Oral Medicine Case Book 49: Plasmablastic lymphoma

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CASE REPORT

A 25-year-old male patient presented at the Oral Medicine Clinic with a painful bleeding lesion on the palate causing him discomfort during speech, mastication, and sleep. The lesion started approximately five months earlier as a small growth that gradually increased in size. The patient was rather vague about his medical history and habits but he did reveal that he smoked two cigarettes per day as well as using cocaine, a habit for which he was receiving therapy, for drug-induced hallucinations, at a local psychiatric hospital. He was not aware of any other medical conditions or allergies. The extra-oral examination revealed nothing of note, however, on intra-oral examination a large and firm pedunculated exophytic soft tissue mass was seen on the hard palate. It covered a large portion of the hard palate extending from the back of the upper incisors posteriorly onto the anterior part of the soft palate and into the right vestibule. It extended laterally to the gingival margins of all the teeth in the first quadrant, resulting in an appearance of gingival hyperplasia. The growth had an erythematous appearance with surface patches of necrosis and other areas that easily bled on touch (Figure 1).

Multiple punch biopsies of the lesion on the hard palate and buccal gingiva were performed and the specimens sent for histopathological investigation. The patient was dismissed with a supply of an antibacterial mouthwash consisting of a 0.2% aqueous solution of chlorhexidine digluconate, to be used twice daily to control superficial infection. He was requested to return a week later for suture removal and further management.

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ACRONYMS

AIDS:	Acquired Immunodeficiency Syndrome
EBER:	EBV-Encoded RNA
EBV:	Epstein-Barr Virus
HHV8:	Human Herpes Virus 8
HIV:	Human Immunodeficiency Virus
NH:	Hodgkin's Lymphoma
NHL:	Non-Hodgkin's Lymphoma
PBL:	Plasmablastic Lymphoma

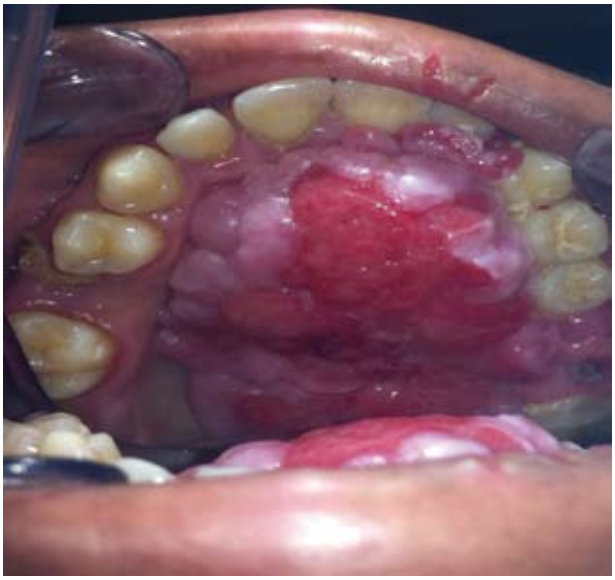

Figure 1: This mirror view shows the exophytic pedunculated soft tissue growth and its erythematous surface with necrotic patches. The growth covers the entire hard palate and extends posteriorly to cover part of the soft palate, as well as extending into the right upper vestibule.

DIAGNOSIS AND MANAGEMENT

The histopathological report revealed stratified squamous epithelial-lined fragments with an underlying diffuse proliferation of large, atypical lymphoid cells. These large neoplastic cells showed plasmacytoid features with vesicular nuclei, coarse chromatin and prominent nucleoli. The cytoplasm was basophilic to amphophilic in nature. Frequent mitoses and apoptotic cells were noted (Figure 2). Immunohistochemical staining was positive for CD38, a plasma cell marker (Figure 3). The proliferation index was very high (Figure 4) and the post germinal centre cell marker MUM-1, was positive (Figure 5). Staining for CD45, CD20 and CD3 were negative in tumour cells. The morphological and immunohistochemical features were consistent with a diagnosis of plasmablastic lymphoma.

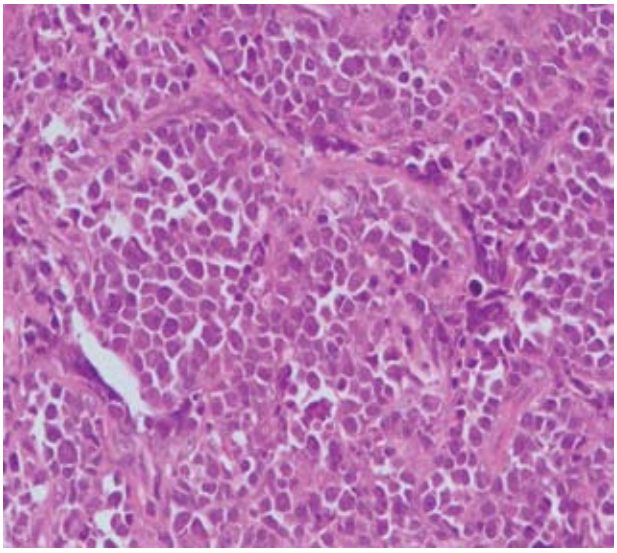

Figure 2: This haemotoxylin and eosin stained slide shows the histological features of plasmablastic lymphoma that consists of a diffuse proliferation of large cells resembling plasmablasts and immunoblasts.

