A biphasic sessile mass of the buccal mucosa

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CLINICAL PRESENTATION

During a routine dental hygiene appointment, a 20-year-old Asian American female was noted to have an asymptomatic, 1.5-cm, sessile nodule of unknown duration on the left buccal mucosa. The patient had been aware of the lesion for several months. It had a biphasic clinical appearance: The inferior aspect had an erythematous, slightly lobular appearance, with intact surface epithelium, whereas the superior aspect was slightly cyanotic, with prominent overlying superficial vessels (Figure 1). The lesion was nontender to palpation. The patient's medical history included current use of oral contraceptives. Dental history included past orthodontic treatment. The patient denied use of tobacco products or history of trauma to the affected area.

Differential Diagnosis

The clinical presentation of the lesion favored that of a reactive lesion versus a benign neoplasm. The differential diagnosis included sclerosing pyogenic granuloma because of the lesion's location in an area that could be easily traumatized, especially considering the patient's history of orthodontic treatment. Pyogenic granulomas are nodular proliferations of reactive, well-vascularized connective tissue with a mixed inflammatory cell infiltrate. The surface epithelium is often ulcerated, but as the lesion ages, the surface ulceration may heal and the lesion may undergo sclerosis. Pyogenic granulomas are common in young adults and show a female predilection. In this case, the lesion was grossly lobular, with prominent vasculature and lack of ulceration, consistent with a pyogenic granuloma that has undergone sclerosis.[1]

Because of the vascular appearance of the lesion, a vascular anomaly, such as a venous malformation, was considered. Venous malformations are congenital lesions that do not regress over time and, instead, grow proportionately with surrounding tissues as the child grows. The lesions may increase in size during puberty and pregnancy. Venous malformations may become painful, a symptom that the current case did not exhibit.[2]

Vascular leiomyoma most often presents as a painless, slowly enlarging submucosal nodule. Although intraoral cases are thought to be derived from smooth muscle surrounding blood vessels, they may or may not demonstrate a vascular clinical appearance. This benign neoplasm is rare in the oral cavity, and it is most commonly noted in the fifth decade.[3]

On the basis of the age of the patient and the location of the lesion, a peripheral nerve sheath tumor was considered. Although intraoral peripheral nerve sheath tumors are relatively infrequent, intraoral cases of neurofibromas and schwannomas are most commonly found in young adults, and the buccal mucosa is not a rare site.[4]

Finally, a minor salivary gland neoplasm, such as a pleomorphic adenoma, was also considered. Pleomorphic adenomas are the most common salivary gland neoplasms, and they generally present as asymptomatic nodules. Although found to occur in patients of a wide age range, they are most typically noted in young adults. Intraoral pleomorphic adenomas are usually found on the palate, but the buccal mucosa is not a rare location.[5]

DIAGNOSIS AND MANAGEMENT

Initial treatment was based on the clinical working diagnosis of a reactive lesion versus a benign neoplasm. The lesion was conservatively excised in the oral surgery clinic with the patient under local anesthesia.

Histopathologic examination revealed a well-delineated, partially encapsulated, cellular mass with an overall solid architecture. The mass was lobulated with numerous fibrous connective tissue septae. Numerous prominent vascular channels lined by large eosinophilic endothelial cells filled with erythrocytes, as well as erythrocyte extravasation with hemosiderin deposition, were also seen.

Superiorly, the lesion was in close proximity to surface mucosa, and laterally, islands of cells infiltrated surrounding connective tissue directly adjacent to minor salivary glands (Figure 2). At high power, lesional cells were noted to have ovoid nuclei and pale, eosinophilic cytoplasm with intracytoplasmic vacuoles.

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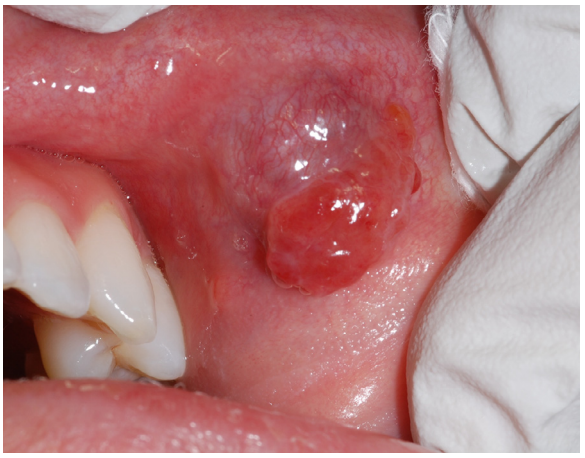

Fig. 1. Clinical presentation of a freely movable, sessile mass with a biphasic appearance, including an erythematous, slightly lobular area against a slightly cyanotic area with prominent overlying superficial vessels.

Pink, amorphous, acellular, colloid-like material was noted in several areas of the tumor (Figure 3A). Mitotic figures were noted in 2 of 10 high-power fields.

