. 2

Hemophagocytic syndrome also called as Hemophagocytic lympho histiocytosis is an uncommon, life-threatening, hyperinflammatory syndrome caused by severe hypercytokinemia due to a highly stimulated but ineffective immune process.3

It is characterized by inappropriate prolonged activation of lymphocytes and macrophages.The name describes the characteristic pathologic finding of macrophages engulfing erythrocytes, leukocytes, platelets and their precursor cells typically seen in bone marrow, spleen and lymph nodes rarely in CNS, skin and peripheral blood.HLH is classified into primary and secondary HLH. Primary HLH may be familial or sporadic associated with immune deficiency syndromes.Secondary HLH may be due to Infections, autoimmune disorders,Malignancy, immunosuppression / Organ transplant.Viral infection especially Epstein—Barr virus (EBV) is the most common trigger for secondary hemophagocytic lymphohistiocytosis (HLH) (29%). Studies have suggested infections, such as Mycobacterium, Plasmodium, hepatitis E, kala azar, malaria, Leptospira, etc., associated with HLH in tropics. 4 Covid and dengue are also associated with HLH. 5,6

We present a case discussion on HLH which later turned out to be due to Acute Myeloid Leukemia and the diagnostic difficulties encountered in general clinical practice.

II. CASE REPORT:

30 years old male painter by occupation, presented with c/o Easy fatiguability for 30 days and low-grade intermittent fever for 2 weeks. He had significant weight loss present not associated with loss of appetiteover 3 months. There was no h/o Cough with expectoration, abdominal complaints, altered bladder, bowel habits.There was no abdominal distension/leg swelling/ oliguria. There was no h/o Bleeding manifestationsor history suggestive of connective tissue disorder.He had no co morbid illness and was an occasional smoker and alcoholic.

Examination was normal except for pallor and splenomegaly.Vital signs: Pulse: Rate – 98 /min, BP – 110 /70 mmHg, Temperature – 98.3 F, Respiratory rate – 20 / min, JVP – not elevated.
Abdomen examination revealed Splenomegaly palpable 5 cm below left costal margin, non-tender, firm in consistency with smooth surface and round border moves with respiration.

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Patient was treated with steroids- intravenous dexamethasone and the platelet count improved on therapeutic dose. Patient was also started on oral Eltrombopag with minimal response.

Total count: 3600 cells/ cumm, DC- Polymorphs- 70%, Lymphocytes 21 %, mid cells- 9%. PCV- 12.6%, RBC count- 1.9 million/ cumm, MCV- 92 fl Platelet count- 13000 cells/ cumm. Sugar, urea, creatinine, electrolytes, thyroid profile were normal. Triglycerides level was 293 mg/dl.ESR was 150 mm/hr, LDH- 150 U/L, serum uric acid was 4.4 mg/dl. Urine analysis was normal and stool occult blood was negative. HHH, RA Factor and ANA were negative;LFT: Total Bilirubin-1.1 mg/dl (Direct- 0.5, Indirect- 0.6), SGOT-29 IU/L SGPT- 19IU/ L.

USG Abdomen showed mild splenomegaly 12.6 cm. Portal vein doppler was normal. CT Chest was normal, CT abdomen showed mild splenomegaly

Urine and Blood cultures were negative. Widal test, Scrub IgM, Lepto IgM and Dengue serology were negative. Direct and indirect antiglobin tests were negative.

Serum iron studies:

