Actas Dermosifiliogr. 2007;98:621-3

CASE REPORT

Focal Epithelial Hyperplasia

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Abstract. Focal epithelial hyperplasia is a rare disease of the oral mucosa caused by the human papilloma virus (HPV). It appears as a benign epithelial growth, usually in the mucosa of the lower lip. It is mainly associated with HPV serotypes 13 and 32 and there is a clear racial predilection for the disease in Native Americans and Eskimos. We describe the case of a 17-year-old girl from Ecuador with multiple papular lesions in both lips that were clinically and histologically consistent with focal epithelial hyperplasia. Analysis by polymerase chain reaction detected HPV serotype 13.

Key words: human papilloma virus, epithelial hyperplasia, Heck disease.

HIPERPLASIA EPITELIAL FOCAL

Resumen. La hiperplasia epitelial focal es una enfermedad poco frecuente de la mucosa oral producida por el virus del papiloma humano. Aparece una proliferación epitelial benigna de predominio en la mucosa del labio inferior. Se asocia fundamentalmente a los serotipos 13 y 32 y existe un claro predominio racial, en indios americanos y esquimales. Presentamos el caso de una chica de 17 años ecuatoriana, con múltiples lesiones papulosas en labio inferior y superior compatibles clínica e histológicamente con hiperplasia epitelial focal. En el estudio por reacción en cadena de la polimerasa se detectó el virus del papiloma humano serotipo 13.

Palabra clave: virus del papiloma humano, hiperplasia epitelial, enfermedad de Heck.

Introduction

Human papilloma virus (HPV) can cause various conditions in the oral mucosa that are characterized by epithelial growths, most of them benign.[1] The most common include papillomas, condylomas, and viral warts, and more rarely focal epithelial hyperplasia (FEH) or Heck disease. It is sometimes implicated in premalignant or malignant diseases, such as leukoplasia or epidermoid carcinoma. Benign oral lesions have been associated with HPV 2, 4, 6, 11, 13, and 32, and malignant lesions with HPV 16 and 18.[1]

FEH is a rare disease of the oral mucosa, of benign course, that normally appears in childhood and is clearly associated with HPV serotypes 13 and 32.

We describe a 17-year-old Ecuadorian girl with FEH who was seen in our department.

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Manuscript accepted for publication November 8, 2006

Case Description

A 17-year-old girl from Ecuador with no relevant personal or family history consulted for asymptomatic lesions on the upper and lower lips, present since age 11, that had spread slowly and progressively. The physical examination revealed numerous, well-defined papules between 3 and 7 mm, of the same color as the adjacent mucosa or pinkish-white, with a smooth surface, and located only on the upper and lower lips (Figures 1 and 2).

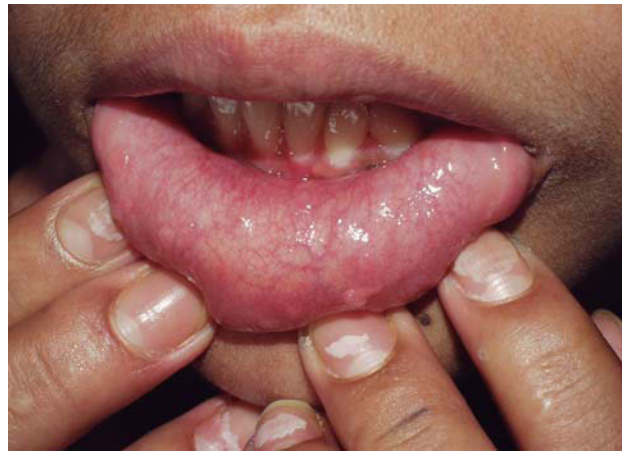

Figure 1. Flat, smooth, mucosa-colored papules.

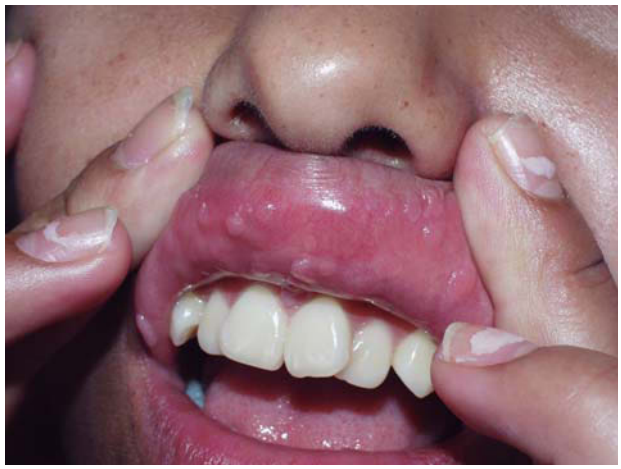

Figure 2. Detailed view of the papules.

