CASE REPORT

Hemophagocytic Lymphohistiocytosis: A Rare Case Report

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Abstract

Hemophagocytic lymphohistiocytosis (HLH) is a life-threatening hyperinflammatory syndrome and is classified into primary and secondary HLH. Primary HLH includes monogenic problems that especially have an effect on the perforin-mediated cytotoxicity of cytotoxic T lymphocytes and herbal killer cells. Secondary HLH happens as a difficulty in diverse settings together with infection, malignancy, autoimmune disease, and postallogeneic hematopoietic stem mobileular transplantation. Both primary and secondary HLH are characterized *via* way of means of out of control hypercytokinemia that affects myelosuppression and vascular endothelium damage. The maximum not unusual place shows of HLH are continual fever refractory to antimicrobial retailers and hyperferritinemia because of hypersecretion of diverse cytokines. To enhance outcome, it is miles critical to discover the problems underlying HLH and offer disorder-suitable treatment.

Keywords: Fever, Hemophagocytic syndrome, Hyperferritinemia, Lymphoma.

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Introduction

Hemophagocytosis

Phagocytosis with the aid of using macrophages of erythrocytes, leukocytes, platelets, and their precursors in bone marrow and different tissues.

Hemophagocytic Lymphohistiocytosis

An uncommon, life-threatening hyperinflammatory syndrome due to excessive hypercytokinemia because of a fairly inspired however useless immune process.

The histological hallmark of HLH is an accumulation of histiocytes in numerous tissues together with faulty cytotoxic function. The innate immunity acts as the first line of protection in opposition to infections. It is mediated with the aid of using phagocytes, neutrophils, and NK cells which collectively provoke phagocytosis, antigen presentation, and activation of the adaptive immune device.

No laboratory check or scientific presentation offers a way to differentiate among primary and secondary. Natural records are comparable for both. Primary HLH is constrained to younger age (80% in <12 months old). In adults, nearly all instances are secondary.

Case Description

An 11-year-old vintage female, student, resident of Khirvi, Sawai Madhopur, Rajasthan, got here to Mahatma Gandhi Hospital with complaints of:

- Fever for 13 days.
- Decreased urge for food for 10 days.
- Slowness of speech for 5 days.
- Altered conduct for 2 days.

Patient was apparently alright 13 days ago, then she developed fever, it was slow onset, slight grade, continuous, associated with bodyache, now no longer related to chills and rigors, relieved with medicines, and no aggravating factors. For this she took Tab Paracetamol and Tab Omnacortil from chemist, however fever persisted.

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After 1 week of fever she began stammering, speaking slowly and non-fluently, became irritable, for which she went to a few neighborhood hospitals, habitual investigations had been achieved and affected person was no longer on any medicines suggested through doctor.

No h/o cough, cold, loose stools, pain abdomen, nausea, vomiting, and dizziness. No recent travel history. No h/o recent vaccination. Patient had no substantial past history. No h/o any drug intake or drug addiction. No recognized drug allergy. She has not attained menarche.

On examination, pulse—110 bpm, BP—106/62 mm Hg, SpO_2—96% on RA, RR—30/min, temperature—100.2°F, GCS—E3V4M4, weight—25 kg.

On CNS examination, patient was dull and drowsy but arousable. Pupils B/L equal and reactive to light. Neck rigidity present. Kernig's and Brudzinski's signs were positive. Cranium and spine: within normal limit. Cranial nerves: no significant finding.

Motor system: Upper limbs power 5/5, lower limbs power 5/5, DTR 2+ in all four limbs, tone in all four limbs normal, no abnormal movements seen.

Sensory system: No numbness, no tingling sensation, no hyperesthesia. Gait could not be assessed as patient was dull and drowsy.

GIT: Soft, non-tender. Mild hepatosplenomegaly was present.

