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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.

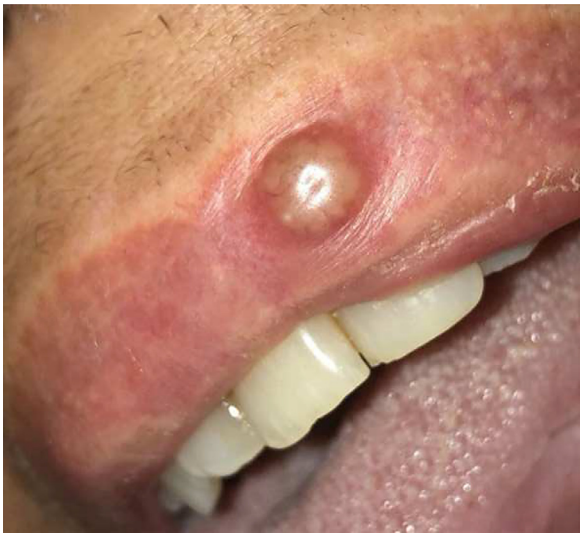

Fig. 1. Ectopic sebaceous glands lateral to the upper lip nodule.

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.

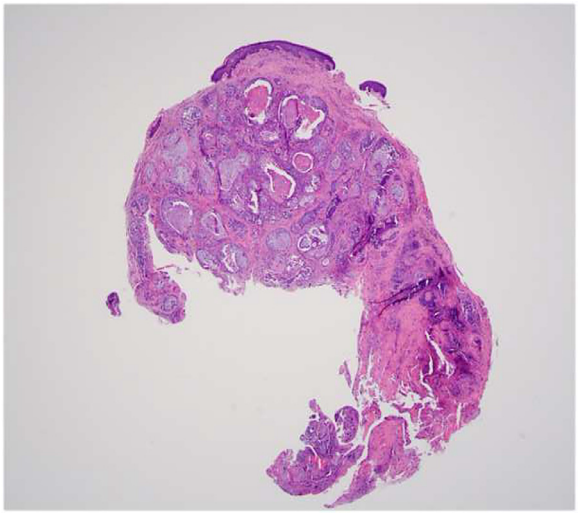

Fig. 2. Unencapsulated tumor composed of solid and cystic areas with mucinous material (hematoxylin and eosin, magnification 2 ×).

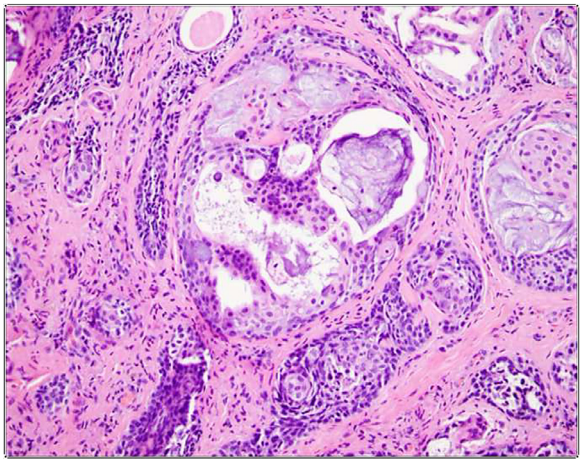

Fig. 3. Squamous, intermediate, and mucous cells in the tumor (hematoxylin and eosin, magnification 10 ×).

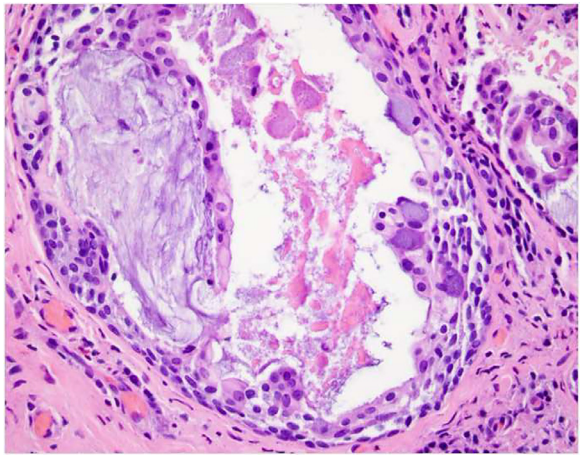

Fig. 4. Squamous, intermediate, and mucous cells in the tumor (hematoxylin and eosin, magnification 20 ×).