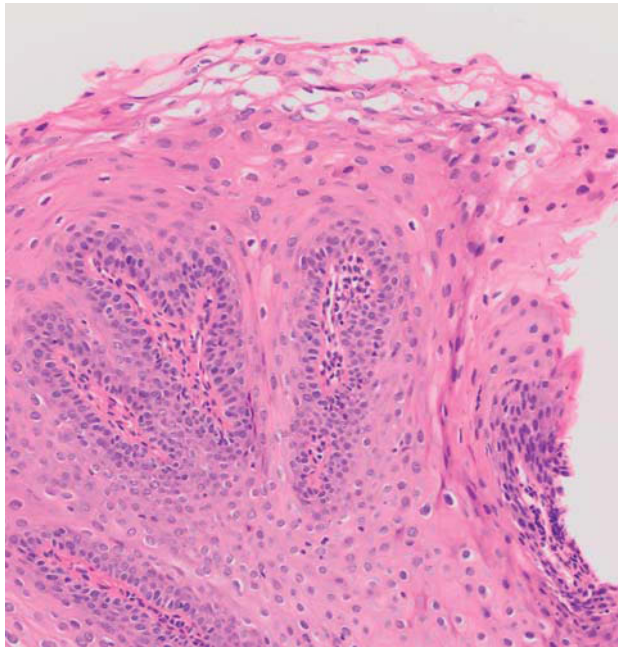

Figura 3. Epidermal hyperplasia, parakeratosis, acanthosis. (Hematoxylin-eosin, ×100.)

The patient had no lesions on the skin or other mucous membranes and denied any high-risk sexual contact or family history of these lesions.

The histological study showed epidermal hyperplasia, acanthosis, mild parakeratosis, and papillary projections with areas of horizontal anastomosis (Figure 3). The superficial layers of the epidermis contained koilocytes and apoptotic or dyskeratotic cells with an apparently mitotic appearance (Figure 4).

Analysis by polymerase chain reaction (PCR) detected HPV 13.

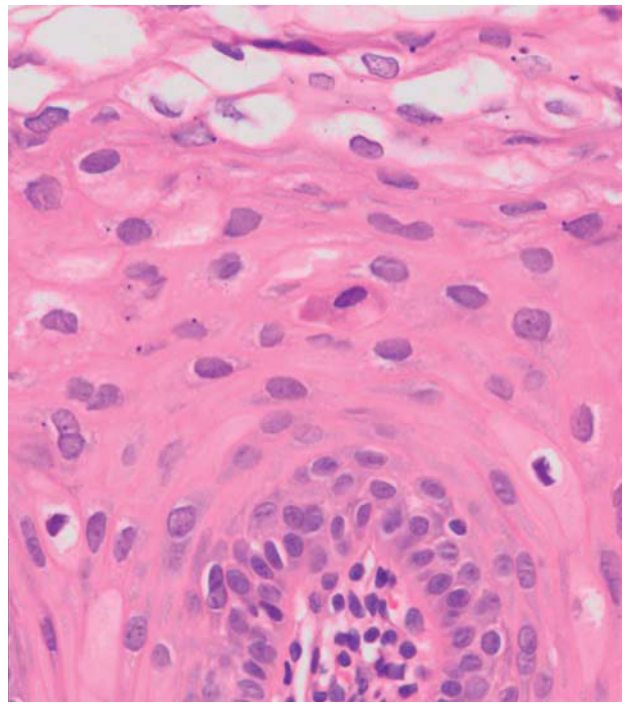

Figure 4. Koilocytes and cells with a mitotic appearance in the epidermis. (Hematoxylin-eosin, ×400.)

Imiquimod therapy 3 times a week was initiated for 3 weeks, without response. The patient did not come for further follow-up.

Discussion

FEH is a benign proliferative disease of the oral mucosa that is rare among white individuals, but with a highly variable prevalence according to geographic area, being as high as 35% in certain ethnic groups.[2] There is a clear predominance among Native Americans, Eskimos, and in some African communities.[3,4]

Onset usually occurs in childhood and adolescence, mainly between 3 and 18 years of age, and the condition is more common among women.[1] It is caused by HPV and 90% of cases are associated with serotypes 13 and 32, more often serotype 13.[5]

This entity has distinctive clinical and histological characteristics. Clinically, it is characterized by multiple flesh-colored papules of 3 to 10 mm that tend toward confluence and produce a cobblestone appearance in the mucosa. The most common site is the lower lip,[6,7] and to a lesser extent, the upper lip, tongue, and buccal mucosa. Involvement of the palate, floor of the mouth, and oropharynx is rare.[6,8]

The histological characteristics include epithelial hyperplasia, elongation and anastomosis of the interpapillary

ridges, parakeratosis, focal acanthosis, focal koilocytosis, and the presence of structures resembling mitotic figures in superficial keratinocytes (cells that show nuclear degenerative changes and simulate mitosis).