Immunoreactivity was positive in the tumor cells for antibodies to pancytokeratin, S-100 protein, and mammaglobin (Figures 3B and 3C) and negative for p63, factor XIIIa, and CD31. The colloid-like material was positive for periodic acid−Schiff stain without digestion (Figure 3D). The key to the diagnosis was provided by fluorescence in situ hybridization analysis, which revealed a rearrangement involving the *ETV6* gene in 73 of 100 examined cells (Figure 4), consistent with the genetic abnormality found in mammary analogue secretory carcinoma (MASC).

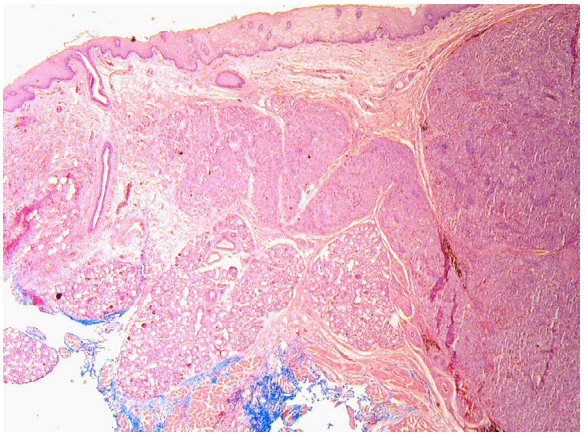

Fig. 2. Interface of neoplasm and adjacent minor salivary gland lobules (hematoxylin and eosin [H&E]; magnification × 20). *A high-resolution version of this slide for use with the Virtual Microscope is available as eSlide: VM05685.*

Additional surgery was planned because of positive surgical margins. Before surgery, computed tomography (CT) and positron emission tomography (PET) scans revealed a necrotic-appearing, fluorodeoxyglucose -avid node in level I of the neck. Definitive surgery consisted of wedge resection and selective neck dissection. Surgical resection achieved negative but close margins, and 1 level 1 B lymph node was positive, with focal extracapsular extension. The patient subsequently received concurrent chemotherapy (weekly cisplatin) and radiation treatment (to a total of 60 Gy).

DISCUSSION

MASC is a rare malignant salivary gland neoplasm, which was initially described in 2010 by Skálová et al.[6] MASC derives its name from its similarities to secretory carcinoma of the breast. These uncommon tumors share several features, including a chromosomal translocation that results in the formation of the *ETV6-NTRK3* fusion gene.[6] Before this, MASC was frequently diagnosed as acinic cell carcinoma, mucoepidermoid carcinoma, adenoid cystic carcinoma, cystadenocarcinoma, or adenocarcinoma not otherwise specified.[6-8] However, unlike acinic cell carcinoma, MASC does not demonstrate zymogen granules, and in contrast to mucoepidermoid carcinoma, it does not exhibit mucicarmine positivity. MASC is not characterized by angular nuclei, as found in adenoid cystic carcinoma, and it exhibits more solid areas of tumor compared with cystadenocarcinoma. Histologically, MASC is often an unencapsulated but well-defined, lobulated mass that may demonstrate variable architectural patterns, including papillary, cystic, tubular, or solid patterns. Lesional cells have a vacuolated cytoplasm with pale, ovoid nuclei, and they are immunoreactive with S-100 protein and mammaglobin antibodies. Intraluminal and cytoplasmic eosinophilic secretions are positive for periodic acid−Schiff stain and diastase resistant.[6,7] Our case demonstrated all these typical features but also demonstrated a highly vascular nature not generally reported, leading to initial consideration of a vascular neoplasm.

The typical MASC presents clinically as an asymptomatic nodule[6,7,9-14] that has enlarged slowly over a period of months to many years.[6,7,9-11,15-17] Most cases of MASC have occurred in the parotid gland,[6,7,14,18] and the mean age at presentation is about 45 years.[6,7,9,18,19] Most reported minor salivary gland tumors have ranged in size from about 0.5 to 2.0 cm.[6,10,12,19] The lesion occurs with almost equal propensity in males and females, with a slightly higher number of cases being reported in males.[7] The size of the lesion in the current case was similar to those in other previously reported cases, but it differed in terms