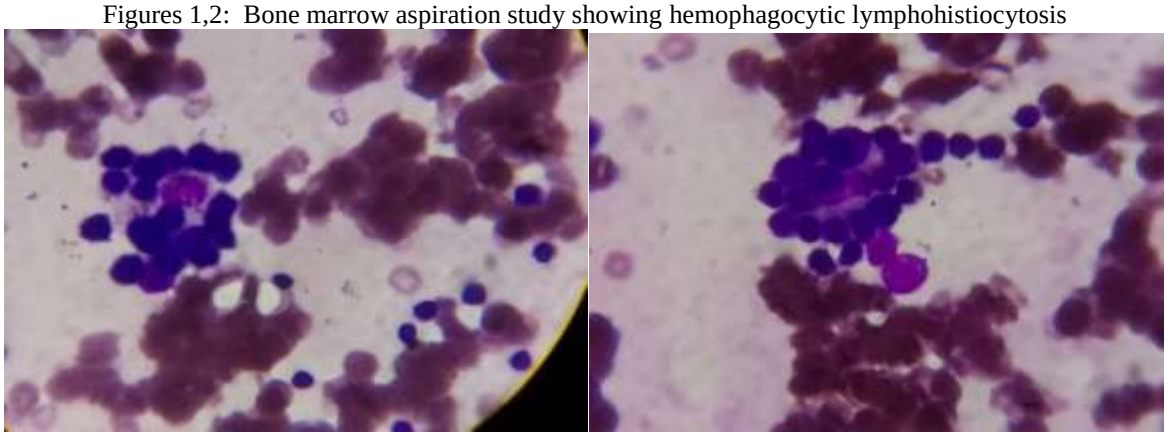
	Patient value	Reference value
Serum ferritin	443 ng/ml	23.9- 336.2
Serum Iron	23 mcg/dl	65-175
TIBC	243 mcg/dl	250-450
Transferrin saturation	10.75 %	20-50

Peripheral smear study: RBCs - reduced in count, shows anisopoikilocytosis, cells are microcytic hypochromic admixed with elongated cells. No hemoparasites are seen; WBCs – Normal in count, morphology and distribution. No atypical cells seen; Platelets – Reduced in count. Reticulocyte count of 0.9%

Bone marrow aspiration study showed: Cellularity – Partially diluted with peripheral blood; Erythroid series – active with predominantly micro normoblastic along with normoblastic maturation; normal Myeloid series, occasional Megakaryocytes and scattered lymphocytes. Large macrophages / Histiocytes engulfing red cell precursors /Erythroblasts were seen.

Bone marrow biopsy: showed trilineage hematopoeisis with erythroid hyperplasia with reduced megakaryocytes; blasts- CD 34 + in 40% blasts, CD 117 + in 30% blasts.

Figures 1,2: Bone marrow aspiration study showing hemophagocytic lymphohistiocytosis



Bone marrow aspiration study repeated after 4 weeks revealed: cellular marrow with myeloid: erythroid 4:1 and30 % blasts suggestive of Acute Myeloid Leukemia. (Fig 3)

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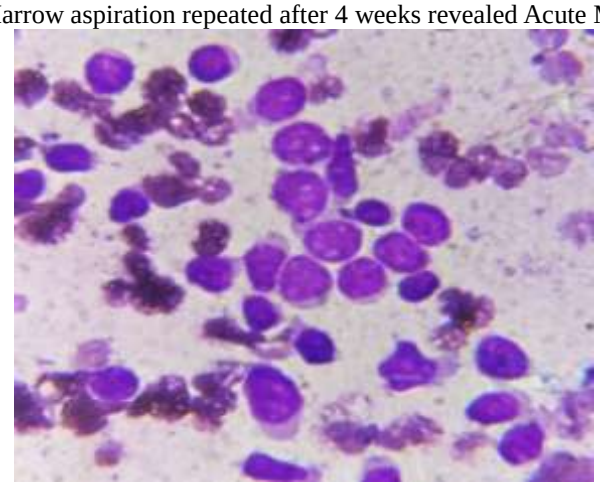
Figure 3: Bone Marrow aspiration repeated after 4 weeks revealed Acute Myeloid Leukemia



III. DISCUSSION:

In HLH-2004 update, for diagnosing HLH, five of the eight criteria must be fulfilled; fever, splenomegaly, bicytopenia, hypertriglyceridemia and/or hypofibrinogenemia, hemophagocytosis, low/absent NK-cell-activity, hyperferritinemia (>500 µg/l), and high soluble interleukin-2-receptor levels (>2400 U/ml).

