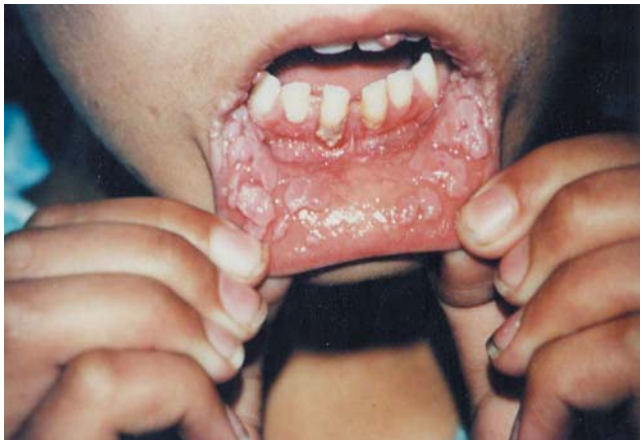
What Is Your Diagnosis?



A 12-year-old boy presented with soft papules and plaques varying from pink to white on the lower and upper labial mucosa, which appeared gradually over one year. The lesions disappeared when the lower lip was stretched.

PLEASE TURN TO PAGE 233 FOR DISCUSSION

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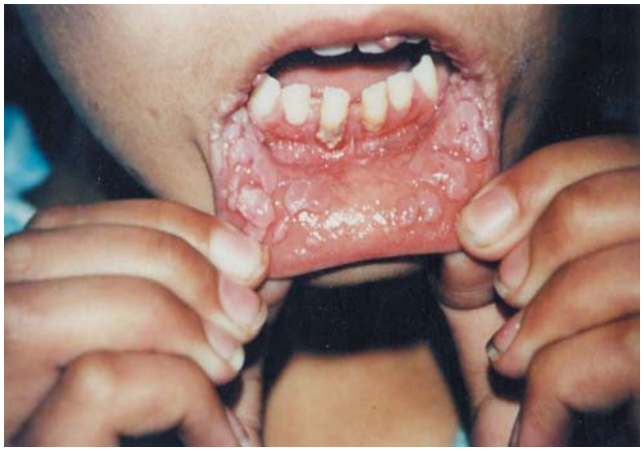
The authors report no conflict of interest.

The Diagnosis: Focal Epithelial Hyperplasia (Heck Disease)



Focal epithelial hyperplasia (FEH) is an uncommon benign cutaneous disorder involving the oral mucosa. FEH usually presents in children with multiple asymptomatic oral papules and plaques.

In 1965, Archard et al[1] reported a series of 19 pediatric patients with FEH, though the first case was observed by Heck, a coauthor of the report, in 1961. Heck noticed multiple "sprinkled" papules over the oral mucosa in an 11-year-old Navajo girl. Archard and colleagues[1] coined the term *FEH* to describe the intraoral papules in several American Indian and Eskimo children. In 1966, Hettwer and Rodgers[2] described FEH in a Polynesian girl, and with esteem for the initial researcher, they named the condition *Heck disease;* the eponym endured in the literature.

FEH predominantly is seen in children, though a few adult cases have been reported. FEH also has been noted in immunocompromised adults, such as patients with human immunodeficiency virus (HIV) infection.[3] Although FEH may appear in various ethnic groups, Eskimos, American Indians, and South Africans may have a distinct predisposition for the condition.[4]

FEH manifests as numerous sessile or pedunculated mucosa-colored or white papules measuring a few millimeters (1–5 mm) in diameter.[1] These papules are nontender and soft with either a smooth or verrucal surface. They may appear discretely or coalesce into plaques. The papules disappear when the mucosa is stretched and may thicken or ulcerate if traumatized.[1] FEH growths usually present on the lower labial and buccal mucosa, though other areas of oral mucosa also may be involved.[5]

FEH can be diagnosed clinically and confirmed histologically with a mucosal biopsy. The histopathologic features of FEH include epithelial hyperplasia of discrete sections of oral mucosa. In particular, the mucosal epidermis demonstrates acanthosis and "clubbing" or horizontal anastomosis of rete ridges.[6]

Although the exact etiology of FEH is unknown, many researchers have speculated on its cause. Genetic predisposition for developing FEH has been proposed based on noted familial occurrences and ethnic predilections.[7] Other potential risk factors include poor nutrition, crowded living conditions, and poor hygiene.[8] However, the most compelling etiologic evidence for FEH is intralesional infection with human papillomavirus (HPV). Based on polymerase chain reaction–DNA testing, the most common HPV types identified with FEH lesions are HPV-13 and HPV-32.[9,10] HPV-13 and HPV-32 have low oncogenic potential, which explains the benign nature of FEH.[10] Furthermore, Moerman et al[11] highlighted reoccurrence of FEH in HIV-infected adults. These observations generated a theory that FEH is a form of viral opportunistic infection in immunocompromised patients, such as those with HIV.[11] FEH may be an important HIV marker, especially because oral lesions are the first sign of HIV disease in 20% to 90% of patients.[11]

The differential diagnosis of FEH includes verruciform xanthoma, verrucous carcinoma, multiple fibromas or papillomas, mucosal neuroma, white sponge nevus, diffuse epithelial hyperplasia, sialadenoma papilliferum, inflammatory papillary hyperplasia, Cowden disease, focal dermal hypoplasia (Goltz syndrome), Darier disease, Crohn disease, and condyloma acuminatum.[4,5,12,13] It is crucial for clinicians to distinguish FEH from condyloma acuminatum in pediatric populations to eliminate suspicion of sexual abuse.[7] Condyloma acuminatum growths are multiple, clustered, verrucal nodules, whereas FEH lesions have more diffuse, soft, and papular characteristics.

Most FEH lesions are asymptomatic with minimal complications; however, some growths may develop into extensive papillomas and produce pain and tenderness. As a result, patients may experience an inability to complete daily activities, which may develop into anorexia and loss of body weight.[14] Furthermore, it has been postulated that FEH lesions presenting in immunocompromised patients are at greater risk for recurrence and malignant transformation.[11] Niebrugge et al[15] described a case of malignant transformation of FEH in one immunocompetent patient; however, Jablonska[16] questioned those findings, stating that oral verrucous carcinoma was mistaken for FEH in their patient.[16]

A variety of treatment options are available for FEH, including CO_2 laser ablation, cryotherapy, electrocoagulation, interferon-α injections, surgical excision, topical podophyllum resin, topical and systemic retinoids, and vitamins.[14,17] However, these treatments have variable results. Topical interferon-β and intramuscular interferon-α-2a, whose mechanism of action is directed against intralesional viral infection and inflammation, was successfully used to treat FEH in one patient.[14,18] Our patient was managed with 3 cycles of cryotherapy, resulting in a moderate decrease in the number and size of mucosal lesions.

Spontaneous regression of FEH papules may occur within a few months to one year after their initial presentation. However, FEH generally is considered a chronic condition with papules persisting or reoccurring for years, yet rarely continuing into adulthood.[12,14]

In addition, based on the high potential for FEH growths to recur or become malignant in immunocompromised patients, the recommendation is to expediently excise the lesions in those patients.[11] Our patient was immunocompetent despite apparent periodontitis (ie, gingivitis and proximal tooth decay).

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