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Case study

In immunocompromised patients, Epstein-Barr virus lymphadenitis can mimic angioimmunoblastic T-cell lymphoma morphologically, immunophenotypically, and genetically: a case report and review of the literature

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Summary The development of lymphomas and solid malignancies in association with immunosuppression is a well-documented occurrence in the medical literature. We report the case of a young man who developed progressive diffuse lymphadenopathy with associated extremely high levels of serum Epstein-Barr virus in the setting of chronic immunosuppressive treatment of glomerulonephritis. Excisional biopsy of a right inguinal node revealed a sclerosing process with the morphologic appearance of angioimmunoblastic T-cell lymphoma with a $CD3^+$, $CD4^+$ immunophenotype. In situ hybridization of Epstein-Barr virus–encoded RNA was positive. Molecular probe studies demonstrated a clonal T-cell population. Upon reduction of immunosuppression, the patient's lymphadenopathy and Epstein-Barr virus titer have resolved without recurrence over 2 years time. This case demonstrates that a benign Epstein-Barr virus–associated process can mimic angioimmunoblastic T-cell lymphoma and should be considered particularly in the setting of immunosuppression, emphasizing the need for close communication with the treating physician in the interpretation of lymph node biopsies.

1. Introduction

The increased propensity for immunodeficient patients to develop neoplasia, including solid malignancies as well as leukemias/lymphomas, has become well recognized in the medical literature as increasing numbers of patients are experiencing marked immunosuppression, either as a direct result of disease, such as in HIV/acquired immunodeficiency syndrome, or from iatrogenic causes, such as in the posttransplant setting. Lymphomas are known to occur in the setting of primary immune disorders [1], HIV infection [2], posttransplant [3], or immunosuppressive treatment of a variety of disorders, usually in the setting of autoimmune disease [4]. Of these, posttransplant lymphoproliferative disorders (PTLDs) have been the most extensively studied.

PTLDs are most commonly Epstein-Barr virus (EBV) associated [5] and are classified within a spectrum ranging

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from "early lesions," which resemble reactive proliferations; to polymorphic PTLDs, which meet some but not all the criteria for lymphoma; and finally, to monomorphic PTLDs, which are indistinguishable from lymphomas [3]. Many of these lesions will regress with cessation of immunosuppression, the earlier the lesion within the spectrum the greater the likelihood of remission [6]. Within the monomorphic PTLDs, a variety of lymphomas have been reported, including B-cell lymphomas, T-cell lymphomas, and Hodgkin lymphomas [3]. The most common B-cell neoplasms include diffuse large B-cell lymphoma, Burkitt lymphoma, and plasma cell myeloma/plasmacytoma [3]. Reported T-cell neoplasms include peripheral T-cell lymphoma not otherwise specified, hepatosplenic T-cell lymphoma, T-cell large granular cell leukemia, adult T-cell leukemia/lymphoma, nasal type extranodal NK/T-cell lymphoma, mycosis fungoides/Sezary syndrome, and anaplastic large-cell lymphoma, cutaneous or otherwise [3]. Lymphoproliferative disorders associated with immunosuppression outside the transplant setting are less well studied but encompass a similar spectrum of lesions [4].

Angioimmunoblastic T-cell lymphoma (AITL) comprises 15% to 20% of peripheral T-cell lymphomas but only 1% to 2% of non-Hodgkin lymphomas overall, occurring most commonly in middle-aged and elderly people with an equal incidence in men and women [7]. AITLs are often associated with EBV [8] and an aggressive course [9]. Patients present most commonly with lymphadenopathy, hepatosplenomegaly, polyclonal hypergammaglobulinemia, and rash [9]. Morphologically, lymph nodes show partial effacement of the lymph node architecture, with proliferation of high endothelial venules surrounded by clusters of small to medium-sized lymphocytes with pale cytoplasm [7]. An expansion of B immunoblasts, sometimes clonal, is also often seen [10]. Neoplastic T cells express pan-T-cell antigens such as CD2, CD3, CD5, and usually CD4 [7], although rare CD8-positive cases have been reported [11]. Other antigens commonly expressed by the neoplastic cells include PD-1, CD10, CD21, and CXCL-13 [7].

