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Case Challenge
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Yellow Papule on the Ventral Tongue

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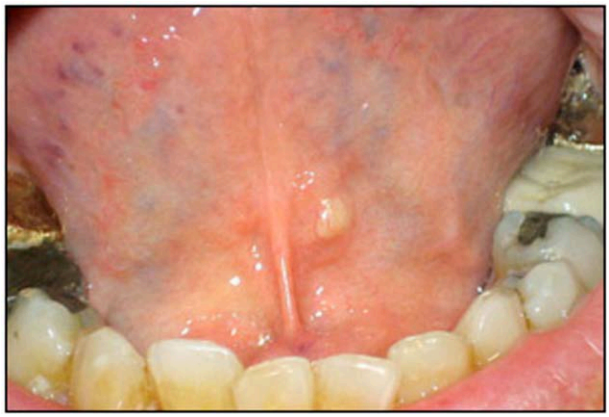


The following Case Challenge is provided in conjunction with the American Academy of Oral and Maxillofacial Pathology.

Case Summary

A 71-year old Caucasian male presented to the Dental Clinic at the University at Buffalo's School of Dental Medicine, New York, USA, for routine dental care. Upon oral examination, an asymptomatic yellow papule with a broad base and superficial vasculature is seen in the left ventral side of the tongue. The lesion demonstrated a soft consistency upon palpation. The overlying lingual mucosa was unremarkable. The patient was not aware of the presence of this lesion.

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

Diagnostic Information

Medical History

The patient's medical history was significant for Type II diabetes, hypertension, hyperlipidemia, and benign prostatic hyperplasia. His current medications included glyburide/metformin hydrochloride (2.5/500 mg, twice a day with food), enalapril maleate (5 mg, daily), simvastatin (10 mg, daily), tamsulosin hydrochloride (0.4 mg, daily), aspirin (81 mg, daily), and over-the-counter multivitamins.

Clinical Findings

The patient was alert and in no acute distress. No evidence of lymphadenopathy, facial asymmetry, or neural deficit was observed. An intraoral examination revealed a single, smooth, well-demarcated, yellow papule (Figure 1). The lesion measured 3–5 mm across, was firm to palpation, and asymptomatic. The patient denied traumatizing the area, and the overlying mucosa was intact. The lesion was completely excised under local anesthesia (1.8 mL of 2% lidocaine with 1:100,000 epinephrine). The specimen was fixed in 10% buffered formalin and submitted for microscopic examination.

Microscopic Findings

Microscopic examination revealed a wedge of mucosa surfaced by nonkeratinizing stratified squamous epithelium with short, blunt rete pegs. The subjacent fibrous connective tissue contained adipocytes, capillaries, interspersed fibroblasts, and scattered lymphocytes. The submucosa consisted of lobules of mature adipocytes. The main feature in the lamina propria was a cyst lined by stratified squamous epithelium that lacked rete pegs and showed lymphocytic exocytosis (Figure 2).

The cystic fibrous connective tissue wall contained lymphoid aggregates with germinal centers showing the presence of tingible body macrophages (Figure 3).

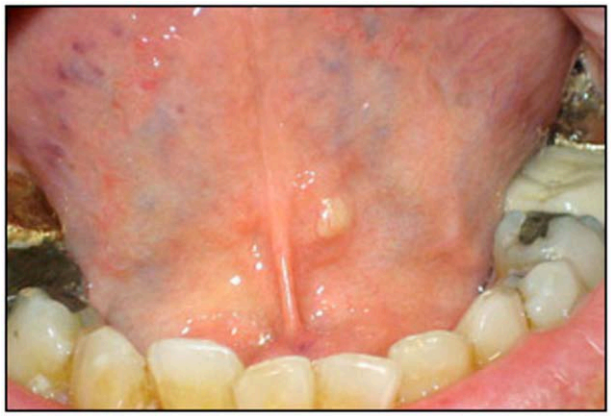


Figure 1. A yellow papule with a broad base and superficial vasculature is seen on the left ventral side of the tongue. The lesion demonstrated a soft consistency upon palpation.

