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HOT TOPIC

The ectomesenchymal chondromyxoid tumor: a review

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The ectomesenchymal chondromyxoid tumor is a relatively recently described neoplasm that appears to involve uniquely the oral cavity, particularly the tongue. Thirty well-accepted cases have been reported since the initial description of this lesion in 1995. While a wide age range (9–78 years) has been documented, most of these tumors are diagnosed from the third to sixth decades of life. No sex predilection is seen. The size of the neoplasm is typically <2 cm, and most affect the anterior dorsal tongue. The duration of the lesion was difficult to gauge, probably due to the asymptomatic nature of the process. Some tumors, however, were well documented to have been present for as long as 10–20 years. Histopathologically, the ectomesenchymal chondromyxoid tumor is characterized by a well circumscribed, but unencapsulated, lobular growth pattern. Varying degrees of cellularity are noted, with the lesional cells often set in a myxoid, chondroid or hyalinized background. Immunohistochemical studies reveal positivity of the lesional cells for antibodies directed against glial fibrillary acidic protein, cytokeratins, S-100 protein and CD-57 in the majority of tumors. Treatment consists of conservative surgical excision, and while recurrence is possible, it has been noted in <10% of reported cases.
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Keywords: neoplasm; tongue; benign

Introduction

In 1995, Smith *et al* provided the initial description of a benign neoplasm of the dorsal tongue that they termed 'ectomesenchymal chondromyxoid tumor (ECMT)'. Prior to the recognition of the lesion as a distinct entity, it was probably diagnosed as a variant of neurofibroma, cartilaginous choristoma, myoepithelioma, soft tissue myxoma, or a reactive process such as oral focal mucinosis or mucocele. The information that currently exists regarding ECMT is derived from the original report of 19 cases in addition to several small series of cases (Kannan *et al*, 1996; De Visscher *et al*, 2003; Kaplan *et al*, 2004) and a few isolated case reports (Van der Wal and van der Waal, 1996; Carlos *et al*, 1999; Ide *et al*, 2003; Goveas *et al*, 2006), all totaling 30 examples. With the advent of diagnostic immunohistochemical studies, identification of specific markers of molecular differentiation was possible, allowing pathologists to distinguish neoplasms such as this from other entities with similar histopathologic features.

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Clinical features

Most of these neoplasms have been identified on the anterior aspect of the dorsal tongue of an adult patient (Figure 1), and typically the lesions have been asymptomatic. Infrequently, the tumor has been documented on the posterior tongue (Carlos *et al*, 1999).

Affected patients have ranged in age from 9 to 78 years of age, with a median age of 39 years. The majority of tumors have been detected in the third through the sixth decades of life. No sex predilection has been noted. Most of the reports describing tumor size have indicated that the lesion measured between 1 and 1.9 cm (12 cases), while seven tumors were <1 cm in diameter, and five were 2 cm or greater in diameter.

Histopathologic features

On low-power microscopic examination, the ECMT typically appears as lobular sheets of cells that are usually demarcated from the surrounding skeletal muscle fascicles and connective tissue (Figure 2). In most cases, the lesion is unencapsulated, although loosely compressed connective tissue is often evident at the interface of the tumor and the adjacent normal tissue. Occasionally, muscle bundles appear to be entrapped by the neoplastic proliferation at the periphery of the tumor (Figure 3); however, extensive invasion of the adjacent normal tissue is not observed (Smith *et al*, 1995; De Visscher *et al*, 2003). Three characteristic histopathologic patterns are usually discernable in each of these tumors, including cellular, myxoid, and chondroid areas, and the proportions of these may vary from lesion to lesion.

