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Rare Aggressive B-Cell Lymphomas: Challenge for a Pathologist, Challenge for a Clinician 1. Plasmablastic lymphoma

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Abstract

Plasmablastic lymphoma (PBL) is aggressive B-cell lymphoma. It has unique diagnostic challenges and limited therapeutic options. PBL is strongly associated with HIV infection. It commonly presents with extranodal masses, frequently involving the oral cavity. Novel therapeutic approaches, including proteasome inhibitors, immunomodulatory agents, and immunotherapy strategies, show promise but remain under investigation.

Keywords: Plasmablastic Lymphoma; HIV Infection; CD20; Oral Cavity; Stem Cell Transplantation; Antiretroviral Therapy

Abbreviations: PBL: Plasmablastic Lymphoma; EBV: Epstein-Barr Virus; HAART: Highly Active Antiretroviral Therapy; SCT: Stem Cell Transplantation; EBER: EBV-Encoded RNA; PBM: Plasmablastic Myeloma; EBV+ DLBCL: EBV-Positive Diffuse Large B-Cell Lymphoma; PEL: Primary Effusion Lymphoma

Introduction

Plasmablastic lymphoma (PBL) is a subtype of diffuse large B-cell lymphoma (DLBCL). PBL has morphological and immunophenotypic features that overlap with both multiple myeloma and DLBCL. PBL predominantly affects adult males, though cases have also been reported in children [1]. The disease is often linked to EBV, particularly in HIV/AIDS patients and in those with other immunosuppressive states [1]. South Africa represents the region with the highest HIV/AIDS burden in the world that is why PBL incidence is high in South Africa [2]. Epstein–Barr virus (EBV) infection, MYC gene rearrangement, and various other molecular alterations have been implicated in the pathogenesis of PBL [1].

It has also been diagnosed in immunocompetent individuals [1]. PBL can involve any organ or system. Rapidly growing ulcerating, bleeding, and painful soft tissue masses, often in the oral cavity (in over half of the patients) or extranodal masses in HIV-positive patients is the typical clinical presentation in PBL. Most of these patients present clinically with advanced stage (ie, stage III or IV). PBL follows an aggressive clinical course characterized by rapid progression, high relapse rate, and poor survival with standard therapies [1].

Pathogenesis

The cell of origin of PBL is plasmablast. Plasmablast is an activated B cell that undergoes somatic hypermutation and class-switch recombination in germinal centers [1]. The pathogenesis of PBL remains poorly understood [2]. EBV shows a strong association with PBL pathogenesis especially in HIV-associated cases [2]. The recurrent translocation t (8;14) involving C-MYC and IGH genes is present in approximately half of all PBL cases. It is regarded as an important molecular event in its development [2].

Diagnosis

PBL poses distinct diagnostic and therapeutic challenges [3] being a rare type [1], has unusual morphology and negative CD20 expression [3]. PBL diagnosis relies on clinical suspicion confirmed by comprehensive pathological confirmation [1]. The best pathological diagnostic approach is to obtain large tissue sample for evaluation. Incisional, excisional, or core needle biopsies are preferred over fine-needle aspiration biopsies [3]. The immunophenotype of PBL is characterized by positive expression of classic plasma cell differentiation markers (such

as CD79a, IRF- 4/MUM-1, BLIMP-1, CD38, and CD138), negative B-cell markers (such as CD20, PAX-5 expression, and variable CD19 and CD45 expression).

Some cases have a positive aberrant expression of T-cell markers (such as CD2, CD3, CD4, or CD8). Proliferation markers (such as Ki-67) are expressed by almost all the neoplastic cells. CD10, BCL2, and BCL6 expressions (consistent with a non-germinal center origin) are uncommon. EBV-encoded RNA (EBER) or EBV Latent Membrane Protein 1 (LMP-1) expression is detected in 66% of the cases. Molecular study revealed presence of detectable MYC rearrangements in two-thirds of cases [3]. Like other common aggressive lymphomas, staging should be done using positron emission tomography/computed tomography (PET/CT) scanning. PBL is clinically staged using the Lugano modification of the Ann Arbor staging system [3].

Differential diagnosis [3]

PBL must be distinguished from other related entities with overlapping features

- **Plasmablastic Myeloma (PBM)**

Both PBM and PBL are morphologically and immunophenotypically similar. Presence of EBER within the neoplastic cells in the setting of an underlying HIV infection strongly supports PBL diagnosis. If there is serum monoclonal paraprotein, renal involvement, and lytic bone lesions consider PBM diagnosis.

