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Prevalence of Epstein-Barr Virus in Oral Lichen Planus in Korea

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Dear Editor:

Lichen planus (LP) is a unique and chronic inflammatory disorder that affects the skin, mucous membranes, nails, and hair. Oral involvement in LP (OLP) occurs in 2% to 3% of the population approximately[1]. The etiopathogenesis of OLP is only partially understood, but it is thought to be a multifactorial process involving genetic, psychological and infectious factors[2]. Viral infections have recently been linked with OLP. Until now, the correlation between Epstein-Barr Virus (EBV) and OLP has been the discussed by many studies, in which several techniques for EBV detection have been used; immunohistochemistry[3], PCR and nested PCR (nPCR)[4,5], *in situ* hybridization[6]. LP of the lips is an uncommon condition that can present with leukoplakic areas that appear somewhat similar to actinic cheilitis (AC) which is defined as actinic keratosis of lips. White reticulated clinical features were similar between AC and OLP. However, there has been no report that AC is associated with EBV. Therefore we studied the prevalence of EBV in histologically diagnosed OLP cases and AC cases as a control.

The study was conducted on formalin fixed paraffin embedded tissue specimens of clinicopathologically confirmed 30 OLP cases and 30 AC cases from July 2007 to November 2017 at Ajou University Hospital. This study was approved by the Institutional Review Board of the Ajou University (AJIRB-MED-KSP-14-052). Written informed consent was obtained. Ambiguous cases were excluded. We also retrospectively evaluated the medical records including age, gender, localization and the histopathological type. The existence of EBV was investigated by BenchMark® Autostainer, an automated staining instrument, and the INFORM EBER Probe (Ventana Medical Systems, Tucson, AZ, USA). It was carried out in accordance

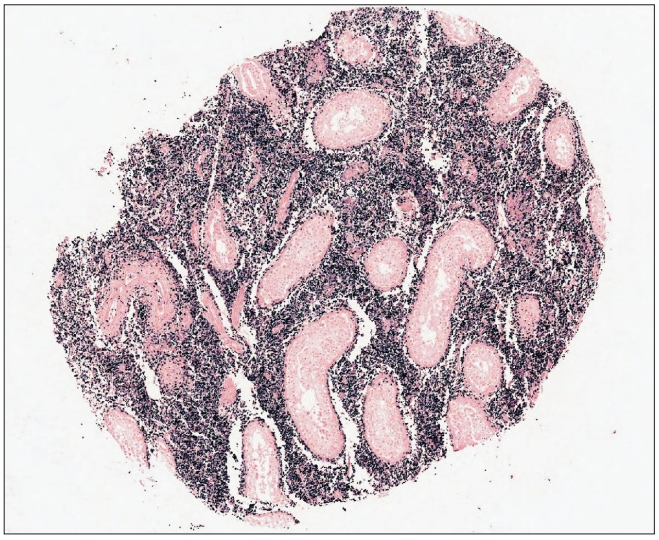

Fig. 1. The control tissue from the testis of the NK/T cell lymphoma patient whose sample showing strong bluish dots *in situ* hybridization (×10).

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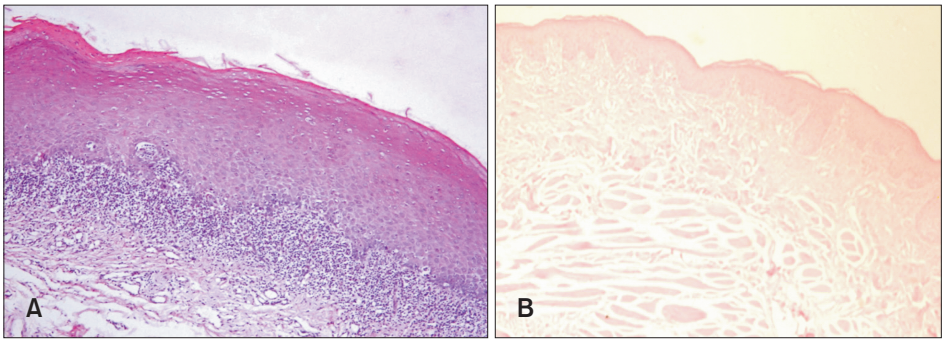

Fig. 2. (A) Oral lichen planus (H&E, ×40). (B) Epstein-Barr virus in situ hybridization of oral lichen planus case (*in situ* hybridization, ×40).