We describe in an immunocompromised patient the pathologic findings of an EBV-associated lesion that mimicked AITL morphologically, immunophenotypically, and genetically.

2. Case report

Clinical presentation: A 16-year-old African American male initially diagnosed at 18 months of age with nephrotic syndrome secondary to focal segmental glomerulosclerosis presented with diffuse lymphadenopathy, which had been

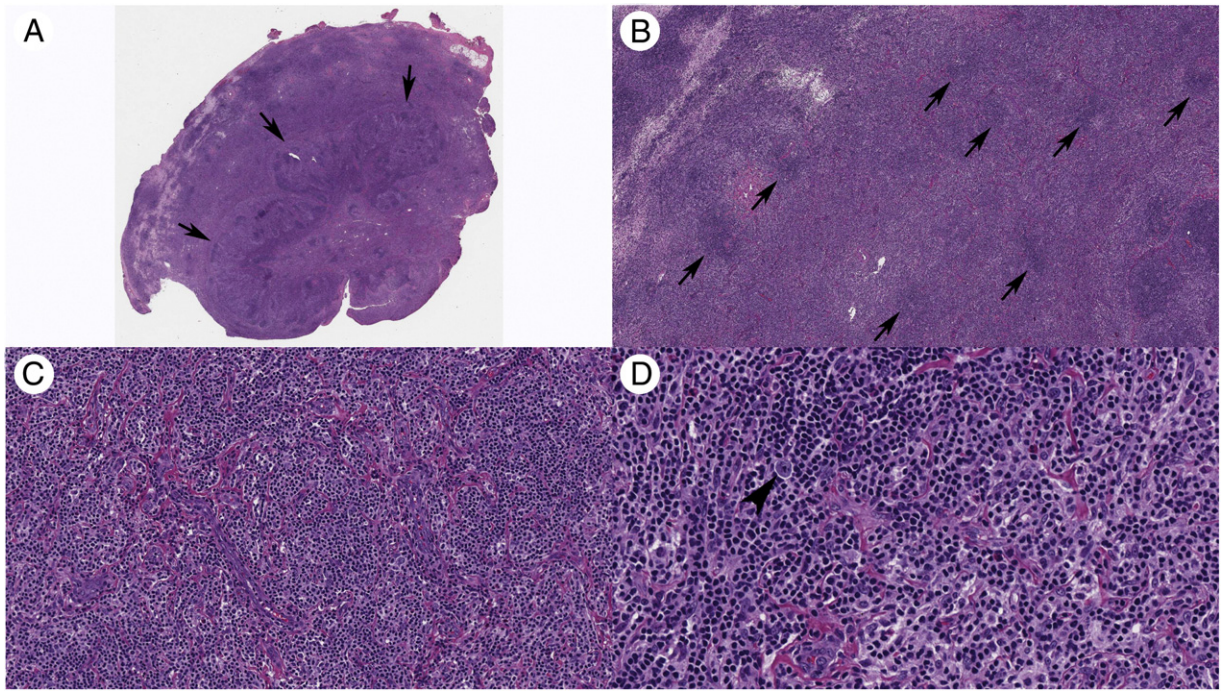

Fig. 1 A, A photomicrograph of an H&E-stained section shows outlines of residual lymph node (arrows) beyond which expansive sheets of lymphoid cells extend into perinodal soft tissue (original magnification ×0.6). B, A photomicrograph of an H&E-stained section shows a moth-eaten appearance of residual germinal centers (arrows) (original magnification ×4). C, A photomicrograph of an H&E-stained section shows numerous arborizing epithelioid venules lined by plump endothelial cells, surrounded by numerous cells with small dark nuclei with abundant pink or clear cytoplasm (original magnification ×20). D, A photomicrograph of an H&E-stained section shows arborizing epithelioid venules surrounded by cells with abundant pink or clear cytoplasm (right side of photomicrograph) immediately adjacent to a residual B-cell area (left side of photomicrograph) within which is seen a large immunoblastic cell (arrowhead) (original magnification ×40).