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CASE REPORT

Intra-oral HIV-associated Burkitt's lymphoma with mandible involvement

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Summary Although Burkitt's lymphoma (BL) of the oral cavity is very uncommon in human immunodeficiency virus (HIV)-infected patients, its occurrence is highlighted as one of the earliest clinical manifestations. This report deals with the first occurrence of intra-oral HIV-associated BL with plasmacytoid differentiation and mandibular involvement. It also serves to illustrate the importance of histological and immunohistochemical analyses of oral lesions to indicate the possibility of HIV-infection.

Introduction

In the most recent World Health Organization (WHO) classification, Burkitt's lymphoma (BL) is separated into three clinical variants: endemic BL, non-endemic BL, and human immunodeficiency virus (HIV)-associated BL.[1] Additionally, three subtypes of HIV-associated BL have been suggested by the WHO:[1] classic BL, BL with plasmacytoid differentiation and atypical BL. This report has documented an intra-oral case of HIV-associated BL with plasmacytoid differentiation and mandibular involvement. It also serves to illustrate the importance of histological and immunohistochemical analyses of oral lesions to indicate the possibility of HIV-infection.

Case report

A 28-year-old Chinese man presented with a 4-week history of a painful swelling on his right cheek (Fig. 1A). The patient did not have any known drug allergies, and had a history of cigarette smoking, alcohol consumption, and betel-quid chewing. No other significant previous medical history was noted apart from gastric disease and a recent

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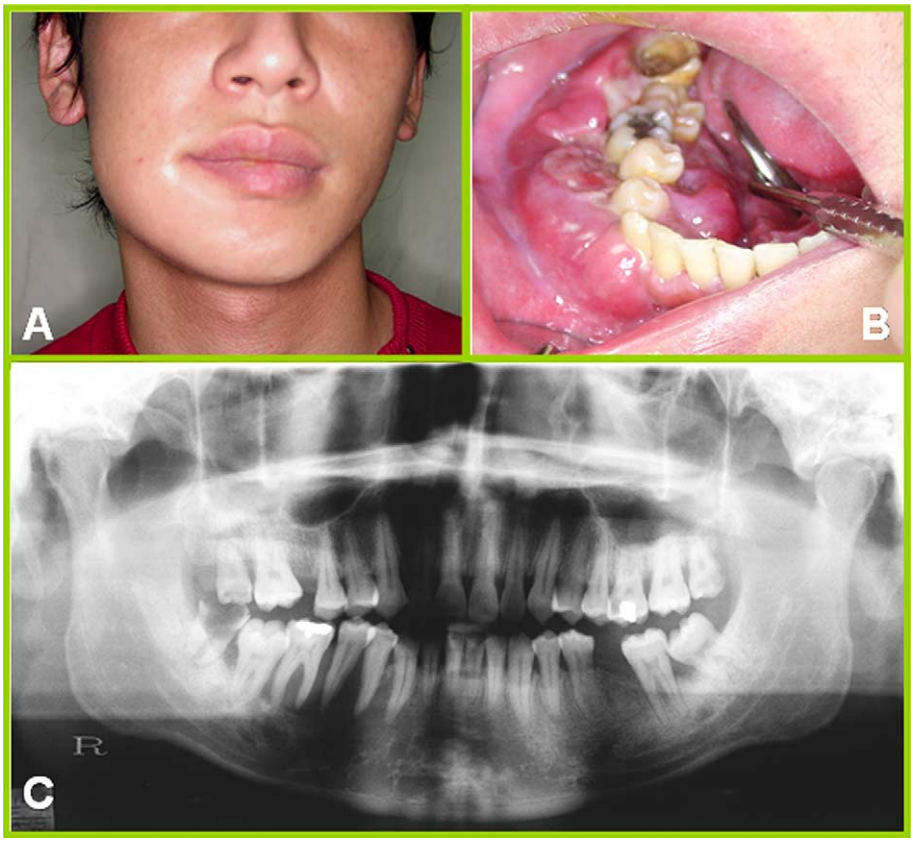

