Oral Diseases (2004) 10, 240–243

http://www.blackwellmunksgaard.com

CASE REPORT

Focal epithelial hyperplasia (Heck's disease): report of two cases with PCR detection of human papillomavirus DNA

PR Jayasooriya[1], S Abeyratne[2], AW Ranasinghe[3], WM Tilakaratne[1]

[1]*Department of Oral Pathology, Faculty of Dental Sciences, University of Peradeniya, Peradeniya;* [2]*Oral and Maxillofacial unit, Base Hospital Matale;* [3]*Department of Oral Medicine, Faculty of Dental Sciences, University of Peradeniya, Peradeniya, Sri Lanka*

Focal epithelial hyperplasia (FEH) (Heck's disease) is essentially a benign oral infection produced by the human papillomavirus (HPV). Although this condition is known to exist in numerous populations and ethnic groups, it is relatively rare in South-East Asia. The following report is based on two cases of adult FEH with histopathological features in favour of the disease. In addition, polymerase chain reaction was performed to detect the presence of HPV DNA in the lesions in order to confirm the histopathological diagnosis.
Oral Diseases (2004) **10**, 240–243

Keywords: focal epithelial hyperplasia; human papillomavirus; polymerase chain reaction

Introduction

Focal epithelial hyperplasia (FEH) or Heck's disease was first described in Native Americans in 1965 (Archard *et al*, 1965). Today it is known to exist in numerous populations and ethnic groups such as Eskimos, North, South, and Central American Indians (Archard *et al*, 1965; Odell and Morgan, 1998). In these populations almost 40% of the children seem to be affected (Odell and Morgan, 1998). However, the disease is relatively rare in the Asian continent (Odell and Morgan, 1998).

In majority of the cases FEH is caused by sub types of human papillomavirus (HPV) 13 and 32 (Odell and Morgan, 1998). A site-specific predilection for keratinized and non-keratinized surfaces has been observed in these two types of HPV respectively (Morrow *et al*, 1993). Moreover, HPV 32 tends to cause the disease in the older age groups while HPV 13 seems to be equally involved in the development of the disease in both young and old patients (Nelson *et al*, 2002).

Focal epithelial hyperplasia primarily occurs in children with no gender predilection (Carlos and Sedano, 1994). Recently, the occurrence of FEH in human immunodeficiency virus (HIV) infected patients has also been reported (Marvan and Firth, 1998). The lips, buccal mucosa and tongue appear to be the frequently affected sites while the floor of the mouth, soft palate and the oro-pharynx seem to be affected rarely (Carlos and Sedano, 1994). Occasionally lesions may also occur at multiple sites (Carlos and Sedano, 1994). Treatment is not usually indicated as the lesions may undergo spontaneous regression particularly in children (Morrow *et al*, 1993). However, when the lesions are traumatized or aesthetically unacceptable excision may be indicated by means of scalpel, cryo or laser surgery (Morrow *et al*, 1993).

The following report is based on two cases of adult FEH in Sri Lanka. Polymerase chain reaction (PCR) analysis of HPV DNA from the lesions was undertaken.

Case report 1

A 42-year-old female was referred to the Department of Oral Medicine, Faculty of Dental Sciences, University of Peradeniya, Sri Lanka for investigation of multiple gingival nodules. The patient's medical history was unremarkable. Intraoral examination revealed a number of elevated, sessile, smooth surface nodules involving both upper and lower lingual and buccal gingivae. The lesions were soft on palpation and were covered by whitish mucosa. The lesions were not ulcerated or inflamed. The size of the lesions ranged from 2 to 10 mm in diameter. The patient claimed that the lesions had been present from adolescence. A clinical differential diagnosis of viral warts or multiple papillomas was proposed. The largest lesion in relation to the lower 65 region was excised under local anaesthesia and submit-

Correspondence: Dr W M Tilakaratne, Department of Oral Pathology, Faculty of Dental Sciences, University of Peradeniya, Peradeniya, Sri Lanka. Tel: 94 8 387500, Fax: 94 8 38948, E-mail: wmtilak@pdn.ac.lk
Received 13 June 2003; revised 30 January 2004; accepted 4 February 2004

ted for histopathological examination. Microscopically the H&E stained sections showed a mucosal nodule covered by parakeratinized stratified squamous epithelium with marked acanthosis. A few scattered koilocytes and occasional mitosoid bodies were observed in the upper layers of the epithelium. The corium was fibrosed with a compartmentalized lymphoplasmacytic infiltrate. These histopathological features together with clinical features helped to arrive at the diagnosis of FEH. The larger lesions were excised without complications and thereafter the patient was lost to follow-up.

