A rare case of angioimmunoblastic T-cell lymphoma-associated hemophagocytic lymphohistiocytosis

Elizabeth Ko, MD[1], Carson Wills, PhD[1], Gustavo Torres, MD[2], Kevin Rakszawski, MD[3]

[1]Penn State College of Medicine, Department of Internal Medicine

[2]Penn State Health Milton S. Hershey Medical Center, Department of Pathology

[3]Penn State Health Milton S. Hershey Medical Center, Department of Medicine, Division of Hematology and Oncology

Introduction

Hemophagocytic lymphohistiocytosis (HLH) is a rare, life-threating hematologic disorder characterized by immune dysregulation leading to systemic inflammation and organ failure. While primary HLH is mediated by known genetic mutations that induce NK and cytotoxic T cell overstimulation, secondary HLH is associated with immune dysfunction in the setting of immunodeficiency, autoimmune disease, or malignancy, most frequently lymphoma.[1] Angioimmunoblastic T-cell lymphoma (AITL) is an uncommon and aggressive subtype of mature peripheral T-cell lymphoma, which can mimic a variety of inflammatory and neoplastic processes, and which is rarely associated with HLH.[2]

Methods

This noncontrolled, observational case report focuses on one patient diagnosed with AITL-associated HLH at a large academic medical center.

Results

A 53-year-old female with no significant past medical history presented in the setting of a one-month history of extensive lymphadenopathy, intermittent fevers, and diarrhea. Labs on arrival were significant for anemia and thrombocytopenia, elevated fibrinogen and ferritin, decreased fibrinogen and elevated interleukin receptor 1. CT of the abdomen/pelvis demonstrated hepatosplenomegaly and extensive lymphadenopathy, and bone marrow biopsy demonstrated hemophagocytosis, concerning for secondary HLH of unknown etiology.

Results Continued

An extensive infectious and autoimmune workup was significant for positive EBV, HBcAb, HSV, and Lyme titers. In the setting of a frequent transfusion requirement, cytopenia workup was significant for cold autoantibodies and peripheral blood smear exhibiting circulating plasmacytoid lymphocytes and immunoblasts. The patient underwent excisional lymph node biopsy, which demonstrated AITL.

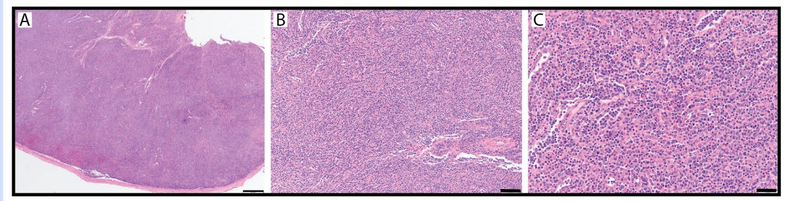

Figure 1| Hematoxylin and eosin stain of excisional lymph node biopsy.

A. Low power demonstrates complete effacement of normal nodal architecture. The subcapsular sinus remains partially open, and high endothelial venules are seen with hyalinized walls. Scale bar, 500µm. **B.** 10x power demonstrates large immunoblasts with pleomorphic nuclei mixed with eosinophils. Scale bar, 100µm. **C.** 20x power demonstrated neoplastic cells invading the lumen of endothelial venules. Scale bar, 50µm.