Figure 1 (A) A painful swelling was noted on the patient's right cheek; (B) an ulcerative swelling was noted in the right posterior mandible extending from the buccal vestibule to the lingual side; (C) panoramic radiography revealed an ill-defined irregular radiolucency extending from the distal side of tooth 44 to mesial side of tooth 48 and above the lower border of the mandible.

hospitalization for unknown fever in another hospital. Extra-oral examination revealed right facial asymmetry (Fig. 1A) and paralysis over the right lower lip. Intra-oral examination revealed a painful ulcerative mass, approximately 4×6 cm in diameter, extending from the right lower posterior buccal vestibule to the lingual side (Fig. 1B). Grade II mobility of the right mandibular second pre-molar and first molar were noted. Also, a tender lymph node could be palpated over the right submandibular area. Panoramic radiography revealed an ill-defined irregular radiolucency without a corticated margin, extending from the distal side of tooth 44 to the mesial side of tooth 48 and above the lower border of the mandible; the right inferior alveolar canal also appeared to be involved (Fig. 1C). A clinical impression of the malignancy was rendered and an incisional biopsy was subsequently performed under local anesthesia.

Histological examination showed a typical ''starry sky'' appearance with an infiltrate of neoplastic lymphoid cells on low-power magnification (Fig. 2A). Under higher magnification, these medium-sized neoplastic lymphoid cells were characterized by abundant basophilic cytoplasm and an eccentric nucleus, suggestive of plasmacytoid differentiation (Fig. 2B). Immunohistochemical staining showed that these neoplastic lymphoid cells were negative for CD45RO, lambda, CD30, bcl-2 and bcl-6, but positive for CD20 (Fig. 2C), kappa, and *c-myc* (Fig. 2D). Immunological examination was negative for anti-Epstein Barr virus immunoglobulins. High labeling indices with prominent nuclear staining for Ki67 (Fig. 2E) and p53 (Fig. 2F) were, however, noted. These histological and immunohistochemical findings were suggestive of an HIV-associated BL with plasmacytoid differentiation.[2] We were therefore alerted to the fact that the patient was likely to be HIV-positive, although he denied having homosexual and heterosexual behavior.

One week subsequent to tumor histopathology, the diagnosis of HIV-associated malignancy in the mandible was explained to the patient, and a serology test for HIV was positive. Unfortunately, the patient failed to show up to be admitted for further

