A Case of Oral Plasmablastic Lymphoma and Review of Current Trends in Oral Manifestations Associated With Human Immunodeficiency Virus Infection

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Plasmablastic lymphoma (PBL) is a rare and aggressive type of non-Hodgkin lymphoma that in 2000 was classified as a distinct type of lymphoma related to acquired immune deficiency syndrome by the World Health Organization after the first reports of the disease surfaced in 1997. PBL is strongly associated with human immunodeficiency virus (HIV) infection and often occurs within the oral cavity. Despite intensive chemotherapy regimens and combinational antiretroviral therapy, the prognosis of PBL in HIV-infected patients remains poor. This article describes a case of oral PBL and a literature review of current trends in oral manifestations associated with HIV infection.

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Plasmablastic lymphoma (PBL) is a recently described non-Hodgkin lymphoma (NHL). In the United States and most developed countries, NHL represents the most common malignancy related to the human immunodeficiency virus (HIV), followed by Kaposi sarcoma.[1] PBL was accepted by the World Health Organization (WHO) 2000 classification as a distinct type of lymphoma related to acquired immune deficiency syndrome (AIDS) subsequent to increasing case reports after the first report in 1997 by Delecluse et al.[2,3] Oral PBL continues to be strongly associated with HIV infection in male patients (92% of the time), as found in a review by Sarode et al[4] of 68 cases of PBL specifically including the oral cavity.[3,5] From 1991 to 2005, the US AIDS population has expanded 4-fold, consisting mostly of patients at least 40 years old.[1] In 2011 there were 872,990 persons living with diagnosed HIV infection in the United States[6] and 35.3 million worldwide as of 2012.[7] One can expect an increase in HIV-related and non–HIV-related malignancies in patients diagnosed with HIV as this population continues to live longer. This report describes a case of PBL in the maxilla in a patient with previously undiagnosed AIDS. A literature review of oral PBL and changing trends in oral manifestations of HIV infection is included.

Report of Case

A 52-year-old man presented to the emergency room of Parkland Memorial Hospital (Dallas, TX) with the chief complaint of 4 weeks of worsening right-sided facial swelling. The patient reported loosening of teeth on the upper right during the past 4 weeks. He consumed alcohol on rare occasions and denied any history of tobacco or recreational drug use. The oral and maxillofacial surgical service was consulted to respond to a suspected odontogenic infection. The emergency room workup showed the patient to have AIDS, with a CD4 count of 134 and an HIV viral load of 223,446, which was previously unknown to the patient.

Extraoral examination disclosed a mild diffuse swelling of the right malar region with no overlying skin changes in this Caucasian patient. No cervicofacial lymphadenopathy was appreciated. An approximately 2- ×2-cm erythematous and lobulated soft

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gingival mass was observed on the buccal mucosa adjacent to the maxillary right first and second molars which were severely carious. The maxillary right first and second molars exhibited class III mobility.

Panoramic radiographic examination showed extensively carious maxillary right first and second molars, with associated periodical radiolucencies that extended apically into the right maxillary sinus as an opacified and well-delineated mass (Fig 1). Computed tomography showed erosion of periapical bone extending into the right maxillary sinus floor adjacent to the maxillary right first and second molars. The right ethmoid and right frontal sinuses also were opacified (Fig 2).

The otolaryngology service performed endoscopic evaluation of the right paranasal sinuses because of concern for invasive fungal sinusitis. No obvious mucosal necrosis was found, although endoscopy did confirm some edematous and inflamed fibrous debris within the right maxillary sinus, which was thought to be secondary to an infected tooth.

The maxillary right first and second molars were extracted under local anesthesia. At this time the decision was made to perform a biopsy to definitively diagnose the gingival mass (Fig 3).

Microscopic examination showed an oral mucosa with extensive underlying diffuse infiltration, with medium to large cells exhibiting plasmacytic differentiation. There was a high degree of mitotic activity and abundant cellular debris present. Cytologically unremarkable plasma cells were seen underlying the squamous epithelium (Fig 4). Immunohistochemical examination also was performed with CD79a, CD20, CD3, PAX-5, KI-67, CD45, and in situ hybridization for κ, λ, and Epstein-Barr virus (EBV), which showed atypical cells exhibiting the following immunophenotype: $CD79a^{+}$, CD20 (minimally positive), $CD3^{-}$, $CD5^{-}$, $CD138^{-}$, $PAX\text{-}5^{-}$, $BCL2^{+}$, $CD10^{-}$, $BCL6^{-}$, Ki-67 (= 90%), $CD45^{+}$, in situ hybridization κ^{+}, λ^{-}, and EBV^{+}. The diagnosis was EBV^{+} PBL.