Blood Investigations

	Outside	*Day 1*	*Day 2*	*Day 3*	*Day 4*	*Day 5*	*Day 6*	*Day 10*
WBC ($\times 10^3$) N/L (%/%)	2 68/27.3	0.79 27/12	0.91	1.16	2.53	4.59	5.44	6.50
HB (gm/dL)	10.9	8.8	8.2	5.5	5.2	8.2	8.5	10.6
PLT ($\times 10^3$)	67	21	18	3	40	35	12	51
Sr. bilirubin (total) (mmol/L)	0.8		0.5					
SGOT (U/L)	115.9	205.4		289.1		143.6		
SGPT (U/L)	62	34.7		53				
ESR (mm/hr)	38							
CRP (mg/L)	103.8							
Sr. creat (mg/dL)		0.2		0.6	0.4			
Sr. electrolytes (mmol/L) (NA/K/CL)		123.2/3.04/93	135.8/2.6/104.9	135/4/102				
Reticulocyte counts			0.5					
LDH (U/L)			1350				764.3	
Ferritin (µg/L)			17,500					
Fibrinogen (mg/dL) PT/INR			148 38.8/3.5			14.2/1.19	12.5/1.045	
D-dimer				2780				

Discussion

The clinical features of HLH are extremely variable but the disease generally presents with fever associated with multiple organ involvement/failure. Although a definite consensus does not exist, diagnosis of HLH in adults is usually based on the HLH-2004 diagnostic criteria, which are validated for children and commonly applied, but not validated for adults. Hemophagocytic lymphohistiocytosis can be diagnosed if there is a mutation in a known causative gene or if at least 5 of 8 diagnostic criteria are met.

Diagnostic Criteria

Clinical criteria	• Fever
	• Splenomegaly
Laboratory criteria	• Cytopenia: affecting 2 of 3 lineages in the peripheral blood
	• Hb <90 gm/L
	• Platelets $<100 \times 10^9$/L
	• Absolute neutrophil counts $<1 \times 10^9$/L
	• Hypertriglyceridemia and/or (fasting triglyceride level ≥3 SD) or hypofibrinogenemia (≤3 SD of normal for age)
	• Hyperferritinemia (>500 µg/L)*
	• Increased CD 25 level (≥2400 U/L)
	• Low or absent NK function
Histopathological criteria	Hemophagocytosis in marrow, spleen, or lymph nodes with no evidence of malignancy

*A higher ferritin level >3000 µg/L is considered highly indicative of HLH

A scoring machine, the "H rating," has been additionally evolved to estimate the opportunity of HLH in person sufferers. The rating consists of graded scientific and laboratory parameters, which includes immunosuppression, fever, organomegaly, stages of triglycerides, ferritin, alanine aminotransferase, fibrinogen, diploma of cytopenias, and the presence of hemophagocytosis at the bone marrow aspirate. An H rating ≥250 confers a 99% opportunity of HLH, while a rating ≤90 confers a <1% age opportunity of HLH.[1]

Prompt remedy of HLH is critical, however, the best assignment to a hit final result is the put off in analysis because of its rarity, variable scientific presentation, and absence of specificity of the scientific and laboratory findings. Hemophagocytic lymphohistiocytosis as scientific presentation of a non-Hodgkin's massive B-mobileular lymphoma is extraordinarily uncommon in scientific exercise however seven sufferers with periferal B-mobileular lymphoma related to HLH had been already reported.[2] In all the seven cases, the histologic subtype became diffuse massive B-mobileular lymphoma and the phenotype became C19+, CD20+, S-Ig+, CD10–, with co-expression of CD5 in a few cases. The pathogenesis of HLH became because of hypercytokinemia brought on *via* way of means of a proliferation of reactive CD8+ cells and secretion of numerous proinflammatory cytokines and chemokines from neoplastic cells.[2] In our case, the preliminary scientific photograph cautioned sepsis as a primary diagnostic hypothesis. Furthermore, the nutrition B12 deficiency, the absence of leukopenia, and the positivity of antiplatelet antibodies have strongly misled the proper diagnosis. Only the reaction to corticosteroid remedy and hyperferritinemia shifted the point of interest to a shape of dysregulation of the immune machine and brought about the following execution of bone marrow aspiration, whose reaction, however, got here too past due and did now no longer permit any centered remedy.

In conclusion, HLH is an unprecedented sickness that has to be continually taken into consideration every time there may be a

dubious scientific photograph blended with symptoms and signs which include fever and inflammation, specifically withinside the aged and/or frail population (eight), setting collectively each the laboratory factor and the instrumental data.

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