

# Invasive Squamous Cell Carcinoma of the Oral Mucosa Associated with HPV Type 53

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A 77-year old man presented with a fungating mass on the oral mucosa and lip, which had an irregular margin. An incisional biopsy of the mass revealed an invasive squamous cell carcinoma. PCR analysis detected HPV DNA in the biopsy specimen. The HPV type was determined as HPV-53 by direct cycle sequencing. This is the first report of HPV-53 in an oral malignant tumor. (*Ann Dermatol* (Seoul) 19(1) 19~21, 2007)

**Key Words:** HPV-associated cancer, HPV type 53, Invasive squamous cell carcinoma, Oral cancer, Oral squamous cell carcinoma

## CASE REPORT

A 77-year old Korean man presented with a fungating mass on the right aspect of his lower lip, which had been growing for 5 months. He was a non-smoker, with no history of alcohol consumption, betel quid use or excessive sun exposure. His past medical history was significant for prostate cancer and transurethral resection without additional adjuvant chemotherapy six months before. At that time, he was also found to have latent syphilis and treated with penicillin. The skin lesion was an irregular, round (1.5 cm by 1.5 cm), whitish fungating mass extending from the right angle of the mouth to the right one-sixth of the lower lip. It was relatively well-demarcated and had a verrucous surface. The mass was excised and diagnosed histopathologically as a verrucous carcinoma. Surgical margins were clear and CT of the head and neck showed no evidence of metastasis. After ten months, the patient came back with recurrence of the mass detected by

the patient 4 months prior. This time, it was 1.5 cm by 2.0 cm with a more irregular shape than previously. The margin was infiltrating the lip and buccal mucosa resulting in indistinct demarcation (Fig. 1). An incisional biopsy revealed an invasive squamous cell carcinoma (Fig. 2). He was transferred to the department of plastic surgery for wide excision. HPV DNA was detected in the biopsy specimen by PCR using MY09/MY11 primers (MY09: 5'-CGT CCM ARR GGA WAC TGA TC-3', MY 11: 5'-GCM CAG GGW CAT AAY AAT GG-3'). We determined the HPV type as HPV-53 by direct cycle sequencing (Fig. 3).

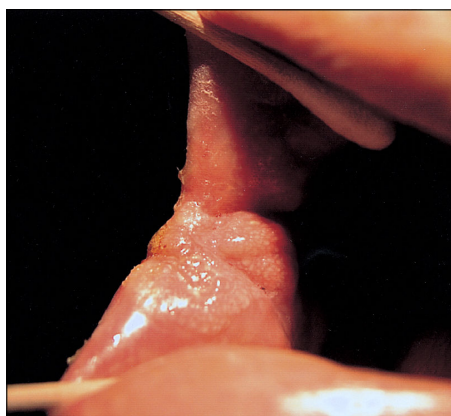
## DISCUSSION

Oral squamous cell carcinoma (OSCC) is a common cancer whose significant risk factors are smoking, alcohol, betel quid use, sun exposure and immunosuppression. Recently many researchers have suggested that HPV infection is a causative factor of OSCC<sup>1</sup>. While it is well known that HPV infection is a significant risk factor for cervical cancer, its relationship with oral malignant tumors has not been fully characterized yet. In 1985, de Villier<sup>2</sup> first detected HPV DNA in oral carcinoma, and many studies have confirmed this finding. A review of articles from 1982 to 1997 showed that the detection

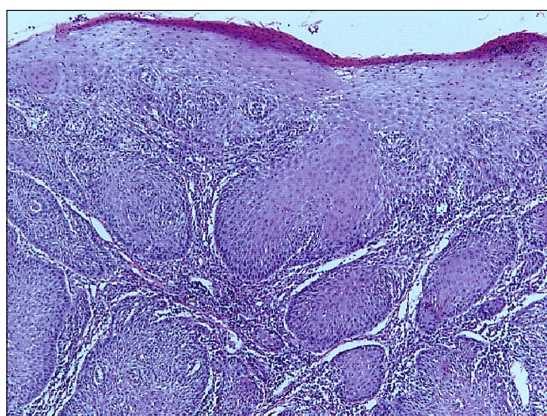
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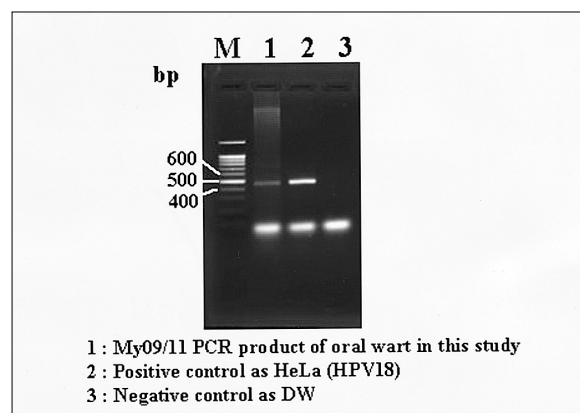
**Fig. 1.** Verrucous-surfaced, white, fungating mass with an irregular margin on the oral mucosa.



**Fig. 2.** Invasive squamous cell carcinoma infiltrating into the deep dermis (H & E,  $\times 100$ ).

rate of HPV in OSCC was up to 46.5%<sup>3</sup>. The most frequently detected types were HPV 16 and 18, suggesting an important role for these viruses in malignant transformation<sup>3</sup>. Other various types of HPV were detected in oral cancers, although their detection rates were much lower than those of HPV-16 and 18<sup>3</sup>.

In this study we demonstrated HPV-53 infection in an invasive, oral squamous cell carcinoma. To our knowledge, this is the first report of detection of HPV-53 in a malignant lesion of the oral mucosa. This virus had originally been detected in benign lesions of female genitalia and leukoplakia. Until now, only six cases have been reported in the literature where HPV-53 was isolated from cancer lesions<sup>4-6</sup>. The specimens were all from cervical squamous cell carcinoma, among which only two were found to have a single infection of that virus.



**Fig. 3.** Detection of HPV DNA in the biopsy specimen by PCR. The band of 450 bp was detected and identified as HPV 53 by direct cycle sequencing.

The other four cases harbored another high-risk HPV type, along with HPV-53. The rarity of reports on HPV-53 in malignant tumors rendered it difficult to define the oncogenic status of the virus. While some researchers classify HPV-53 as a high-risk type<sup>4,7,8</sup>, others regard it as not associated with malignant transformation<sup>5,9,10</sup>.

In the present study, HPV-53 was the only HPV type isolated from the biopsy specimen. There was no evidence of infection by other HPV types, especially, high-risk types such as HPV-16, 18, 31, 33 or 35<sup>3</sup>. The singular presence of HPV-53 in an invasive OSCC in a patient with no other risk factors, supports the recent suggestion that HPV-53 is a probable high-risk type associated with malignant progression of epithelial lesions. In particular, it was unique that HPV-53 had been isolated from a malignant tumor of the oral cavity such as OSCC, other than from cervical cancer. We tried to determine the HPV status of the previous verrucous carcinoma, but have failed to detect any HPV in that lesion. Further studies on more HPV-53 positive cancers are required to define the oncogenicity of HPV-53.

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