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Testicular Plasmablastic Lymphoma in an HIV-Negative Patient: A Rare Case Presentation

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Abstract

Plasmablastic lymphoma (PBL) is a very rare disease and it is usually considered a human immunodeficiency virus (HIV)–related B-cell lymphoma that carries a poor prognosis. It mostly involves the oral cavity, lungs, nasal cavity, gastrointestinal tract, lymph node, and skin. Therapeutic regimens like dose-adjusted etoposide, vincristine, doxorubicin, cyclophosphamide, and prednisone (DA-EPOCH) have shown better results in these aggressive lymphomas. We report a rare case of PBL in an HIV-negative patient who presented to the clinic with a complaint of left testicular swelling for 3 months. Ultrasound showed an enlarged left testicle. He underwent a left orchiectomy and the pathology showed PBL with involvement of the spermatic cord margin. Positron emission tomography scan showed hypermetabolic mediastinal and hilar lymph nodes. He was started on DA-EPOCH but showed no response. Accordingly, salvage therapy with bortezomib in addition to ifosfamide carboplatin and etoposide (B-ICE) chemotherapy was initiated with remarkable response. Several other regimens can be used in the refractory setting; however, the evidence is mostly based on retrospective analysis.

Keywords

testicular plasmablastic lymphoma, hematology, oncology

Introduction

Plasmablastic lymphoma (PBL) is a rare and aggressive type of non-Hodgkin's lymphoma (NHL) that shares pathological features with plasma cell myeloma (PCM). In addition to human immunodeficiency virus (HIV), it is also associated with Epstein-Bar virus (EBV) and immunosuppression in HIV-negative patients, for example, post transplantation.[1,2] The overall survival rate is between 6 and 19 month in both HIV-positive and HIV-negative patients with PBL.[1] It often involves the oral cavity, lungs, nasal cavity, gastrointestinal tract, lymph node, and skin. We report a rare case of left testicular plasmablastic lymphoma in a 63-year-old HIV-negative patient.

Case History

A 63-year-old male with a history of previously treated hepatitis C presented to the clinic with a complaint of left testicular swelling for 3 months. On physical examination the left testicle was significantly enlarged. No clinically palpable lymphadenopathy could be appreciated. Ultrasound scan of the left testicle showed an enlarged testicle. Serology results were negative for HIV, hepatitis B surface antigen, and hepatitis B core antibody. Hepatitis C antibody was positive; however, hepatitis C polymerase chain reaction was undetectable. The remaining laboratory workup including complete blood count, serum lactate dehydrogenase, β-human chorionic gonadotropin, α-fetoprotein, and calcium levels were all within normal limits. Subsequently, he underwent a radical left orchiectomy. His pathology examination showed plasmablastic lymphoma (Figure 1). Tumor cells were positive for CD38, CD 43, CD 45, CD 56, CD 138, MUM1, C-MYC, lambda, and EBER ISH (EBV-encoded RNA in situ hybridization), but were negative for CD2, CD3, CD4, CD5, CD7, CD10, CD15, CD20, CD23, CD30, CD34, CD79a, kappa, PAX-5, BCL-2, BCL 6, cyclin D1, ALK-1, CK IT, EMA, MPO, D2-40, and HHV 8. The proliferation index as indicated by Ki-67 immunohistochemistry was 90%. Cytogenetic analysis revealed noabnormality. Positron emission tomography (PET) scan showed hypermetabolic

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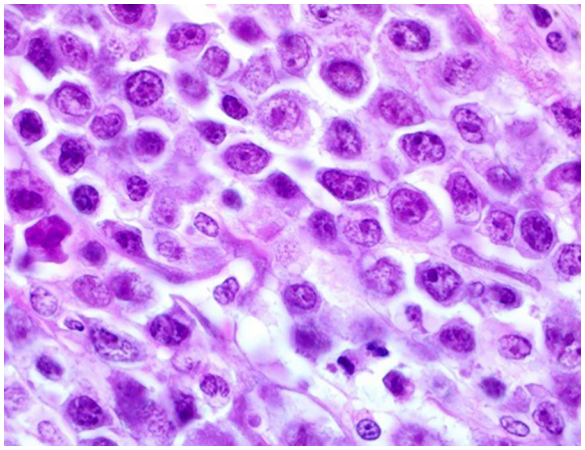

Figure 1. Tumor composed of malignant plasmablastic cells with fairly abundant pink cytoplasm, round to irregular shaped nuclei, open chromatin, and occasional prominent nucleoli.

