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Case Report

Plasmablastic lymphoma: A report of 2 cases with review of literature

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ABSTRACT

Plasmablastic lymphoma (PBL) is an aggressive subtype of non-Hodgkin lymphoma initially described in extra-nodal sites in an immunocompromised and later in immunocompetent patients. PBL remains a diagnostic challenge due to morphological overlap with various other entities and also due to similarities on immunohistochemistry with plasma cell myeloma. In spite of therapeutic advances, PBL remains an aggressive disease with high fatality rate. We describe 2 cases of this uncommon neoplasm; both in immunocompromised patients.

KEY WORDS: Immunocompromised, immunohistochemistry, non-Hodgkin lymphoma

INTRODUCTION

Plasmablastic lymphoma (PBL) is a distinct clinico-pathological entity and is now considered a subtype of diffuse large B-cell lymphoma (DLBCL), seen more often in HIV-infected patients but is not rare in immunocompetent [1] patients also. In spite of therapeutic advances, PBL remains an aggressive disease with high fatality rate with only two studies reporting longer patient survival [2,3]. The diagnosis of PBL is challenging, due to its morphologic overlap with various other disease processes.

CASE REPORTS

Case 1

A 49-year-old female patient presented to the Ophthalmology Department of Kasturba Hospital with a complaint of swelling in the left eye with a 2-week history of pain radiating to the neck and head over the ipsilateral side. The patient was a known case of retropositive illness since 5 years. She had completed antitubercular therapy for tuberculous lymphadenopathy in 2013. Her physical examination was within normal limits

except left eye proptosis and multiple maculopapular skin lesions. On local examination, the patient had abaxial proptosis with lagophthalmos and severe ptosis along with exposure keratopathy. Computed tomography (CT) [Figure 1] study confirmed of a retrobulbar ill-defined soft tissue density in the intraconal compartment of the left eye. CT study on the right side was unremarkable. Complete blood counts and metabolic profile revealed no abnormality. Peripheral smear examination showed features of hemolytic anemia. Direct Coomb's test was positive. CD4 counts done around the same time was 91.74 cells/mL, and CD4/CD8 ratio was 0.11. An endonasal incisional biopsy of left orbital mass was performed, and tissue was submitted for examination. Histopathologic examination showed large abnormal lymphoid cells, with many showing plasmacytic differentiation. On immunohistochemistry, tumor cells were positive for CD138 and negative for cytokeratin, CD79a, CD20, and CD3 [Figure 2]. A final diagnosis of non-Hodgkin lymphoma (NHL) of plasmablastic type was made. Serum electrophoresis was requested to rule out monoclonal gammopathy. Subsequently, the patient was lost to follow-up.

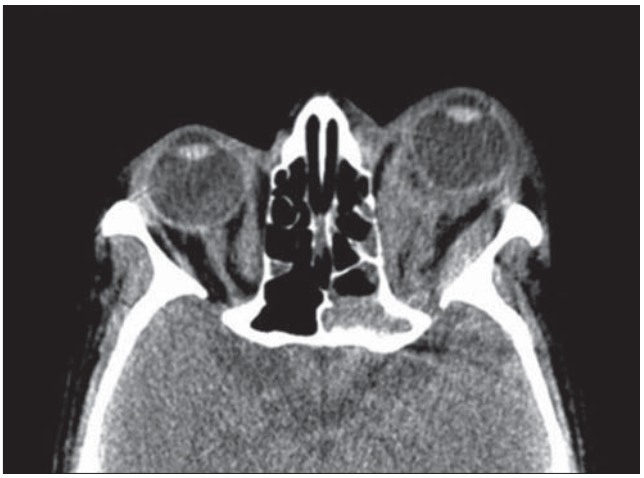

Figure 1: Computed tomography image of lesion in the left orbit

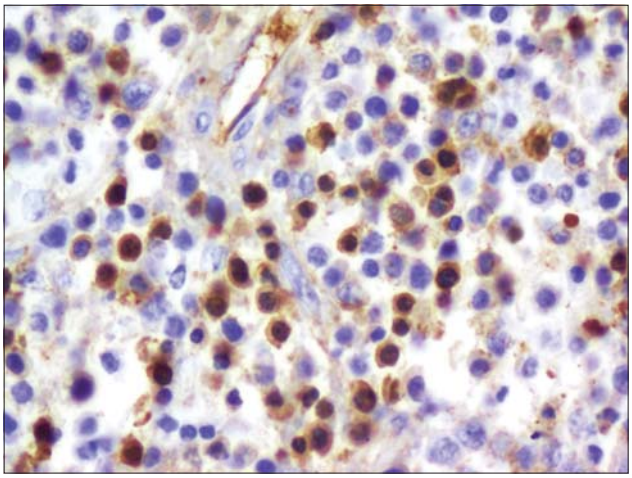

Figure 2: Positive lymphoid cells (CD138, ×400)

