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CASE REPORT

A case of HIV-negative plasmablastic lymphoma of the bone marrow with a unique immunophenotype

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Key Clinical Message

We present an interesting case of plasmablastic lymphoma, which is a rare type of non-Hodgkin lymphoma that is typically diagnosed in HIV-positive patients and has an immunophenotype that overlaps with multiple myeloma. Our patient is unique because he is HIV-negative, has primary bone marrow disease, and has an atypical immunophenotype.

Keywords

Aggressive lymphoma, B-cell lymphoma, bortezomib, HIV-associated lymphoma, non-hodgkin lymphoma, plasmablastic lymphoma, rare lymphoma.

Case Presentation

A 62-year-old male presented to the emergency department of a Boston VA facility with fatigue and back pain. The patient stated that he has had worsening lower back and hip pain for 2 months, as well as a 45-pound weight loss. The patient denied fever, chills, night sweats, adenopathy, dyspnea, and chest pain. The patient's medical history was significant for coronary artery disease with coronary artery bypass grafting, ischemic cardiomyopathy with an ejection fraction of 35%, peripheral vascular disease, diabetes, atrial fibrillation, transient ischemic attack, and venous thromboembolism. On physical examination, the patient had no palpable lymphadenopathy, splenomegaly, or peripheral edema. Subsequent laboratory work revealed a white blood cell count of 3.37 K/μL (absolute neutrophil count of 2200), a hemoglobin of 7.5 g/dL with a mean corpuscular volume of 95 fL, and a platelet count of 189 K/μL. Lactate dehydrogenase was not elevated, and testing for HIV was negative. Serum protein electrophoresis and immunofixation were not evaluated at the time of initial diagnosis. The patient was admitted for further workup and PET-CT revealed several FDG-avid foci with lytic correlate on CT, particularly the L5 vertebral body and the left femur with an SUV Max of 6.4. Additionally, there were small FDG avid right common iliac nodes and a more pronounced FDG avid (SUV Max, 4.9) right pelvic sidewall node.

The above findings prompted a bone marrow biopsy, which revealed a hypercellular bone marrow (100%) that was replaced with sheets of immature precursor-like cells with fine nuclear chromatin and prominent nucleoli. The predominant cells appear to have plasmacytic/plasmablastic differentiation (Fig. 1, long arrow). Immunoblastic cells are also seen in a scattered distribution (Fig. 1, short arrow). Immunohistochemistry was positive for LCA, CD117, CD79A, lambda immunoglobulin light chain, BCL2, EMA, and MYC protein expression (60–70%). Of note, the KI-67 proliferation index was 70–80%. Pertinent negative stains were as follows: CD19/20, CD38/138, CD56, CD30, CD10, PAX5, MUM1, HHV8, EBV, BCL6, ALK1, and TDT. The morphologic findings are most consistent with plasmablastic lymphoma, despite the atypical immunophenotype.

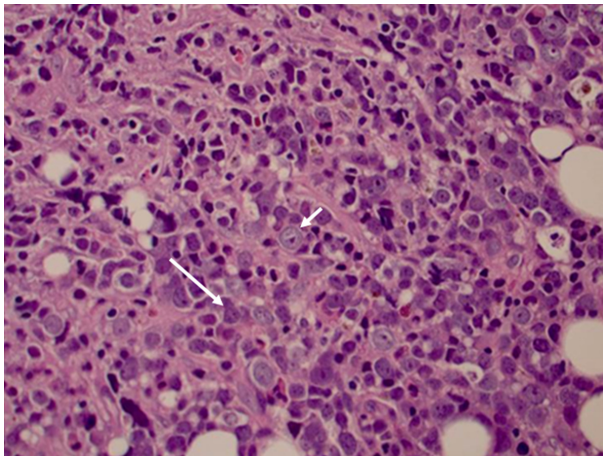

Figure 1. Plasmablastic Lymphoma (400x). The small arrow identifies an immunoblast, and the large arrow identifies a cell with plasmablastic differentiation.