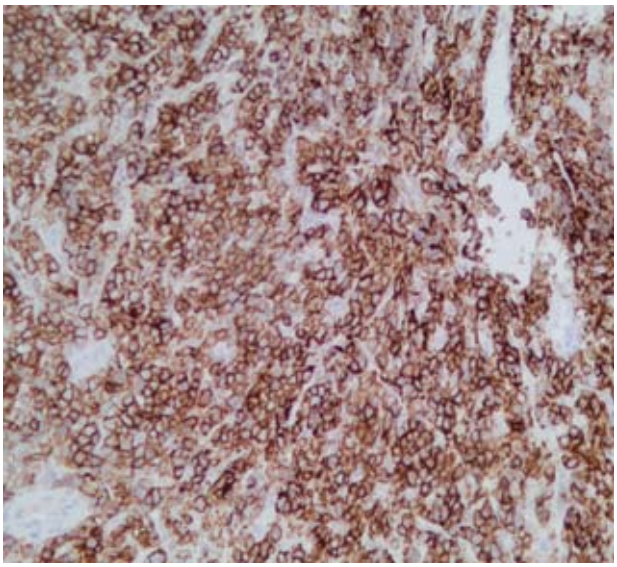

Figure 3: The plasmablastic lymphoma cells are strongly and diffusely positive for CD38

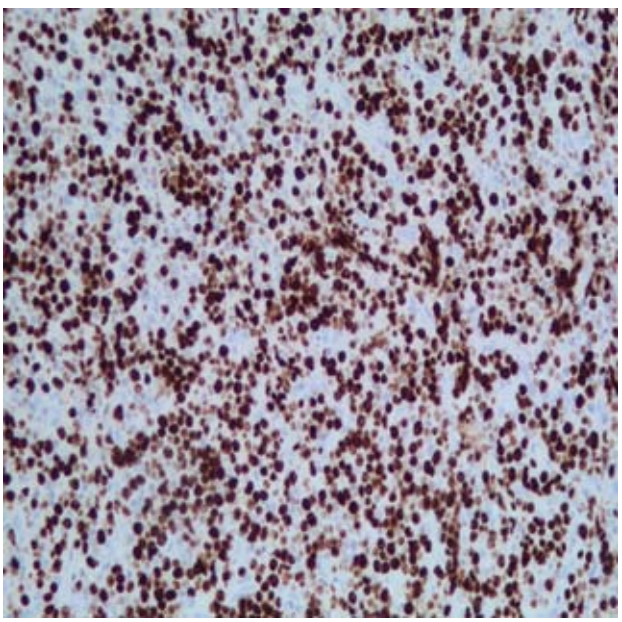

Figure 4: The measured proliferative index is very high (Ki67 > 90%).

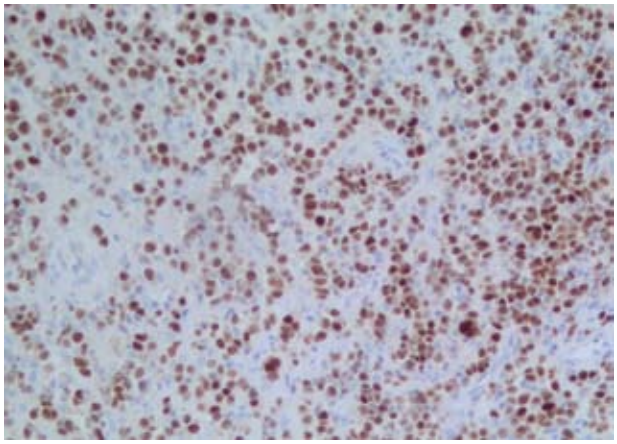

Figure 5: The immunohistochemical stain MUM-1 is positive in the atypical cells.

At the succeeding appointment the histopathological report was discussed with the patient and he was referred to the Lymphoma Clinic at the nearby tertiary hospital for further management. The patient also received counselling before being referred for retroviral testing. The patient turned out to be HIV-positive with a CD4 count of only 124. At the time of publication, the patient was on anti-retroviral medication, had completed his first course of chemotherapy and was doing reasonably well.

DISCUSSION

Neoplasms arising from lymphoid tissue are generically referred to as lymphomas and are broadly divided into the Hodgkin's lymphoma (HL) and non-Hodgkin's lymphoma (NHL) groups. NHL is a heterogeneous group of malignant lymphomas distinguished from HL by the absence of the giant Reed-Sternberg cells that are characteristic of the latter. NHL is the more common type of lymphoma and is further divided into follicular and diffuse types. Plasmablastic lymphoma (PBL) is a subtype of the diffuse large B-cell lymphoma. PBL was first described as recently as 1997 as a lymphoma presenting in the oral cavity of HIV-positive individuals. It was seen to consist mainly of large cells having the characteristics of differentiating plasma cells (plasmablasts), hence the term 'plasmablastic lymphoma of the oral cavity' was coined for this type of lymphoma. Subsequently, PBL was also described as occurring in other extranodal sites and in the 2008 World Health Organisation classification of lymphomas the descriptive phrase "of the oral cavity" was dropped from the terminology. Although most reported cases are in fact seen in HIV-positive persons, it may also occur in other immunodeficiency states and PBL is thus not considered to be an AIDS-defining disease.[1,2]

