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CLINICAL PATHOLOGIC CONFERENCE CASE 1: AN ULCERATED NODULAR MASS ON THE RIGHT HARD PALATE

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Clinical Presentation: A 30-year-old Hispanic male presented to an oral surgeon with a 2.5 cm × 1 cm ulcerated nodular mass on the right lateral hard palate (Figure 1). The mass extended from the lateral palatal margin to the midline and antero-posteriorly from the rugae to the distal aspect of tooth #2. The surface was ulcerated and covered by a yellow fibrinous exudate focally with a violaceous erythematous pigmentation in other areas. The mass had raised borders and was painful and tender to palpation. As per the patient, the mass was present for a month, and he thought he had burnt the roof of his mouth after consumption of pizza. There was no bone involvement in the radiographs according to the oral surgeon. His medical history was significant for hypertension, heart murmur, and asthma.

Differential Diagnosis: Given the clinical presentation of an ulcerated mass in the lateral hard palate, the differential diagnosis for this case should include variety of pathologies that affect the lateral hard palate. They can be grouped under 3 main categories: neoplastic, reactive/inflammatory, and infectious. The differential diagnosis for neoplastic category includes the following: lymphoma, Kaposi's sarcoma, myeloid sarcoma, salivary gland neoplasms, melanoma, sinonasal neoplasms or odontogenic cysts/neoplasms breaking through maxilla, squamous cell carcinoma, and mesenchymal neoplasms. The reactive/inflammatory category includes pyogenic granuloma, necrotizing sialometaplasia, and palatal abscess. The infectious category includes deep fungal infections because immunocompromised patients can have a tumor-like clinical presentation.

Diagnosis and Management: Microscopic examination of the submitted biopsy specimen revealed a palatal mucosal ulceration surfaced by fibrin and enmeshed neutrophils (Figures 2A, 2B). There was diffuse infiltration of large, pale-staining mononuclear cells with indented vesicular nuclei that resembled histiocytes (Figure 2C) and a large number of eosinophils, fewer plasma cells and lymphocytes, and hemorrhage interspersed among histiocyte-like cells (Figure 2D). By immunohistochemistry, the histiocyte-like cells were strongly and diffusely positive for CD1a and S100, confirming the presence of Langerhans cells (Figures 2E, 2F). The overall histopathologic features were consistent with Langerhans cell histiocytosis/disease. Because there was no bone involvement, a diagnosis of peripheral Langerhans cell disease was rendered. The patient was referred for further evaluation and appropriate management and no additional information was available.

Discussion: Langerhans cell histiocytosis (LCH) or Langerhans cell disease represents a spectrum of clinicopathologic disorders that are characterized by neoplastic proliferation of $CD1a^+/CD207^+$ Langerhans cells in the background of eosinophils, lymphocytes, plasma cells, and multinucleated giant cells.[1] It can range between a unifocal bony or cutaneous involvement with excellent prognosis to a disseminated multiorgan manifestation with poor prognosis. Therefore, the treatment may vary from conservative curettage or surgical excision in unifocal lesions to chemotherapy with corticosteroids for patients with disseminated multifocal lesions.[2] The pathogenesis of LCH has always been controversial, but recent studies favor it as a neoplastic process with monoclonal proliferation of Langerhans cells, and 40% to 60% of LCH harbor BRAF v600e mutations.[3,4] A majority of LCH is seen in children younger than 15 years of age; however, it can be encountered in any age range of population. Single or multiple bone lesions are the most common clinical presentation with jaws affected in 10% to 20% of all cases. If the disease ruptures the jaw, gingival ulcerations or proliferative masses may develop. Nevertheless, there are rare cases of oral soft tissue or peripheral LCH without any bony involvement.[5-14]

Though LCH represents a mere 1 to 4 cases per million annually, peripheral LCH is even more rare, with only16 cases previously reported in the English literature to date.[5-14] A summary of these previously reported peripheral LCH cases with the present case is shown in Table I. The age of patients ranged from 3 months to 69 years and a majority of the cases were in males. Most of the cases manifested as painful gingival/hard palate ulcerations. Only 3 cases including our case presented as a proliferative nodular mass, which can mimic other palatal malignancies. The cases were treated with different treatment modalities

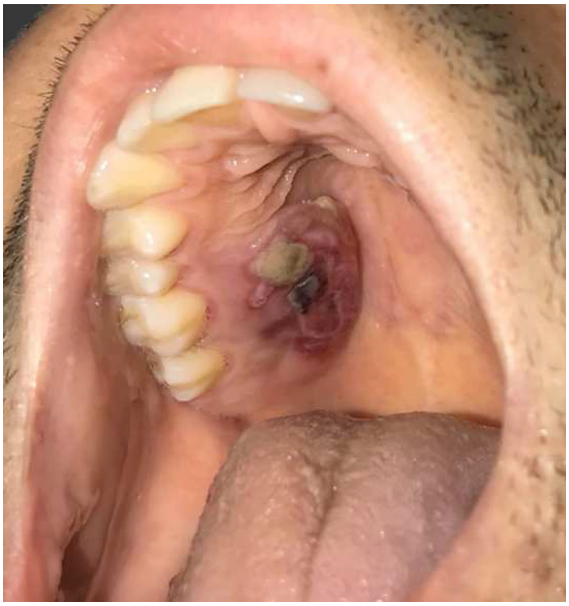

Fig. 1. Clinical photograph showing an ulcerated nodular mass on right hard palate.

