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CASE REPORT

Oral Hairy Leukoplakia Which Occurred as a Presenting Sign of Acute Myeloid Leukemia in a Child

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Oral hairy leukoplakia (OHL) is caused by the reactivation of a previous Epstein-Barr virus (EBV) infection in the epithelium of the tongue. Most lesions are characterized by corrugated whitish patches on the lateral border of the tongue. It is frequently associated with AIDS, but cases in patients with other immunosuppressed states have also been reported. In leukemia patients, OHL is rarely encountered, and appears only after chemotherapy. We report a case of OHL which occurred as a presenting sign of acute myeloid leukemia (AML) in a previously healthy 15-year-old child. A 15-year-old boy presented with a whitish patch on the left lateral border of the tongue. The biopsy specimen revealed papillomatosis, hyperkeratosis, acanthosis and ballooning degeneration in the stratum spinosum. The patient was EBV seropositive, and PCR analysis of EBV DNA in the lesional tissue was positive. After the diagnosis of OHL in dermatologic department, the patient was referred to pediatrics due to the abnormal peripheral blood smear, and was diagnosed with AML. **(Ann Dermatol 22(1) 73～76, 2010)**

-Keywords-
Acute myeloid leukemia, Ebstein-Barr virus, Oral hairy leukoplakia

INTRODUCTION

Oral hairy leukoplakia (OHL) was first described by Greenspan et al.[1] in 1984. It is characterized by whitish patches with a corrugated or hairy surface most commonly on the lateral borders of the tongue. Its distinctive feature is produced by the proliferation of mucosal epithelium, which is caused by the reactivation of a previous Epstein-Barr virus (EBV) infection[2]. As the histopathology features are not pathognomonic, the demonstration of EBV in the lesional tissue is essential for a definite diagnosis[3]. OHL is found most commonly in patients infected with HIV and is regarded as an early sign and prognostic factor of a HIV infection[4]. It can also be associated with other immunosuppressed conditions, such as an organ or bone marrow transplantation, chemotherapy, hematological malignancies and the long term use of systemic steroid[5,6]. Occasionally, cutaneous manifestations, such as leukemia cutis, pyoderma gangrenosum, erythema nodosum and chronic urticaria may be the first symptom or signs of leukemia. However, there are no reports of OHL being a presenting sign of leukemia[7-12].

We report a case of OHL that occurred as a presenting sign of acute myeloid leukemia (AML) in a previously healthy 15-year-old child.

CASE REPORT

A 15-year-old boy presented with a whitish patch on the left lateral border of his tongue that had lasted for several months. The patient was a player in his middle school soccer team. He appeared healthy and denied any prior medical problems. He had no subjective symptoms but the lesion had recently increased in size. A physical examination revealed corrugated whitish patches on the left border of the tongue, which were so adhesive that they could not be scraped by a tongue depressor (Fig. 1). The differential diagnosis of the lesion included oral candidiasis, oral lichen planus and oral hairy leukoplakia.

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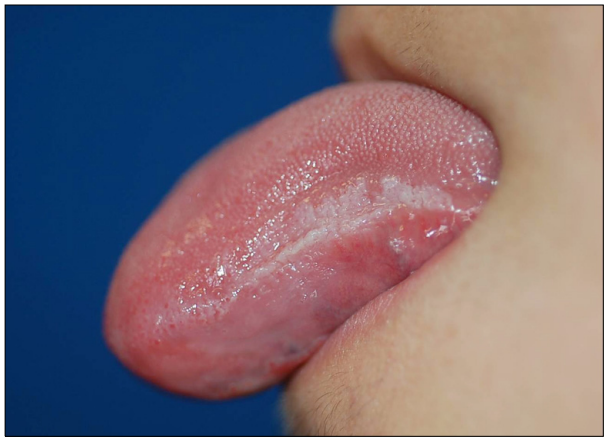

Fig. 1. Tightly adhered whitish patches are located unilaterally in the left border of the tongue showing slightly hairy projections.