Case report 2

A 65-year-old male patient was referred for persisting, multiple, whitish nodules to the Oral and Maxillofacial unit of the Base Hospital Matale, Sri Lanka. On examination, he presented with white soft nodules of 5–10 mm in diameter on the right side of the buccal mucosa (Figure 1). The past medical history and the family history were unremarkable. According to the information a clinical differential diagnosis of squamous cell papilloma and verruca vulgaris was proposed. The lesions were excised under local anaesthesia to arrive at a definitive diagnosis. The H&E stained sections showed the mucosa covered by acanthotic parakeratinized stratified squamous epithelium. Virally damaged cells (koilocytes) (Figure 2) and mitosoid bodies (Figure 3) were present in the upper prickle cell layers. These histopathological features together with the clinical features were consistent with FEH. Considering the diagnosis and the benign nature of the disease no treatment was attempted and this was explained to the patient.

Analysis of HPV DNA by PCR

DNA extraction and verification

Three to five 10-μm thick sections from each paraffin embedded block were collected to 1.5 ml sterile microcentrifuge tubes for DNA extraction. Briefly, the tissues were deparafinized with xylene. Thereafter, the tissues were placed in 200 μl of TE buffer (0.5 M ethylenediaminetetraacetic acid, 1 M Tris-HCl) and 20 μg ml^{-1} proteinase K and incubated overnight at 37°C. Following the inactivation of Proteinase K the supernatant was purified with phenol:chloroform:isoamyl alcohol solution (25:24:1) and DNA precipitated with 100% ethanol. Finally the DNA pellet was resuspended in 20 μl of TE buffer. PCR with β-Globin primers PCO3/PCO4 indicated the presence of amplifiable DNA in both cases.

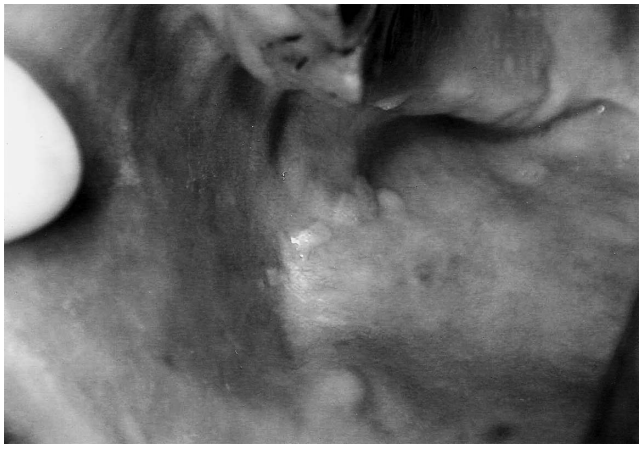

Figure 1 Clinical photograph to show the multiple lesions of Focal epithelial hyperplasia on the right buccal mucosa in a 65-year-old male patient

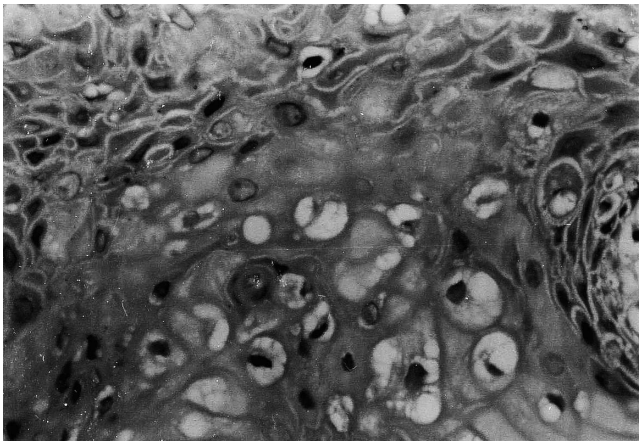

Figure 2 Photomicrograph to show virally damaged cells or koilocytes on the superficial keratinocytes (×400)