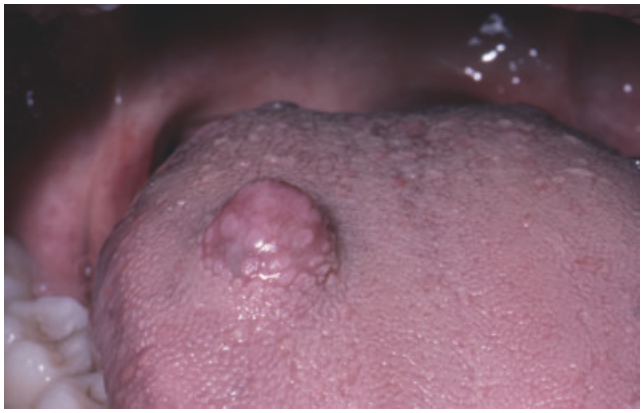

Figure 1 Characteristic clinical presentation of the ectomesenchymal chondromyxoid tumor, in this case affecting the anterior dorsal tongue of a 33-year-old man (Kannan *et al*, 1996)

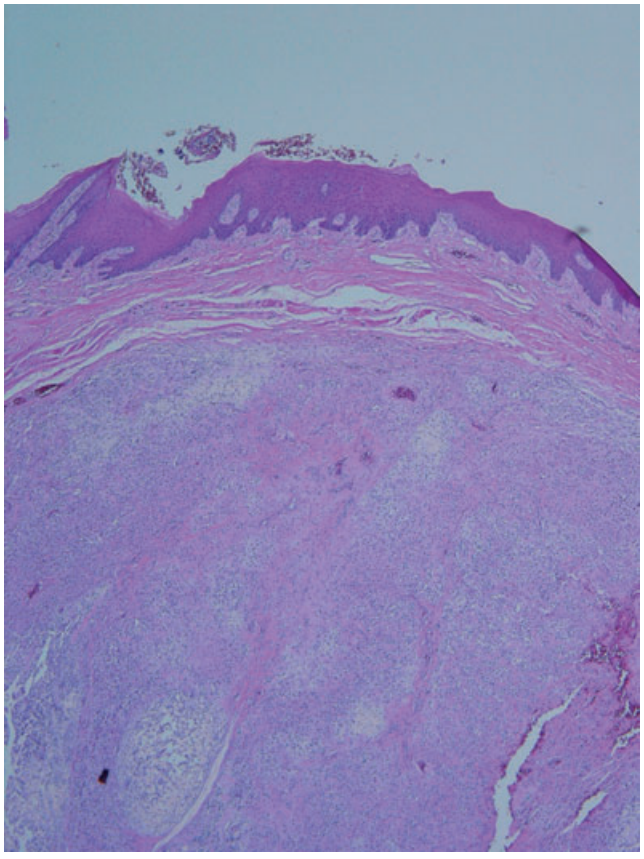

Figure 2 This low-power photomicrograph shows a relatively demarcated tumor mass in the superficial aspect of the dorsal tongue mucosa; hematoxylin and eosin, original magnification ×20

In the cellular regions, the lesional tissue is characterized by lobular collections of relatively uniform cells that contain moderate amounts of eosinophilic to faintly basophilic cytoplasm (Figure 4). Cytoplasmic boundaries may be indistinct. The cells can be round, polygonal, ovoid or fusiform in shape, depending on the area of the tumor that is examined (Figure 5). The nuclei are generally rather small and uniform, although

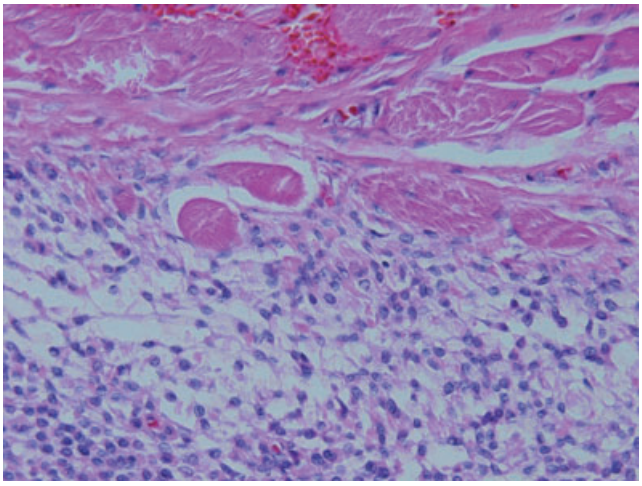

Figure 3 The lack of a well-developed capsule is seen in this photomicrograph that depicts lesional cells of the ectomesenchymal chondromyxoid tumor intermingling with adjacent fascicles of skeletal muscle; hematoxylin and eosin, original magnification ×100

