Clinical Pathology Conference Cases Presented at the Combined Annual Meeting of the American Academy of Oral and Maxillofacial Pathology and International Academy of Oral Pathology, June 22–29, 2018

CLINICAL PATHOLOGY CONFERENCE CASE 1: AN EXOPHYTIC MASS ON THE LEFT ANTERIOR TONGUE

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Clinical Presentation: A 74-year-old male of Northern European descent presented for evaluation of an asymptomatic swelling of his tongue. Clinical examination revealed an approximately 2-cm exophytic mass involving the left anterior dorsolateral tongue (Figure 1). The surface was crenated from the adjacent dentition; however, the mucosa was intact and of normal color, with the exception of focal erythematous zones with thin, yellowish borders, consistent with a background of benign migratory glossitis. The patient was apparently not aware of the duration of the lesion or its evolution over time. His medical history was unremarkable.

Magnetic resonance imaging (MRI) was performed, and the mass appeared isointense compared with surrounding muscle with subtle heterogeneity on the T1-weighted sequence (Figure 2A). On the T2-weighted sequence, the lesion was uniformly hyperintense, with well-defined borders and a lobular morphology (Figure 2B).

Differential Diagnosis: Given the clinical presentation of a mass on the tongue, the differential diagnosis for this case had to be quite broad to include benign mesenchymal neoplasms, such as schwannoma, lipoma, leiomyoma, myofibroma, solitary fibrous tumor, ectomesenchymal chondromyxoid tumor, and granular cell tumor. Developmental cystic processes, such as epidermoid cyst, as well as salivary gland malignancies, such as mucoepidermoid carcinoma and polymorphous adenocarcinoma, could also be included. The hyperintense nature of the mass on T2-weighted MRI, however, was most compatible with high fluid content (either free fluid or high-bound water), excluding many of the solid tissue tumors. In addition, the lobular morphology ruled out the possibility of an epidermoid cyst or other developmental cystic processes.

Limiting the differential diagnosis to entities that fit with *both* the clinical presentation and MRI findings narrowed the diagnostic considerations considerably, with plexiform schwannoma, vascular anomaly, ectomesenchymal chondromyxoid tumor, and low-grade salivary gland malignancy, such as mucoepidermoid carcinoma, being reasonable considerations.

Schwannoma, also called *neurilemmoma*, is a benign, slow-growing neoplasm originating from the Schwann cells of the nerve sheath generally arising between ages 20 and 50 years. Although schwannomas of the head and neck region account for 25% to 45% of all extracranial cases, only 1% to 12% of these occur intraorally, most commonly involving the tongue.[1] Schwannomas are generally solitary, encapsulated tumors; however, a multinodular morphology (plexiform schwannoma) is a unique anatomic variant that represents approximately 23% of head and neck cases.[2] On MRI, schwannomas consistently appear isointense to muscle on the T1-weighted sequence, with a homogenous hyperintense signal seen on T2-weighted images.[1]

Fig. 1. Oral examination revealed an exophytic mass involving the left anterior dorsolateral tongue.

Vascular malformations are developmental anomalies that may become clinically significant in adult life as dilated blood vessels gradually enlarge in response to local trauma or increasing age. Approximately 40% of low-flow lesions arise in the head and neck region, and although the blood-filled spaces often impart a reddish-blue hue, the observed color can vary, depending on depth of the lesion.[3] On T2-weighted MRI, vascular malformations characteristically appear hyperintense and lobulated, with a low to intermediate signal observed on the T1-weighted sequence.[3]

Ectomesenchymal chondromyxoid tumor (ECT) is a rare, benign soft tissue neoplasm that exhibits a striking predilection for the dorsal tongue. It typically presents between the first and eighth decades of life as a slow-growing, painless mass, ranging in size from 0.5 to 2.0 cm.[4] Given the rarity of this entity, characteristic imaging findings are difficult to discern. Yoshioka et al. provided MRI for 1 case, which showed a low-level signal with contrast enhancement on the T1-weighted sequence.[5]

Mucoepidermoid carcinoma (MEC) is the most common malignancy affecting the minor salivary glands. It occurs across a broad age range, with greatest incidence between the third and sixth decades of life.[6] Although it may arise at any oral mucosal site that contains salivary gland tissue, MEC shows a predilection for the palate, retromolar region, floor of the mouth, and buccal mucosa, with involvement of the tongue being quite rare.[6,7] Features of MEC on MRI vary, depending on tumor grade, with the possibility for mucin-rich cystic areas appearing hyperintense on T1 and T2-weighted sequences.[8]