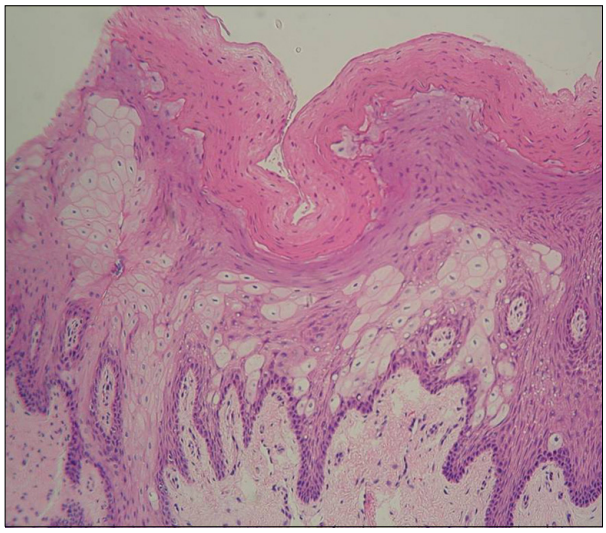

Fig. 2. Hyperkeratosis, parakeratosis, acanthosis, ballooning degeneration in the stratum spinosum and vacuolated cells with small, round, deeply basophilic nuclei surrounded by a narrow clear halo are shown (H&E, ×100).

The laboratory tests including routine blood tests, peripheral blood smear tests, HIV and EBV antibody, were carried out. There was no fungal element on the KOH mount. The mucosal biopsy specimen revealed papillomatosis, hyperkeratosis, parakeratosis, acanthosis and ballooning degeneration in the upper stratum spinosum (Fig. 2). The high-power view revealed vacuolated cells with small, round, deeply basophilic nuclei surrounded by a narrow clear halo, which were compatible with oral hairy leukoplakia (Fig. 3). The patient was HIV seronegative on EIA but EBV seropositive (EBV anti-VCA IgG). There was a very low platelet count with $25\times10^3/\mu l$ (normal range, $140\times10^3/\mu l$ to $400\times10^3/\mu l$). While white blood cell count was adequate in number, blasts

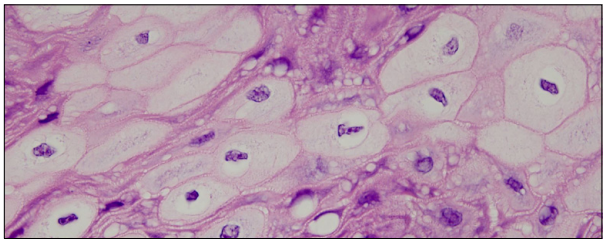

Fig. 3. Cytoplasmic halo surrounding the nucleus and peripheral margination of chromatin in the nucleus are shown (H&E, ×1,000).

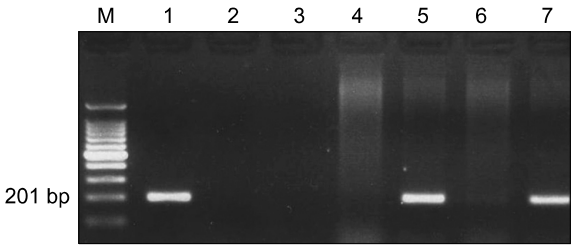

Fig. 4. Positive result shows the EBV band 201 bp region of the EBV *Bam*HI W repeat. M: marker, Lane 1: EBV positive control, Lane 2: patient negative control, Lane 3: negative control (D.W), Lane 4: patient sample 1 (100 ng/dl), Lane 5: patient sample 1 (50 ng/dl), Lane 6: patient sample 2 (100 ng/dl), Lane 7: patient sample 2 (50 ng/dl).

(10%) were found. The lesional tissue was examined to demonstrate an EBV infection using immunohistochemistry and in situ hybridization, but these showed doubtful results. A polymerase chain reaction (PCR) was performed to detect EBV DNA using a primer to the EBV W fragment. Positive control was the Hank-1 cell line, which is a case of B-cell lymphoma. 50 ng/dl of DNA of the lesional tissue showed a distinct band that was comparable to the positive control (Fig. 4). The lesion was diagnosed definitely as oral hairy leukoplakia.