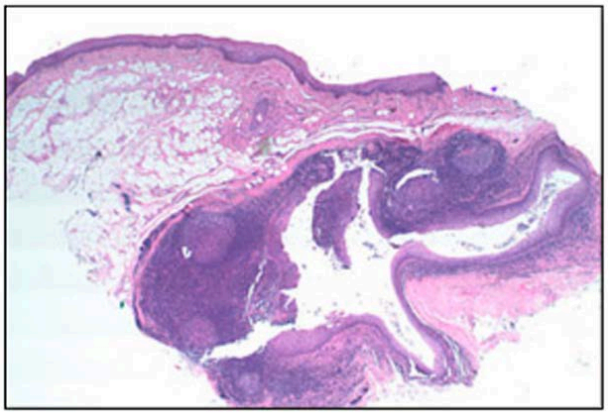


Figure 2. The specimen is covered by surface epithelium. The subjacent connective tissue contains lobules of mature adipocytes, an excretory salivary duct, and a cyst. A cystic cavity lined by stratified squamous epithelium is seen in the lower right side of the field of the photomicrograph. Low-power magnification (hematoxylin and eosin).

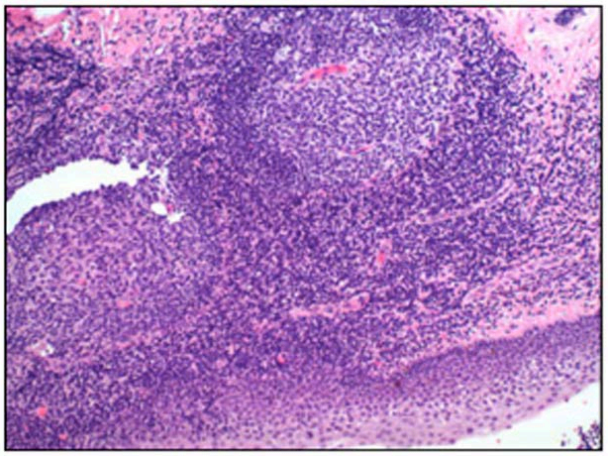
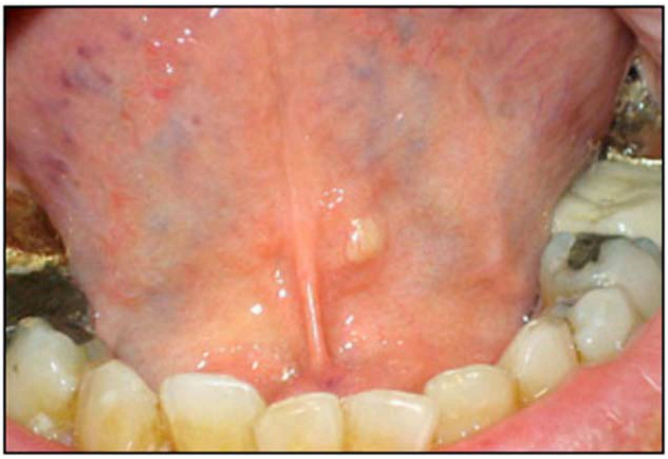


Figure 3. The cystic lining is surrounded by lymphoid aggregates with germinal centers. Medium-power magnification (hematoxylin and eosin).

Can you make the diagnosis?

A 71-year old Caucasian male presented for routine dental care. Upon oral examination, an asymptomatic yellow papule with a broad base and superficial vasculature is seen in the left ventral side of the tongue.



