WJPMR, 2026, 12(5), 94-96

Review Article

WORLD JOURNAL OF PHARMACEUTICAL AND MEDICAL RESEARCH

www.wjpmr.com

Impact Factor: 7.555

ISSN (O): 2455-3301

ISSN (P): 3051-2557

Coden USA: WJPMBB

SECONDARY HEMOPHAGOCYTIC LYMPHOHISTIOCYTOSIS: A REPORT OF 10 CASES AND LITERATURE REVIEW

Sami Zarhloul*, Youssef Bighouab, Yousra Manar, Chaimae Dadi, Nouama Bouanani

Department of Hematology, Cheikh Khalifa International University Hospital, Mohammed VI University of Health Sciences, Casablanca, Morocco.

***Corresponding Author: Sami Zarhloul**

Department of Hematology, Cheikh Khalifa International University Hospital, Mohammed VI University of Health Sciences, Casablanca, Morocco. **DOI:** https://doi.org/10.5281/zenodo.19908973

How to cite this Article: Sami Zarhloul*, Youssef Bighouab, Yousra Manar, Chaimae Dadi, Nouama Bouanani. (2026). Secondary Hemophagocytic Lymphohistiocytosis: A Report of 10 Cases and Literature Review. World Journal of Pharmaceutical and Medical Research, 12(5), 94–96.

Article Received on 03/04/2026 **Article Revised on 23/04/2026** **Article Published on 01/05/2026**

ABSTRACT

Hemophagocytic lymphohistiocytosis (HLH) is a rare but life-threatening hyperinflammatory syndrome characterized by uncontrolled immune activation and excessive cytokine release. Secondary HLH is more commonly observed in adults and is typically triggered by infections, malignancies, or autoimmune diseases. The present study aimed to describe the clinical, biological, etiological, therapeutic, and prognostic characteristics of secondary HLH in a Moroccan tertiary care center. A retrospective descriptive study was conducted including 10 adult patients diagnosed with secondary HLH between January 2017 and December 2020. Clinical presentation, laboratory findings, underlying etiologies, treatment strategies, and outcomes were analyzed. Fever and splenomegaly were the most common clinical manifestations. Marked hyperferritinemia was observed in all patients, while cytopenias and hypertriglyceridemia were present in the majority of cases. Infectious etiologies accounted for 40% of cases, followed by malignancies (30%) and autoimmune diseases (20%). All patients received corticosteroid therapy, and etoposide was administered in 60% of cases. The overall mortality rate reached 60%. Secondary HLH remains a diagnostic and therapeutic emergency with a poor prognosis. Early recognition and prompt initiation of appropriate therapy are essential to improve patient outcomes.

KEYWORDS: Hemophagocytic lymphohistiocytosis; macrophage activation syndrome; cytokine storm; hyperferritinemia; Epstein-Barr virus.

INTRODUCTION

Hemophagocytic lymphohistiocytosis (HLH) is a severe systemic inflammatory disorder resulting from dysregulated immune activation. It is characterized by excessive proliferation and activation of macrophages and cytotoxic T lymphocytes, leading to a massive release of pro-inflammatory cytokines, commonly referred to as a "cytokine storm." This uncontrolled inflammatory response results in widespread tissue damage and multi-organ dysfunction.

HLH is classically divided into primary (genetic) and secondary (acquired) forms. While primary HLH is associated with genetic defects affecting cytotoxic function, secondary HLH is more commonly encountered in adults and is triggered by infections (notably viral infections such as Epstein-Barr virus), hematological malignancies, and autoimmune disorders.

The clinical presentation is often nonspecific, including prolonged fever, hepatosplenomegaly, and cytopenias, which frequently leads to delayed diagnosis. The HLH-2004 diagnostic criteria and the HScore are commonly used tools; however, their application in adult populations remains challenging.

Given the rarity of HLH and the limited data available in North African populations, this study aimed to describe the clinical and biological profile of secondary HLH cases managed in our institution and to compare our findings with the existing literature.

MATERIALS AND METHODS

This retrospective descriptive study was conducted in the Department of Hematology at Cheikh Khalifa International University Hospital in Casablanca,

Morocco, over a period extending from January 2017 to December 2020.

Adult patients aged 16 years or older with a diagnosis of secondary HLH, established according to the HLH-2004 criteria (at least five of eight criteria fulfilled), were included in the study.

