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LETTER TO THE EDITOR

Lymphocytic Hypereosinophilic Syndrome Evolving to Fatal Hemophagocytic Lymphohistiocytosis: Cytokine Signatures

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SUMMARY

Background: **This study documents a rare case of lymphocytic variant hypereosinophilic syndrome (L-HES) [1], progressing to fatal hemophagocytic lymphohistiocytosis (HLH).**
Methods: **A 70-year-old female with eosinophilia (85.6%) underwent cytokine profiling, flow cytometry, and bone marrow examination.**
Results: **A Th2-to-Th1 cytokine shift (IL-5↓/IFN-γ↑) preceded HLH onset. Despite therapy, the patient succumbed to refractory disease.**
Conclusions: **Cytokine monitoring may predict L-HES-to-HLH transformation, suggesting JAK inhibitors for high-risk cases.**
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KEYWORDS

Lymphocytic Hypereosinophilic Syndrome, Hemophagocytic Lymphohistiocytosis, cytokine profiling, IL-5, IFN-γ

CASE PRESENTATION

A 70-year-old female presented with leukocytosis (41.53 x 10^9/L) and eosinophilia (85.6%). Flow cytometry identified aberrant $CD3^+CD4^+CD7^-$ T-cells (6.95%) [2,3], and bone marrow biopsy confirmed eosinophilic infiltration (Figure 1A). Within 8 months, she developed HLH with cytopenias, hyperferritinemia (2,422 ng/mL), and hypofibrinogenemia (< 0.9 g/L), supported by bone marrow hemophagocytosis (Figures 1B) and HScore 187 (Table 1) [4,5].

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Table 1. Laboratory evolution from L-HES to HLH.

Parameter	August 2022 (L-HES diagnosis)	April 2023 (HLH diagnosis)
WBC (x 10 < sup > 9 </sup >/L)	41.53	1.2
Eosinophils (%)	85.63	0
Ferritin (ng/mL)	-	2,422
Fibrinogen (g/L)	-	0.82
IFN-γ (pg/mL)	-	3,602
IL-6 (pg/mL)	-	147.38

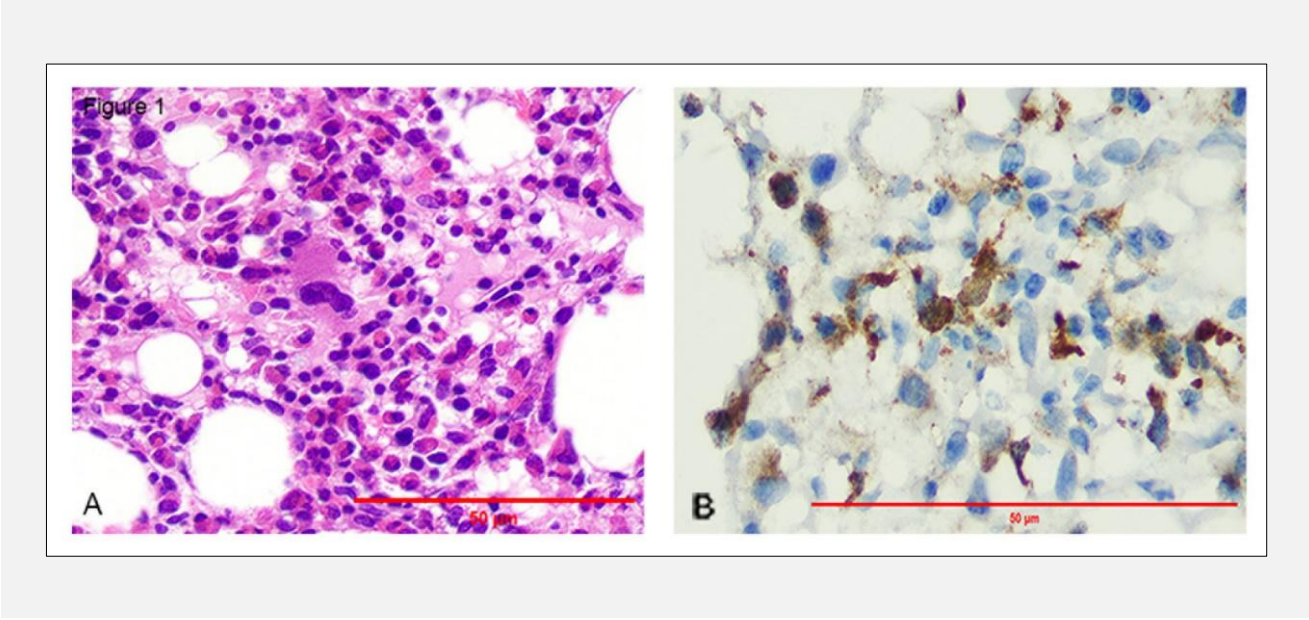

Figure 1. (A) Bone marrow eosinophilia (H&E, 400 x), (B) Hemophagocytosis (CD68 IHC, 1,000 x).

DISCUSSION

This case highlights three critical insights:
1) Pathogenesis: The Th2-to-Th1 shift (IL-5↓/IFN-γ↑) suggests clonal T-cell evolution, consistent with Faguer et al.'s findings on JAK inhibition in L-HES [6].
2) Diagnostic Utility: Extreme eosinophilia (> 80%) and IFN-γ > 1,000 pg/mL may serve as early HLH predictors [4,7].
3) Therapeutic Implications: HLH-94 failure supports trials of JAK inhibitors (e.g., ruxolitinib) in similar cases [5,8,9].

Ethics Approval:
Retrospective analysis exempted by Ganzhou People's Hospital Ethics Committee (Helsinki compliant).

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Declaration of Interest:
All authors declare no conflicts of interest.

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