Diagnosis and Management: A punch biopsy was performed of the lesion. Microscopic examination revealed an unencapsulated tumor composed of solid and cystic areas with mucinous material (Figure 2). High power view revealed the tumor to be composed of squamous, intermediate, and mucous cells (Figures 3, 4). Necrosis, cellular pleomorphism, and marked mitotic activity were not present. Additionally, there were no sebaceous elements in the specimen. The mucinous material and mucous cells were positive for mucicarmine stain. A diagnosis of low-grade mucoepidermoid carcinoma was rendered.

Discussion: The palate is consistently the most common location for intraoral minor salivary gland tumors.[11-16] Other common sites of minor salivary gland tumors include the buccal mucosa, retromolar area, and lips.[12,17,18] Several retrospective studies suggests that the majority of minor salivary gland tumors are benign.[11-15] However, other reviews suggest that most minor salivary gland tumors are malignant.[16,19] Despite the conflicting data in the literature, the general rule of thumb is that minor salivary glands have a higher probability of being malignant.[20]

The lips can also be involved with salivary gland tumors. With the minor salivary glands of the lips, the tumors in the upper lip are much more likely to be benign when compared to the lower lip.[21] In the lower lip, the most common malignancy was mucoepidermoid carcinoma.[21] Synthesizing retrospective studies of the number of cases limited to intraoral mucoepidermoid carcinomas (MECs), the lips are involved in MEC about 5% relative to other intraoral locations (Table I).

MEC is salivary gland malignancy composed of mucinous, intermediate, and squamoid tumor cells forming cystic and solid patterns.[4] MEC is the most common malignant tumor in intraoral salivary glands and occurs over a wide age range.[11] Clinically, intraoral MECs present as painless firm nodules that can appear bluish, red-purple, or magenta.[22-24] Rarely, MECs presented as ulcerated or exophytic in presentation.[23]

Our case of an intraoral minor salivary gland MEC was rare in both its location and color. The yellowish color of the submucosal nodule on the cutaneous surface was an unusual presentation for MEC arising in a minor salivary gland. We speculate that the coloration was due to its proximity to the vermillion surface, and had the lesion been more proximal to the mucosal surface it would have appeared as the more classically described bluish coloration.

Most intraoral MECs present as low-grade and are well differentiated.[21,24,25] Thus, wide local excision is effective in preventing local recurrence.[24] As in our case, the tumor was low-

Table I. Summary of retrospective studies of intraoral mucoepidermoid carcinoma

Authors	Intraoral MEC total	MEC lips (total)	MEC upper lip	MEC lower lip
Melrose et al.[23]	54	3	1	2
Olsen et al.[24]	54	4	—	4
Auclair et al.[22]	143	10	2	8
Pires et al.[26]	75	1	1	—
Lopes et al.[27]	27	—	—	—
Totals	353	18	4	14

MEC, mucoepidermoid carcinoma.

grade, and the patient was referred for a wider excision. The excision was free of residual tumor and the patient has no signs of recurrence 12 months after surgery.

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CLINICAL PATHOLOGIC CONFERENCE CASE 3: AN EXPANSILE SINONASAL MASS WITH OCCULAR AND NEUROLOGIC SYMPTOMS

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Clinical Presentation: A 19-year-old African American female presented with facial asymmetry and prominent left facial swelling for 2 years. The patient reported loss in her sense of smell and blurred vision as well as 2 episodes of severe headaches shortly before presentation. She also indicated little to no improvement when she used medications for headaches. On physical examination, facial asymmetry with bulging left maxillary bone and left upward proptosis was noted. Extraocular muscle movement and cranial nerves II-XII were grossly intact and symmetrical. Rhinoscopy showed a markedly deviated nasal septum to the right without turbinate hypertrophy. Oropharyngeal examination showed good dentition, no palatopharyngeal mass, and fully mobile and symmetric tongue and palate. Computed tomography (CT) images showed an extradural mass, measuring $81.2 \times 44 \times 39$ mm, involving the left nasal cavity and paranasal sinuses with mass effect on the left orbit and skull base. Magnetic resonance imaging was subsequently performed and revealed a lobulated, well-defined heterogeneously enhanced expansile lesion with calcified matrix and soft tissue component involving the left maxillary sinus with extension into the left nasal cavity, frontal and ethmoid sinuses, and medial wall of the left orbit (Figures 1A and 1B). The patient received debulking of the lesion via endoscopic surgery, and a tissue specimen was submitted for microscopic examination.