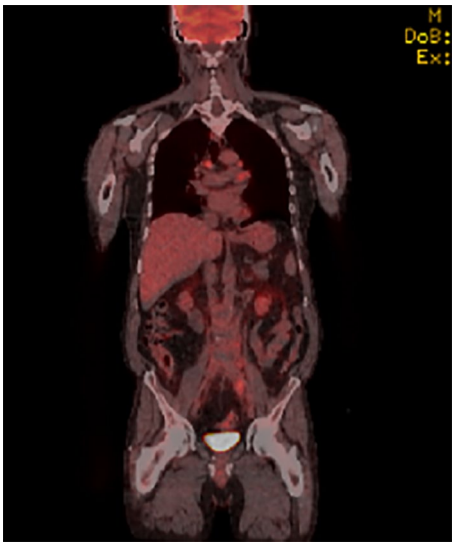

Figure 2. Positron emission tomography scan obtained before initiation of chemotherapy showing hypermetabolic mediastinal and hilar lymph nodes.

mediastinal and hilar lymph nodes (Figure 2). There was a relatively symmetric increased medullary tracer activity in the bilateral proximal femurs, favored to represent red marrow reconversion. A bone marrow biopsy with aspirate revealed no evidence of bone marrow involvement. Given the overlap between PBL and PCM, serum-protein electrophoresis, immunofixation electrophoresis, and free light chain done showed no monoclonal protein. He was started on systemic chemotherapy with dose-adjusted etoposide, prednisone, vincristine, cyclophosphamide, and doxorubicin

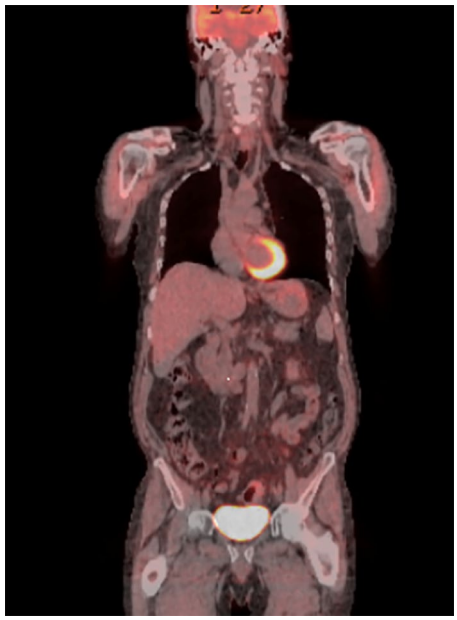

Figure 3. Surveillance positron emission tomography scan obtained following chemotherapy with B-ICE consistent with complete remission.

(DA-EPOCH). He was also treated with allopurinol for tumor lysis prophylaxis. After 2 cycles of DA-EPOCH, a repeat PET scan showed increased hypermetabolic activity in the mediastinum consistent with refractory disease. We reviewed the medical liteature and found few reports of cases with improved outcome utilizing multiple myeloma therapies.[3,4] Accordingly, the decision was made to start salavage systemic chemotherapy with bortezomib, ifosfamide, carboplatin, and etoposide. A surveillance PET scan (Figure 3) obtained at the time of submission was consistent with remission.