Two days after the mucosal biopsy, the patient complained of a 2 cm-sized hematoma on the biopsy site, which was probably due to severe thrombocytopenia. The patient was referred to the pediatric department, where he was diagnosed with acute myeloid leukemia (AML M2) after a bone marrow biopsy. At that time, a poor outcome was expected because chromosomal analysis showed 8-trisomy. Induction chemotherapy was started immediately, but it failed and was followed by neutropenic fever. After a 3 month struggle against the leukemia, he died of septic shock.

DISCUSSION

The EBV is transmitted mainly through the saliva[13]. It is

not only lymphocytotrophic but also epitheliotrophic, and can cause pharyngeal mucosal lesions including OHL and nasopharyngeal carcinoma[3].

OHL usually affects both lateral borders of the tongue[4]. Unilateral involvement, as in our case, has been reported albeit rarely[14-16]. The histology findings of OHL include filiform hyperkeratosis, parakeratosis and acanthosis with a vacuolar alteration of epithelial cells[4]. Among them, the vacuolar alteration of prickle cells is the most characteristic feature[4]. The condition is either diffuse or focal, and each vacuolated cell has small, round, deeply basophilic nuclei surrounded by a narrow clear halo and by pale-staining cytoplasm[4]. OHL should be differentiated from white sponge nevus, frictional keratosis, lichen planus and idiopathic leukoplakia[17]. Among them, the clinical and histopathology findings of idiopathic leukoplakia are similar to those of OHL[17]. To confirm OHL, demonstration of the EBV in the lesional tissue is essential because the histopathology features on conventional optical microscopy are not pathognomonic. The EBV can be detected by immunohistochemistry, in situ hybridization, or a PCR. In situ hybridization is the most accurate, and is considered the gold standard technique in diagnosis[3]. In our case, the EBV was detected by PCR, and 'in situ hybridization' showed an inconclusive result. The EBV *Bam*HI W repeat was used as the primer and the Hank-1 cell line (a B-cell lymphoma line) was used as the positive control[18]. As EBV DNA strains are present in the saliva of EBV-seropositive persons, there is a possible risk of contaminating the scraped tissue with saliva (false positive in PCR analysis). However, in case of using a biopsy specimen, as in the present case, PCR analysis is as specific and sensitive for the detection of EBV as in situ hybridization[3]. Successive treatment modalities using a range of topical agents, such as tretinoin solution, podophylline resin, gentian violet or antiviral agent, have been reported[4,16,19-21].

Since the first report in 1984, OHL has been observed mainly in AIDS patients[4,22-24]. However, OHL has been reported in other immunosuppressed patients, including those with ulcerative colitis, pemphigus vulgaris, bullous pemphigoid, Behcet's syndrome, multiple myeloma, and leukemia[5,6,16,17,25]. Although rare cases of OHL in healthy people have been reported, OHL is believed to occur in immunosuppression as a rule[14,15].

OHL is not regarded as a prognostic factor of diseases other than AIDS. However, previous cases of OHL with hematologic malignancies have been reported in patients after chemotherapy, whose state of immunosuppression would be more severe than a malignancy per se[5,16,25]. Therefore, it was assumed that the OHL might also be associated with an advanced state or poor prognosis in leukemia. In this case, trisomy 8 was observed by chromosomal analysis and the course of the disease was very rapid and poor. In AML, cytogenetics at diagnosis can have important prognostic significance, and a number of chromosomal abnormalities have been identified[26]. Among these abnormalities, trisomy 8 is the most common numerical aberration in AML, and its presence indicates a poor progonosis[26]. The early recognition of OHL is very important considering the high possibility of an underlying immunodeficiency and the potential indicator of a poor prognosis.

Various skin diseases can be associated with leukemia, and some can occur as the presenting sign of leukemia. These include leukemia cutis, pyoderma gangrenosum, erythema nodosum, and chronic urticaria[7-12]. However, OHL has never been reported as the presenting sign of leukemia. To our knowledge, this is the first report of OHL as a presenting sign of acute myeloid leukemia.

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