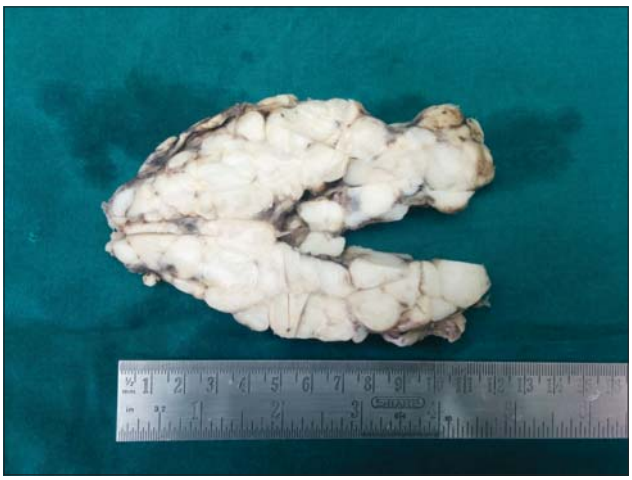

Figure 3: Large multinodular mass

Case 2

A 42-year-old male patient presented to the Surgery Department of Kasturba Hospital with complaints of pain and swelling over right leg for 4 years with a recent history of excruciating pain over the right lower limb making him inactive. The patient was a known case of retropositive illness on treatment at a local hospital. His physical examination was unremarkable. Local examination revealed a swelling measuring 7 cm × 4 cm on the extensor aspect of the leg which was hard in consistency, tender, and mildly erythematous. Magnetic resonance imaging study of the right leg revealed multiple lobulated septate enhancing soft tissue lesion (hypointense on T2-weighted imaging [T2W1] when compared to subcutaneous fat, hyperintense on short inversion time inversion recovery, isointense on T1W1) within the intramuscular and intermuscular compartment of extensor digitorum longus extending from the proximal leg till proximal part of foot where it was extending deep to the tendons of extensor compartment. Complete blood count and metabolic profile were within normal limits. The patient underwent an excisional biopsy, and the resected mass was submitted for histopathology examination [Figure 3]. Microscopy showed nodules and islands of neoplastic lymphoid cells, many being large to medium sized with hyperchromatic nuclei, single to multiple small nucleoli, moderate amount of eosinophilic cytoplasm, suggestive of plasmacytic differentiation, with interspersed binucleate and bizarre forms [Figures 4, 5a and b]. Tumor cells were CD138 positive, CD20 and CD3 negative. The final diagnosis of NHL-PBL was made. No bone marrow infiltration was identified. The patient was referred to oncology for further management.

DISCUSSION

PBL is a rare lymphoid neoplasm that was first described in retropositive patients. It has been subsequently described in patients with immunosuppression due to other causes. It accounted for 2.6% of AIDS-related lymphoma in the study by Carbone [4]. Since the first report of PBL in 1997 by Delecluse *et al*. [5], the spectrum of anatomical site of involvement by PBL has widened enormously. Various sites from where PBL has been recorded include skin [6], breast [7], gastrointestinal tract [8], central nervous system [9], male genitourinary system, and bones [10]. Table 1 summarizes the spectrum of involvement