- **EBV+ Diffuse Large B-Cell Lymphoma (EBV+ DLBCL)**

EBV+ DLBCL typically affects older adults. Malignant cells in EBV+ DLBCL can have a plasmablastic morphology and retain B-cell markers like CD20.

- **Primary effusion lymphoma (PEL)**

PEL is closely linked to HHV8 infection and typically presents with pleural or pericardial effusion or ascites.

- **ALK + DLBCL**

Both are aggressive CD20-negative subtypes that may exhibit plasmablastic morphology. ALK-positive DLBCL is ALK (anaplastic lymphoma kinase) driven protein, and has cytogenetic anomalies involving the ALK gene, such as the translocation t (2;17) and others. Furthermore, it is not associated with HIV infection or expression of EBER.

- **HHV8-positive LBCL**

Both are aggressive CD20-negative lymphomas that can be seen in patients with underlying HIV infection. HHV8+ LBCL has strong association with HHV8 infection. It can be also differentiated by underlying IgA- or IgG-lambda light chain restriction and closely related to HHV8-associated multicentric Castleman disease [3].

Risk Stratification and Prognosis

Poor survival rates have been observed in numerous literature reviews in patients with PBL. Worse survival was noted in patients aged ≥60 years, advanced clinical stage, and in high intermediate and high International Prognostic Index scores. The median OS of PBL patients was 15 months, and the 3-year OS rates was 40%. In another study, the 3-year OS rate of 248 PBL patients between 2010 and 2016 using the Surveillance, Epidemiology, and End Results (SEER) database was 54% [3].

Treatment

Most patients will require systemic antineoplastic therapy [3]. Treatment of early-stage disease with four courses of EPOCH combination chemotherapy with or without bortezomib followed by 30 Gy of consolidative radiotherapy improves their outcomes [1]. Six cycles of EPOCH with or without bortezomib for advanced disease stages [3]. Adding targeted agents, including proteasome inhibitors and anti-CD38 monoclonal antibodies, to the combination chemotherapy can enhance outcomes in advanced disease [1].

HAART (Highly active antiretroviral therapy) is necessary for treatment of all PBL with HAART-naïve HIV-positive patients. Optimal outcomes require more effective treatment combinations in patients with HIV-positive having low CD4+ counts or having high HIV viral loads. Spontaneous regression on HAART has been noted in HIV-positive individuals in some case reports [3]. Frail patients, those with CNS involvement, and those with cardiac, renal, or hepatic dysfunction should be managed according to current NCCN guidelines for DLBCL [3].

SCT: autologous SCT has been explored in patients with PBL in first remission and in relapse. Autologous SCT may be considered in patients with high-risk disease (such as those with HIV-negative, high IPI score, and the presence of MYC gene rearrangements) during first complete remission (CR1) when feasible. The advent of HAART has made autologous SCT a viable option for HIV-positive patients. Limited data on allogeneic SCT case reports in PBL is available. In relapsed patients, consider incorporating bortezomib, daratumumab, or lenalidomide, followed by autologous SCT for chemo sensitive disease [3].

Future Direction

Daratumumab (a CD38-targeting monoclonal antibody) has shown promising activity in PBL. Other emerging therapeutic options are immunomodulatory agents such as lenalidomide or pomalidomide particularly in relapsed or refractory PBL cases. PD-1 and PD-L1 are also promising but still experimental in PBL. Although chimeric antigen receptor T-cell therapy (CAR-T) is still limited in its application, it shows promising potential [3].

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Conclusion

PBL still has bad prognosis, limited response to standard chemotherapy regimens and high relapse rates. Early recognition, accurate diagnosis, and the development of targeted therapies are essential to improve patient outcomes. Continued research into the molecular biology of PBL and clinical trials exploring innovative treatment modalities will be critical in addressing the unmet needs for this rare devastating lymphoma.

References

1. Castillo JJ (2025) When immature plasma cells form lymphoma: how to improve on diagnostics and treatment of plasmablastic lymphoma? Hematology Am Soc Hematol Educ Program 2025(1): 564-570.
2. Fonseca FP, Robinson L, van Heerden MB, van Heerden WFP (2021) Oral plasmablastic lymphoma: A clinicopathological study of 113 cases. J Oral Pathol Med 50(6): 594-602.
3. Ramirez-Gamero A, Martínez-Cordero H, Beltrán BE, Florindez J, Malpica L, Castillo JJ (2024) Plasmablastic lymphoma: 2024 update on diagnosis, risk stratification, and management. Am J Hematol 99(8): 1586-1594.

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