Case Report

Plasmablastic lymphoma of the testis in a human immunodeficienecy virus patient – report of a rare entity

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ABSTRACT

Testicular lymphoma is the second most common extra nodal lymphomas. It is a highly lethal disease with a median survival of 1–2 years. In human immunodeficiency virus (HIV) patients, primary testicular lymphomas are estimated to comprise > 6% of testicular tumors, and they tend to occur in younger patients. Testicular lymphoma can occasionally be the initial manifestation of the disease in HIV patients.Plasmablastic lymphoma (PBL), which is considered as a variant of diffuse large B-cell lymphoma is a highly aggressive tumor with poor prognosis. PBL has a well-established association with HIV infection and occurs most commonly in the oral cavity. The presentation at extra nodal sites and absence of usual hematolymphoid markers makes its diagnosis more difficult. PBL of the testis as the primary lesion in HIV patients has not been reported so far. We report a case of PBL presenting as a primary testicular lesion in a HIV patient with a grave prognosis.

Key words: Human immunodeficiency virus infection, plasmablastic lymphoma, testis

INTRODUCTION

Testicular lymphoma is the second most common extranodal lymphoma, and it is a highly lethal disease with very poor prognosis. Primary testicular lymphomas in human immunodeficiency virus (HIV) patients are estimated to comprise > 6% of testicular tumors and tend to occur at an younger age. Plasmablastic lymphoma (PBL), a variant of diffuse large B-cell lymphoma is a highly aggressive tumor with a grave prognosis. PBL has a well-established association with immune suppression, particularly with HIV infection.[1]

Plasmablastic lymphoma is a B-cell neoplasm that corresponds to the differentiation stage between a B immunoblast and a plasma cell. It is an incompletely characterized entity without universal agreement on the minimum diagnostic criteria. The neoplastic population is monomorphic or admixed with immature plasma cells.[2] The presentation at extra nodal sites and negativity for usual hematolymphoid markers makes the diagnosis difficult. We present probably the first case of PBL presenting as the primary testicular tumor in a HIV patient. The patient died within 4 months after the diagnosis. The differentiating features of PBL and the etiopathogenesis are discussed briefly.

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CASE REPORT

A 26-year-old male, a known case of HIV since 2011, presented with the complaints of left scrotal swelling of 1-month duration. Physical examination did not reveal any significant findings but for the firm swelling of left testis. Ultrasound examination of left testis revealed altered echo texture. Fine needle aspiration cytology of the left testicular swelling was suggestive of seminoma. Orchiectomy was done, and the specimen was sent for histopathological examination.

Grossly the test is measured 5 cm × 6 cm × 9 cm, and the spermatic cord measured 8 cm in length. C/S of the test

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is showed irregular grayish white nodular areas. Largest nodule measured 3 cm × 3 cm. Foci of hemorrhage and necrosis were seen.

Microscopic examination showed a tumor almost totally replacing the testis. Remnant seminiferous tubules could be seen at places [Figure 1]. The tumor was seen as diffuse sheets of large round to oval or irregular cells with prominent round hyperchromatic nucleus and moderate basophilic cytoplasm. The nucleus had thick nuclear membrane, condensed chromatin and 2–5 nucleoli in some cells. Majority of cells showed single eosinophilic nucleolus. Plasmacytoid cells and occasional plasma cells were seen in the tumor [Figure 2]. The tumor cells were seen involving the entire testis and adnexae as diffuse sheets and extending into the paratesticular area. Many bizarre cells, binucleate and multinucleate cells were also seen. Brisk mitosis with many atypical mitoses was seen [Figure 3].

The lesion was diagnosed as the plasmablastic variant of diffuse large B-cell lymphoma. The diagnosis was confirmed by our collaborating hospital in Spain by immunohistochemical (IHC) studies [Figures 4-6]. The patient declined to take the radiotherapy and was lost for follow-up. 3 months later it was found that he died at home.

DISCUSSION

Testicular lymphoma is uncommon and constitutes 1–9% of all testicular neoplasms. Secondary involvement of the testis in patients with lymphoma is far more common than primary testicular lymphoma.[3]

Primary testicular lymphomas generally occur in the elderly. In HIV patients, primary testicular lymphomas are estimated to comprise 5% of testicular tumors and tend to occur in younger patients. Primary testicular lymphoma has been reported as the initial manifestation of the disease in HIV patients.[4,5] In 1997, Delecluse *et al*. reported a series of PBL arising in the oral cavity of HIV patients.[1] PBL has a well-established association with immune suppressive

