

Study of Plasmablastic Lymphoma: Our 3 years' experience at a Tertiary Care Oncology Institute

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Abstract

Background: Plasmablastic Lymphoma (PBL) is a rare aggressive subtype of B cell Lymphoma commonly associated with HIV infection. However, PBL is also seen in other immunodeficient and immunocompetent individuals. Because of its rarity and lack of expression of markers used in establishing an initial hematopoietic lineage, it poses a diagnostic challenge to pathologists.

Aim and Objective: To study cases of PBL at a Tertiary Care Oncology Institute, Hyderabad. To summarize the current knowledge on clinical and pathological characteristics, differential diagnosis, therapeutic and prognostic factors.

Observations and Results: Twenty cases of Plasmablastic Lymphoma were studied. In addition to Hematoxylin and Eosin staining, Immunohistochemistry was done for further diagnosis. Most of the cases were diagnosed as Poorly differentiated neoplasm on H&E, followed up with IHC, which was positive for CD138 and Ki67.

Conclusion: To increase awareness towards PBL and to avoid misdiagnosis.

Keywords: Plasmablastic lymphoma; B cell lymphomas; HIV infection; Immunodeficiencies

Introduction

Plasmablastic Lymphoma was first described by Delecluse in 1997 in oral cavity of HIV positive patient [1]. It is a rare clinico pathological entity, a distinct subtype of Diffuse Large B cell Lymphoma accounting for 2% of AIDS related Lymphomas [1,2]. The histological appearance of most of the lesions showed infiltration by monomorphous population of large cells which showed minimal expression of B cell antigens on IHC. With cells showing immunoblast morphology and immunophenotype of plasma cell, this tumor was named as PBL [2]. Because of its rarity, most of the clinical data was collected from medical archives. The aim of this study is to review cases of PBL along with their diagnostic morphology (H & E & IHC) and analyses the therapeutic and prognostic features.

Materials and Methods

Medical records of 20 cases of Plasmablastic Lymphoma were collected over a period of three years from July 2015 to July 2018 at a Tertiary Care Oncology Institute. Clinical history and other investigations were documented in all the cases. All Extra nodal and Nodal Lymphomas in pediatric and adult age group which were diagnosed according to WHO (2017) Classification, with clinico pathological features were included. All the cases of Myeloma were excluded based on clinical, biochemical, Radiological and morphological findings.

All the biopsy specimens from various sites were received in Formalin and embedded in paraffin and serially sectioned, stained with Hematoxylin and Eosin and an initial histological diagnosis was made. Further 3 microns sections were taken on positively charged slides for IHC with various antibodies, for further evaluation and confirmation of diagnosis.

Observations and Results

Of the 325 cases of Non-Hodgkin's Lymphoma, there were 20 cases

of PBL (20/ 325-6%) Peak age of incidence was 40 years with male preponderance and with male to female ratio of 3:1.

Patients are categorized based on their immunological status as follows: HIV positive PBL (n=11/ 20-55%), HIV negative PBL (n=9/20-45%).

HIV - positive PBL: 11 /20

Of the 11 positive cases with PBL, 8 (73%) were males with a median age at presentation of 38 years. Extra nodal presentation was most frequent 10/11-(90%), 3/11-(27%) of which involved oral cavity/ jaw, 3/11-(27%) sino-nasal tract, anorectal mass in 2/11-(18%). Most of the patients presented with advanced clinical stage and with B-symptoms.

HIV - negative PBL: 9/20

Female patients were affected relatively in higher proportion than HIV - positive PBL and occurs in older patients with a median age at presentation of 44 years and involvement of oral cavity (5/9-55.5%) been most common. There were 2 pediatric cases in our study.

Pediatric cases

Of the 2 pediatric cases of PBL reported, one was male and other female with age of 13 years at presentation and both the cases were HIV- negative. Lymph node and sino nasal tract were the sites of involvement.

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Clinical features: Most of the patients presented at an advanced stage of disease with dysphagia, generalised weakness, lymphadenopathy, bleeding per rectum and painful defecation.

All these patients were subjected to basic hematological and biochemical investigations - which were within normal limits. Radiological investigations- showed mass lesions in few cases. Bone Marrow Aspiration was within normal limits.

