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A case report of a hemophagocytic lymphohistiocytosis secondary to an extranodal NK/T-cell lymphoma

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Abstract

Hemophagocytic Lymphohistiocytosis (HLH) is a rare, life-threatening hyperinflammatory syndrome resulting from inappropriate and dysregulated activation of NK cells, CD8+ cytotoxic T-cells, and macrophages. HLH is classified as primary (familial) or secondary, with the latter triggered by factors such as infections, autoimmune disorders or malignancies, particularly Hodgkin and non-Hodgkin lymphomas. Diagnosis typically follows HLH-2004 criteria, and management focuses on addressing the underlying disease. The authors report a case of Hemophagocytic lymphohistiocytosis secondary to an extranodal Natural Killer (NK)/T-cell lymphoma in 52-year-old man, born in China, with a history of hepatitis B infection, presented to the emergency department with disseminated skin lesions, anorexia, weight loss and fever.

Description

A 52-year-old man, born in China, with a history of hepatitis B infection, presented to the emergency department with disseminated skin lesions, anorexia, and weight loss over six months. He also reported vespertine fever (39.5ºC) for two weeks. The patient denied other symptoms, recent travel, or contact with animals.

On physical examination, multiple painful erythematous nodules were observed on both lower limbs, some of which were ulcerated with necrotic borders. Small, soft lymphadenopathy was also noted in the right jugular chain. Laboratory tests revealed leukopenia (2,100/mm^3) and thrombocytopenia (64,000/mm^3) without anemia, hypofibrinogenemia (93 ng/dL)) with normal aPTT and INR; mild creatinine elevation (1.26 mg/dL); slight increased liver enzymes (alanine aminotranferase: 93 U/L; aspartate aminotransferase: 129 U/L), elevated lactate dehydrogenase (1,749 U/L), hypertriglyceridemia (346 mg/dL), and hyperferritinemia (22,959 ng/mL). Serological tests were negative for human immunodeficiency virus, hepatitis B and C, Human T-lymphotropic virus, syphilis, leishmania, *Mycoplasma pneumoniae*, Cytomegalovirus, Epstein–Barr virus, and parvovirus.

Thoracic-abdominal-pelvic computed tomography identified a 29 mm cystic lesion in the superior mediastinum and a 24 mm subpleural nodule in the left lower lobe, with no other significant findings.

The patient was hospitalized and underwent bone marrow aspiration and biopsy, along with a cutaneous lesion biopsy.

Bone marrow aspiration suggested a reactive medullary process with hemophagocytosis (Figures 1 & 2), with no atypical populations identified on immunophenotyping. Bone marrow biopsy showed mild dyserythropoiesis. Skin biopsy demonstrat-

ed diffuse infiltration of pleomorphic small-to-medium lymphocytes within the panniculus, angiocentric necrosis with vasculitis, and nodular lymphoid aggregates in the dermis, consistent with a high-grade lymphoma. Immunohistochemical revealed lymphocytes positivity for CD3, CD4, CD56, and TIA-1 and negativity for CD20, CD8 and CD123. Ki-67 staining was nearly 100% positive, and Epstein-Barr virus-encoded small RNAs were detected.

The diagnosis of Hemophagocytic Lymphohistiocytosis (HLH) secondary to an extranodal Natural Killer (NK)/T-cell lymphoma was established. The patient began treatment with the CHOEP protocol (cyclophosphamide, doxorubicin, vincristine, etoposide and prednisolone) but succumbed to multiagent pneumonia one month later.

HLH is a rare, life-threatening hyperinflammatory syndrome resulting from inappropriate and dysregulated activation of NK cells, CD8+ cytotoxic T-cells, and macrophages [1,2]. HLH is classified as primary (familial) when associated with inherited genetic mutations or secondary, triggered by factors such as infections, autoimmune disorders or malignancies, particularly Hodgkin and non-Hodgkin lymphomas [1,2].

Extranodal NK/T-cell lymphomas, though rare in Europe and North America, are the most prevalent subtype of lymphoproliferative disorders associated with lymphoma-related HLH in Asia [1,3]. Diagnosis often follows HLH-2004 criteria [1]. Prompt recognition and treatment are critical due to the high mortality rate, with an overall mortality of 41% [2] without intervention. Management focuses on addressing the underlying disease, with the HLH-94 protocol – steroids and etoposide – showing favorable outcomes in critically ill patients.

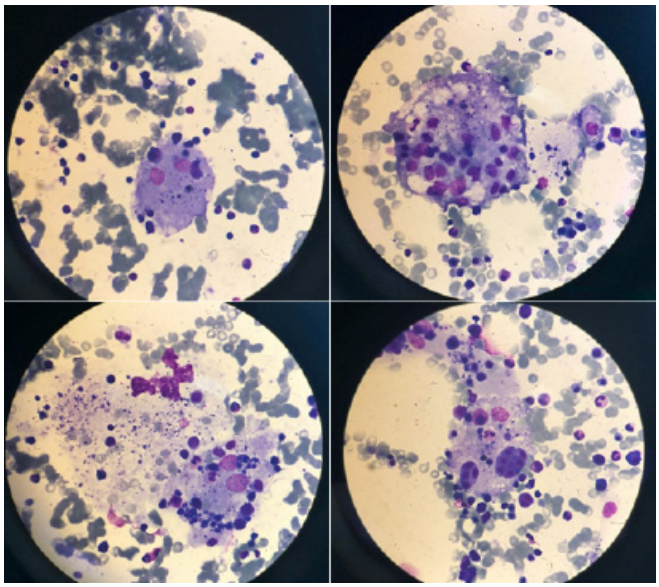

Figure 1: Hemofagocytosis, fagocytosis by macrophages in bone marrow aspiration smear. May–Grünwald–Giemsa stain, ×1000 magnification.

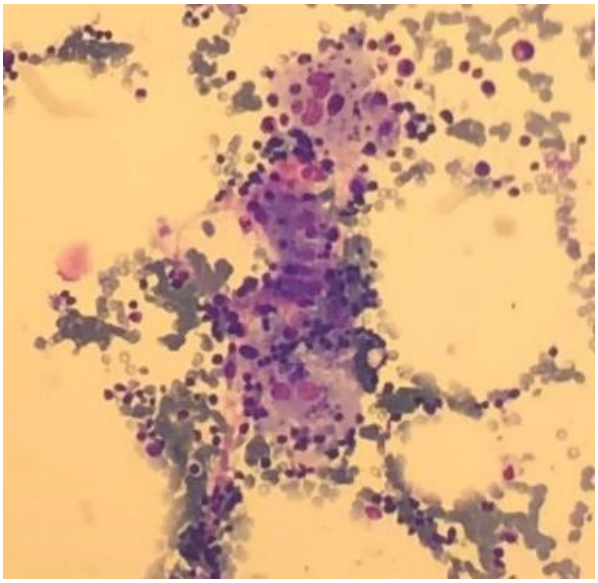

Figure 2: Hemofagocytosis, fagocytosis by macrophages in bone marrow aspiration smear. May–Grünwald–Giemsa stain, ×100 magnification.

Conclusion

HLH represents a medical emergency requiring rapid recognition and treatment. Diagnosis requires high suspicion, particularly in patients with persistent fever, cytopenias, and hyperinflammatory markers. Identifying and managing the underlying triggers is crucial for prognosis. This case highlights the need for awareness of rare conditions like extranodal NK/T-cell lymphoma-associated HLH, particularly in patients from regions where such malignancies are more prevalent.

Disclosures: The authors claim no conflicts of interest.

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