The patient was initiated on dose-adjusted EPOCH (etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin), and his course was complicated by multiple episodes of severe neutropenic sepsis. A bone marrow biopsy after three cycles revealed no residual lymphoma cells. Subsequently, the patient received one more cycle of DA-EPOCH and then entered a surveillance protocol due to his inability to tolerate further chemotherapy.

Discussion

Plasmablastic lymphoma (PBL) is an aggressive and very rare type of lymphoma that displays some features of diffuse large B-cell lymphoma (DLBCL), and some features of multiple myeloma (MM) [1]. This tumor was first described in the oral cavity of HIV-positive patients in 1997 [2]. Subsequently, the tumor has been described in regions other than the oral cavity, particularly in HIV-*negative* patients [3]. Differences between HIV-positive and HIV-negative cases of PBL are significant. Clinically, HIV-positive patients have a stronger male predominance, younger age of onset, and classically manifest with EBV-positive oral cavity lesions. Additionally, HIV-positive patients with PBL respond to antiretroviral medications and have improved overall survival [4]. In a recent review of 76 cases of HIV-negative PBL, one-third of the cases were immunosuppressed, and 89% had extranodal involvement [3]. Extranodal disease in the bone marrow was found in 13% of patients.

Obtaining a definite diagnosis is critical. Morphologically, our patient's tumor was consistent with PBL. The immunophenotype, though, was more complicated. PBLs typically lose classic B-cell markers (CD19, CD20, and PAX5) and gain plasma cell markers (CD38, CD138, and MUM1) [5]. Our patient was negative for both the traditional B-cell markers as well as the traditional plasma cell markers. To consider an aggressive B-cell lymphoma, such as diffuse large B-cell lymphoma (DLBCL), the traditional B-cell markers would be positive. At the other end of the spectrum is MM, which would have negative B-cell markers, but would express plasma cell markers. Plasmablastic myeloma (PBM) is a diagnostic consideration, but there is usually some component of mature plasma cells in the bone marrow specimen. Furthermore, PBM would typically express plasma cell markers and is generally found in patients with pre-existing MM [1]. *MYC* gene rearrangements have been described in 49% of patients with PBL according to one study [6]. While our patient did not have fluorescence *in-situ* hybridization (FISH) testing, he was positive for MYC protein expression by immunohistochemistry. The final diagnosis of PBL was based on the morphology, atypical immunostains, and the exclusion of other hematologic malignancies.

Management of PBL is challenging, and the prognosis is dismal with <40% of patients living beyond two years [1]. The National Comprehensive Cancer Network (NCCN) guidelines state that "standard CHOP is not adequate therapy"[7]. Listed alternative regimens are CODOX-M/IVAC (cyclophosphamide, vincristine, doxorubicin, methotrexate/ifosfamide, etoposide, and cytarabine), DA-EPOCH, and HyperCVAD (hyperfractionated cyclophosphamide, vincristine, doxorubicin, dexamethasone alternating with methotrexate and cytarabine). HIV-positive patients should receive antiretroviral therapy [7]. Autologous stem cell transplant may have a role as consolidation for patients with high-risk disease [5]. Responses to novel agents have been described in case reports. Of interest is the proteasome inhibitor bortezomib, which is a logical agent to study because of its proven efficacy in MM. Several case reports have shown significant responses to bortezomib alone or in combination with chemotherapy [8, 9]. One case series has described the efficacy of a novel combination regimen, bortezomib-EPOCH (V-EPOCH), in three patients [10]. The immunomodulating agent lenalidomide has been shown to have some efficacy in at least one case report [9]. The suggested initial approach to PBL in a recent review article is as follows: six cycles of DA-EPOCH (with or without bortezomib) and intrathecal prophylaxis with each cycle [11]. The authors of that review also recommend consideration of autologous stem cell transplant for eligible candidates. Further studies evaluating the efficacy of novel agents targeting plasma cells, as well as other novel therapeutics, are critically needed.

Authorship

CD: Contributed to the clinical case, writing the manuscript, and editing the manuscript. SS: Contributed to the clinical case, writing the manuscript, and editing the manuscript.

Conflict of Interest

None declared.

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