Primary plasmablastic lymphoma of the central nervous system in an immunocompetent man: A case report and review of literature

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ABSTRACT

Plasmablastic lymphoma (PBL) is an aggressive non-Hodgkin lymphoma classically occurring in individuals infected with human immunodeficiency virus (HIV). It has a predilection for the oral cavity and jaw. However, recent case reports have shown this variety of lymphoma in the stomach, lung, nasal cavity, cervical lymph nodes and jejunum in HIV-negative individuals. In this manuscript we report a case of primary PBL of brain in an HIV-negative heterosexual man, who presented with multiple episodes of seizures and hemiparesis. It proved a diagnostic challenge as initial stereotactic brain biopsy showed only few necrotic fragments and possibility of glioblastoma multiforme was rendered. Later patient underwent craniotomy and subsequent histopathology combined with immunohistochemistry led us in making a correct diagnosis of extramedullary PBL. Extensive systemic work up failed to reveal any disease outside the central nervous system. Only single case of primary PBL of brain in HIV-negative individual has been reported until date. To the best of our knowledge, this is the second report to suggest such an association.

Key words: Central nervous system, human immunodeficiency virus-negative, plasmablatic lymphoma, primary

INTRODUCTION

Plasmablastic lymphoma (PBL) is most frequently an AIDS-related non-Hodgkin lymphoma (NHL) and is usually confined to the oral cavity and jaws, although involvement of distant sites may occur.[1] It is a rapidly progressive tumor usually seen in human immunodeficiency virus (HIV) infection with advanced immunodeficiency (CD4 < 200 cells/ml) and is an AIDS defining illness.[2] In the recent years, cases of PBL have been reported involving the lungs, stomach, cervical lymph nodes, nasal cavity and jejunum in HIV-negative individuals.[3,4] Herein, we report a rare case of PBL found in the brain of an HIV-negative man.

Access this article online	
Quick Response Code:	Website: www.ijns.in
	DOI: 10.4103/2277-9167.146839

CASE REPORT

A 50-year-old heterosexual HIV-negative man presented with multiple episodes of seizures and progressive right hemiparesis of 1-week duration. Clinical examination revealed grade 4 spastic hemiparesis on the right side. On magnetic resonance imaging of the brain, there was a heterogeneous mass lesion in the left posterior frontal region [Figure 1a]. Patient underwent stereotectic brain biopsy, which showed a small fragment of highly pleomorphic cells along with large areas of necrosis. A possibility of glioblastoma multiforme was suggested. There was no history of noticeable lumps, unexplained fevers, drenching sweats, or weight loss. General physical examination was unremarkable, with no palpable lymphadenopathy or hepatosplenomegaly. Based on progressive symptoms and increased size of the lesion the patient underwent craniotomy and decompression of the lesion. The surgical specimen sent for histopathology consisted of multiple light brown tissue pieces, altogether measuring 6 × 5 × 4 cm. Microscopic examination showed diffuse sheets of highly atypical cells having large round nuclei, coarse chromatin and 1 or 2 prominent nucleoli. Tumor nuclei

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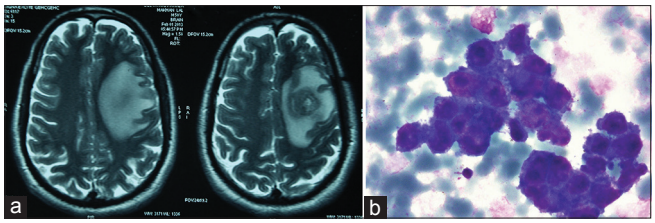

Figure 1: (a) Magnetic resonance imaging of the brain showing heterogeneous lesion in the left posterior frontal region. (b) Cytological smear showing atypical lymphoid cells with plasmablastic differentiation (May-Grunwald-Giemsa, ×400)

were slightly eccentrically placed. There were foci of necrosis and mitotic activity was brisk [Figure 2a]. On immunohistochemistry, tumor cells were positive for vimentin, CD38, CD138 [Figure 2b and c] and epithelial membrane antigen. Pancytokeratin, lung malignancy (thyroid transcription factor-1 and cytokeratin-7), melanoma (S-100, Melan-A and HMB-45) and other lymphoid markers (CD20, CD3, CD79a, CD56, CD45, ALK, and CD30) were all negative. Immunostaining for Epstein-Barr virus (EBV) was negative. Ki-67 index was 90% [Figure 2d]. Cytological examination of the cerebrospinal fluid fluid showed large atypical lymphoid cells showing plasmacytoid and immunoblastic differentiation, having basophilic cell cytoplasm, eccentric nuclei with 1-2 prominent nucleoli [Figure 1b]. Based on the clinical presentation, morphology and immunophenotype, the patient was diagnosed as having an extramedullary plasmablastic tumor consistent with plasmablastic NHL. There was no history of use of any immunosuppressive medications. He was an ex alcoholic, nonsmoker, and he denied any high risk behavior. Complete blood counts, liver and kidney function tests were within normal range. HIV, hepatitis B virus and hepatitis C virus serologies were negative. Radiological evaluation with computed tomography scan of chest/abdomen/bone did not show any other focal lesion. Further evaluation, that is, bone marrow biopsy was done to exclude plasma cell dyscrasias, which was normal with no marrow infiltration. Serum and urine protein electrophoresis were normal without presence of a paraprotein or free light chains.