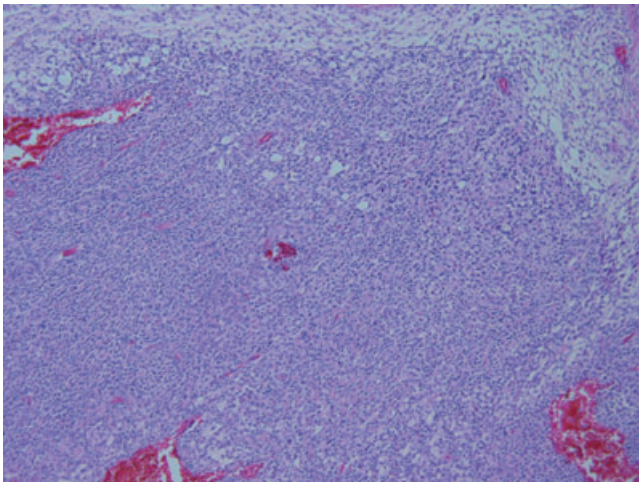

Figure 4 This medium-power photomicrograph demonstrates one of the more cellular zones of the ectomesenchymal chondromyxoid tumor; hematoxylin and eosin, original magnification ×50

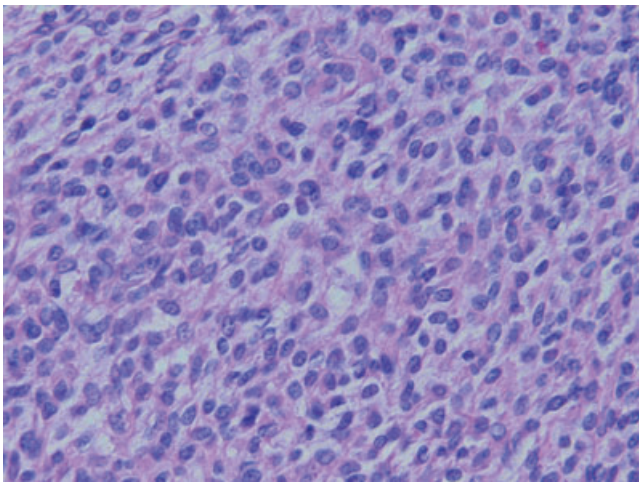

Figure 5 This high-power photomicrograph depicts one of the cellular areas of the tumor; hematoxylin and eosin, original magnification ×200

some lesions may have foci of nuclear atypia, characterized by variation in nuclear size, evidence of nuclear hyperchromatism, or the presence of binucleated or multinucleated cells. Nuclear inclusions and 'cup-shaped' nuclei have also been described (Smith *et al*, 1995). Nucleoli that are typically small and inconspicuous are seen in approximately half of the lesional cells. Mitotic figures are rarely observed.

In the myxoid zones, the lesional tissue is composed of spindle-shaped cells that are set in a background of glycosaminoglycans and delicate collagen fibers (Figures 6 and 7). In these myxoid regions, the tumor cells are often arranged as cords and strands that form a net-like or reticular pattern (Kannan *et al*, 1996).

In the chondroid areas, the lesional tissue is comprised an amorphous material with lacunae that contain the lesional cells (Figure 8). Sometimes the chondroid material is rather eosinophilic (Figure 9), but usually it has a basophilic staining quality (Figure 10). In most ECMTs, the chondroid component occupies a relatively modest portion of the tumor area histopathologically (De Visscher *et al*, 2003).

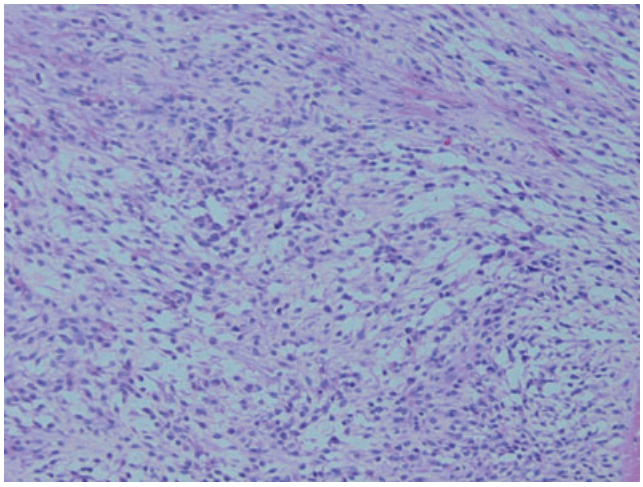

Figure 6 This medium-power photomicrograph demonstrates one of the more myxoid zones of the ectomesenchymal chondromyxoid tumor; hematoxylin and eosin, original magnification ×50