Table 1: Spectrum of PBL involvement

Study	Number of cases	Sex	Age	Location	HIV status
Delecluse *et al*. [5]	16	14 M/2 F	27-75	Oral cavity	15/16
Carbone [4]	5	4 M/1 F	25-34	Oral cavity	5/5
Brown *et al*. [19,20]	1	M	35	Oral cavity	+
Pruneri *et al*. [21]	1	F	43	Oral cavity	-
Porter *et al*. [22]	1	M	36	Oral cavity	+
Flaitz *et al*. [23]	1	M	50	Oral cavity	+
Robak *et al*. [24]	1	F	56	Oral cavity	-
Borrero *et al*. [25]	1	M	36	Oral cavity	+
Gaidano *et al*. [26]	12	10 M/2 F	25-57	Oral cavity	12/12
Nasta *et al*. [27]	1	M	44	Mediastinum	+
Chetty *et al*. [15]	4	1 M/3 F	23-56	1 Nasal/3 ano-rectal	4/4
Nguyen *et al*. [28]	1	M	42	Nasal cavity	-
Nicol *et al*. [29]	1	F	68	Leg skin	-
Ojanguren *et al*. [30]	2	2 M	57,30	Perianal	1/2
Cioc *et al*. [31]	4	4 M	31-51	2 oral cavity,1 oropharynx,1 nasopharynx	4/4
Hirosawa [32]	1	M	58	Oral cavity	-
Corti *et al*. [33]	1	M	39	Oral cavity	+
Samoon *et al*. [34]	1	F	30	Oral cavity, breast	-
Romero *et al*. [9]	1	M	39	CNS	-
Urrego *et al*. [35]	1	M	45	CNS	+
Shuangshoti *et al*. [36]	1	M	37	CNS	+
Zhang *et al*. [37]	1	M	32	CNS	-
Mathews *et al*. [38]	1	M	40	CNS	+
Huang *et al*. [8]	1	M	21	Stomach	-
Liang *et al*. [7]	1	F	50	Breast	-
Chagas *et al*. [39]	1	F	46	Anal canal	+
Jiang *et al*. [40]	1	F	76	Neck	-
Cao *et al*. [41]	1	F	75	Duodenum	+
Isfahani *et al*. [42]	1	M	30	Anal canal	+
Yasuhara *et al*. [43]	1	F	50	Maxillary sinus	-
Radhakrishnan *et al*. [12]	1	M	7	Oral cavity	+
Dales *et al*. [6]	1	M	45	Skin	+
Schichman *et al*. [10]	1	M	41	Nasal sinus, testicles, bone	+

PBL: Plasmablastic lymphoma, CNS: Central nervous system

of PBL cases reported in the literature. However, orbital involvement is uncommon [Table 2]. The mean age of PBL presenting in HIV-positive and -negative cases is 39 years and 54 years, respectively [11]. It is a rare disease in children [12]. Men outnumber women in cases of PBL in HIV-positive cases [13]. Two morphological subtypes of PBL have been described in the literature [14]. The first and most common subtype is characterized by monomorphic tumor cell population with minimal or no plasmatic differentiation. The second type includes PBL with plasmacytic differentiation which shows tumor cells with differentiation to mature plasma cells, i.e., round to oval cells with an eccentric nucleus and some with prominent nucleolus. A distinct perinuclear hof in the cytoplasm may also be present [13]. In the present study, both the cases presented with the features of plasmacytic differentiation. Differentiating PBL from other lymphoma subtypes is challenging. The differential diagnosis includes immunoblastic DLBCL, anaplastic lymphoma kinase-positive DLBCL, Burkitt lymphoma, and plasmacytoma. PBLs are differentiated from immunoblastic DLBCL and Burkitts lymphoma based on their pattern on immunohistochemistry. Further, PBL shows CD138 positivity which is uncommon in DLBCL [5,15]. DLBCL shows CD20 positivity, the latter if present, is patchy and heterogeneous in PBL. A major diagnostic challenge lies in differentiating PBL from plasmacytoma, especially if the latter has anaplastic or plasmablastic morphology. In such a scenario, correlation with the clinical context, i.e., immunocompromised state, extra-nodal involvement, lack of bony involvement, and absence of monoclonal gammopathy is useful to rule out plasma cell neoplasm.

Table 2: Literature review of PBL cases with ocular involvement

Study	Number of cases	Sex	Age	Site	HIV status
Morley *et al*. [44]	2	M, M	40, 49	Ocular	-/NA
Barkhuysen *et al*. [45]	1	F	50	Ocular	+
Valenzuela *et al*. [17]	1	F	41	Ocular	+
Degnan and Levy [18]	1	M	43	Ocular	NA
Colomo *et al*. [14]	2	M/M	37/55	Ocular	+/NA
Mulay *et al*. [46]	3	F/F/M	45/45/48	Ocular	+/+/-
Present case	1	F	49	Ocular	+

The pathogenesis of PBL remains unclear. It has been proposed that it develops from the post-germinal center, terminally differentiated, active B-cell in transition from immunoblasts to plasma cells [13]. Many of these tumors are also positive for Epstein-Barr virus, suggesting role for these viruses in oncogenesis. Various studies have documented MYC gene rearrangement in cases of PBL [8]. In addition to retroviral positive patients, PBL has also been described in the setting of solid organ transplant recipient and in patients with autoimmune diseases.