Data were collected from medical records and included demographic characteristics, clinical features, laboratory findings, bone marrow examination results, underlying etiologies, therapeutic interventions, and clinical outcomes.

A descriptive statistical analysis was performed. Continuous variables were expressed as mean values, and categorical variables as percentages.

RESULTS AND DISCUSSION

A total of 10 patients were included in the study, with a mean age of 41.5 years. A slight male predominance was observed (60%).

Fever was present in 80% of patients and represented the most consistent clinical manifestation. Splenomegaly was observed in 70% of cases. All patients presented with a marked deterioration of general condition.

Marked hyperferritinemia was observed in all patients, frequently exceeding 5000 µg/L. Cytopenias involving at least two hematological lineages were identified in 90% of cases. Hypertriglyceridemia and hypofibrinogenemia were also commonly observed.

Bone marrow examination demonstrated hemophagocytosis in the majority of patients, supporting the diagnosis.

Infectious etiologies were the most frequent (40%), particularly viral infections such as Epstein-Barr virus. Malignancies, mainly lymphomas, accounted for 30% of cases, while autoimmune diseases represented 20%. No etiology was identified in one patient.

All patients received corticosteroid therapy. Etoposide was administered in 60% of cases according to the HLH-94 protocol. Despite treatment, the overall mortality rate remained high at 60%, mainly due to septic complications and multi-organ failure.

DISCUSSION

Hemophagocytic lymphohistiocytosis represents a severe hyperinflammatory condition driven by profound immune dysregulation. The pathophysiology is primarily characterized by impaired cytotoxic activity of natural killer (NK) cells and CD8+ T lymphocytes, leading to persistent antigenic stimulation and uncontrolled macrophage activation. This results in excessive cytokine production, including interferon-gamma, interleukin-6, and tumor necrosis factor-alpha, which ultimately leads to multi-organ damage.

One of the major challenges in HLH lies in its nonspecific clinical presentation. The overlap with severe infections or septic syndromes frequently leads to delayed diagnosis. In our study, persistent fever, cytopenias, and hyperferritinemia were the most consistent diagnostic clues.

Hyperferritinemia remains a key biological marker in HLH. Extremely elevated ferritin levels (>10,000 µg/L) have been shown to strongly suggest the diagnosis, although they are not entirely specific. In our cohort, ferritin elevation was universal, highlighting its diagnostic importance.

The predominance of infectious etiologies observed in our series is consistent with data reported in developing countries. Epstein-Barr virus plays a central role due to its ability to infect T lymphocytes and promote excessive immune activation. Malignancy-associated HLH, particularly in lymphomas, is associated with a poorer prognosis and often requires combined therapeutic strategies targeting both HLH and the underlying malignancy.

The HLH-2004 protocol remains the standard of care and includes corticosteroids and etoposide. However, its efficacy in adult populations is variable, and treatment-related toxicity remains a concern. Despite appropriate therapy, the mortality rate remains high, as illustrated in our study.

Recent therapeutic advances have focused on targeted immunomodulation. Agents such as ruxolitinib, a Janus kinase inhibitor, and emapalumab, an anti-interferon-gamma monoclonal antibody, have shown promising results in refractory cases by specifically targeting the cytokine storm.

Early diagnosis and prompt initiation of therapy are the most critical determinants of prognosis. The use of diagnostic tools such as the HScore may facilitate earlier recognition in clinical practice.

CONCLUSION

Secondary hemophagocytic lymphohistiocytosis is a life-threatening condition associated with a high mortality rate. Its diagnosis remains challenging due to nonspecific clinical features.

Early recognition, rapid initiation of appropriate therapy, and identification of the underlying cause are essential to improve patient outcomes.

ACKNOWLEDGEMENT

None.

REFERENCES

1. La Rosée P, et al. Blood, 2019; 133(23): 2465–2477.
2. Griffin G, et al. Best Pract Res Clin Rheumatol, 2020; 34(4): 101515.
3. Schram AM, Berliner N. Blood, 2015; 125(19): 2908–2914.
4. Ramos-Casals M, et al. Lancet, 2014; 383(9927): 1503–1516.
5. Fardet L, et al. Arthritis Rheumatol, 2014; 66(9): 2613–2620.
6. Al-Samkari H, Berliner N. Annu Rev Pathol, 2018; 13: 27–49.
7. Brisse E, et al. Front Immunol, 2021; 12: 631747.
8. Park HS, et al. Eur J Haematol, 2021; 106(4): 546–553.