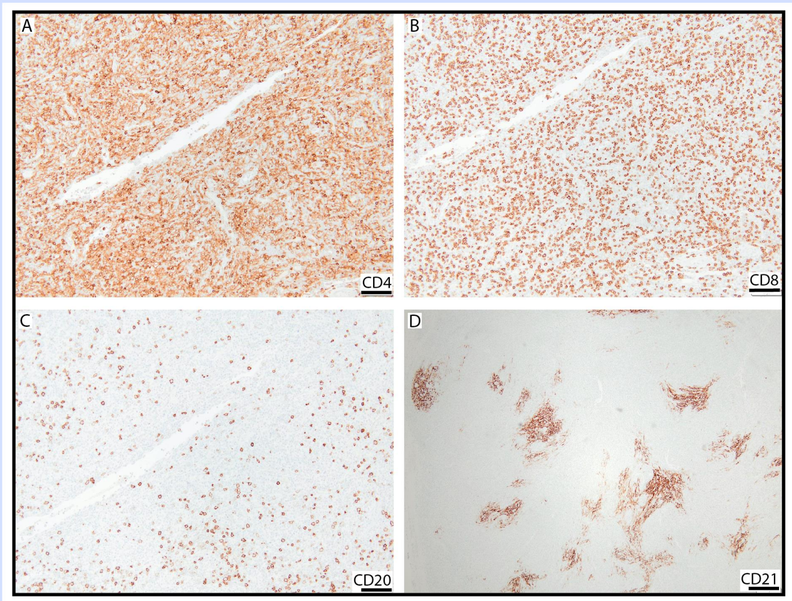

Figure 2| Immunohistochemistry of lymph node biopsy demonstrates T cell proliferation.

A. CD4 immunostain highlights neoplastic cells. Scale bar, 100µm. **B.** CD8 immunostain highlights reactive cytotoxic T cells. Scale bar, 100µm. **C.** CD20 immunostain highlights B cells. Scale bar, 100µm. **D.** CD21 immunostain highlights the expanded and abnormal follicular dendritic cell meshwork. Scale bar, 100µm.

After confirmation, the patient was started on induction chemotherapy with cyclophosphamide-hydroxydaunorubicin, vincristine, etoposide, and prednisone, with improvement in symptoms and lymphadenopathy.

Results Continued

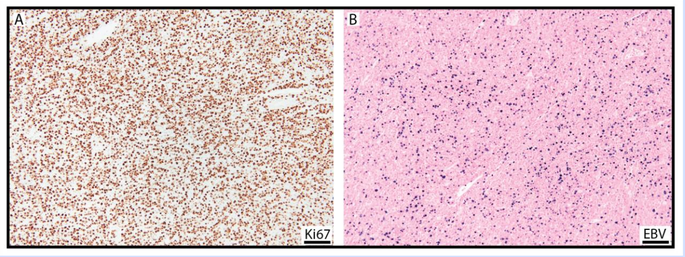

Figure 3| Immunohistochemistry of excisional lymph node biopsy demonstrates high proliferation index and reactivation of Epstein–Barr virus (EBV).

A. Ki-67 immunostain highlights 80-90% of large neoplastic cells, indicating high proliferation index. Scale bar, 100µm. **B.** Ish-EBV (EBER) positive B-cells, highlights reactivation of EBV. Scale bar, 100µm.

Conclusions

AITL is a rare and aggressive malignancy, which is infrequently associated with secondary HLH. Clinicals should maintain a broad differential while pursing the workup of a patient with newly-diagnosed HLH.[1,3]

References

1. Henter JI, Horne A, Aricó M, Egeler RM, Filipovich AH, Imashuku S, Ladisch S, McClain K, Webb D, Winiarski J, Janka G. HLH-2004: Diagnostic and therapeutic guidelines for hemophagocytic lymphohistiocytosis. Pediatr Blood Cancer. 2007 Feb;48(2):124-31. doi: 10.1002/pbc.21039.

2. Lunning MA, Vose JM. Angioimmunoblastic T-cell lymphoma: the many-faced lymphoma. Blood. 2017 Mar 2;129(9):1095-1102. doi: 10.1182/blood-2016-09-692541.

3. Xie Y, Jaffe ES. How I Diagnose Angioimmunoblastic T-Cell Lymphoma. Am J Clin Pathol. 2021 Jun 17;156(1):1-14. doi: 10.1093/ajcp/aqab090.

Acknowledgements

We would like to acknowledge the Penn State Health Department of Internal Medicine, the Division of Hematology/Oncology, the Department of Pathology, and the Flow Cytometry Core for their support of this project.