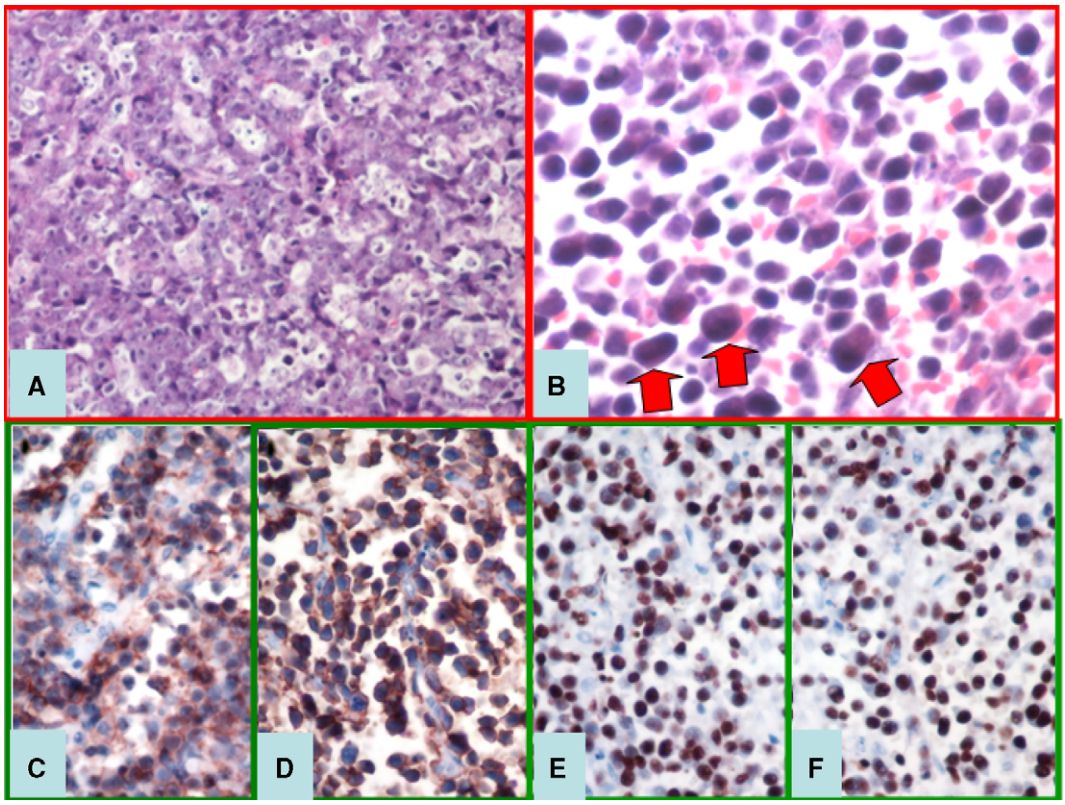

Figure 2 (A) A typical ''starry sky'' appearance with an infiltrate of atypical lymphoid cells was noted (Hematoxylin eosin × 40); (B) plasmacytoid differentiation of the neoplastic lymphoid cells with abundant basophilic cytoplasm, and an eccentric nucleus could be seen, with some examples indicated by the arrows (Hematoxylin eosin × 100). Immunohistochemical stainings showed that the neoplastic lymphoid cells were positive for CD20 (C), *c-myc* (D), Ki67 (E) and p53 (F) (×100).

tests, such as a whole-body computer tomographic scan, bone scintigraphy, a complete hemogram and CD4 level, as well as the staging of the lymphoma, and has been lost for follow-up since then. Although the molecular cytogenetic analysis for *myc* translocation between chromosomes 8 and 14, which is regarded as the hallmark test for BL,[2] could not be performed due to the lack of available fresh tissue samples, the diagnosis of HIV-associated BL could be confidently confirmed from the histological and immunochemical analyses for this patient.

Discussion

The ulcerative intra-oral swelling with extensive mandibular bone destruction and mandibular nerve paresthesia suggest a malignant neoplasm with mandibular involvement. This case also highlights the possibility of detecting HIV-infection from the histological examination of intra-oral lesions.

As aforementioned, three variants of HIV-associated BL have been suggested by the WHO.[1] To our knowledge, this is the first reported case of intra-oral BL with plasmacytoid differentiation. Such a subtype of BL has been assumed to be almost unique to patients with AIDS.[2]

Immunosuppressed individuals, due to HIV-infection in this case, have been shown to be at significantly higher risk for lymphomas, which are the second most common malignancy seen in HIV-infected individuals, whereas Kaposi's sarcoma is the most common.[2] It has been predicted that up to 25% of cases of lymphoma will be associated with, and occur as a result of, HIV-infections.[3] Reviews of the English-language medical literature show that the oral manifestation of BL in HIV-infected individuals is very uncommon and only three cases have been histologically identified in adults.[4,5] Hernandez Vallejo et al.[6] (1989) has reported the periodontal findings in an AIDS patient with BL occurred in the axillary lymph nodes; however, no histological examination has been confirmed for the intra-oral lesions. All of these reported BLs in HIV-infected

individuals, including the current case, were found to have mandibular involvement.[4,5] Moreover, it has been highlighted that BL in an HIV-infected person may be one of the first clinical findings.[2,4,5]

Most recently, Lim et al.[7] has compared the outcomes of patients with HIV-associated BL and HIV-associated diffuse large-cell lymphoma (DLCL) after treatment with CHOP (cyclophosphamide, doxorubicin, vincristine, prednisone) or M-BACOD (methotrexate, bleomycin, cyclophosphamide, etoposide) in pre-highly active anti-retroviral therapy (HAART) versus HAART eras. It has been concluded that the survival of patients with HIV-associated DLCL has improved in the HAART era, whereas survival of similarly treated patients with HIV-associated BL remained poor. Our patient did not receive any treatments and the prognosis could not be predicted.

In conclusion, although BL of the oral cavity is very uncommon in HIV-infected patients, its occurrence is highlighted as one of the earliest clinical manifestations. This report deals with the first occurrence of intra-oral HIV-associated BL with plasmacytoid differentiation and mandibular involvement.

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