CASE REPORT

Plasmablastic lymphoma of the anus: a case report

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Abstract

Plasmablastic lymphoma (PBL) is a rare variant of diffuse large B-cell lymphoma which has been most commonly reported in jaw and oral cavity in Human Immunodeficiency Virus (HIV) infected patients. A handful of cases have been reported in the extra-oral sites. Plasmablastic lymphomas should be differentiated from other large cell lymphomas as these lymphomas have very short survival and poor response to chemotherapy. We present a case of PBL in an HIV infected patient with history of recurrent anal fistulotomies.

Key words

Plasmablastic lymphoma

1 Introduction

In 1997, Delecluse *et al*. reported a series of 16 cases of plasmablastic lymphoma (PBL) in HIV patients [1]. With subsequent reporting of more than 200 cases of PBL, the spectrum of PBL has expanded which is now thought to be a heterogeneous disease [2]. Plasmablastic differentiation refers to diffuse proliferation of immunoblastic cells with a plasma cell or a terminally differentiated B-cell immunophenotype. Every plasmablastic lesion in the HIV positive patient is not plasmablastic lymphoma. The differential diagnosis is wide and includes diffuse large B-cell lymphoma (DLBCL) with immunoblastic differentiation, ALK positive DLBCL, secretory variant of DLBCL, primary effusion lymphoma, large B-cell lymphoma arising in HHV-8 associated multicentric Castleman's disease and plasmablastic transformation of multiple myeloma (MM) or solitary plasmacytoma.

2 Case presentation

A 40 year old African-American male patient presented with increasing perirectal/anal pain and drainage from an anal fistula for the past few months. At this presentation there was no history of fever, weight loss or night sweats. His past medical history was significant for an HIV infection that was diagnosed 18 years ago and he has been maintained on HAART regimen. His CD4 count at this presentation was 363/mm^3. His past surgical history was notable for recurrent fistulotomies and placement of a seton stitch three years ago. Physical examination revealed no hepatosplenomegaly or lymphadenopathy. Examination under anesthesia revealed several firm areas with mild inflammation and underlying abscess cavities. Multiple biopsies were obtained.

The histopathological features were remarkable for ulcerated squamous mucosa with underlying diffuse infiltrate of atypical large cells with round nucleus, vesicular chromatin, prominent single nucleolus and moderate amount of cytoplasm (see Figure 1). The neoplastic cells were positive for MUM1, BCL-2, CD10, EMA (focal) and CD138. These cells were negative for CD45, CD20, CD30, CD3, CD4, CD8, CD56, ALK-1, HHV-8 and BCL-1 immunostains. CD38 staining was non-contributory. The EBV in-situ hybridization (EBER) stain was strongly positive in the neoplastic cells (see Figure 2). The morphological, immunohistochemical and EBER staining favored a diagnosis of plasmablastic lymphoma. He was treated with Etoposide, Prednisone, Vincristine (Oncovin), Cyclophosphamide and Dexamethasone. He initially responded well to chemotherapy but lost to follow-up after six cycles. He later returned with extensive progression of the disease with peritoneal involvement and succumbed to the illness.

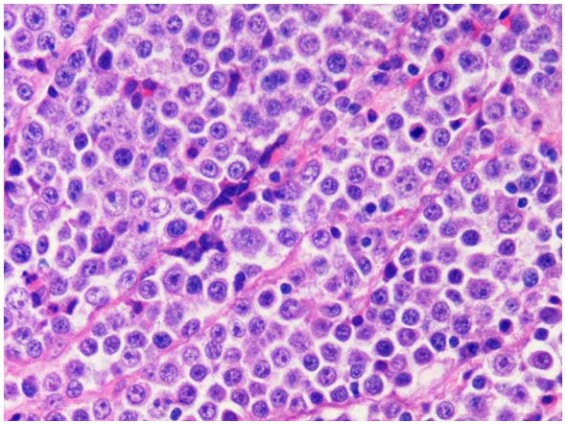

Figure 1. The mucosa showed diffuse infiltration of medium to large sized cells with round nucleus, vesicular chromatin, prominent single nucleolus and moderate amount of cytoplasm, H&E 40×.

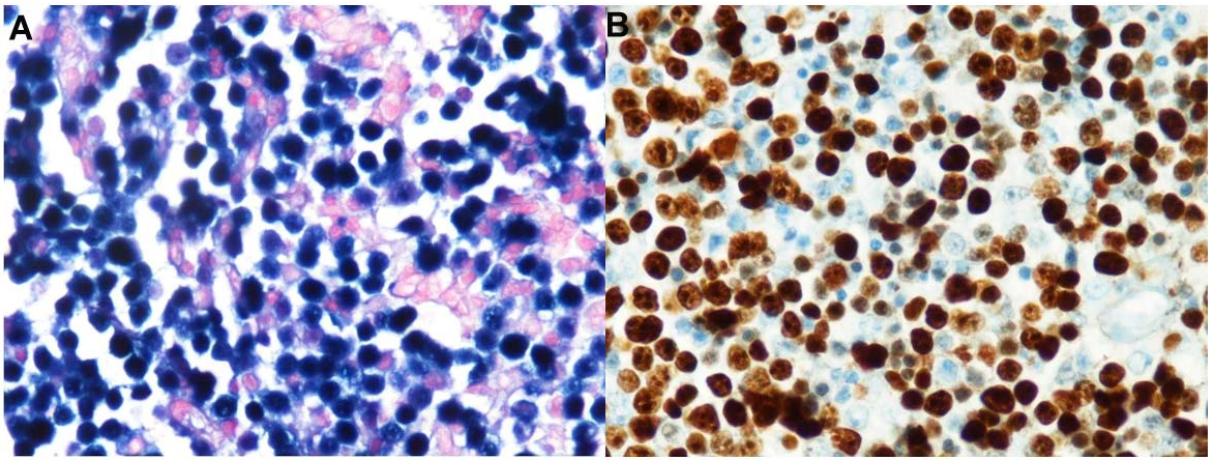

Figure 2. The neoplastic cells stained positive for EBER in situ hybridization (A) and displayed a high proliferation rate by Ki-67 (B)