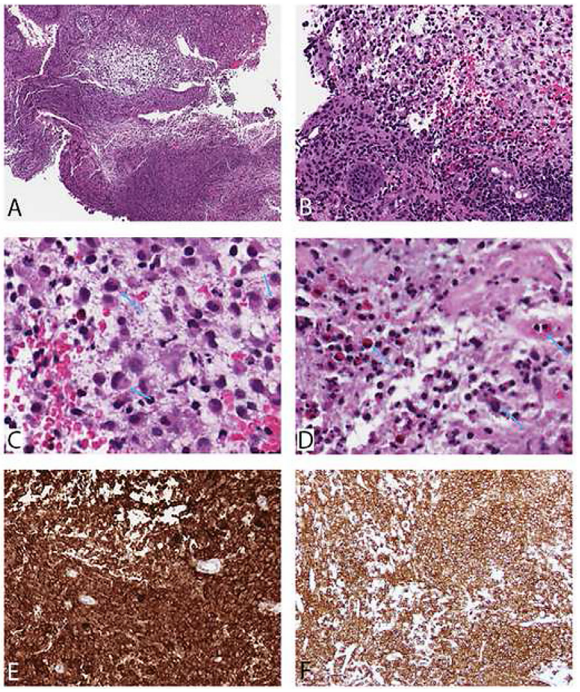

Fig. 2. (A). Palatal mucosal ulceration surfaced by fibrin (hematoxylin and eosin, original magnification 4 ×). (B). Proliferation of histiocyte-like cells with mixed inflammatory cell infiltrate and hemorrhage (hematoxylin and eosin, original magnification 20 ×). (C). High power showing infiltration of large, pale-staining histiocyte-like cells with indented vesicular nuclei (hematoxylin and eosin, original magnification 40 ×). (D). Large number of eosinophils, fewer plasma cells and lymphocytes, and hemorrhage interspersed among histiocyte-like cells (hematoxylin and eosin, original magnification 40 ×). (E). Histiocyte-like cells shows strong and diffuse immunoreactivity with CD1a confirming the diagnosis of Langerhans cell histiocytosis (original magnification 20 ×). (F). Langerhans cells also show strong and diffuse immunoreactivity with S100 (original magnification 20 ×).

Table I. Previously reported oral soft tissue associated Langerhans cell histiocytosis without any bony involvement along with the present case

Cited by	Age/Sex	Location	Clinical features	Treatment
Present case	30/M	Hard palate	Painful ulcerated nodule	Not available
Bedran et al.[5]	2/M	Gingiva	Painful ulcerated nodule	Vinblastine and steroid
Yashoda et al.[6]	50/M	Labial mucosa	Painful ulceration	Surgical excision
Kilic et al.[7]	41/F	Hard palate	Ulceration	Chemotherapy
Fistarol et al.[8]	24/M	Gingiva	Painful ulceration	CO_2 laser ablation and topical triamcinolone acetonide
Mortellaro et al.[9]	2/F	Gingiva	Not available	Wait and watch
	2.5/F	Hard palate	Not available	Chemotherapy
	0.25/M	Vestibule	Not available	Chemotherapy
Manfredi et al.[10]	23/M	Hard palate and gingiva	Painful ulceration	Vinblastine and steroid
Milián et al.[11]	50/M	Hard palate	Painless ulceration	Triamcinolone acetonide injection
	52/F	Gingiva	Painful ulceration	Radiotherapy
Cleveland et al.[12]	63/M	Gingiva	Ulcerated nodule	Surgical excision
	32/M	Hard palate	Painless ulceration	Wait and watch
	60/M	Vestibule	Corrugated leukoplakia	Lost to follow-up
Finney et al.[13]	27/M	Gingiva	Ulceration	Surgical excision
	69/M	Gingiva	Ulceration	Radiotherapy
Bottomley et al.[14]	65/M	Hard palate	Painful ulceration	Vinblastine/ prednisone

such as surgical excision, chemotherapy with corticosteroid, radiotherapy, and wait and watch approach. No additional information was available for our patient after referral for further evaluation and appropriate management.

In summary, we present a case of oral soft tissue/peripheral LCH manifesting as a proliferative nodular mass on hard palate with no bony involvement. The diagnosis of peripheral nodular lesions of LCH could be a challenge because its clinical features can mimic other oral malignancies. Therefore, recognition of the histopathologic features of LCH is important to avoid misdiagnosis and to establish the correct treatment.

