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Multiple Bumps on Lips and Tongue

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The following Case Challenge is provided in conjunction with the UT Health San Antonio School of Dentistry faculty.

A 54-year-old Hispanic female who recently immigrated to the United States from Honduras has bumps on her lips.

After you have finished reviewing the available diagnostic information, make the diagnosis.

Diagnostic Information

History of Present Illness

The patient is a 54-year-old Hispanic female who recently immigrated to the United States from Honduras. She comes to your clinic with a chief complaint of, "Can you tell me what these bumps are on my lips?" She notes she has had them since childhood and they have never bothered her, and up until now she never felt different from everyone else. However, since moving here she perceives the people at her new job look at her funny and she wants to know what she has. She has been married for 30 years, has three healthy children and 4 grandchildren. Nobody else in her family has similar lip bumps. A biopsy of the lower labial mucosa was performed. After you have finished reviewing the available diagnostic information, make the diagnosis.

Medical History

- Pertinent medical history: hypertension x 15 years; 3 day hospitalization in 1990 due to a motor vehicle accident (concussion, broken forearm); 3 uncomplicated pregnancies
- Medications: Losartan, calcium, vitamin D3
- Adverse drug effects: none
- Pertinent family history: maternal: diabetes type 1; paternal: noncontributory; siblings: 4 healthy brothers, 1 sister with diabetes type 2
- Social history: denies tobacco use; drinks 1 -2 beers per night x 30 years; denies recreational drug use

Clinical Findings



Figure 1. Multiple sessile, focally pigmented, papulonodular lesions on labial vermilion border and perioral skin.



Figure 2-3. Multiple sessile, confluent, "cobblestone" nodules present on the upper and lower labial mucosa.



Figure 4. Multiple nodules on dorsal tongue surface.

Histopathologic Findings

Histologic sections of the biopsy show a mucosal soft tissue fragment exhibiting epithelial hyperplasia with a vaguely papillated architecture, elongated rete ridges, acanthosis, and irregular hyperparakeratosis. There are proliferative epithelial changes with increased cellularity, disordered maturation, mild reactive cytologic atypia, dyskeratosis, binucleate cells, mitosoid cells, and basal mitotic activity.



Figure 5. Low power histologic image showing epithelial hyperplasia with increased cellularity and hyperparakeratosis.



Figure 6. High power histologic image showing viral cytopathic changes with mild cytologic atypia, binucleate cells, dyskeratosis and a mitosoid cell.

Select Diagnosis

Can you make the diagnosis

54 year-old-female concerned about multiple bumps on her lips and tongue.



Select the Correct Diagnosis

- A. Molluscum contagiosum
- B. Multifocal epithelial hyperplasia (Heck disease)
- C. Verruciform xanthoma
- D. Multiple hamartoma syndrome (Cowden syndrome)

Molluscum contagiosum

Choice A. Sorry, this is not the correct diagnosis.

Molluscum contagiosum (MC) is a contagious cutaneous epithelial proliferation caused by a DNA poxvirus.¹⁻³ The virus is spread by direct sexual or nonsexual contact as well as by shared clothing, towels, bedding and communal baths or pools. The disease primarily affects children, adolescences and young adults. After an incubation period of several weeks, multiple small clustered, pink, umbilicated papules develop on the skin of the face, neck, trunk or genitalia. Involvement of the oral mucosa is uncommon. The lesions are usually asymptomatic but may occasionally be tender or pruritic. Histologically, the lesions display epithelial hyperplasia with a central crater containing keratinaceous curd-like material exhibiting infectious viral inclusions (Henderson-Paterson bodies). MC tends to spontaneously regress after several months. The lesions can be treated by curettage or cryotherapy if symptomatic or of cosmetic concern. MC may be more florid and persistent in immunocompromised patients. No apparent malignant potential has been noted. The clinical and histologic findings for MC do not support the diagnosis for this case.

Please re-evaluate the information about this case.

Multifocal epithelial hyperplasia (Heck disease)

Choice B. Congratulations! You are correct.