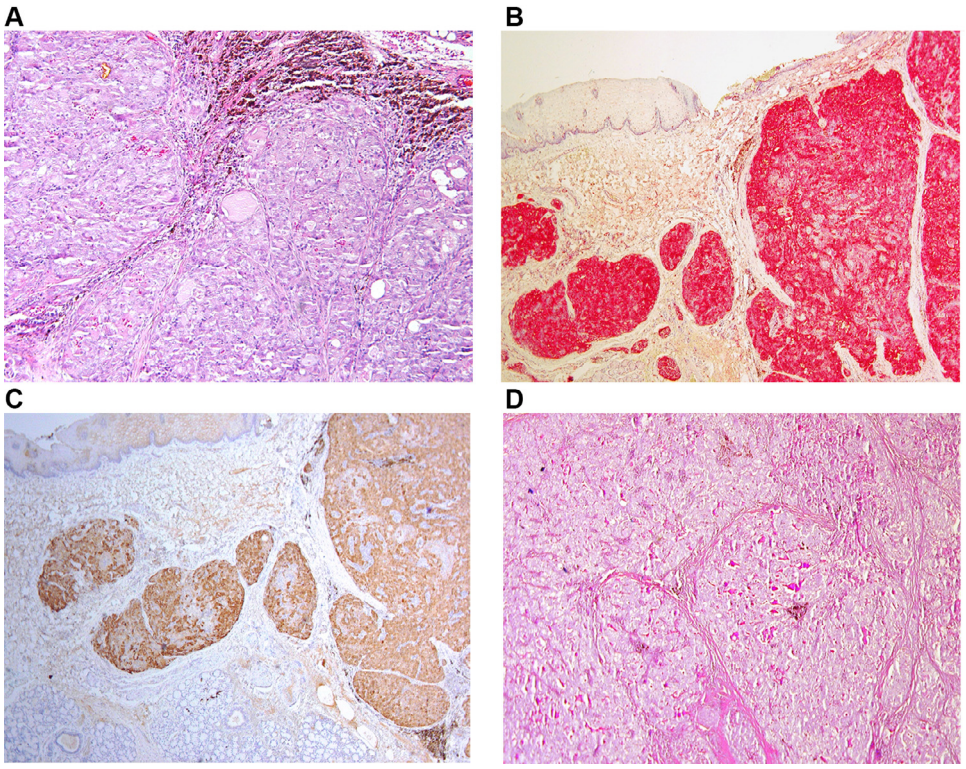

Fig. 3. **A**, Lesional cells, extracellular colloid-like material and hemosiderin (hematoxylin and eosin [H&E]; magnification × 100). **B,** Immunoreactivity for antibodies to S-100 protein (magnification × 40). *A high-resolution version of this slide for use with the Virtual Microscope is available as eSlide: VM05684.* **C,** Immunoreactivity for antibodies to mammaglobin (magnification × 40). *A high-resolution version of this slide for use with the Virtual Microscope is available as eSlide: VM05683.* **D,** Colloid-like material demonstrated positivity with periodic acid−Schiff (PAS) stain (magnification × 200). *A high-resolution version of this slide for use with the Virtual Microscope is available as eSlide: VM05686.*

of anatomic location and patient age. The most significant difference was its biphasic clinical presentation that included a highly vascular component.

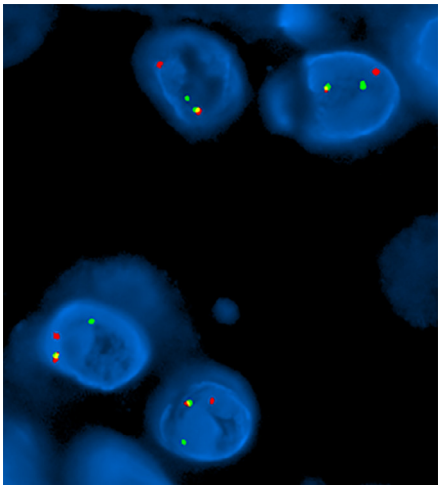

Fig. 4. Fluorescent in situ hybridization break-apart rearrangement probe (Abbott Molecular, Abbott Park, IL) demonstrating break of the *ETV6* gene (red: 5' *ETV6* signal; green: 3' *ETV6* signal; yellow: intact *ETV6* locus).

Treatment of MASC varies, depending on the clinical presentation, and most often includes surgical resection with or without neck dissection. In general, for malignant salivary gland tumors with close margins, perineural invasion, large size (stage T3 or T4), or histologic lymph node involvement, radiation therapy is recommended as postoperative treatment.[7,20,21] Among patients with MASC, 20% have received radiation treatment, and less than 5% have received both radiation and chemotherapy,[7] as did our patient.

Assessment of prognosis and response to treatment is challenging because of the limited number of cases reported with long-term follow-up. MASC is currently treated as a low-grade carcinoma with an overall favorable prognosis, but with the caveat that there is a risk of regional lymph node metastasis. One study reported that in approximately 20% of patients, tumors were present in the regional lymph nodes.[9] Four patients have been reported to have succumbed to the disease.[7] An average overall disease-free survival time of 92 months has been reported; there are currently no defined grading or staging criteria that indicate a poor prognosis, although aggressive cases have tended to present as larger tumors.[9] At 2 years after definitive

surgical resection, our patient had no evidence of disease.

Although more than 100 cases of MASC have been reported, data regarding this tumor are still relatively limited because of its rarity and recent recognition. This case adds to the known number of cases of MASC with lymph node involvement, and it also contributes to the overall knowledge of this rare malignancy by reporting a variation in histopathology. Our case had a benign clinical presentation that belied the malignant nature of the lesion. Its presentation varied from the typical clinical presentation of MASC in terms of biphasic clinical features, patient age, anatomic location, and positive metastasis. Histologically, this lesion was noted to be highly vascular, a feature not widely reported in MASC.

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