Extraoral disease involvement was ruled out with positron emission tomography, transthoracic echocardiography, plain chest radiography, computed tomographic examination of the abdomen and pelvis, brain magnetic resonance imaging, bone marrow biopsy, and lumbar puncture. Subsequently, multiple specialists were recruited to manage AIDS and oral PBL. The patient was started on combinational antiretroviral therapy (cART) in the form of Atripla (efavirenz, emtricitabine, and tenofovir; Bristol-Myers Squibb, New York, NY) and began chemotherapy with rituximab, etoposide, doxorubicin, vincristine, prednisone, and cyclophosphamide (R-EPOCH) for PBL.

Despite being initially responsive, the mass eventually progressed after 5 cycles of R-EPOCH. Next, rituximab, ifosfamide, carboplatin, and etoposide (R-ICE) chemotherapy was used for refractory disease. After the second cycle of R-ICE and approximately 6 months from the initiation of chemotherapy, the mass continued to increase in size. At this point, roughly 7 months from diagnosis, a 40-day salvage radiotherapy course was administered for refractory oral PBL. After 5 cycles of rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisolone (R-CHOP), 2 cycles of R-ICE, and

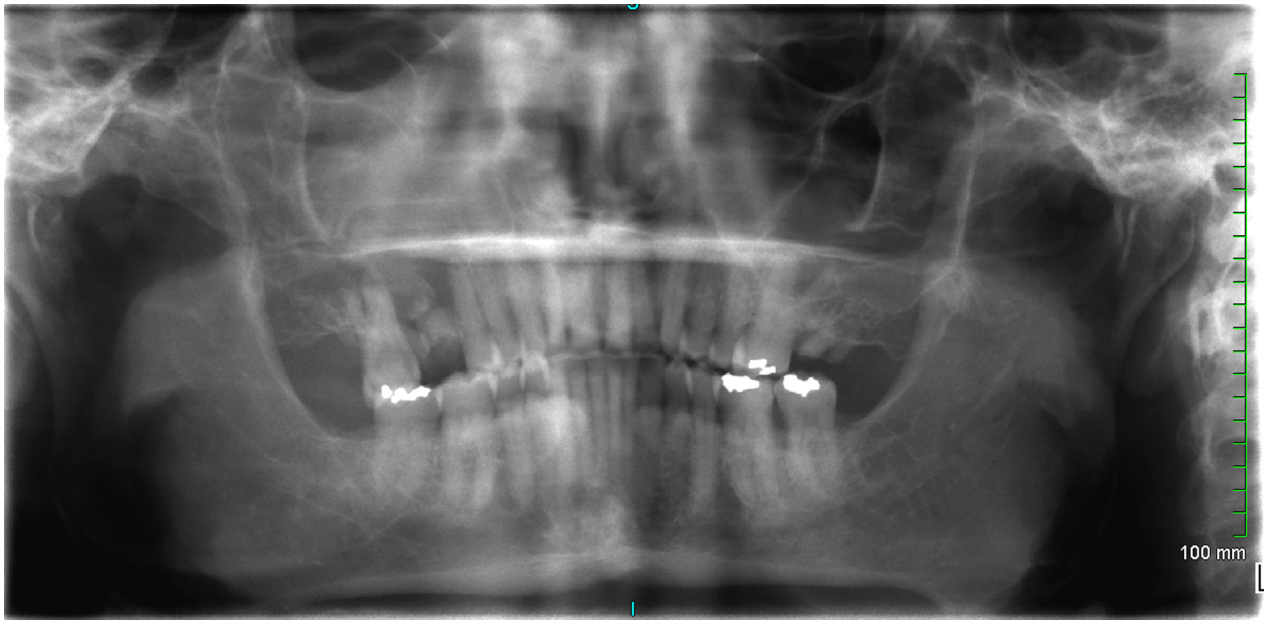

FIGURE 1. Panorex radiograph.

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