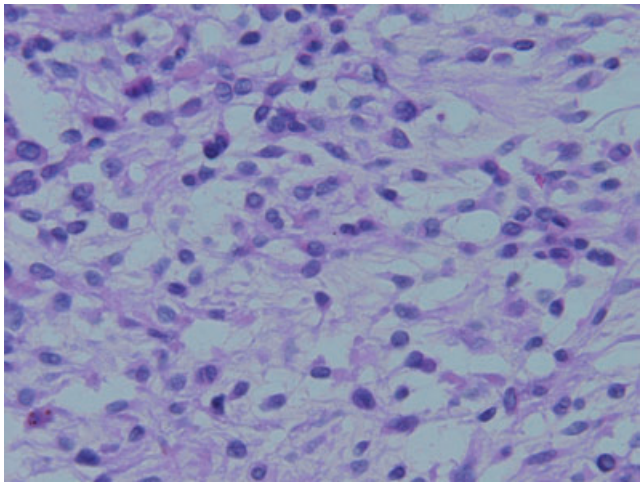

Figure 7 This high-power photomicrograph shows the spindle-shaped cells of the myxoid region; hematoxylin and eosin, original magnification ×200

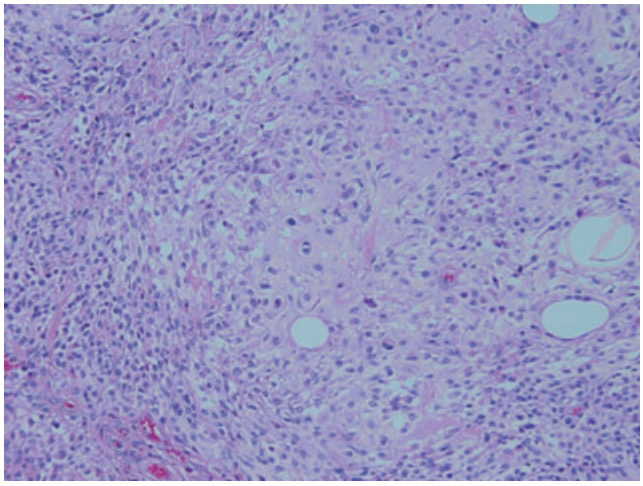

Figure 8 This medium-power photomicrograph demonstrates one of the more chondroid zones of the ectomesenchymal chondromyxoid tumor; hematoxylin and eosin, original magnification ×50

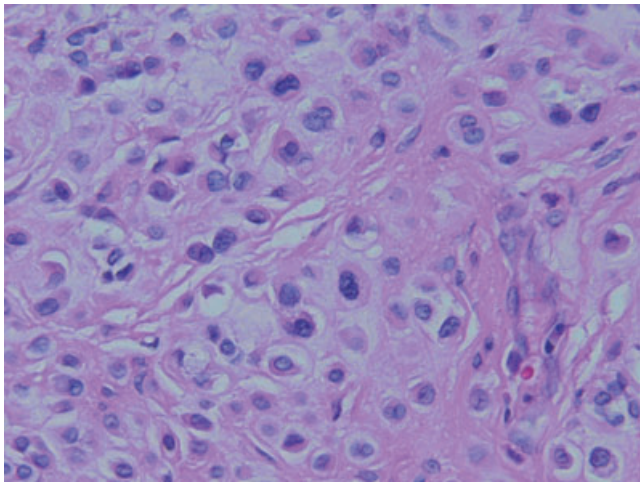

Figure 9 This high-power photomicrograph shows an eosinophilic chondroid pattern that is characterized by lesional cells set in lacunae; hematoxylin and eosin, original magnification ×200

The supporting stroma of the ECMT is generally unremarkable, with relatively few small-caliber blood vessels and partitioning of the tumor lobules by thin bands of fibrous connective tissue.

