Plasmablastic Lymphoma of Gingiva as Primary Oral Manifestation in Previously Undiagnosed HIV Patient – A Case Report
Kamlesh N. Dekate, Vineet Kini, Shwetha V. Kumar, Jigna Pathak, Leela Poonja

Abstract
Non-Hodgkin's lymphomas are the third most common group of malignant lesions in the oral cavity and maxillofacial region. Most such lymphomas have been shown to be predominantly of B-cell lineage. Plasmablastic lymphoma of the oral cavity is an aggressive B-cell lymphoma associated with Human Immunodeficiency Virus infection and is classified as an individual nosological entity by the World Health Organization Classification of Tumours of Hematopoietic and Lymphoid Tissues. It clinically presents with a rapid growth and histologically shows a diffuse pattern with a high mitotic index. Based solely on clinical and microscopic features, separation of Plasmablastic lymphoma from other categories of Non-Hodgkin’s lymphoma is very difficult. Therefore demonstration of distinguishing pattern of expression of immunohistochemical markers is an essential component of the diagnostic protocol. Hence we report a case of Plasmablastic Lymphoma in a healthy person with previously undiagnosed Human Immunodeficiency Virus.

Key words: Malignant Lymphoma; Immunoblastic; AIDS-Related; Non-Hodgkin’s lymphoma; HIV; Immunohistochemistry; CD138.

Introduction
The development of lymphoma in patients with immune dysregulation, induced by the Human Immunodeficiency Virus (HIV) is fully consistent with the known occurrence of lymphoma in other setting of immunologic compromise. Non-Hodgkin’s lymphoma (NHL) represents the most common HIV-associated malignancy, occurring in HIV-infected individuals at 60 times the frequency experienced in an otherwise healthy population.

With the constellation of Acquired Immunodeficiency Syndrome (AIDS) related Non Hodgkin's Lymphoma, four distinct types are AIDS Burkitt’s Lymphoma, Diffuse Large Cell Lymphoma, Immunoplasmacytoid Lymphoma and Primary Effusion Lymphoma. Plasmablastic Lymphoma (PBL) represent a recently categorized subtype of HIV-related Diffuse Large B Cell Lymphoma (DLBCL) based on its blastic morphology, with a marked predilection for oral cavity.

The present case report describes an interesting case of solitary intraoral Plasmablastic lymphoma in an apparently healthy individual who was later diagnosed seropositive for HIV infection. Lymphoma is considered to be a relatively late manifestation of HIV infection but in the present case Plasmablastic lymphoma was the only clinical oral manifestation.

Case Report
A 38 year old male patient reported to the Department of Oral Pathology, MGM Dental College and Hospital, with a chief complaint of painless swelling of gingiva on mandibular anterior region since one and half months. He had no other signs and symptoms before the onset of swelling that gradually grown up to present size.

Intra-orally an exophytic lobulated mass (Fig 1) measuring approximately 3x2 cm in size was present on the anterior region of mandibular gingiva. On palpation the swelling was soft in consistency, and not fixed to the underlying bone. Extra orally, neither facial asymmetry nor cervical lymphadenopathy was observed. Radiographic examination revealed vertical bone loss till the apex in between mandibular left central incisor and mandibular left lateral incisor. The differential diagnosis of pyogenic granuloma, peripheral giant cell granuloma and squamous cell carcinoma were considered.

Histopathologic examination of an excisional biopsy (Fig 2) revealed Parakeratinized, stratified squamous epithelium at one place. The underlying connective tissue showed a
dense, lymphocytic infiltrate of large lymphocytes with sparse, darkly staining cytoplasm and basophilic, pleomorphic, and vesicular nuclei. The overall picture consisted of malignant cells exhibiting eccentric, round nuclei and monotonous distribution of immature lymphocytes with few giant cells. Based on these histological findings, we concluded the lesion to be a form of NHL. For further confirmation we sent the patient for serological (ELISA) examination, for which the patient was found reactive for HIV and Hepatitis B.

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**Figure 1:** Gingival enlargement in the mandibular anterior region

**Figure 2:** Poorly differentiated large lymphocytes with darkly staining cytoplasm and pleomorphic basophilic nucleoli.

Immunohistochemical analysis revealed strong positivity for LCA (Fig 3) and CD138 (Fig 4) and focal positivity for CD30 (Fig 5). Tumor cells were negative for CK, EMA, CD20, CD3, Alk-1, CD34, and MPO. The final diagnosis of Non-Hodgkin Lymphoma-Plasmablastic type was made. The patient was referred to the Tata Cancer hospital for further treatment.