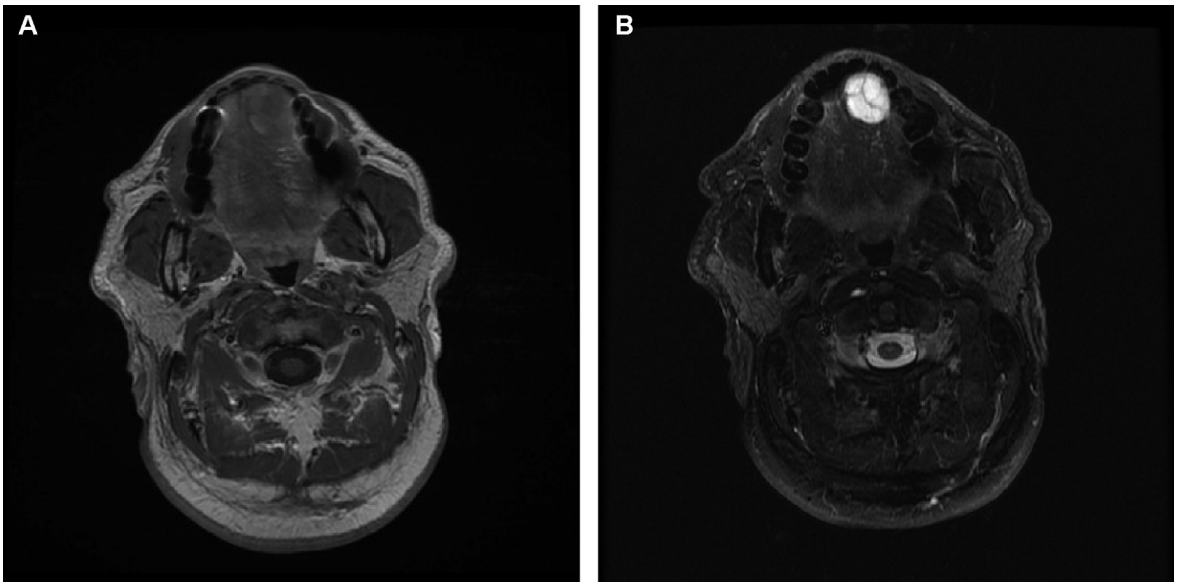

Fig. 2. T1-weighted magnetic resonance imaging (MRI) scan demonstrating the isointense nature of the tongue mass compared with surrounding muscle **(A)** with a homogeneous hyperintense signal with lobular morphology noted on the T2-weighted sequence **(B)**.