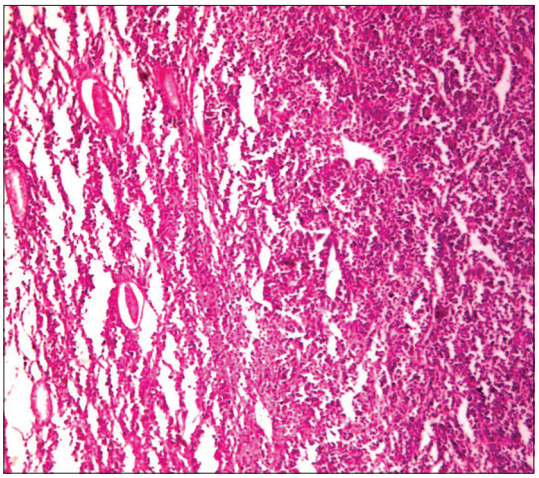

Figure 1: Scanner view of the tumor with remnant seminiferous tubules above, (H and E, ×10)

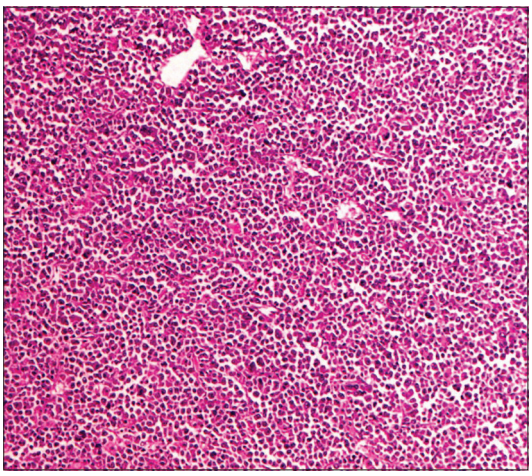

Figure 2: Tumor showing diffuse sheets of plasma cells, plasmacytoid cells and occasional bizarre cell. Low power view, (H and E, ×20)

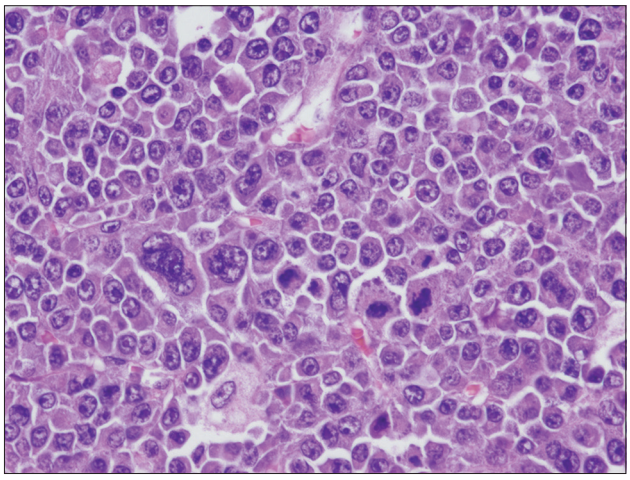

Figure 3: Tumor shows sheets of plasmacytoid cells. Occasional bizarre cell and binucleate cell are seen. High power view, (H and E, ×40)