Histochemical features

While histochemical procedures are less frequently used to assist in the definitive diagnosis of ECMT, several groups have described characteristic findings with certain stains (Smith *et al*, 1995; Kannan *et al*, 1996; Van der Wal and van der Waal, 1996; Ide *et al*, 2003; Kaplan *et al*, 2004). Lesional cells did not stain with the periodic acid-Schiff method (Smith *et al*, 1995; Van der Wal and van der Waal, 1996; Carlos *et al*, 1999). The presence of acid mucopolysaccharides that were diffusely distributed

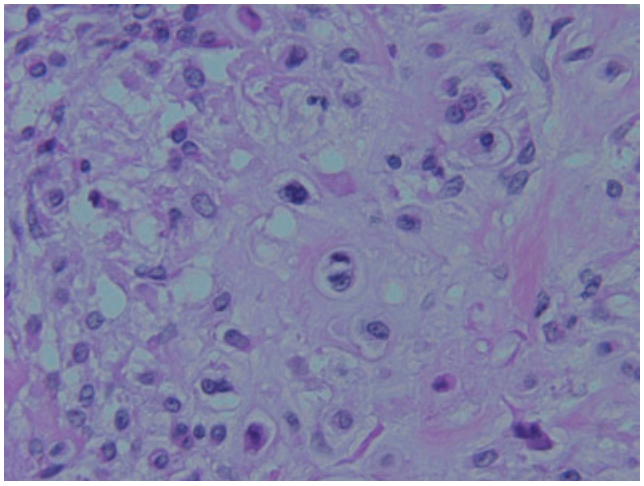

Figure 10 This high-power photomicrograph shows a more typical chondroid pattern with lacunar cells set in a more basophilic homogeneous material; hematoxylin and eosin, original magnification ×300

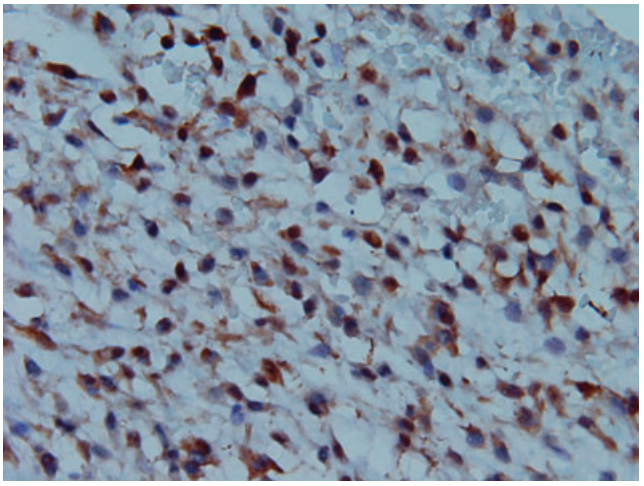

Figure 11 This high-power photomicrograph shows positivity of the lesional cells for antibodies directed against glial fibrillary acidic protein (GFAP); original magnification ×200

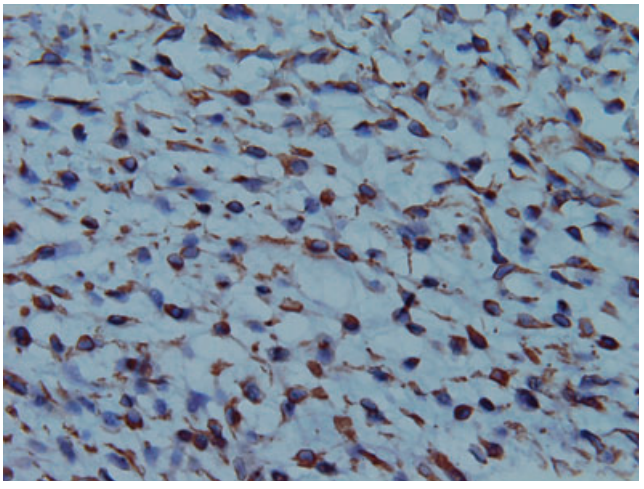

Figure 12 This high-power photomicrograph shows positivity of the lesional cells for antibodies directed against S-100 protein; original magnification ×200