PBL has a strong viral association especially in the presence of severe immunodeficiency such as that induced by HIV infection. The Epstein-Barr virus (EBV), the putative causative agent of infectious mononucleosis and Burkitt's lymphoma, is known to infect B lymphocytes and convert them into immortal lymphoblasts. The presence of such infected cells results in the expression of latent gene products which may promote cell growth and impair apoptosis, thus leading to neoplastic transformation. The virus associated with Kaposi's sarcoma, the Human Herpes Virus 8 (HHV8), may also be involved by its propensity to stimulate lymphomagenesis. Whereas it is thought that EBV plays an important aetiological role in PBL, it seems that the same role for HHV8 is still controversial.[1,2,3] The role of smoking in the development of PBL is uncertain but it is thought to have a synergistic influence.

The mean age of patients with PBL is approximately 39 years with a high male prevalence, however, the latter may be the result of the preponderance of males in the HIV-positive population in developed countries.[4,5] In the African setting, this gender trend may well be reversed due to a different profile of the HIV-positive persons in many African countries. PBL is most often seen in the oral cavity and has a rapidly progressive clinical course. Extra-oral sites affected by PBL include the lung, stomach, ano-rectal region, nasal cavity, maxillary sinuses, pharynx, bone, skin and other soft tissues. According to the literature, such extra-oral PBL lesions are relatively rare, however, this may be due to the difficulty in correctly diagnosing these lesions in remote sites.[6] Moreover, it appears that such lesions occur less commonly in immunocompromised persons than is the case with oral lesions.[1] Lesions usually present as a localised, painful and rapidly growing neoplastic mass, clinically similar to Kaposi's sarcoma, and may infiltrate the adjacent bone.[1,5] Thus an early and accurate diagnosis is essential and can only be achieved by histopathological evaluation, including appropriate immunohistochemical analysis.

The histopathological features of PBL is that of a cellular proliferation in the form of sheets of large lymphoid cells in a background of small mature lymphocytes and macrophages.[3,5,7] The neoplastic infiltrate typically invade the surrounding soft tissue and results in superficial ulceration and necrosis. The neoplastic cells show plasmablastic differentiation in the form of round to oval shaped cells with eccentrically placed nuclei and with abundant eosinophilic cytoplasm.[7, 2] Cells show a high mitotic rate and stain positive for the Ki-67 proliferation index, usually involving 90% of the tumour cells.[3, 5] Mature lymphoid cells, occasional neutrophils and a few eosinophils may also be present.[7] PBL cells also stain positive for plasma cell markers such as CD38, CD138, Vs38c but not for the B-cell antigen, CD20.[3] In addition, the detection of EBV by in situ hibridisation for EBER (EBV-encoded RNA) is helpful in confirming the diagnosis in approximately 60-75% of cases. In the oral cavity the rate of EBV infection is nearly 100%.[8]

The differential diagnosis for patients with a rapidly-growing oral lesion should include infectious and malignant conditions. Infectious lesions that should be considered are the relatively common odontogenic abscesses arising from infection with typical oral flora. Malignant processes should include oral squamous cell carcinoma, metastatic tumours, Kaposi's sarcoma, diffuse large B-cell lymphoma, plasmacytomas and Burkitt's lymphoma.[3]

Management of individuals with PBL include chemotherapy or radiotherapy with or without surgical excision, or a combination of chemotherapy and radiotherapy depending on the stage of the tumour, the systemic symptoms and HIV co-infection.[3,9] The prognosis of PBL is poor and death usually occurs within 1 to 24 months after diagnosis.[7]

CONCLUSION

The present case is a stark reminder that any growth in the oral cavity should be diagnosed as soon as possible in order to get the patient properly managed in cases of life-threatening conditions, such as PBL. It also demonstrates just how rapidly a large PBL lesion can develop and how aggressive these lesions can be. Moreover, it should be noted that PBL patients must be considered positive for HIV infection until proven otherwise. Although HIV-positivity had not been established in this patient at the time of diagnosis, it is highly probable that the patient would be positive for HIV. The patient's habits of tobacco and drug use may have had an effect, however, the history obtained from the patient was so sketchy that no deduction could be made on the possible effect of these noxious habits. Due to the destructive behaviour and poor prognosis of PBL, especially if associated with AIDS, the early diagnosis of both these conditions will allow for appropriate treatment of PBL with chemotherapy, at the earliest possible moment, as well as allow prompt enrolment into a HIV treatment programme in the case of HIV-positive patients. Such measures will undoubtedly help to reduce the morbidity and mortality relating to PBL, and of other possible AIDS-related diseases, thus improving the patient's survival rate and quality of life. Moreover, any oral mass, especially when occurring in immuno-compromised individuals, should be referred for biopsy.

Declaration: No conflict of interest declared.

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