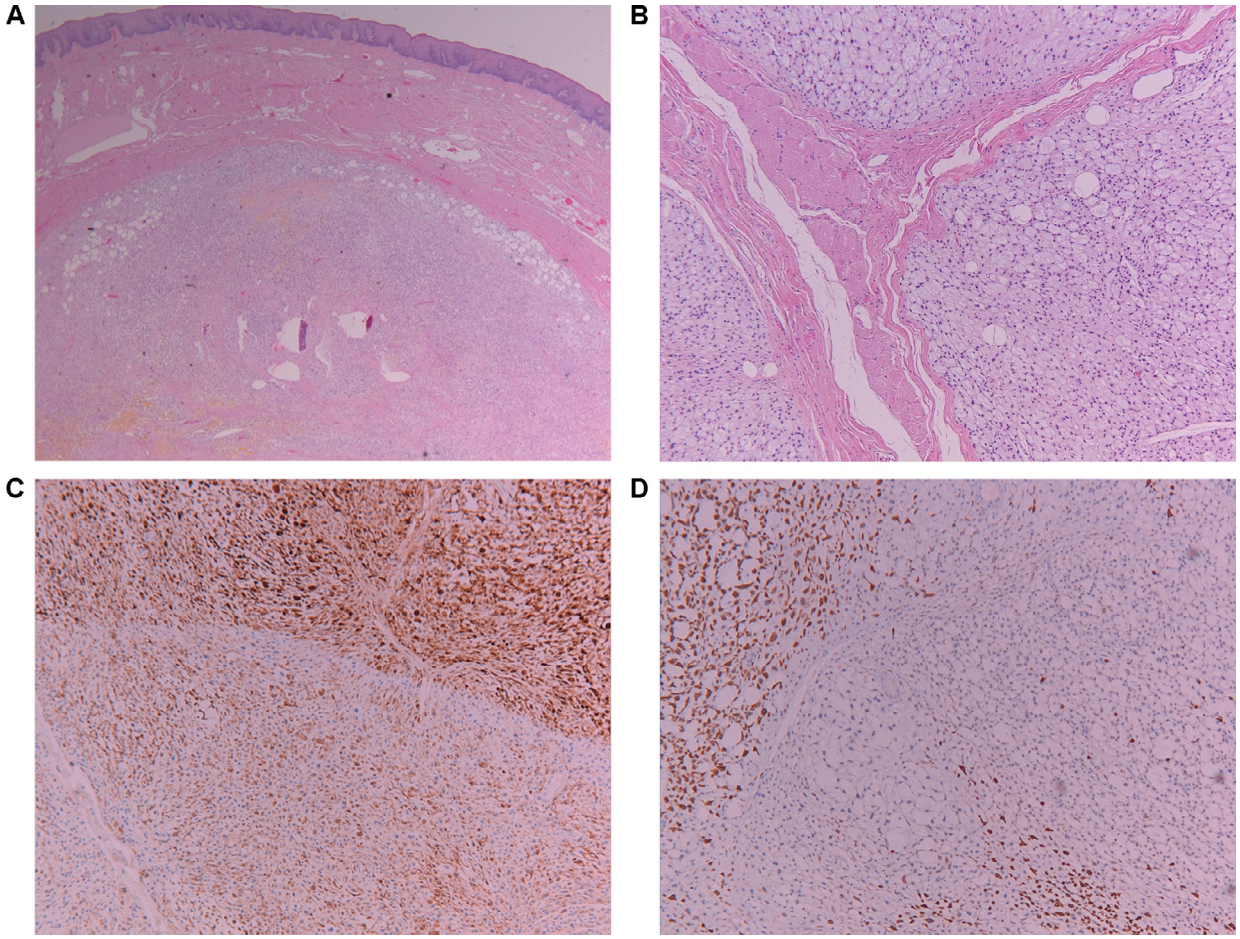

Fig. 3. Histopathologic features of a well-circumscribed, lobulated mass composed of cells with small, round to ovoid nuclei set in a myxoid stroma **(A, B)**. Immunohistochemical analysis shows diffuse, strong positivity of lesions cells to antibodies directed against S100 **(C)** with focal, strong positivity to glial fibrillary acidic protein (GFAP) **(D)**.

Diagnosis and Management: Surgical excision was performed. Macroscopically, the lesion consisted of a well-circumscribed, lobulated, submucosal mass measuring 2.3 cm in diameter. Histopathologic examination revealed a well-circumscribed, but nonencapsulated neoplasm consisting of slightly polymorphous cells that exhibited small, round to ovoid nuclei and eosinophilic cytoplasm set in prominent myxoid stroma containing pseudocystic spaces. Lesional cells were arranged in broad lobules separated by slender fibrous septae (Figures 3A and 3B). The overlying mucosa was unremarkable. Immunohistochemical analysis showed diffuse, strong positivity of lesional cells to vimentin and S100, with more focal, strong expression of glial fibrillary acidic protein (GFAP) (Figures 3C and 3D). Pancytokeratin, p63, smooth muscle actin, CD31, and CD34 were negative, with appropriate reactivity in control tissues. Given the histomorphology and immunohistochemical profile, a diagnosis of ectomesenchymal chondromyxoid tumor was rendered.

Discussion: ECT is a relatively rare neoplasm initially described by Smith et al. in 1995.[9] Two recent extensive reviews of the English language and German language literature confirmed at least 60 reported cases of ECTs, showing a striking predilection for the dorsal tongue, with few extralingual cases reported.[4,10] Age at diagnosis ranges from 7 to 78 years, with no sex predilection. Lesions generally present as a slow-growing, painless mass with minimal chance for recurrence after surgical excision.

Histopathologic features of ECT characteristically show demarcated, lobular sheets of fairly uniform round to ovoid, polygonal, or spindle-shaped cells with small, uniform nuclei. Although mild nuclear atypia can be observed, mitotic figures are rarely noted. Cytoplasmic boundaries may be indistinct, with variable proportions of myxoid to chondroid stroma admixed with cellular zones.[9]

While the origin of ECTs is uncertain, this neoplasm is thought to derive from pluripotent ectomesenchymal cells from the neural crest.[9] This impression is corroborated by tumor expression of GFAP. To further substantiate the neural crest origin, cells derived from ECTs have been shown to be similar to neuronal cells in cell cultures, with expression of homeobox protein-transcription factor (Nanog), GFAP, and microtubule-associated protein 2 (MAP2), and with mRNA real-time polymerase chain reaction analysis demonstrating positivity for octamer binding protein 3/4, transcription factor Sox2, Nanog, MAP2, and CD105.[5]

The *EWSR1* gene rearrangement has been described in a subset of ECTs.[11] This rearrangement has also been reported in soft tissue myoepitheliomas and clear cell hyalinizing tumors of the tongue and, therefore, does not discriminate between these entities.[11,12]

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CLINICAL PATHOLOGY CONFERENCE CASE 2: GINGIVAL OVERGROWTH AROUND A BADLY CARIOUS FIRST MOLAR

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Clinical Presentation: A 10-year-old girl was referred to the oral surgery clinic with a chief complaint of easily bleeding gingival overgrowth of 3 months' duration in the lower right quadrant (Figure 1). The associated right first molar was badly carious, with grade 2 mobility along with the adjacent premolars. On palpation, the buccal and lingual cortical bones associated with first molar were missing. On radiographic evaluation, a periradicular radiolucency with external root resorption was evident (Figure 2). The patient showed developmental delay and had a history of tonsillectomy and chronic cough. Enlarged upper anterior gingiva and enlarged, palpable bilateral submandibular lymph nodes were also noted during clinical examination (Figures 3 and 4).

Differential Diagnosis: Given the clinical presentation of gingival overgrowth around a badly carious tooth, the differential diagnosis for this case had to include either reactive lesions, such as pyogenic granuloma, peripheral giant cell granuloma, local-