Although the pathogenesis is unknown, host factors such as the immune system, malnutrition, and genetic factors, are key aspects of the etiology of this entity.[3] Some adult cases associated with human immunodeficiency virus have been reported.[9,10] A clear family history and association with certain HLAs has been observed, suggesting that individuals can be genetically predisposed to the disease.[3,7] A Mexican study found a significant association with HLA DR4.[4] This allele is relatively common in indigenous populations from Mexico, Guatemala, and Colombia. There appears to be a genetic susceptibility that leads to a specific immunological abnormality in the response to certain HPV types.

The differential diagnosis should consider multiple diseases of the oral cavity, mainly condyloma, viral warts, mucosal neuroma, white sponge nevus, papilloma due to a bite, florid oral papillomatosis, and diffuse epithelial hyperplasia in tobacco chewers.[6,11]

Knowing the serotype may differentiate the condition from other HPV infections of the oral mucosa, since FEH is the only one with specificity between serotypes and pathology, being associated with HPV 13 and 32. Certain diseases are more often associated with certain serotypes,[1] for example, papilloma with HPV 6, 11, 13, 16, and 32 (most often 6 and 11), verruca vulgaris with HPV 2 and 4, and condyloma with HPV 2, 6, 11, 16, and 32 (most often 6 and 11).

The course of FEH is benign, with resolution often occurring spontaneously within months or a few years, but sometimes taking longer.[7,8] Treatment is not therefore necessary and none have been shown to be truly effective, although good response has been reported with destructive methods such as CO_2 laser,[12,13] podophyllum resin, and interferon.[14]

We believe that our patient had FEH, based on her ethnic origin, age at onset, absence of sexual contact, clinical and histological symptoms consistent with the condition, and serotype 13 detected in the PCR study. Based on the data, the patient was diagnosed with FEH.

Conclusion

FEH is an uncommon, relatively unknown condition in Spain, but should be included in the differential diagnosis for oral lesions, particularly those caused by HPV. Because of the increase in immigration from Central and South America, it is now more likely for physicians to encounter this condition in Spain. The course is benign and associated with serotypes of HPV with little or no carcinogenic risk; therefore, aggressive therapy should not be undertaken. The differential diagnosis should include condylomas, particularly in young patients, in order to avoid inaccurate sexual or abuse-related implications.[2,11]

Conflicts of Interest
The authors declare no conflicts of interest.

References

1. Garlick JA, Taichman LB. Human papillomavirus infection of the oral mucosa. Am J Dermatopathol. 1991;13:386-95.
2. Segura R, Toro M, Ceballos A, Aparicio JL, Fuentes H. Focal epithelial hyperplasia. A rare disease in our area. Med Oral Patol Oral Cir Bucal. 2005;10:128-31.
3. Nartey NO, Newman M.A. Focal epithelial hyperplasia: report of six cases from Ghana, West Africa. J Clin Pediatr Dent. 2002;27:63-6.
4. García-Corona C, Vega-Memije E, Mosqueda-Taylor A, Yamamoto-Furusho J, Rodríguez-Carreón A, Ruiz-Morales J, et al. Association of HLA-DR4 with human papillomavirus infection in patients with focal epithelial hyperplasia. Arch Dermatol. 2004;140:1227-31.
5. Delgado Y, Torrelo A, Colmenero I, Zambrano A. Hiperplasia epitelial focal. Actas Dermatosifiliogr. 2005;96:697-9.
6. Michael EJ, Husain S, Zalar G, Nuovo G. Focal epithelial hyperplasia in an Ecuadorian girl. Cutis. 1999;64:395-6.
7. González LV, Gaviria AM. Clinical, histopathological and virological findings in patients with focal epithelial hyperplasia from Colombia. Int J Dermatol. 2005;44:274-9.
8. Jayasooriya PR, Abeyratne S, Ranasinghe AW, Tilakaratne WM. Focal epithelial hyperplasia (Heck's disease): report of two cases with PCR detection of human papillomavirus DNA. Oral Dis. 2004;10:240-3.
9. Moerman M, Danielides VG, Nousia C, Van Wanz F. Recurrent focal epithelial hyperplasia due to HPV13 in an HIV-positive patient. Dermatology. 2001;203:339-41.
10. Viraben R, Aquilina C, Brousset P, Bazex J. Focal epithelial hyperplasia (Heck's disease) associated with AIDS. Dermatology. 1996;193:261-2.
11. Guill CK, Hwang LY, Iyengar V, Hsu S. Asymptomatic labial papules in a teenager. Arch Dermatol. 2002;138: 1509-14.
12. Luomanen M. Oral focal epithelial hyperplasia removed with CO_2 laser. Int J Oral Maxillofac Surg. 1990;19:205-7.
13. Bassioukas K, Danielides V, Georgiou I, Photos E, Zagorianakou P, Skevas A. Oral focal epithelial hyperplasia. Eur J Dermatol. 2000;10:395-7.
14. Akyol A, Anadolu R, Anadolu Y, Ekmekci P, Gurgey E, Akay N. Multifocal papillomavirus epithelial hyperplasia: successful treatment with CO_2 laser therapy combined with interferon alpha-2b. Int J Dermatol. 2003;42:733-5.