Select the Correct Diagnosis

A. Lipoma
B. Granular Cell Tumor
C. Lymphoepithelial Cyst
D. Amyloid Nodule

Lipoma

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

The differential diagnosis of a yellow papule in the oral cavity should include lipoma. The lipoma is a benign neoplasm of mature adipose tissue.[1] Lipomas represent 1 to 5% of all neoplasms of the oral cavity.[2] The most common intraoral locations in descending order of frequency are buccal mucosa, lip, tongue, palate, vestibule, and floor of the mouth.[3]

The clinical presentation of intraoral lipoma is that of a slowly enlarging, smooth-surfaced, well-circumscribed mass of soft tissue that can be sessile or pedunculated.[4] Although intraoral lipomas are typically smaller than 3 cm in size, some can reach a size of 5 to 6 cm across.[5] Superficial lipomas are yellow in color, but deeper lesions display a pink color. They are typically asymptomatic and can be present for many months to years before they are diagnosed. Most lipomas occur in adult individuals around the fourth decade of life and show no gender predilection.[1]

Microscopically, various subtypes of lipoma are recognized. The classic lipoma is well demarcated from the surrounding stroma and is composed of lobules of mature adipocytes separated by vascularized fibrous connective tissue septa.[1] Ocassionally, a thin fibrous capsule may be observed. Sometimes, delicate extensions of adipocytes from the main tumor appear to “infiltrate” surrounding skeletal muscle fibers creating the so-called intramuscular lipoma variant.[5] A combination of neoplastic adipocytes with either blood vessels, chondroid tissue, or smooth muscle result in the presence of other subtypes of lipoma such as angiolipoma, chondroid lipoma, and myolipoma, respectively. Occasional lipomas show an excess amount of collagen fibers (fibrolipoma), a myxoid background (myxoid lipoma), or numerous spindle-shaped mesenchymal cells (spindle cell lipoma).[6,7] When spindle cells are combined with floret-like multinucleated giant cells, the appellation pleomorphic lipoma is used.[3,8]

The treatment for lipoma is surgical excision and recurrence, although possible, is uncommon.[4] If lipomas of the oral cavity are left untreated, they can reach large dimensions and eventually interfere with speech and mastication.[9]

Although lipoma is a legitimate component of the clinical differential diagnosis for the lesion in this case, the microscopic findings are inconsistent with it.

Please re-evaluate the information about this case.

Granular Cell Tumor

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

One of the possible clinical presentations of granular cell tumor (GCT) is a yellow papule or plaque and, thus, it should be considered in the differential diagnosis for this lesion. First described by Abrikossoff in 1926 as "granular cell myoblastoma," the GCT represents a benign soft tissue tumor.[10] The histogenesis of this tumor remains elusive and thus the designation of GCT appears to be the most appropriate term.[11] GCT has been reported in a variety of locations including the skin, esophagus, larynx, stomach, biliary system, and male and female reproductive tract. However, a predilection for the head and neck region has been documented.[11] The most common site of occurrence is the tongue. Forty eight percent of GCT occur on the dorsum, another 15% on the lateral border, and 4% on the ventral surface, accounting for fully two-thirds of all oral cases.[12] GCT can occur in any race, at any age, and displays a predilection for Caucasian women.[13] However, some studies have reported a predilection for African Americans.[14] Although GCT can occur over a wide age spectrum, most cases present between the fourth and sixth decades of life.[15]

Clinically, GCT appears as a solitary submucosal nodule with an intact smooth surface that varies in color from pink to yellow and, sometimes, a white discoloration.[16] However, in up to 25% of cases, multiple lesions can occur.[17] If traumatized, ulceration of the surface may be seen. Unusual polypoid presentations also have been documented in the literature.[18,19]

Microscopically, the lesion shows pseudoepitheliomatous hyperplasia of the overlying epithelium in up to 50% of all cases.[13] This feature may be misinterpreted as squamous cell carcinoma. The stroma contains sheets of tumor cells that are characterized by small nuclei and abundant granular eosinophilic cytoplasm.[11] Immunohistochemical studies have suggested that the tumor cells have either a neural or endocrine genesis.[18] Typically, GCT shows positive staining with S-100 and neuron-specific enolase (NSE).[19] In a few cases, negative results with S-100 and NSE have been reported.[11] A lack of S-100 staining coupled with cytological atypia has prompted the use of the term nonneural granular cell tumor for some lesions.[19,20]

The mainstay of treatment for GCT is conservative, but deep surgical excision is indicated because lesional cells sometimes extend far from the main tumor cell mass into the adjacent tissues.[21] Recurrences are unusual and most likely related to incomplete excision.

