World Journal of Advanced Research and Reviews
eISSN: 2581-9615 CODEN (USA): WJARAI
Cross Ref DOI: 10.30574/wjarr
Journal homepage: https://wjarr.com/

(CASE REPORT)

Secondary Hemophagocytic Lymphohistiocytosis (HLH) in a 40-Year-Old Female: A rare clinical presentation highlighting the importance of early recognition and management

Dawood Khan [1,*], Muhammad Aamir Iqbal [2], Hasnat Ahmed [3], Abdul Mueed Bangash [4], Muhammad Saad [5] and Muhammad Talha [6]

[1] *Department of Internal Medicine, Hayatabad Medical Complex (HMC), MTI, Peshawar, Khyber Pakhtunkhwa, Pakistan.*
[2] *Department of Internal Medicine, Khyber Teaching Hospital (KTH), MTI, Shangla, Khyber Pakhtunkhwa, Pakistan.*
[3] *Department of Internal Medicine, Ayub Teaching Hospital (ATH), MTI, Abbottabad, Khyber Pakhtunkhwa, Pakistan.*
[4] *Department of Internal Medicine, Northwest Health Porter, Valparaiso, Indiana, USA.*
[5] *Department of Internal Medicine, Jewish Hospital Cincinnati, Cincinnati, Ohio, USA.*
[6] *Department of Internal Medicine, Hayatabad Medical Complex (HMC), MTI, Peshawar, Khyber Pakhtunkhwa, Pakistan.*

World Journal of Advanced Research and Reviews, 2025, 27(03), 1228-1230

Publication history: Received on 11 August 2025; revised on 14 September 2025; accepted on 18 September 2025

Article DOI: https://doi.org/10.30574/wjarr.2025.27.3.3187

Abstract

Hemophagocytic lymphohistiocytosis (HLH) is a rare but potentially life-threatening hyperinflammatory syndrome characterized by dysregulated immune activation. We report a case of secondary HLH in a 40-year-old woman with persistent high fever, pancytopenia, hepatosplenomegaly, and hyperferritinemia. The diagnosis was confirmed according to the HLH-2004 diagnostic criteria combined with HScore of 303 (corresponding probability > 99%). The patient responded well to the HLH-2004 regimen of immunosuppressive therapy (dexamethasone, etoposide, and cyclosporine A). This case suggests the importance of maintaining high clinical vigilance and timely intervention in the diagnosis and treatment of adult HLH.

Keywords: Hemophagocytic Lymphohistiocytosis (HLH); Secondary HLH; Hepatosplenomegaly; Hyperferritinemia; HLH-2004 diagnostic criteria; HScore; HLH-2004 regimen; Immunosuppressive therapy; Adult HLH

1. Introduction

Hemophagocytic lymphohistiocytosis (HLH) is a hyperinflammatory disease driven by excessive immune activation that can lead to tissue destruction and multiorgan dysfunction. HLH can be familial or acquired, the latter often caused by infections, malignancies, or autoimmune diseases (1,2). Although HLH is well documented in the pediatric population, it is often missed in adults because of nonspecific symptoms and overlap with other critical conditions such as sepsis or malignancy (3). Although the HLH-2004 criteria were developed for pediatric cases, they are still widely used for adult diagnosis. Additional scoring systems, such as HScore, can further support clinical decision-making. (4,5)

2. Case Presentation

A 40-year-old female presented with fever, fatigue, anorexia, abdominal pain, and general weakness for 2 weeks. She has had intermittent symptoms in the past two years and has been treated with methotrexate and glucocorticoids. Examination showed fever and pallor. Abdominal ultrasound confirmed hepatosplenomegaly.

* **Corresponding author:** Dawood Khan

Laboratory tests revealed pancytopenia (WBC 2.6 × 109/L, HB 8.6 g/dL, platelets 73 × 109/L), hyperferritinemia (2537 ng/mL), hypertriglyceridemia (370 mg/dL), elevated ALT (116 IU/l), and elevated total bilirubin (1.47 mg/dL). Bone marrow biopsy showed active proliferation of bone marrow and hemophagocytosis of histiocytes. ANA spectrum and virus serology (HBsAg, anti-HCV, HIV) were negative. Secondary HLH was diagnosed according to HLH-2004 criteria and HScore. (1,4)