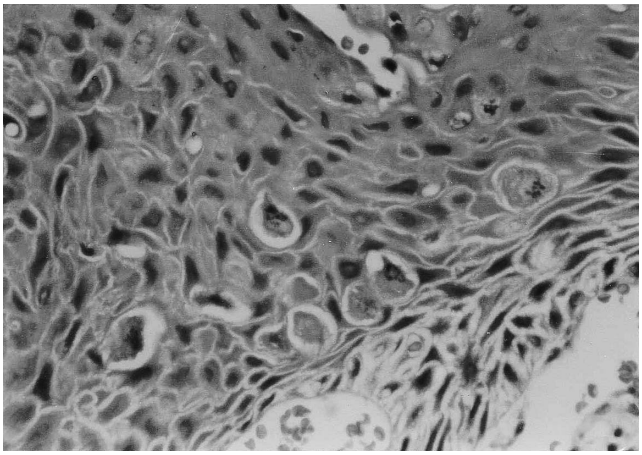

Figure 3 Typical nuclear changes produced by human papillomavirus in focal epithelial hyperplasia (mitosoid bodies) are seen in this microscopic field (×400)

Polymerase chian reaction

Consensus primers MY09/11, which amplify 450 bp of the L1 region of the HPV genome, was used in the PCR reaction. Hot start PCR was performed in a final reaction volume of 50 μl containing 5 μl of DNA sample, 50 mM KCl, 10 mM Tris-HCl, 2 mM each dNTP, 1 U Taq polymerase. The conditions for PCR were as follows, initial denaturation step at 95°C for 15 min followed by 40 cycles at 95°C × 1 min, 55°C × 1 min, 72°C × 1 min with a final elongation step at 72°C for 4 min.

Finally, the PCR amplimers were separated on 2% agarose gel, visualized under UV light and recorded on poloroid film. Accordingly, the results revealed the presence of HPV DNA in the lesions of the second patient while HPV was undetectable in the lesions obtained from the first patient (Figure 4).

Discussion

Focal epithelial hyperplasia is clinically characterized by multiple circumscribed sessile soft elevated nodules of whitish colour or colour similar to adjacent mucosa (Odell and Morgan, 1998). Although these clinical manifestations were found in our cases, FEH was not considered in the clinical differential diagnosis, as the disease is relatively rare in Sri Lanka. The asymptomatic nature of the disease together with the fact that it is commonly associated with poverty leading to the relatively low tendency of such patients to seek treatment, may contribute to the fewer number of cases being reported from South East Asia. However, the prevalence of the disease in certain populations seems to have a genetic predisposition (Odell and Morgan, 1998) Asians may have a relatively low genetic predisposition to the disease.

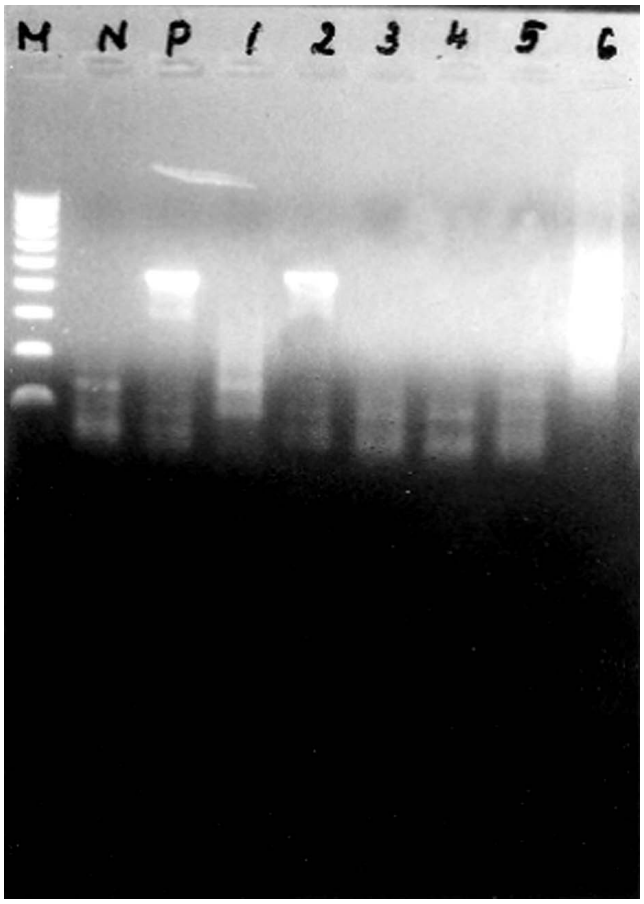

Figure 4 Photograph to show positive samples following gel electrophoresis. Lane 1 – marker, 2 – negative control, 3 – positive control, 4 – case 1 [negative for human papillomavirus (HPV)], 5 – case 2 (HPV positive)