The patient was planned for radiotherapy, but with progressive lesion and deteriorating functional status he expired.

DISCUSSION

Plasmablastic lymphoma is a rare and newly accepted type of aggressive lymphoma, initially described in HIV positive patients and presenting with an oral mass.[1] After 2001, PBL was acknowledged to be a new subtype of diffuse large B-cell lymphoma by the World Health

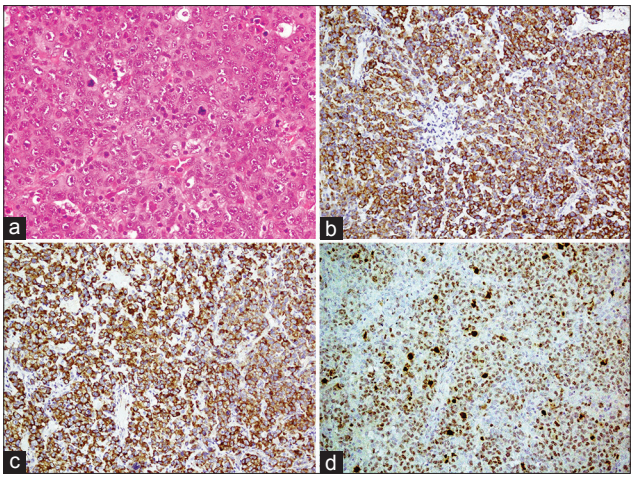

Figure 2: (a) Microphotograph showing diffuse sheets of atypical cells having large round nuclei, prominent nucleoli and numerous mitoses (H and E, ×400). (b) Microphotographs showing CD38. (c) CD138. (d) Ki-67 immunopositivity (immunohistochemistry, ×400)

Organization (WHO). The recent WHO classification of lymphoid neoplasms addresses PBL under separate entity as mature B-cell neoplasms, unlike previously being discussed as variant of diffuse large B-cell lymphoma.[5]

Although the majority of cases occur in the oral cavity of the AIDS patients, extra-oral involvement has increasingly been recognized and the tumor has also been documented in HIV-negative immunocompetent subjects.[3,4] Primary central nervous system (CNS) PBL is a distinctly uncommon disease and very few cases have been reported.[6-9]

The cytological feature of PBL is characteristic and includes large neoplastic cells with plasmacytoid morphology that resemble large immunoblasts. Tumor cells are pleomorphic, arranged in sheets or in glandular pattern with eccentrically located nuclei and prominent nucleoli. Frequent mitosis with areas of tumor cell necrosis and apoptosis are typical. Immunophenotype includes positivity for plasma cell markers (CD138, CD38, and Vs38c) and nongerminal center marker (MUM-1) and negativity, or weakly positive B-cell lineage markers leukocyte common antigen (LCA/CD45, CD20 and PAX-5). CD45 can be positive in PBL in 40-67% of cases.[10] Important differential diagnosis of PBL includes reactive plasmacytosis, malignant lymphoma and malignant melanoma. Increased number of immature plasma cells can be found in reactive conditions such as infectious CNS diseases (viral, neurosyphilis, cysticercosis etc.) or noninfectious conditions such as multiple sclerosis. Single cell necrosis and background apoptosis are not usually found in reactive processes. Malignant

melanoma is positive for S-100, HMB-45 and Melan-A. The etiology of PBL has not been well established. Although EBV and SV40 have been associated with PBL, yet the causal relationship has not been defined. CNS involvement by PBL either primary or secondary carries a dismal prognosis with a short survival time ranging from 3 days to 6 months.[7]

CONCLUSION

We report a case of PBL, an aggressive NHL usually associated with significant and documented immunosuppression, but which can occur in immunocompetent individuals as well. Biopsy, with accurate pathological and immunohistological testing is essential for the correct diagnosis and planning subsequent therapy. Increasing awareness of PBL in HIV-negative individuals and in this location is warranted.

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How to cite this article: Badyal RK, Vasishta RK, Kakkar N, Patra DP, Salunke P, Savardekar A. Primary plasmablastic lymphoma of the central nervous system in an immunocompetent man: A case report and review of literature. Indian J Neurosurg 2014;3:178-80.

Source of Support: Nil, **Conflict of Interest:** None declared.