Concurrent Presentation Of Waldenstrom's Macroglobulinemia and Angioimmunoblastic T-cell Lymphoma

Amar Jariwala
George Washington University - School of Medicine and Health Sciences, amarjari@gwmail.gwu.edu

Fadi Alakeel

Elsie Lee
George Washington University

Donald S. Karcher
George Washington University

Follow this and additional works at: https://hsrc.himmelfarb.gwu.edu/smhs_path_facpubs

Part of the Medical Pathology Commons, and the Pathology Commons

APA Citation
Angioimmunoblastic T-cell lymphoma (AITL) is an aggressive T-cell neoplasm in which patients typically present with generalized lymphadenopathy and constitutional symptoms. AITL is known to be associated with B-lymphocyte abnormalities, including polyclonal hypergammaglobulinemia, Coombs-positive hemolytic anemia, and diffuse large B-cell lymphoma. Waldenstrom’s macroglobulinemia (WM) is a manifestation of lymphoplasmacytic lymphoma (LPL) and is characterized by bone marrow infiltration by a lymphoplasmacytic infiltrate, elevated serum viscosity, and production of monoclonal immunoglobulin IgM (macroglobulin). Herein, we report a unique case of AITL in which the patient presented with clinical and laboratory features of Waldenstrom’s macroglobulinemia (WM), and a subsequent axillary lymph node biopsy showed no evidence of WM/LPL and but exhibited morphologic, immunohistochemical, and molecular features of AITL.

Patient

The patient is a 73 year old African American woman who presented with shortness of breath, nausea, vomiting, and lethargy. Initial work-up showed Coombs-positive hemolytic anemia (Hgb 6.4 gram/dl), leukocytosis (WBC 23,000/dl), lymphadenopathy, splenomegaly and urticaria. Further investigation revealed an elevated IgM (13 gm), serum viscosity of 2.7, renal dysfunction (creatinine of 1.8) and urinalysis showing RBCs and positivity for protein. Bone marrow biopsy showed a lambda light chain-restricted lymphoplasmacytic infiltrate. Examination of the peripheral blood smear showed plasmacytoid lymphocytes. Flow cytometric analysis was performed and showed lambda restricted monoclonal B lymphocytes in the bone marrow and peripheral blood. Also, the B cells in the peripheral blood were positive for clonal immunoglobulin heavy chain gene rearrangement by polymerase chain reaction (PCR). The clinical and laboratory findings were consistent for WM/LPL; however, molecular studies for MYD88 mutation were negative1. The patient received brief chemotherapy for WM and the patient’s IgM monoclonal gammapathy and hemolytic anemia improved and the number of circulating monoclonal B lymphocytes decreased. Subsequently, the patient developed polyclonal hypergammaglobulinemia, increasing serum IgG level and worsening generalized lymphadenopathy. An axillary lymph node biopsy was performed.

Introduction

Histology and Immunohistochemical stains

Histology

Histologic sections of the lymph node showed complete effacement of the nodal architecture by a diffuse to vaguely nodular infiltrate consisting of small to medium size lymphocytes, numerous plasma cells, and scattered eosinophils. Immunoblasts were present singly and in loose clusters, and many exhibited mitotic activity. Rare multinucleated immunoblasts were also seen. In some areas, the infiltrate extended beyond the lymph node capsule, with preservation of the capsule and subcapsular sinus. Prominent blood vessels, including numerous apparent high-endothelial venules, were present throughout. Numerous mature-appearing plasma cells were present throughout the lymph node. A few very small and poorly preserved apparent residual follicles were noted.

Flow Cytometry and Molecular studies

Flow cytometric analysis showed dominance of CD4+ T lymphocytes, with no evidence of an immunophenotypically abnormal lymphocyte population and no evidence of a monoclonal B-cell population. Molecular studies using PCR showed no evidence of clonal rearrangement of the immunoglobulin heavy chain gene (IGH), but did show clonal rearrangement of the T-cell gamma receptor gene (TRG).

Immunohistochemistry and In-Situ Hybridization Studies

In the lymph node, atypical lymphocytes with clear cytoplasm were positive for CD2, CD3, CD5, PD1, with marked predominance of CD4+ cells and a small minority of CD8+ cells. Stains for CD10 and BCL6 showed positivity of varying intensity in widely scattered loose foci of lymphocytes, in some cases adjacent to prominent blood vessels. CD20 and CD79a stains were positive mostly in a few very small apparent residual B-cell follicles, as well as in the immunoblasts. Most of the immunoblasts were also positive for CD30. A CD15 stain was positive mostly in apparent eosinophils. A CD21 stain showed extensive expanded and poorly organized follicular dendritic cell meshworks throughout the lymph node, in many areas surrounding apparent prominent blood vessels. A CD138 stain highlighted numerous positive plasma cells throughout the lymph node. In-situ hybridization (ISH) stains for kappa and lambda light chains showed a kappa:lambda ratio among the plasma cells of approximately 2:1. An ISH stain for EBV (EBER) was positive in rare small cells. An immunohistochemical stain for HHV8 was negative.

Discussion

The findings in the lymph node were consistent with AITL. Classically in AITL, the neoplastic T cells activate and induce proliferation of the polytypic B-cell/plasma cell populations. Rare cases of AITL presenting with clonal proliferation of B cells have been reported, manifested as plasma cell myeloma and rarely plasma cell leukemia2,3. A rare case of biclonal gammapathy has also been reported4. The present case is the first reported example of concurrent presentation of WM and AITL. Because of the known association of AITL with B-lymphocyte abnormalities, including polyclonal hypergammaglobulinemia, Coombs positive hemolytic anemia, and diffuse large B-cell lymphoma, the patient’s WM is proposed to be pathogenetically related to AITL. Many of the B-cell abnormalities seen with AITL are thought to be related to immune dysregulation and poor control of EBV associated with AITL. This case illustrates a previously unreported form of B-cell lymphoma in association with AITL and suggests a possible pathogenetic connection to this T-cell lymphoproliferative disorder. Further investigation and research is needed to understand the underlying pathogenetic mechanism.

References