The clinical presentation of the present case warranted the inclusion of GCT in the differential diagnosis. However, the absence of granular tumor cells in the biopsy specimen argues against a diagnosis of GCT.

Please re-evaluate the information about this case.

Lymphoepithelial Cyst

Choice C. Congratulations! You are correct.

The clinical presentation, location, and microscopic findings of this lesion established a diagnosis of oral lymphoepithelial cyst.

Lymphoid tissue aggregates are normally found in the pharynx and the oral cavity. They concentrate in Waldeyer's ring (palatine/lingual tonsils and pharyngeal adenoids), the floor of the mouth, the ventral surface of the tongue, and the soft palate.[22] These lymphoid aggregates are intimately associated with epithelial crypts from the overlying mucosa, which can fill up with keratin.[23] It is believed that these crypts may crimp off at the surface, thus resulting in the formation of a lymphoepithelial cyst.[5]

Lymphoepithelial cysts represent 16.3% of all nonodontogenic jaw and cystic lesions found in the oral cavity and they appear with more frequency in young adults.[24,25] The floor of the mouth is the most common location, followed by the ventral surface of the tongue, and then the posterior lateral lingual borders.[25] Clinically, the oral lymphoepithelial cyst presents as a small, sessile papule or nodule, usually less than 1.0 cm in diameter, with white to yellow discoloration covered by an intact, smooth mucosa. This cyst is asymptomatic unless traumatized. In addition, some patients may complain of tumefaction and, occasionally, oozing of the cyst contents.[26]

Microscopically, the oral lymphoepithelial cyst is lined by a parakeratinized, stratified squamous epithelium lacking rete pegs. Occasionally, goblet cells are seen in the cystic lining and the cystic lumen may be filled with desquamated keratinocytes. Furthermore, the cystic wall contains lymphoid tissue with or without germinal centers. The germinal centers may vary considerably in size. The lymphoid tissue component may either completely encircle the cyst or be restricted to a small pericystic area.[26]

Surgical excision is the mainstay of treatment for oral lymphoepithelial cyst. The prognosis is excellent and recurrence is not expected.[27]

Amyloid Nodule

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

Amyloidosis represents a group of heterogeneous disease processes characterized by the extracellular deposition of amorphous fibrillar proteins called amyloid.[28] More than 25 distinct biochemical forms of amyloid have been characterized.[29] Estimates show that every year, eight out of one million people will develop amyloidosis.[30] The deposition of amyloid can occur systemically or be limited to specific organ involvement.31 Various forms of systemic amyloidosis have been identified and include primary (AL) or myeloma-associated, secondary (AA), hemodialysis-associated, and heredofamilial subtypes.[32] Amyloidosis may affect the head and neck region and has a predilection for the tongue. This may present either as a generalized macroglossia associated with AL amyloidosis/ multiple myeloma or as localized individual pink to yellow nodules with no associated systemic disease.[28]

On light microscopy examination of H&E stained sections, amyloid appears as a homogeneous eosinophilic amorphous material. This material stains positive with Congo red preparations, showing a typical apple-green birefringence when subsequently viewed under polarized light.[31,33] Regardless of the biochemical subtype, a common feature of all the different types of amyloid is its protein folding pattern known as a “ß-pleated sheet.” This is responsible for the homogeneous staining characteristic of all the various types of amyloid.[34]

The mainstay of treatment for AL amyloidosis is chemotherapy.[35] For AA amyloidosis, the therapeutic approach is directed to control of the underlying infection.[32]

An amyloid nodule is an example of a limited and localized form of amyloidosis, where surgical excision would be expected to be curative.[36]

An asymptomatic yellow nodule of the tongue may represent an amyloid nodule and could be included in the differential diagnosis of the lesion presented in this article. However, the microscopic findings of the biopsy are a strong argument against a diagnosis of solitary amyloid nodule.

Please re-evaluate the information about this case.

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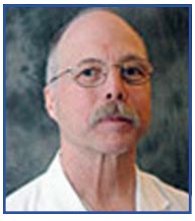

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