Fine Needle Aspiration Cytology of lymph node showed plasmacytic differentiation. Further biopsy was sent from these mass lesions for histopathological evaluation. Most of the cases showed diffuse sheets of monomorphous population of large cells with moderate to scant cytoplasm, large round central to eccentric nucleus with vesicular chromatin, prominent nucleoli, apoptotic bodies, necrosis, mitotic figures, intratumoral and peritumoral neutrophilic infiltrate, with sinusoidal pattern and angioinvasive pattern in two cases (Figure 1).

Based on the histomorphological findings and clinical sites our initial diagnosis was of Poorly Differentiated Carcinoma (12/20,60%), and the others were initially diagnosed as probably Anorectal Carcinoma (3/20,15%), Round Cell Tumor (2/10, 10%), Lymphoproliferative Disorder (2/10, 10%) and Sinonasal Carcinoma (1/20, 5%) . However all these cases were further subjected to IHC analysis.

As histomorphology was inconclusive, a panel of markers was done to rule out all the probable differentials, which includes an initial panel of markers like PCK, LCA, Vimentin and S100. When the results of the initial panel were inconclusive a further panel of markers was done which includes B cell markers (CD20, CD19, PAX5), T cell markers-CD3, melanoma-HMB45, proliferation marker Ki67, and CD56. All these markers were negative except for Ki67 which was high in all

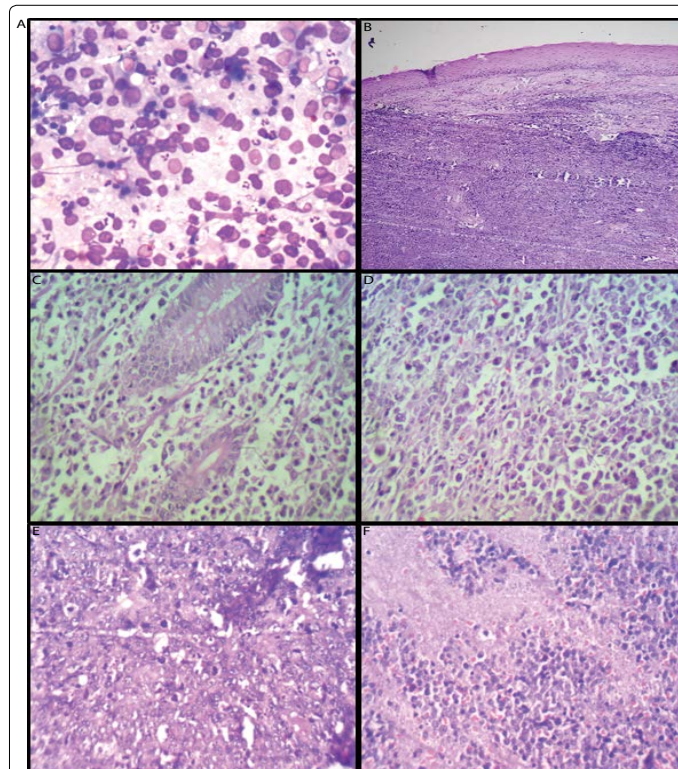


Figure 1: (A) Aspiration Cytology of lymph node showing plasmacytic differentiation, (B) Biopsy of tonsil showing mucosal sparing, (C,D) Anorectal mass showing plasmacytic and plasmablastic differentiation in HIV negative patient, (E,F) Apoptosis and Necrosis.

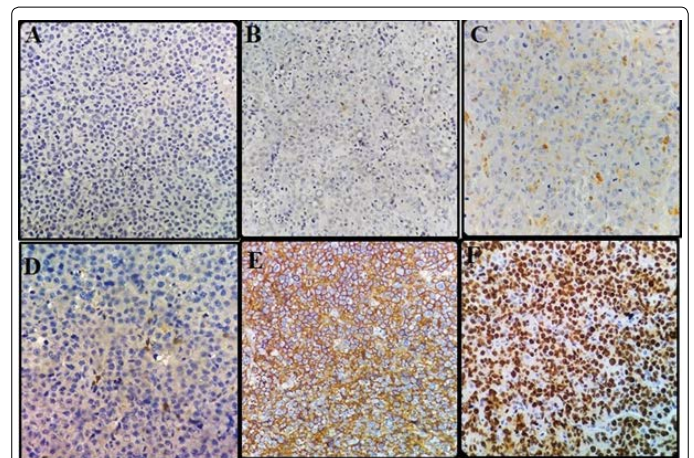


Figure 2: Immunohistochemistry showing (A) LCA-dim positive, (B) CD20-negative, (C) PAX5-negative, (D) CD3-negative, (E) CD138-positive, (F) Ki67-high.

