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A case of intraoral plasmablastic lymphoma spontaneously regressed after biopsy in HIV-negative patient

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ABSTRACT

Plasmablastic lymphoma (PBL) is a rare and aggressive subtype of non-Hodgkin's lymphoma that predominantly occurs in the oral cavity of individuals infected with human immunodeficiency virus (HIV) and Epstein-Barr virus (EBV). However, it has been reported that it often occurs in HIV negative patients. In addition, although it is rare, there are cases where spontaneous withdrawal occurs without treatment. We describe a case of the PBL of oral mucosa type that occured in the mandibular gingival. The patient was a 69-year-old man who visited our hospital because of the growth of a gingival swelling in the right mandibular first molar buccal region. The swelling was identified as a spherical tumor with a smooth surface of about 10 mm in diameter. This was diagnosed clinically as a granulomatous epulis, and we performed resection biopsy to establish definite diagnosis. From the histopathological and immunohistological search of the biopsy specimen, the extract was diagnosed as PBL. The patient was HIV-negative; confirmed as a result of the blood test. Afterwards, the biopsy section followed a good healing process, and we are continuing regular follow-up observation, but we do not recognize recurrence.

1. Introduction

Plasmablastic lymphoma (PBL) is one of the highly aggressive and poor prognostic non-Hodgkin's lymphoma initially described as occurring in the oral cavity of human immunodeficiency virus (HIV)-positive individuals [1]. There is no definite standard treatment for PBL, and poor prognosis cases often die within one year after diagnosis [2]. PBL has been reported to occur in HIV-positive patients, however it is related to other immunodeficiency conditions, such as immunosuppression by using immunosuppressive drugs and immune function deterioration due to aging [3]. There seems to be no apparent difference in the prognosis of PBL due to the presence or absence of infection with HIV, however patients with HIV-negative PBL tend to be elderly, and some cases have recently been shown to follow a unique clinical course [4]. Epstein-Barr virus (EBV) infection has been prominently observed in PBL cases in elderly compared to PBL cases associated with other immunodeficiency states [3]. Although cases of spontaneous regression of low-grade lymphoma have often been reported, there are few cases where malignant lymphoma spontaneously disappears without treatment [5–7]. It has occasionally been reported that diffuse large B-cell lymphoma (DLBCL) spontaneously regressed after patients taking methotrexate discontinue immunosuppressive drugs [8]. We describe a case of rare PBL that spontaneously regressed after biopsy, despite no treatment being done.

2. Case report

A 69-year-old man was referred to our hospital owing to growth of a gingival swelling in the right mandibular first molar buccal region. He had suffered from recurrent gingival swelling of this region for a month before his visit. At the first visit, a physical examination revealed an exophytic gingival tumor in the right mandibular first molar buccal gingival region (Fig. 1A). This was recorded as a spherical tumor with a smooth surface of about 10 mm in diameter. On the dental X-ray image, bone loss due to the mesial root hemisection was observed, but there was no obvious abnormal finding (Fig. 1B). In addition, the patient had no significant medical history, including autoimmune disease, and had not taken any immunosuppressive drugs. We diagnosed clinically that

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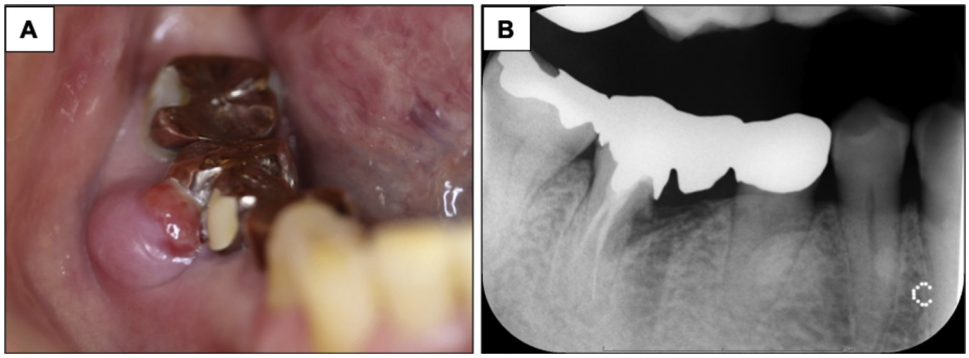

Fig. 1. A: Intraoral photo and dental x-ray image at first visit. The gingiva of the mandibular gingival molar region was swollen with hemisphere-shaped masses covered with smooth and reddish mucosa. B: On the dental X-ray image, there was no obvious abnormal finding.