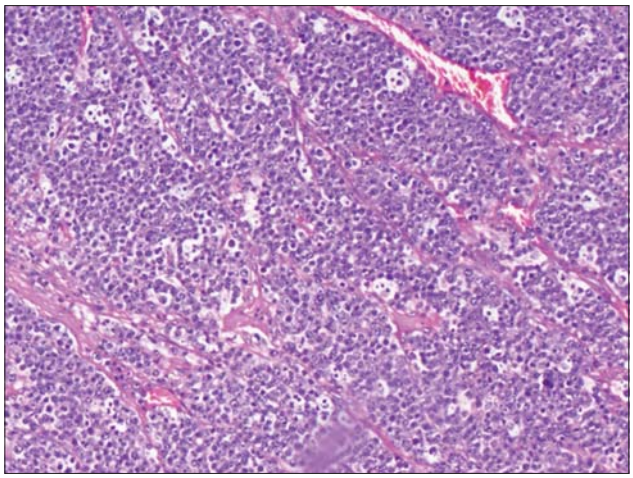

Figure 4: Abnormal lymphoid cells with starry sky pattern due to interspersed tangible body macrophages (H and E, ×100)

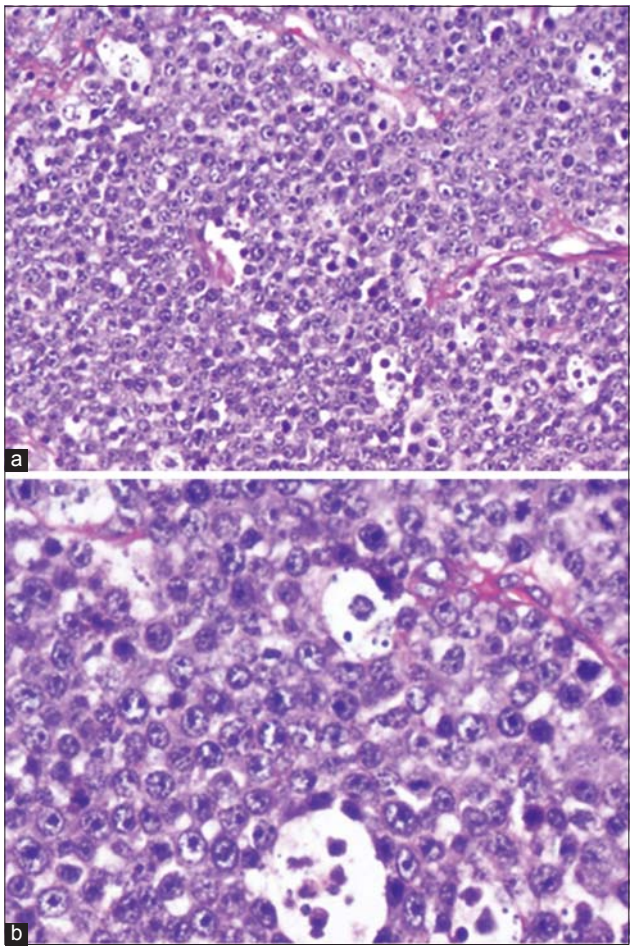

Figure 5: (a and b) Abnormal lymphoid cells with many plasmacytoid features and few bizarre forms (H and E, ×400)

PBL has an aggressive course. Rafaniello Raviele *et al.* [16] reported the prevalence of disease-related deaths is 59.6% during a mean period of 10.4 months from diagnosis and 58.6% during a mean period of 6.2 months for the extraoral type. Both our patients were, however, lost to follow-up after diagnosis.

At present, there is no standard therapeutic regimen for the treatment of PBLs. A robust management system to minimize disease-related mortality remains to be developed.

CONCLUSION

PBL is best classified as DLBCL, having predilection for extra-nodal sites in immunocompromised patient. Awareness of this entity and careful evaluation of lesions with plasmablastic morphology, especially in immunocompromised patients is useful in the recognition of this disease.

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