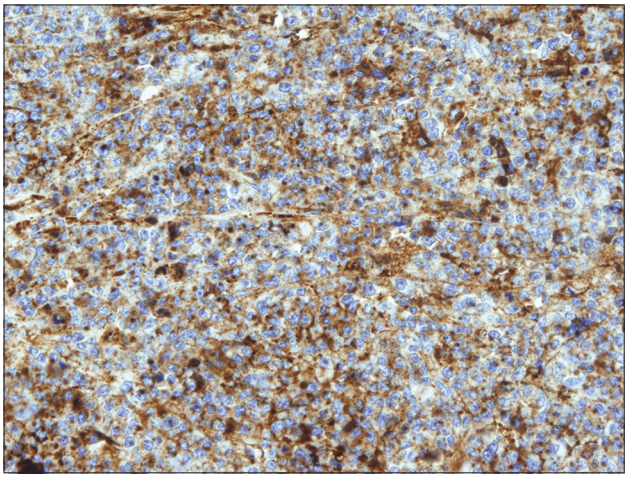

Figure 4: Tumor cells showing positive CD138

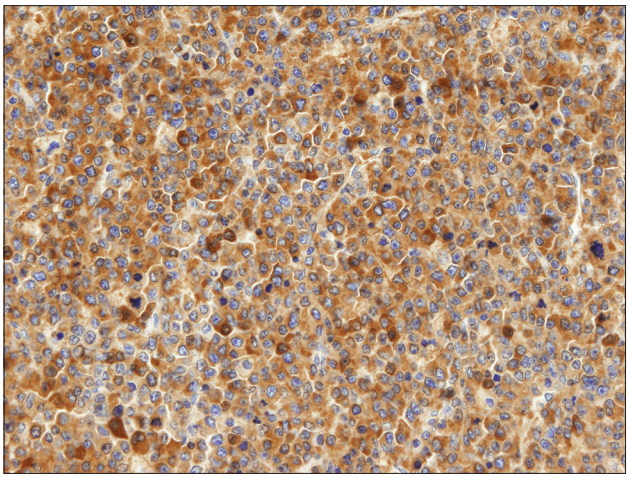

Figure 5: Tumor cells showing cytoplasmic kappa immunoglobulin

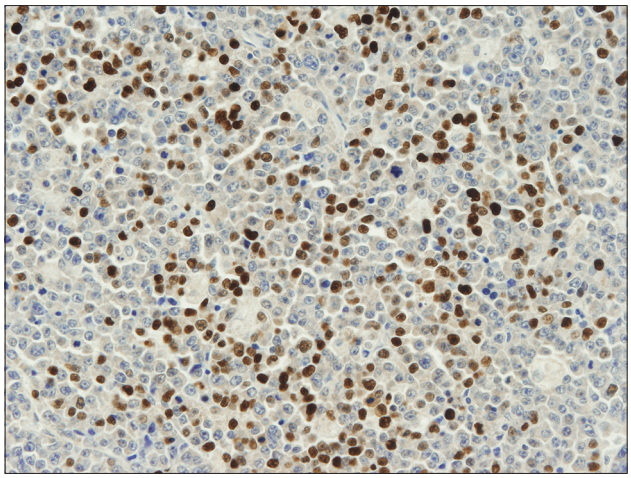

Figure 6: Tumor cells showing positive Epstein–Barr virus-encoded RNA

states like HIV infection, solid organ transplantation and steroid therapy for autoimmune disease.[6]

Plasmablastic lymphoma is a B-cell neoplasm that corresponds to the differentiation stage between a B immunoblast and a plasma cell. It is presently listed in the WHO classification as a variant of DLBCL. Morphologically the neoplastic population is monomorphic or admixed with immature plasma cells.[3] It is extremely difficult to distinguish PBL from anaplastic lymphoma and plasmablastic plasmacytoma. Plasmacytic PBL closely resembles plasmacytoma; however it shows brisk mitotic and apoptotic activity.[4] The neoplastic cells are monomorphic and show admixed immature or mature plasma cells. Because of this morphology it is extremely difficult to distinguish PBL from plasmablastic plasmacytoma. Immuno phenotype confirms that the cells are in the differentiation stage between B immunoblast and a plasma cell.

Immunohistochemistry of PBL shows CD45 negative, CD20 negative, CD79a positive/negative, Pax-5 negative, CD38 positive and CD138 positive. There is a variable expression of cytoplasmic immunoglobulin. Epstein–Barr virus (EBV) is positive in 60–75% of cases and heron hepatitis B virus is positive in a small proportion of cases. In the present case, IHC study showed positive CD79a-1, CD138, Ki-67, kappa, MUM1-1 and negative CD20, CD45, lambda, and Pax 5.

Vega *et al*. found that the only significant difference between multiple myeloma (MM) and PBL was the presence of EBV-encoded RNA (EBER), which was positive in all PBL cases and negative in all MM cases, with or without HIV infection.[7] They suggested that when considering a single case with differential diagnoses between MM and PBL, a positive EBER result makes the diagnosis of MM unlikely. In the present study, EBER was positive [Figure 6].

Patients with HIV infection are at higher risk of acquiring PBL, which primarily involves an oral cavity. Involvement of the testis by PBL as the sole lesion and as the primary presentation is not recorded so far. Only four cases of PBL secondarily involving the testis are on record.[8] We are probably presenting the first case of PBL involving the testis only and presenting as the primary testicular tumor in a HIV patient.

Human immunodeficiency virus patients tend to have more aggressive type PBL and are likely to die earlier when compared with non-HIV patients having PBL. In the present study, the patient died within 3 months of the diagnosis.

In most HIV patients the persistent paraproteinemia has been shown to contain high anti-HIV activity suggesting that the HIV infection provided the antigenic stimulation for excessive immunoblastic production and may thereby have predisposed the patient to clonal expansion of a malignant phenotype.[9] The mechanisms of HIV-induced neoplasia are not clearly understood, though immune suppression is the most suggested mechanism. Another theory is that HIV may promote oncogenic viruses such as EBV and HHV8.

Antiretroviral therapy and the resulting prolonged survival in HIV disease have modified the form of presentation of HIV-associated malignancies. Early years of HIV epidemic saw the predominance of Kaposi's sarcoma, and more recent years have been associated with increased incidence of non-Hodgkin lymphoma. It is not clear whether PBL will continue to increase as a percentage of HIV-associated diseases, but it is clear that this tumor is very aggressive in its course.

CONCLUSION

We conclude that HIV patients can develop aggressive lymphomas at extra nodal sites. Testicular swelling in HIV

patients should be investigated thoroughly to exclude extra nodal lymphoma as it is shown that PBLs are very aggressive.

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