Focal epithelial hyperplasia primarily occurs in children (Carlos and Sedano, 1994). However, the cases reported in the present study are adult patients who were above the average age range. Moreover, in populations where the disease is endemic among children the adults seem to have minimal evidence of residual oral lesions indicating spontaneous regression of the disease (Morrow *et al*, 1993). However, the fact that the first patient had had lesions from adolescence indicates that some lesions may persist in to adulthood without spontaneous regression.

Although, squamous cell papilloma and verruca vulgaris were considered in the clinical differential diagnosis the lesions were finally diagnosed as FEH according to both clinical and histopathological features. Microscopically epithelial hyperplasia in FEH presents as an abrupt and considerable focal acanthosis. The thickened epithelium extends upwards without extending in to underlying connective tissue. Hence, the regional rete ridges are at the same depth as normal retes. The ridges are widened, confluent and club shaped. Koilocyte changes and mitosoid bodies are present in the superficial keratinocytes. Histopathologically, FEH was differentiated from papilloma and viral warts by its lack of pronounced surface projections and presence of mitosoid bodies. However, the first case showed only a few mitosoid bodies. A previous report (Carlos and Sedano, 1994) indicates the necessity to perform serial sectioning to identify mitosoid cells, as they may not be present in a single section.

The PCR analysis revealed the presence of HPV in only one patient. Degradation of DNA in paraffin embedded specimens, with time, may have influenced the negative results of the second case (Mies, 1994). Moreover, a previous report (Qu *et al*, 1997) has also indicated the primers that amplify small segments of the HPV genome to be more suitable for detection of HPV when using DNA extracted from paraffin embedded specimens. The use of consensus primers that amplified a relatively large segment (450 bp) of the L1 region, may have also contributed to negative results.

Recent reports have indicated the presence of FEH in HIV infected patients (Marvan and Firth, 1998). Therefore, it is increasingly possible that the General Dental Practitioner in the Asian Continent will encounter this relatively uncommon condition more frequently in the future. Hence, this report also aims to educate and inform General Dental Practitioners so that they will be able to recognize, diagnose and manage patients with FEH.

Acknowledgements

We thank Mrs I. K Rambukewela for providing technical support for PCR analysis of HPV DNA.

References

Archard HO, Heck JW, Stanley HR (1965). Focal epithelial hyperplasia: an unusual oral mucosal lesion found in Indian children. *Oral Surg Oral Med Oral Pathol* **20:** 201–212.

Carlos R, Sedano HO (1994). Multi focal papillomavirus epithelial hyperplasia. *Oral Surg Oral Med Oral Pathol* **77:** 631–635.

Marvan E, Firth N (1998). Focal epithelial hyperplasia in an HIV positive man. An illustrated case report and review of literature. *Aust Dent J* **43:** 305–310.

Mies C (1994). Molecular biological analysis of paraffin-embedded tissues. *Human Pathol* **25:** 550–560.

Morrow DJ, Sandhu HS, Daley TD (1993). Focal epithelial hyperplasic (Heck's disease) with generalized lesions on the gingiva. A case report. *J Periodontol* **64:** 63–65.

Nelson BL, Schafer DR, Bosy TZ (2002). The typing of the human papillomavirus within an older patient population. *J Dent Res* IADR Abstract #0897.

Odell EW, Morgan PR (1998). Focal epithelial hyperplasia. In: Neville AM, Walker F, Taylor CR, (eds) *Biopsy Pathology of Oral Tissues*. Chapman & Hall Medical: London, pp. 143.

Qu W, Jiang G, Cruz Y *et al* (1997). PCR detection of human papillomavirus: comparison between MY09/11 and GP5+/6+ primer systems. *J Clin Microbiol* **35:** 1304–1310.