**Discussion**

Plasmablastic lymphoma is a rare neoplasm that is intimately associated with HIV. In the series of 191 AIDS-related non-Hodgkin’s Lymphoma studied at single institution during the year 1984-1997, Plasmablastic Lymphoma accounted for 2.6% of the cases. The first 16 cases were described by Delecluse et al in 1997 as highly malignant DLBCL of the oral cavity. Chang et al study results suggest that Plasmablastic lymphoma is best classified as sub-type of DLBCL at genomic level."

**Figure 3:** Immunohistochemistry shows strong positive for LCA.

**Figure 4:** Tumor cells show positive for CD 138.

**Figure 5:** Tumor cells show focal expression of CD 30.
Extra oral site of PBL includes the oropharyngeal, nasopharyngeal gastric, cutaneous, pulmonary, sacroccocygeal, pericardial, anorectal, nasal, paranasal or submandibular region. Intra orally gingiva and palate are the most commonly affected sites, although primary involvement of the jaw bones had also been reported. In the present case, a 38 year old man was diagnosed with PBL on gingiva of the mandibular anterior region. A review of literature shows oral PBL occurs in the age range of 7-75 years. The gender distribution shows male predilection of 6.3:1. Out of 65 cases of PBL reviewed by Sarode et al, 28 (43%) occurred in gingiva, 8 (12%) on palate, 4 (6%) on the floor of mouth and 19 (20%) were listed as occurring in the oral cavity. Few cases were reported to arise after extraction of tooth.

The present case was diagnosed HIV-positive prior to the immunohistochemical confirmation of PBL. In the literature, 59 of 65 (95%) patients were HIV-positive which were diagnosed before or after diagnosis of oral PBL. Raghu Radhakrishnan, reported a case of Plasmablastic lymphoma with vertical transmission of HIV in a child through parents. One reported case was, PBL located on the gingiva as HIV-negative but without explanation of immunosuppression status. Two cases were reported to affect immunosuppressed post-transplant non-HIV patients. One case of Richter Syndrome associated with PBL was reported in non-HIV patient. Nicolas Dupin et al reported PBL associated with multicentric Castleman disease having HIV-negative.

In the literature, Scheper et al reported a case of PBL with history of Hepatitis B. In our case serum sample was found to be positive for Hepatitis B.

Recognition of PBL confined to the gingiva is important to avoid confusion with other gingival enlargement like pyogenic granuloma, peripheral/central giant cell granuloma, malignancy like squamous cell carcinoma. Thus it is necessary to include PBL in differential diagnosis of solitary gingival enlargement in an apparently healthy individual as in our case and case reported by Desai RS et al.

The diagnosis of PBL solely depends on immunohistochemistry. The recognition of this variant of non-Hodgkin’s lymphoma is characterized by plasma cells morphology and expression of plasma cell associated antigens.

Morphologically differential diagnosis of PBL includes poorly differentiated carcinoma, anaplastic large cell lymphoma, and immunoblastic variant of DLBCL, Burkit's lymphoma and anaplastic plasmacytoma. Anaplastic large cell lymphomas are not immunoreactive for CD138 and CD38 whereas, PBL is reactive. Absence of immunoreactivity for cytokeratin helps to distinguish from carcinoma. PBL is negative for CD 20, while a blastic variant of DLBCL is negative for CD 138. In Burkit’s lymphoma and DLBCL, CD20 and LCA immunoreactivity is uniformly present while CD 138 and VS38c antigen immunoreactivity is absent.

The identification of Ebstein Barr Virus (EBV) specific RNAs in the neoplastic cells in PBL as of the immunodeficiency, may suggest an active role of virus in lymphogenesis. In present case we were unable to detect EBV status. As there is no established definitive treatment plan, treatment option may vary. It may consist of combination of chemotherapy or local excision followed by radiation. Despite the localization, the prognosis of PBL is poor.

Robert Armstrong reported a case of HIV-associated PBL with complete remission using Highly Active Anti-Retroviral Therapy (HAART) as well as traditional lymphoma therapy. Barkhuysen R et al reported a case of PBL mimicking orbital cellulitis showing regression with HAART.

Conclusion
In conclusion, this report mainly emphasizes the importance of clinical, morphologic, immunohistochemical and laboratory data in the specific diagnosis of Plasmablastic lymphoma from the differential diagnosis of solitary gingival enlargement in an apparently healthy individual with previously undiagnosed HIV-infection.

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Acknowledgement
We sincerely thanks Dr. Mukta Ramdwar, Tata Memorial Hospital, for her kind support in immunohistochemical analysis and Dr. Sheetal Awachar for her valuable guidance.

References

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Source of Support: Nil, Conflict of Interest: None Declared.