Multifocal epithelial hyperplasia (MEH)^{1,4-5} is a human papillomavirus driven squamous epithelial proliferation that has been associated with HPV types 13 and 32.1 The disease is endemic in certain ethnic populations including Native Americans and Hispanics. Some cases show a familial pattern. These findings indicate a possible genetic susceptibility. MEH occurs most often in children and adolescents but can occasionally be seen in adults. There may be a slight female gender predilection. The lesions develop most often on the lips, buccal mucosa and tongue. MEH presents as sessile, smooth surfaced, papulonodular lesions that may coalesce to give a cobblestone appearance. The lesions on the tongue may present as exophytic, papillomatous nodules. Histologically, the lesions show epithelial hyperplasia with elongated rete ridges, acanthosis, and parakeratosis. There are epithelial viral cytopathic changes including increased cellularity, binucleate cells, koilocytes and mitosoid cells. Mitosoid cells are characteristic of MEH and appear as arrested mitotic figures with dyskeratotic cytoplasm in the spinous layer of the epithelium. MEH often undergoes spontaneous regression over a period of moths to years. Treatment may not be necessary. A biopsy can be performed for diagnostic purposes. Irritated or esthetically concerning lesions can be excised. Immunosuppressed patients may have florid involvement. The lesions can sometimes recur. There does not appear to be the potential for development of malignancy.

Verruciform xanthoma

Choice C. Sorry, this is not the correct diagnosis.

Verruciform xanthoma (VX) is believed to be a hyperplastic and inflammatory response to irritated or damaged epithelium.^{1,6-7} Usually there is no obvious cause for VX. However, some cases have been associated with lichen planus, lupus erythematosus, graft versus host disease, pemphigus vulgaris, epithelial dysplasia and squamous cell carcinoma. No definitive relationship with human papillomavirus has been demonstrated. Unlike cutaneous xanthomas, VX is not related to hyperlipidemia. VX occurs most often on the oral mucosa with the gingiva, alveolar mucosa, palate and tongue being the most common intraoral locations. VX usually presents as a solitary asymptomatic roughened white to yellow-tan keratotic plaque. Most lesions are less than 2 cm in size. VX most often develops in white middle-aged to older adults. Histologically VX exhibits verrucoid to papillary epithelial hyperplasia with uniformly elongated rete ridges and hyperparakeratosis. The connective tissue papillae contain an infiltrate of macrophages with clear foamy cytoplasm. Nonspecific chronic inflammation is often present at the base of the lesion. No viral cytopathic changes are seen. Treatment of VX is conservative surgical excision. If present, management of any associated conditions should also be addressed. VX has no malignant potential unless related to epithelial dysplasia or carcinoma in situ. The clinical and histologic findings for VX do not support the diagnosis for this case.

Please re-evaluate the information about this case.

Multiple hamartoma syndrome (Cowden syndrome)

Choice D. Sorry, this is not the correct diagnosis.

Multiple hamartoma syndrome (Cowden syndrome) is a rare genetic disorder related to mutation of the PTEN (phosphate and tensin) gene on chromosome ^{10.8,9} The disease is most often inherited as an autosomal dominant condition. The disease is characterized by multiple hamartomatous growths and the development of benign and malignant neoplasms. Skin signs of the disease first manifest in the second decade. Patients present with multiple facial trichilemmomas, palmar/ plantar keratosis, hemangiomas, neuromas, lipomas and cutaneous xanthomas. Thyroid goiter, adenoma and carcinoma may also develop. Women often have fibrocystic disease of the breast and have an increased risk of breast cancer. There may also be multiple benign intestinal polyps. Benign and malignant tumors of the female genitourinary tract may also be seen. Oral manifestations include multiple mucosal papules involving the tongue, buccal mucosa and gingiva. An increased incidence of periodontal disease, dental caries, and a high arched palate vault has been reported. Biopsy of the oral papules shows only a nonspecific epithelial and fibrovascular hyperplasia. Patients with the multiple hamartoma syndrome require continued close long term follow-up for the development of malignant tumors. These patients should also receive genetic counseling. The clinical and histologic findings for multiple hamartoma syndrome do not support the diagnosis for this case.

Please re-evaluate the information about this case.

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