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CLINICAL PATHOLOGIC CONFERENCE CASE 2: LONG-STANDING NODULE OF UPPER LIP

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Clinical Presentation: A 62-year-old female presented to the emergency clinic with a carious and symptomatic mandibular second molar (tooth #18). Incidentally, a nodule was noted on her upper lip (Figure 1). According to the patient, the asymptomatic nodule had been present for several years with little change in size. Upon clinical examination, the nodule was firm and palpable from both the cutaneous and the mucosal aspects, revealing that it was centered within the substance of the lip.

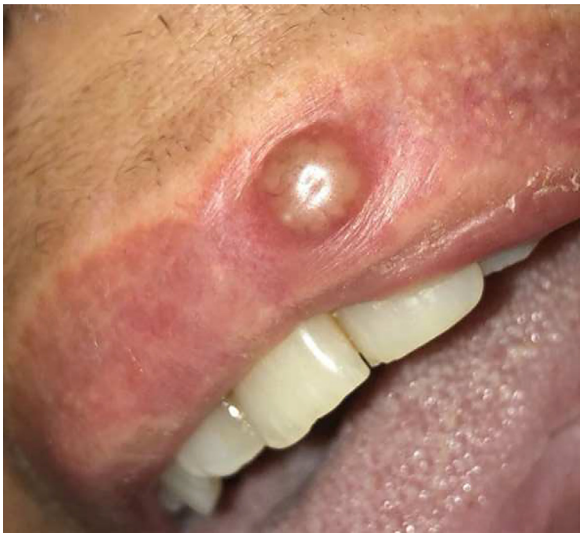

Fig. 1. Ectopic sebaceous glands lateral to the upper lip nodule.

The patient's medical history included type II diabetes mellitus, hypercholesterolemia, acid reflux, and osteoarthritis. Her medications included aspirin, lisinopril, Lipitor, metformin, omeprazole, folic acid, methotrexate, calcium, and naproxen.

Differential Diagnosis: Because of the yellowish hue of this longstanding submucosal nodule of the upper lip, a diagnosis of a benign tumor of the pilosebaceous unit was favored.

Sebaceous glands are usually found in association with hair follicles, the so-called pilosebaceous unit. Ectopic sebaceous glands without attached follicles can appear as 1- to 3-mm yellow papules near the mucocutaneous junctions particularly in the upper lip and in the buccal mucosa (i.e., Fordyce granules).[1] Ectopic sebaceous glands were present in this patient's upper lip lateral to the nodule (Figure 1). Sebaceous adenomas are benign sebaceous tumors that can appear as yellow nodules, usually about 5 mm in greatest dimension. These tumors typically arise on the head and neck regions of older individuals.[2] Furthermore, sebaceous adenoma arising in patients with visceral carcinoma may be associated with Muir-Torre syndrome. Patients with Muir-Torre syndrome often have multiple sebaceous tumors, keratoacanthomas, epidermal cysts, colonic polyps, and gastrointestinal carcinomas.[3] Careful examination of the family history, past medical history, and consideration of screening for mutations in DNA mismatch repair genes MLH1, PMS-2, MSH-2, and MSH-6 should be performed in sebaceous tumors with unusual clinical and/or histologic features.

Salivary gland tumors can also present as a long-standing upper lip submucosal nodule. The canalicular adenoma is a benign minor salivary gland tumor with a predilection for occurring in the upper lip. According to the World Health Organization, 80% of canalicular adenomas present in the upper lip.[4] Clinically, canalicular adenoma presents as a firm, movable nodule, and yellow coloration to the tumor has been previously reported.[5]

Other considerations are benign mesenchymal tumors, such as neural tumors (i.e., schwannoma/neurilemmoma), and those that might impart a yellow hue, such as lipoma or granular cell tumor. Neurilemmoma is a slow-growing, benign tumor of Schwann cells. It presents clinically as a painless nodule that is often firm on palpation. Although not uncommon in the head and neck, occurrence in the upper lip is rare.[6] Lipomas are benign soft tissue neoplasms of mature adipose tissue. Oral lipomas can occur on the lip as an asymptomatic circumscribed mass with a mean size of 2 cm.[7] When lipomas are superficial, they can impart a yellowish color.[8]

Oral granular cell tumor is a benign tumor thought to be of Schwann cell origin, composed of a nonencapsulated mass of plump cells with granular cytoplasm. Clinically, it appears as a pink to yellow submucosal mass with normal overlying epithelium. A large series found that oral granular cell tumors had a 2:1 female predilection, with a patient age range from 7 to 70 years, and occurrence in the upper lip reported at 4%.[9] Interestingly, in pediatric patients, 25% of cases have been reported to occur in the lip.[10]

Although the patient denied any cosmetic injectables to the lips, a foreign body granuloma could also have been a consideration if the history was compatible.