In 2009, a modified diagnostic criterion was proposed:

1. Molecular diagnosis of hemophagocytic lymphohistiocytosis (HLH) or X-linked lymphoproliferative syndrome (XLP).
2. Or at least 3 of 4:(Fever, Splenomegaly, Cytopenias (minimum 2 cell lines reduced), Hepatitis)
3. And at least 1 of 4:(Hemophagocytosis, hyperferritinemia, raised sIL2Rα, Absent or very decreased NK function
4. Other results supportive of HLH diagnosis: (Hypertriglyceridemia, Hypofibrinogenemia, Hyponatremia)

Defects in the function of Natural killer (NK) cells and Cytotoxic T cells have been found in HLH patients. The inappropriate activation of T cells and macrophages produce proinflammatory cytokines, including IFN-γ, TNF-α, IL-6, IL-10, IL-12, & soluble IL-2 receptor-α (sCD25). The hypercytokinemia and pathologic activation of T cells and macrophages result in multiorgan dysfunction that can rapidly lead to death. 7

Our patient who presented with fever, pancytopenia, splenomegaly, hyperferritinemia, hypertriglyceridemia and bone marrow hemophagocytic lymphohistiocytosis fits into the diagnosis of HLH. Probably a viral infection had incited the HLH syndrome. In our patient HLH was diagnosed before the diagnosis of AML which shows that an extensive work up should be done to find out and follow up for a hematological malignancy.

IV. CONCLUSION:

HLH is encountered in a patient with leukemia in 10 % cases according to literature but in our case HLH had preceded the diagnosis of leukemia. Primary care physicians should keep a high index of suspicion for HLH as early diagnosis and treatment reduces morbidity and mortality. HLH should be routinely suspected in a patient with unexplained fever with pancytopenia and multiorgan failure.

REFERENCES

[1]. Vargas-Carretero CJ, Fernandez-Vargas OE, Ron-Magaña AL, Padilla-Ortega JA, Ron-2qGuerrero CS, Barrera-Chairez E. Etiology and clinico-hematological profile of pancytopenia: experience of a Mexican Tertiary Care Center and review of the literature. Hematology. 2019 Dec;24(1):399-404.

[2]. Delavigne K, Bérard E, Bertoli S, Corre J, Duchayne E, Demur C, Mansat-De Mas V, Borel C, Picard M, Alvarez M, Sarry A, Huguet F, Récher C. Hemophagocytic syndrome in patients with acute myeloid leukemia undergoing intensive chemotherapy. Haematologica. 2014 Mar;99(3):474-80. doi: 10.3324/haematol.2013.097394. Epub 2013 Oct 18. PMID: 24142998; PMCID: PMC3943310.

[3]. Amisha, Malik P, Pathania M, Rathaur VK, Kaeley N. Hemophagocytic lymphohistiocytosis as a diagnostic consideration of fever of unknown origin

with pancytopenia and chronic liver disease. J Family Med Prim Care. 2019 Apr;8(4):1504-1507. doi: 10.4103/jfmpc.jfmpc_190_19. PMID: 31143751; PMCID: PMC6510086.

[4]. Kim YR, Kim DY. Current status of the diagnosis and treatment of hemophagocytic lymphohistiocytosis in adults. Blood Res. 2021 Apr 30;56(S1): S17-S25. doi: 10.5045/br.2021.2020323. PMID: 33935031; PMCID: PMC8094004.

[5]. Jeyakanthan T, Ladel L, Khandpur B, Tan WY, Nasir SA. Coronavirus Does It Again: Post-COVID-19 Hemophagocytic Lymphohistiocytosis (HLH). Cureus. 2023 Feb 21;15(2):e35275. doi: 10.7759/cureus.35275. PMID: 36968874; PMCID: PMC10036136.

[6]. Munshi A, Alsuraihi A, Balubaid M, Althobaiti M, Althaqafi A. Dengue-Induced Hemophagocytic Lymphohistiocytosis: A Case Report and Literature Review. Cureus. 2021 Dec 5;13(12):e20172. doi: 10.7759/cureus.20172. PMID: 35003998; PMCID: PMC8724679.

[7]. Alexandra Filipovich. Hemophagocytic lymphohistiocytosis (HLH) and related disorders. Hematology Am Soc Hematol Educ Program (2009) 2009 (1): 127–131.https://doi.org/10.1182/asheducation-2009.1.127