Discussion

Plasmablastic lymphoma was originally reported mostly in HIV-positive patients. However, PBL in HIV-negative patients have now been identified.[5,6] Although the exact incidence of PBL is unknown, it accounts for about 2% to 3% of all AIDS-related lymphomas.[1,2,7] Furthermore, HIV-positive patients are generally diagnosed at an earlier age with PBL.[1,8,9] About a third of HIV-negative patients have some form of iatrogenic immunosuppression, for example, post organ transplantation.[7,8,10] It occurs mostly in the oral cavity, nasal cavity, skin, gastrointestinal tract, and less commonly in the testicles.[1,9,11]

PBL is characterized by plasmablasts, which are lymphoid cells that have lost the characteristic B-cell surface markers and acquired plasma cell surface markers.[12] Molecular and genetic studies suggest that it arises from

activated B cells in transition from immunoblast to plasma cell that fail to undergo apoptosis in the post germinal center.[1,4] EBV infection has also been reported to be associated with PBL[8-10] and it may be one of the distinguishing factors between PBL and PCM.[13,14] Due to several mechanisms associated with EBV antigens, EBV infection prevents apoptosis of B-cells.[2] Other studies have found that genetic alterations involving the MYC oncogene that cause overexpression of the MYC protein may play a major role in the pathogenesis of PBL.[1,8,9] In patients with a history of EBV infection, MYC rearrangements have been found to occur more often leading to a more aggressive clinical course of PBL.[1,7]

One of the important differential diagnoses for PBL is PCM. They have similar morphological and immunophenotypic features and both express plasma cell markers without the classic B-cell markers. Features such as the absence of renal dysfunction, lytic bone lesions, and bone marrow involvement are suggestive of PBL.[12,13,15] The morphology and phenotype of this case was consistent with PBL; however, lack of any immunosuppression or evidence of EBV infection makes this case was unusual. The main differential diagnosis considered was PCM. Although similar, it is important to distinguish between these 2 entities as treatment for the 2 are different. Absence of bone marrow involvement or hypercalcemia in our patient makes PCM an unlikely diagnosis.

Patients with PBL usually present at an advanced stage (III and IV) regardless of their HIV status and the prognosis is generally poor.[8,10,11] While some studies have reported worse prognosis in HIV-negative patients that are immunosuppressed, others have reported no significant difference in the overall survival when compared with HIV-positive patients.[7,10,16] According to Lin and colleagues,[5] features associated with better survival include the use of antiretroviral therapy in HIV-positive patients and autologous stem cell transplantation. In contrast, features that are associated with poor outcome include late stage of the Ann Arbor classification system, patients who test negative for EBV and cases not responsive to treatment.[9,17] Our patient presented with several poor prognostic factors such as late stage disease (stage III) and HIV-negative PBL.

Given the unfavorable outcome of PBL and expression of myeloma markers, physicians have tried agents that are routinely used in the treatment of multiple myeloma. There is reportedly a favorable response to treatment of PBL using proteasome inhibitors such as bortezomib in addition to standard chemotherapy.[3,4,16] Its mechanism of action involves targeting the hypothesized pathogenesis of PBL, which is targeting plasmablasts that fail to undergo apoptosis.[4] As in this case with the addition of bortezomib, there was improvement as demonstrated by the repeat PET scan. Furthermore, studies have also suggested the use of hematopoietic stem cell transplant as there may be a possible benefit in the setting of relapsed and refractory disease.[7,9]

Conclusion

PBL has an extremely poor prognosis, and its treatment remains a challenge. The role of bortezomib in addition to standard chemotherapy and stem cell transplant are still evolving. They may evolve as the new guidelines for the management of PBL. The progression of PBL is associated with the translocation of MYC oncogene. Therefore, if the re-arrangement of the MYC oncogene is studied further, it will lead to a greater level of understanding on the mechanism of PBL. This can influence pharmacological research and chemotherapeutic regimen in the future.

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Declaration of Conflicting Interests

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Ethics Approval

Our institution does not require ethical approval for reporting individual cases or case series.

Informed Consent

Verbal informed consent was obtained from the patient for his anonymized information to be published in this case report.

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