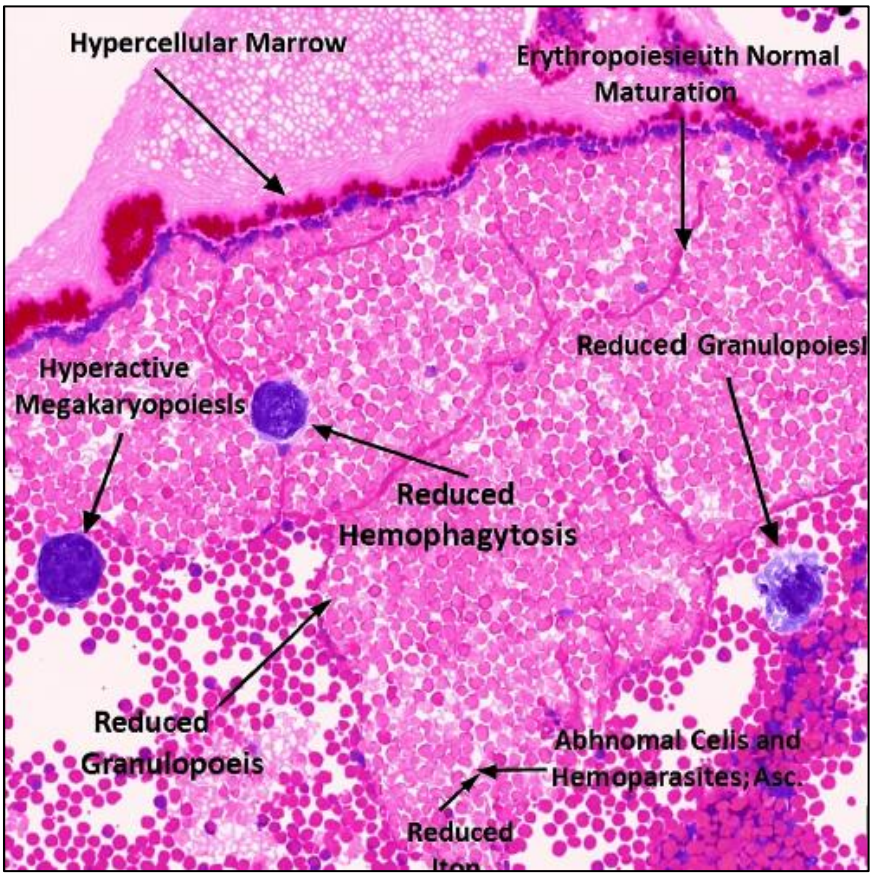

Figure 1 Bone marrow aspirate showing hypercellular marrow with hyperactive megakaryopoiesis, reduced granulopoiesis, and reduced hem phagocytosis, consistent with secondary HLH

Table 1 HScore Calculation of our patient

Parameter	Patient Finding	Score
Known Immunosuppression	Yes (Methotrexate, Steroids)	18
Temperature ≥38.4°C	Yes	33
Organomegaly	Hepatosplenomegaly	38
Cytopenias (≥2 lineages)	Yes	34
Ferritin ≥2000 ng/mL	2537 ng/mL	50
Triglycerides ≥354 mg/dL	370 mg/dL	64
AST ≥30 IU/L	116 IU/L	19
Hemophagocytosis	Present in marrow	35
Fibrinogen ≥250 mg/dL	597 mg/dL	0

Total Score: 303 → Corresponds to >99% probability of HLH [5].

3. Discussion

Secondary HLH in adults can be triggered by a variety of infections, autoimmune diseases, or malignancies (2,3). The diagnosis is difficult because of the overlap of symptoms with sepsis and other diseases. The patient in our case meets the 6 criteria of HLH-2004: fever, splenomegaly, cytopenia, hyperserotonemia, hypertriglyceridemia, and hemophagocytosis. A calculated HScore of 303 based on the criteria developed by Fardel et al further validated the diagnostic probability of > 99% (5).

The patient was started on HLH-2004 with intravenous dexamethasone and etoposide, followed by Cyclosporine A. Supportive care includes blood component infusion and monitoring of organ function. Within the first week, his clinical and hematological indices improved, confirming a good response to treatment.

4. Conclusion

Adult-onset HLH remains a diagnostic challenge; if missed, the risk of death is extremely high. This case highlights the diagnostic value of the HLH-2004 criteria and HScore, as well as the importance of early initiation of immunochemotherapy. Timely identification and multidisciplinary management are essential to improve the prognosis of patients with HLH.

Compliance with ethical standards

Disclosure of conflict of interest

No conflict of interest to be disclosed among authors.

Statement of informed consent

Informed consent was obtained from all individual participants included in the study.

References

[1] Henter J-I, Horne A, Aricó M, Egeler RM, Filipovich AH, Imashuku S, et al. HLH-2004: Diagnostic and therapeutic guidelines for hemophagocytic lymphohistiocytosis. Pediatr Blood Cancer. 2007 Feb;48(2):124–31.

[2] Ramos-Casals M, Brito-Zerón P, López-Guillermo A, Khamashta MA, Bosch X. Adult haemophagocytic syndrome. Lancet. 2014 Apr 26;383(9927):1503–16.

[3] Machowicz R, Janka G, Wiktor-Jedrzejczak W. Similar but not the same: Differential diagnosis of HLH and sepsis. Crit Rev Oncol Hematol. 2017 Jun; 114:1–12.

[4] Jordan MB, Allen CE, Weitzman S, Filipovich AH, McClain KL. How I treat hemophagocytic lymphohistiocytosis. Blood. 2011 Oct 13;118(15):4041–52.

[5] Fardet L, Galicier L, Lambotte O, Marzac C, Aumont C, Chahwan D, et al. Development and validation of the HScore, a score for the diagnosis of reactive hemophagocytic syndrome. Arthritis Rheumatol. 2014 Sep;66(9):2613–20.