neoplastic cells. As the diagnosis was inconclusive further IHC analysis was carried out which included - ALK and CD138. ALK was negative and CD138 was positive in all tumor cells. Hence a final diagnosis of PBL was made based on histomorphological and immunohistochemical analysis correlation (Figure 2).

Discussion

Plasmablastic Lymphoma is a rare aggressive, high grade neoplasm with overlapping features of Myeloma as well as Lymphoma with plasmacytoid morphology and negative for B cell and T cell markers. Hence it cannot be readily classified as B cell and T cell neoplasm.

Most of the cases in our study were males [2] with median age at presentation were 40 years [1,2]. Most common site of involvement was oral cavity [2].

Majority of these lesions had morphological features of monomorphous population of diffuse sheets of large cells showing plasmacytoid differentiation at places with moderate to scant cytoplasm, large round nucleus with vesicular chromatin, prominent nucleoli, apoptotic bodies and necrosis [3].

Differential Diagnosis

In our study the differential diagnosis considered were site specific like Carcinoma, Melanoma, Lymphomas- Diffuse Large B cell Lymphoma, ALK Positive Large B cell Lymphoma, and Plasmablastic Plasma cell Myeloma [4].

Based on histomorphology and Immunohistochemistry Carcinoma was ruled out as PCK was negative and ruled out Melanoma as S100 and HMB45 was negative.

Similar to PBL, ALK-positive Large B cell Lymphoma is a rare subtype of B cell Lymphoma, with large immunoblast like cells that lack expression of pan B-cell markers and express plasma cell related antigens. Unlike PBL, as the name suggests these neoplastic cells are positive for ALK in a granular, cytoplasmic staining pattern [5].

Immunoblastic Diffuse Large B cell Lymphoma is also a differential diagnosis but expression of pan-B cell antigens (ie. CD20, CD19, PAX-5) differentiates it from PBL which is negative for these markers [6].

But the most challenging distinction is from Plasmablastic (Anaplastic) plasma cell myelomas as, these two entities are similar in

morphology and immunophenotypic features. The distinction is based on clinical, laboratory and radiographic findings like hypercalcemia, renal dysfunction, paraproteinemias, osteolytic lesions and diffuse bone marrow involvement which favor plasmablastic plasma cell myeloma. In contrast, HIV infection, high Ki index and absence of CRAB features favor PBL [7,8].

Prognosis and therapy

The prognosis of Plasmablastic Lymphoma is poor with a median survival of 8 months [2]. In our study most of the patients were treated with combination of Chemotherapy and Radiotherapy. Of which Chemotherapy was given to 11 of the 20 patients (55%) with an aggressive regimen with EPOCH (Etoposide, Prednisolone, Oncovirin, Cyclophosphamide, Doxorubicin) in contrast to treatment for DLBCL which is inadequate to treat PBL. Remission was seen in four patients. Two patients were treated with Radiotherapy as palliative treatment to control epistaxis, then treated with Chemotherapy. Nine cases did not receive any treatment because of early death [9-12].

Conclusion

PBL is hard to diagnose and hard to treat lymphoma especially in immunocompromised patients. Hence awareness is important in the diagnosis of a suspected Lymphoma that lacks expression of markers for B cell and T cell lineage.

Appropriate use of IHC and clinical, laboratory and radiographic findings are crucial for establishing correct diagnosis. Intensive and aggressive treatment is required. Prolonged relapse free course following ECHOP and Anti-Retroviral therapy suggests that HIV patients even with advanced stage Plasmablastic Lymphoma may have prolonged survival and equivalent to cure. Further studies with targeted therapies have a potential to make long term responses possible for a greater number of patients.

In Indian scenario detailed clinical history, retroviral status and with minimal and limited IHC markers, these Lymphomas,

though difficult to diagnose, should be kept in mind, especially in immunocompromised patients-both adults and pediatric age groups which helps in correct diagnosis.

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