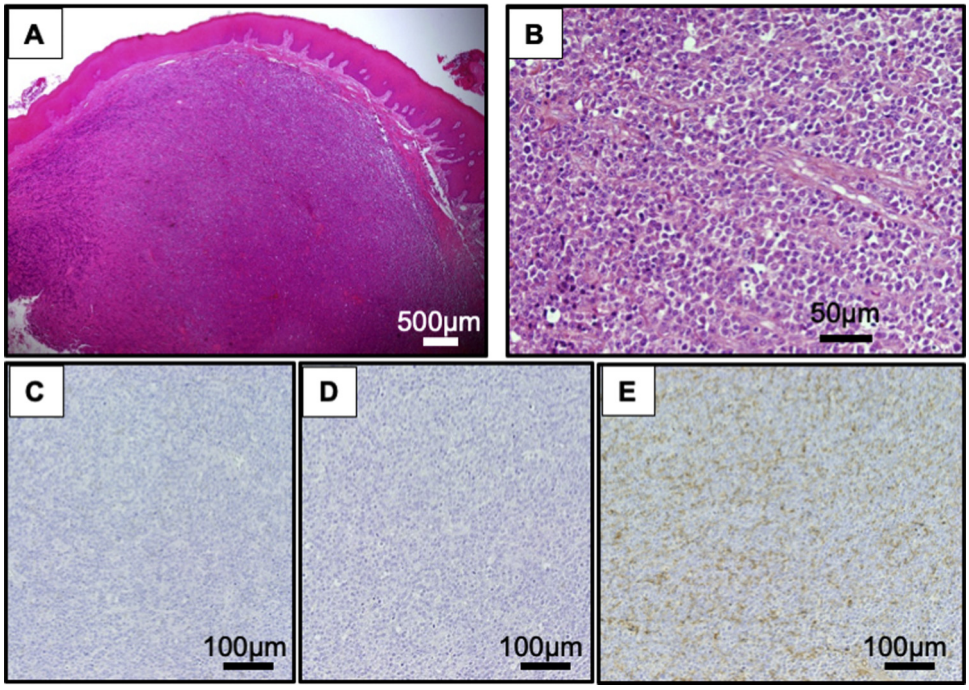

Fig. 2. Histologic and immunohistochemical features of biopsy specimens. A: HE(scale bar; 500 μm). B: HE(scale bar; 50 μm). C: CD3 (scale bar; 100 μm). D: CD20(scale bar; 100 μm). E: CD138(scale bar; 100 μm).

there was a granulomatous epulis, and we performed a resection biopsy to establish definite diagnosis.

Histological examination was carried out. A diffuse lymphocyte infiltration was observed under the epithelium by hematoxylin and eosin staining (Fig. 2A, B). Infiltrating lymphocytes were medium to large, with nuclei arranged in wheels (Fig. 2B). As a result of immunohistochemical (IHC) staining, it was negative for CD3 • CD20 and positive for CD138, so differentiation into plasma cells was recognized (Fig. 2C–E). Almost no positive cells were observed for Igκ-ISH and Igλ-ISH via in situ hybridization (Fig. 3A, B). Therefore, we could not determine the light chain restriction. As determined via in situ hybridization, neoplastic cells were partly EBV-encoded RNA (EBER)-positive and Ki-67 labeling index was about 30% (Fig. 3C, D). Based on the histopathological findings above, we first considered that it was likely lymphoma. As a histological type, we diagnosed as "plasmablastic lymphoma (PBL)" from tumor morphology, developmental site and marker.

Two weeks after resection biopsy, there was no tumor recurrence in the same area, and no problem in the healing process (Fig. 4). We referred the patient to the blood tumor internal medicine in our hospital for whole-body examination. In the blood test data following excision biopsy, the white blood cell count and platelet count were normal, and there was no abnormality in the ratio of each granulocyte in the white blood cell image (Table 1). There were also no abnormal values in C-reactive protein (CRP), lactate dehydrogenase (LDH), soluble interleukin 2 receptor (sIL-2R), which are items that may increase in lymphoma. Virus capsid antigen (VCA) that is expressed upon dissolution infection with EBV was negative for IgM antibody and positive for IgG antibody. And EBV nuclear antigen (EBNA) that is expressed upon latent infection with EBV was positive. From these results, it was found that EBV was not an acute phase although there was a prior infection.

Since then, we have been conducting strict follow-up regularly along with the blood tumor internal medicine, but thus far it has been 2 years with no sign of relapse.

3. Discussion

PBL is a rare malignant lymphoma within the oral cavity of HIV-positive patients as a spontaneous site. Delecluse et al., who first reported PBL in 1997, reported 16 PBLs occurring in the oral cavity, 15 of which were HIV-positive and only 1 was HIV-negative elderly [1]. However, there are reports that the number of PBL cases in HIV-