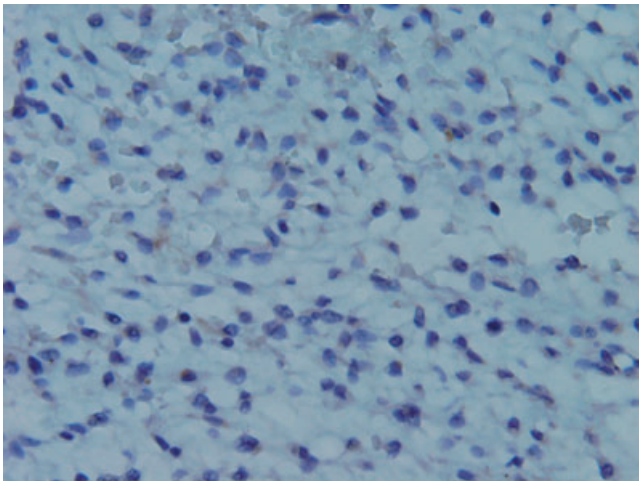

Figure 13 This high-power photomicrograph shows a lack of immunoreactivity of the lesional cells for antibodies directed against CD-57 in this particular tumor; original magnification ×200

was confirmed with aldehyde fuchsin staining (at pH 1.0 and 1.7) and with alcian blue staining (pH 0.4 and 2.5), and the intensity was not reduced after digestion with testicular hyaluronidase prior to staining (Smith *et al*, 1995; Kannan *et al*, 1996). Staining was particularly intense in the chondroid areas. One group reported that the more chondroid areas stained with alcian green (Kaplan *et al*, 2004), although mucicarmine staining also highlighted these areas (Smith *et al*, 1995). Masson's trichrome stain identified some collagen production within the lesion, but this was not a prominent feature in most of these tumors (Smith *et al*, 1995). Peculiar 'myxoglobulosis'-like bodies were described in one lesion, and these stained with both mucicarmine and alcian blue (Ide *et al*, 2003).

Immunopathologic features

The immunopathologic profile of the ECMT appears to be consistent with neural crest differentiation (De Visscher *et al*, 2003). Antibodies directed against glial fibrillary acidic protein (GFAP) (Figure 11) and S-100 protein (Figure 12), as well as vimentin, show a highly predictable pattern of positivity for the lesional cells (Kaplan *et al*, 2004). Antibodies directed against cytokeratins, CD57 (Leu-7), and smooth muscle actin can also identify immunoreactivity in approximately 40–75% of the cases (Figure 13). Antibodies directed against desmin and epithelial membrane antigen show immunoreactivity only sporadically. Antibodies directed against antigens associated with myoepithelial differentiation, such as calponin, smooth muscle myosin heavy chain, and p63, do not exhibit immunoreactivity with the lesional cells (Goveas *et al*, 2006).

Treatment and prognosis

Conservative surgical excision is the appropriate treatment for this benign neoplasm. Only two instances of

recurrence have been described, suggesting a recurrence rate of approximately 7%. Local re-excision proved to be curative for one of these lesions, but no follow-up information was given for the other tumor (Smith *et al*, 1995).

Discussion

Ectomesenchymal chondromyxoid tumor is a relatively rare benign neoplasm that was initially delineated by Smith *et al* (1995). To date, convincing examples of this tumor have been described involving only the tongue, with the majority of cases seen in the anterior tongue. Most of the reported patients have been adults, and no sex predilection has been noted. The tumor presents as a slow-growing submucosal nodule that is asymptomatic and non-tender on palpation.

The clinical differential diagnosis for ECMT primarily would include benign mesenchymal proliferations, such as focal fibrous hyperplasia, myofibroma, neurofibroma, granular cell tumor, schwannoma, leiomyoma, or rhabdomyoma. Given the lack of salivary gland tissue in the anterior dorsal tongue, a benign salivary gland tumor would not be a likely consideration.