3 Discussion

The most frequent sites of involvement for plasmablastic lymphoma are the oral cavity, head and neck. The reported extra-oral sites of involvement include stomach [3], small bowel [4], colon and ano-rectum [5, 6]. Rare cases arising in extramucosal sites such as bone, lung, lymph node, spleen, mediastinum, testis, and spermatic cord have been published. PBL has been reported to occur 8-10 years after acquiring HIV infection. However, with increasing use of HAART and prolonged survival, the latency period is increasing. In our case, this patient developed PBL 18 years after the initial infection. The CD4 counts are usually less than 200/mm^3 at the time of presentation [7]. Our patient had a CD4 count of 363/mm^3 at the time of presentation.

Exact pathogenesis of PBL and other AIDS related lymphomas is not clear. EBV positivity has been frequently reported in various types of lymphoma arising in the setting of immunodeficiency. Although CD4 counts were maintained (> 200/mm^3) in our patient, he was in probable state of relative immunosuppression. Reactivation of EBV infection in states of relative immunosuppression can cause unmasking of some clones of B-cells at the sites of long standing chronic inflammation. A similar case of anal PBL has been described in HIV negative patient with a history of ischiorectal abscess and anal fistula [7]. A close follow up should be advised in HIV infected patients with similar chronic mucocutaneous inflammatory lesions while keeping in mind the possibility of lymphomatous transformation.

The morphological features of PBL include diffuse monomorphic proliferation of large cells, round nuclei with coarse chromatin and prominent nucleoli and abundant cytoplasm [8]. Some authors have reported that plasmacytic differentiation is more likely to be seen in extra-oral type of PBL [9, 10]. On the other hand, others have reported plasmacytic differentiation in large percentage (57%) of oral PBL [11]. The immunophenotype of PBL is characteristic which shows down regulation of CD20 and other B-cell markers and expression of CD38 and CD138. However, the plasma cell markers may not always be strongly expressed and this probably depends upon the stage of differentiation of the plasmablast. In such cases, use of other markers of plasma cell differentiation such as BLIMP-1/PRDM1 and XBP1 may be helpful [12]. Some authors have reported that extra-oral type of PBL is more likely to show CD56 expression as compared to the oral type [10]. Further studies are needed to find out whether extra-oral type of PBL represents a distinct subset.

The differential diagnosis in this case is extensive including DLBCL with immunoblastic differentiation, ALK positive DLBCL, secretory variant of DLBCL, primary effusion lymphoma, large B-cell lymphoma arising in HHV-8 associated multicentric Castleman disease (HHV8 MCD) and plasmablastic type of multiple myeloma or solitary plasmacytoma. DLBCL-NOS cells usually do not have prominent basophilic cytoplasm and exhibit positivity for CD45 and CD20. DLBCL can be difficult to rule out especially if the tumor cells show weak expression of CD20. ALK positive DLBCL can be easily differentiated due to CD30 and ALK-1 expression. Primary effusion lymphoma shows similar plasmablastic morphology and is positive for HHV-8 in almost all cases. Large cell lymphoma arising HHV8 MCD can pose diagnostic problems. HHV8 MCD is a rare node based disease and shows characteristic morphology. A plasmacytoma with plasmablastic morphology is a difficult differential diagnosis. However, diffuse strong EBV positivity in the clinical setting of HIV infection, and lack of monoclonal paraproteinemia favor a diagnosis of plasmablastic lymphoma. It is noteworthy to mention here that some cases of multiple myeloma (MM) and plasmablastic lymphoma may have identical immunophenotype. A clinical correlation is essentially required in such cases. Rare cases of plasmacytoma have been reported that showed EBV positivity [13]. A recent study reported immunohistochemical analysis of 35 cases of PBL and compared it with 111 cases of DLBCL. A limited panel of CD20, PAX5, BLIMP-1 and XBP1 is reported to be useful to differentiate PBL from DLBCL [12]. The prognosis is usually very poor and reported survival is less than a year. Hansara *et al*. reported a better overall survival in patients with PBL of extra-oral sites when compared to patients with oral PBL [10]. Some authors have described a better prognosis in HIV positive patients with PBL as compared to HIV negative patients with PBL [14]. In HIV patients HAART administration and immunosurveillance restoration correlate with better survival.

Despite the ever increasing number of cases of PBL, some issues remain controversial such as exact role of HIV and EBV in pathogenesis, whether oral and extra-oral types of PBL truly represent two distinct subtypes and clinico-pathologic differences between HIV positive and HIV negative PBL. Long standing chronic mucocutaneous inflammatory lesions in immunocompromised patients need close follow-up. More cases should be reported to facilitate further studies on pathogenesis and biological behavior of these lymphomas. This case report is our effort to contribute towards the number of cases of extra-oral type of plasmablastic lymphomas.

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