with the manufacturer's instructions. The tissue area injected with paraffin was de-diluted, enzyme digested by ISH-PROTEASE-1, and this section was applied with the INFORM EBER probe, a hybridization solution, to warm up and incubate. Hybridization detection was carried out, counterstained, and covered with nuclear Fast Red. The proton staining was identified as a blue nuclear dot. To analyze results of *in situ* hybridization samples, we set strongly expressed EBV-positive tissue from the testis of the NK/T cell lymphoma patient. This tissue sample was used as a positive control (Fig. 1). A total of 30 cases of OLP and 30 cases of AC were included in the study. The average age of patients was 64 years and 54 years, and the total sex ratio (male-to-female) was 9:21 and 21:9 respectively. In OLP patients, 20 patients had lesions in buccal mucosa and 10 in lower lip. On the other hand, all AC patients had lesions in lower lip.

As a result, in our *in situ* hybridization analysis of EBV, all cases revealed negative in EBV (Fig. 2). This was an unexpected result considering that some of the previous studies proved OLP is related to EBV so far. However, as our positive control showed numerous bluish dots which means EBV positive by our *in situ* hybridization method, we could predict there are no flaws in our methods itself. In fact, so far there has been no consistent results on whether EBV is significantly detected in lesions of OLP. Yildirim et al[3] analyzed 65 cases of OLP by immunohistochemical staining and found EBV was statistically significantly found in patient group than the control. Also, nPCR conducted by Sand et al.[4] revealed presence of EBV in 26.1% of the patients compared to 7.3% of the control. However nPCR by Vieira Rda et al.[5] and recent study by Danielsson et al.[6] using *in situ* hybridization found no relationship between EBV and OLP.

EBV infection varies by race and region, and the causes of LP also vary by genetic, psychological, and infectious factors. Our results suggest that the LP lesion of Korean patients has few possibility with pathologically related to EBV. Therefore, the hypothesis that EBV can't be related to the etiopathogenesis of OLP may lead to changes at least in Korea.

In this study, only OLP involving only lips and buccal mucosa was used, and all patients involved in buccal mucosa showed reticular form. Therefore, further study will be needed to enroll more patients and to use those with various clinical and location settings.

CONFLICTS OF INTEREST

The authors have nothing to disclose.

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A Case of Smooth Muscle Actin-Positive Cutaneous Spindle Cell Squamous Cell Carcinoma

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Dear Editor:

An 83-year-old female presented with a solitary nodule on the right preauricular region for 4 months. Physical examination revealed a 1.4×1.2 cm^2 sized skin-colored deeply palpable nodule with central ulceration (Fig. 1A). Dermoscopy showed central ulceration with scales, crusts, and blood spots surrounded by arborizing vessels and adjacent whitish veil appearance (Fig. 1B). A punch biopsy was performed and histopathological examination revealed atypical proliferation of keratinocytes with solar elastosis and the pan-dermal proliferation of atypical spindle cells (Fig. 1C~F). In immunohistochemical (IHC) staining to rule out mesenchymal tumors, tumor cells were positive for vimentin and smooth muscle actin (SMA) (Fig. 1G, H). However, CD34, CD68, and S-100 were negative. In pan-cytokeratin stain to rule out epidermal tumors, tumor cells were diffusely positive (Fig. 1I). Given these findings, the diagnosis was cutaneous spindle cell squamous cell carcinoma (SpSCC). Subsequent ultrasonography to check regional lymph node metastasis of head and neck area showed no abnormal findings, however, the tumor grew rapidly to a preoperative size of 2.7×2.0 cm^2 (Fig. 1J). Wide excision, with deep margin of the superficial muscular aponeurotic system, was performed followed by reconstruction with a full-thickness skin graft. Post-surgical histopathological examination revealed atypical spindle cell proliferation with epidermal connection, poorly differentiated tumor cells with nuclear pleomorphism and high mitotic activity (Fig. 1K, L). Deep margin involvement of the tumor cells was also noted (Fig. 1M); however, the patient refused adjuvant radiotherapy. Five months later, local recurrence was identified and further aggressive excision was considered.

SpSCC is a rare variant of SCC; it shows spindle cell differentiation and can invade deeply into the subcutis[1]. They com-

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