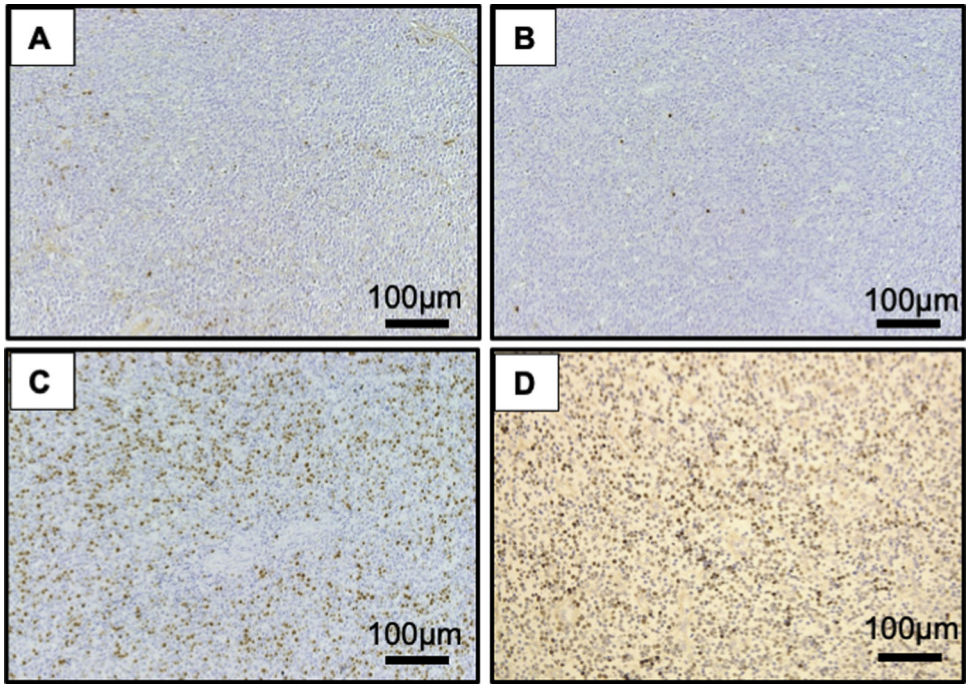

Fig. 3. Histologic and in situ hybridization features of biopsy specimens. A: Igκ-ISH (scale bar; 100 μm). B: Igλ-ISH (scale bar; 100 μm). C: Ki-67 (scale bar; 100 μm). D: EBER-ISH (scale bar; 100 μm).

Fig. 4. Intraoral photo taken 2 weeks after resection biopsy. There was no tumor recurrence in the same area, and the healing process was well developed.

Table 1
Blood test result.

WBC	6,050/μl	CRP	0.28 mg/dl
PLT	18.4×10^4 /μl	LDH	162 U/l
Neutr	53.1%	sIL-2R	401U/ml
Lympho	31.2%	EBVVCA-M	< 10
Mono	11.1%	EBVVCA-G	320
Eosino	4.1%	EBNA	20
Baso	0.4%	HIV	negative

negative patients have been increasing [2,3,9,10]. HIV-positive PBL is thought to be associated with EBV and human herpesvirus 8 (HHV-8) infection due to immunodeficiency [11,12]. Meanwhile, it is reported that HIV-negative PBL has less relation to EBV and has a high incidence in elderly people [2].

Unlike other HIV-associated B cell lymphomas, PBL indicates unique immunological features that scarcely expresses CD20, which is a common lymphoid antigen. In addition, CD138 is strongly positive for PBL and is used as one diagnostic marker for PBL [1,13]. However, the strange aspect of our case is not the pathological findings but the clinical course that spontaneously regressed despite lack of treatment. In our case, the margin of the excision product was tumor-positive. Nevertheless, there is no recurrence and normal healing without any treatment following biopsy. The lymphoma classification revised by WHO in 2016 proposes "EBV positive mucocutaneous ulcer (EBV-MCU)" as a recognition of a new lymphoproliferative disorder (LPD) [14]. This disease is regarded as an EBV-related LPD associated with immunodeficiency by aging regardless of the presence or absence of HIV infection, and cases that have spontaneous regressed have been reported in the past [15,16].

The concept of EBV-MCU is first reported as a clinicopathologic entity with Hodgkin-like features and a self-limited, indolent course, generally responding well to conservative management [15]. EBV-MCU is a recently recognized B cell lymphoproliferative disorder caused by latent EBV infection and causing ulcers in the oral mucosa, skin and others. Indeed in our case, the patient was positive for EBNA and suspicion of latent infection with EBV (Table 1). It has been reported in the past that the onset of EBV-MCU is associated with immunosuppression by the use of immunosuppressants such as methotrexate [17]. EBV-MCU in such patients successfully responds to modest measures aimed at correcting the underlying immunosuppression. In the case we experienced, the patient had no history of using immunosuppressants, however, elder aging may attribute immunosuppressive factors. The positive EBER was suggested to be related to EBV-related lymphoproliferative diseases. Although there are no recurrence findings at the present time, in general, since plasmablastic lymphoma is a poor prognosis case, we believe that strict follow-up is also necessary in the

future. In recent years, EBV-MCU has been proposed as a new B cell lymphoproliferative disease. Although this disease is histologically difficult to distinguish from malignant lymphoma in the oral cavity, it follows a good healing process with no treatment. It is the same process in our case and we cannot to deny the possibility of an EBV-MCU. We think that confirmation of careful clinical course in future and correspondence are necessary.

Ethical approval

The patient has provided permission to publish these features of this case, and the identity of the patient has been protected.

Conflict of interest

The authors report no conflicts of interest.

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