The histopathologic differential diagnosis is more diverse and can include a variety of lesions with a myxoid component, such as oral focal mucinosis, nerve sheath myxoma/neurothekeoma, soft tissue myxoma, glial choristoma, and ossifying fibromyxoid tumor of soft parts. Tumors with a chondroid component also may enter into consideration, including cartilaginous choristoma and extraskeletal myxoid chondrosarcoma. Given the lack of salivary gland tissue in the anterior dorsal aspect of the tongue, it would be highly unlikely for a mucocele, myoepithelioma or pleomorphic adenoma to arise in this region. Nevertheless, these lesions have been mentioned as histopathologic diagnostic possibilities (Smith *et al*, 1995). Many reports of ECMT specifically state that no salivary gland tissue was identified in the sections (Smith *et al*, 1995; Van der Wal and van der Waal, 1996; De Visscher *et al*, 2003; Ide *et al*, 2003; Kaplan *et al*, 2004; Goveas *et al*, 2006).

The histogenesis of the ECMT remains speculative. The immunohistochemical profile suggests that this lesion has some relationship to the neural group of neoplasms, but whether it arises directly from neural cells in the tongue or from primitive mesenchymal cells that undergo neural differentiation during tumorigenesis remains unclear (Kaplan *et al*, 2004; Goveas *et al*, 2006). Currently, some investigators believe that this neoplasm is neither derived from, nor differentiates toward, a myoepithelial cell phenotype (Kaplan *et al*, 2004; Goveas *et al*, 2006); however, others feel that myoepithelial differentiation cannot be completely excluded (Woo *et al*, 2005).

Although one palatal tumor has been reported as representing an ECMT (Nigam *et al*, 2006), the appropriate documentation to support this diagnosis was not presented (Ide, 2006). Because the site of this particular lesion was so peculiar, convincing histopathologic and immunopathologic findings should have been documented in this report. No characteristic cellular zones were identified however, and no immunohistochemical studies were performed. For these reasons, the diagnosis of this lesion remains in doubt.

Conversely, the prevalence of ECMT may be greater than what is currently accepted (De Visscher *et al*, 2003). For instance, some reports of 'pleomorphic adenoma' or 'myoepithelioma' involving the tongue may actually represent examples of ECMT (Ide *et al*, 2003). Although the example described by Rogers *et al* (1989) involved the ventral tongue of a 12-year-old girl, and therefore could have been a pleomorphic adenoma, the description of the histopathologic features was very suggestive of ECMT. Another example identified by Ide *et al* was reported as a myoepithelioma that clinically was a submucosal nodule of the anterior dorsal midline of the tongue in a 65-year-old man (De Las Casas *et al*, 2001). One of the photomicrographs showed intermingling of the lesional cells with adjacent fascicles of skeletal muscle, a feature more commonly associated with ECMT than myoepithelioma. The lesional cells were diffusely and intensely immunoreactive for antibodies directed against S-100 protein, while more focal immunoreactivity was seen with antibodies directed against GFAP and muscle-specific actin. The authors also mentioned that no salivary gland tissue was identified in the sections. In a series of five tumors reported as pleomorphic adenomas occurring in juveniles, one of these lesions was found in the tongue of an 18-year-old female (Jorge *et al*, 2002). Minimal clinical or immunopathologic information was reported, however, the authors noted that the tongue lesion was the only one that was unencapsulated. Tanigaki *et al* (2004) described what they believed to be a pleomorphic adenoma of the lateral tongue, although their clinical photograph suggested that it involved the dorsum of the tongue as well. Cytokeratin positivity and S-100 negativity suggested to the authors that this lesion was not a chondroma. No mention was made of the histopathologic features, although one might conclude from their histopathologic differential diagnosis that chondroid areas were present. Furthermore, no mention of other immunohistochemical reactions was made. The photomicrographs that appear in the manuscript show a demarcated tumor that is unencapsulated in some areas. In addition, no evidence of ductal structures is seen, thus raising the question as to whether this might actually be an ECMT.

In conclusion, it is important to distinguish this interesting, unusual neoplasm from other potentially significant tumors that could develop in the submucosa of the dorsal tongue so that an appropriate conservative approach to surgical excision will be made.

Author contributions

Dr Carl M Allen wrote the entire manuscript and took both the clinical photograph and the photomicrographs used in the submission.

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