Ectomesenchymal Chondromyxoid Tumour of the Tongue. A Review of Histological and Immunohistochemical Features

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Abstract. *Background*: *Ectomesenchymal chondromyxoid tumour (ECT) is a rare, benign neoplasm of uncertain histogenesis, which appears to exclusively involve the oral cavity, particularly the tongue. Case Report: We report the case of a 27-year-old woman with a 0.7 cm tumoral lesion of 3 months' duration on the dorsum of the tongue. Histologically, it comprised well-circumscribed, unencapsulated lobular proliferations of fusiform and polygonal cells, with varying degrees of cellularity, with neoplastic cells often set in a myxoid, chondroid or hyalinized background. Immunohistochemistry revealed positivity of the neoplastic cells for antibodies directed against S-100, glial fibrillary acidic protein and vimentin, plus negativity for CD-57(leu-7), epithelial membrane antigen, smooth muscle actin, desmin and cytokeratin AE1-AE3. The diagnosis was consistent with ECT. Total excision was performed and there has been no recurrence after 10 months' follow-up. Conclusion*: *This is the 37th case reported in the English language literature; ECT is characterized microscopically by a biphasic myxoid and chondroid pattern. Immunohistochemical expression of S100, glial fibrillary acidic protein and vimentin, very helpful in confirming diagnosis, suggest a probable mesenchymal and neural origin of this rare entity.*

Ectomesenchymal chondromyxoid tumors are extremely uncommon. The first report was by Smith *et al*. (1) in 1995, who described a unique chondromyxoid lesion they called "ectomesenchymal chondromyxoid tumor" (ECT). ECT occurs almost exclusively in the anterior tongue, and only 37 cases have been reported to date, including the present one (1-13). Most documented lesions have affected the (anterior) tongue; however one palatal tumour has been described (3).

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Clinically, ECT presents as slow-growing, painless, firm, well-circumscribed nodules of the anterior dorsal tongue in the submucosa, covered by normal oral mucosa; the duration ranges from a few months to several years. Patients have reported minor local complaints, including local pressure and purulent discharge rarely; These lesions have ranged in size from 0.3 to 2.0 cm, in patients aged 9 to 78 years (2, 3, 9), with no predilection for either sex (2, 3). Diagnosis of ECT is based on the clinical, light microscopic, and immunohistochemical aspects.

We present an additional case of ECT and review the histological and immunohistochemical features of all previously reported cases, thus enabling pathologists to distinguish neoplasms such as this from other entities with similar histopathological features.

Case Report

A 27-year-old woman was referred for evaluation of a swelling of the anterior dorsum of the tongue with a 0.7 cm tumoural lesion of 3 months' duration. Clinical examination revealed a nodular, firm, mobile mass. Her medical history was otherwise non-contributory.

The lesion was completely excised under local anaesthesia. The histology was reported as ECT, and the patient remains well with no evidence of recurrence 10 months after surgery.

Histopathology. The surgical specimens were fixed in 10% buffered formalin and embedded in paraffin.

Histopathological examination of the excised lesion demonstrated a well-circumscribed multinodular tumour located within the connective tissue and striated muscle, extending to the overlying mucosa. Within the lesion, cartilaginous differentiation was noted. The lesion was composed of ovoid to spindle-shaped cells in a myxoid stroma (Figure 1). Chondroid differentiation was noted in some areas (Figure 2).

Immunohistochemistry. Immunohistochemical analysis was carried out with antibodies directed against pancytokeratins, vimentin, S100 protein, desmin, smooth-muscle actin (SMA), epithelial membrane antigen (EMA) and glial fibrillary acidic protein (GFAP) through an avidin-biotin-peroxidase method. Positive and negative controls were included in all reactions, following the manufacturer's indications (Table I). Slides were evaluated for intensity of staining and proportion of tumour cells stained.

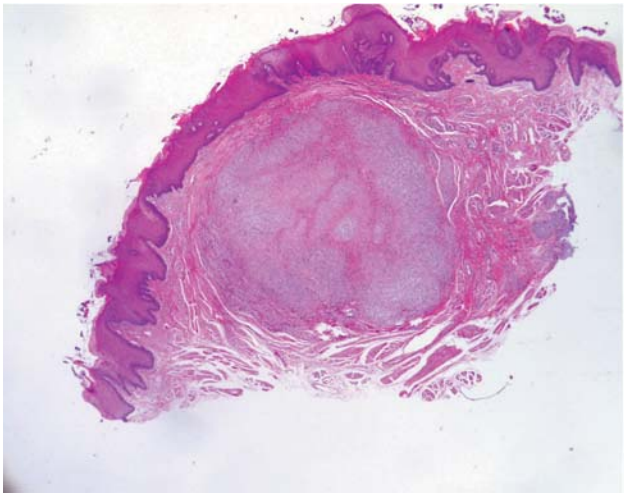

Figure 1. *Low-power photomicrograph showing a demarcated tumour mass in the superficial aspect of the dorsal tongue mucosa (haematoxylin-eosin, original magnification ×20).*

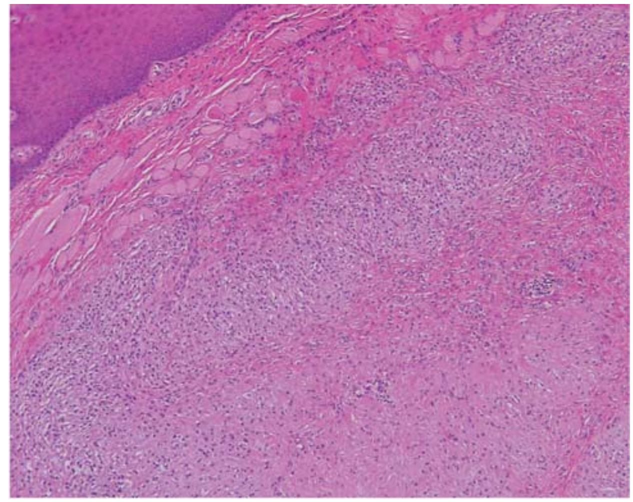

Figure 2. *Photomicrograph showing the underlying connective tissue, containing an infiltrating tumour composed of lobules of small cells exhibiting uniform ovoid to spindle-shaped nuclei set in pale-staining eosinophilic cytoplasm. Small collections of larger cells containing foamy cytoplasm are also visible. The lesional stroma is diffusely myxoid in appearance. In some areas, the cells appear to be set in lacunae, chondroid cells (haematoxylin-eosin, original magnification ×40).*

Table I. *Immunohistochemical findings.*

Marker	Clone	Dilution	Antigen retrieval	Source	Results	Country
S100	Polyclonal	1:1000	None	Dako	+	Denmark
GFAP	Polyclonal	1:4000	None	Dako	+	Denmark
CKs	AE1/AE3	1:50	Microwave citrate ph 6	Dako	_	Denmark
VIMENTIN	V9	1:100	None	Dako	+	Denmark
SMA	1A4	1:100	None	Dako	_	Denmark
CD57 (LEU-7)	TB01	1:40	None	Dako	_	Denmark
DESMIN	D33	prediluted	Microwave citrate ph 6	Neomarkers	_	United Kingdom
EMA	E29	1.50	None	Dako	_	Denmark

CKs, Cytokeratins; EMA, epithelial membrane antigen; SMA, smooth muscle actin; GFAP, glial fibrillar acid protein.

Results

The immunohistochemical findings are summarized in Table I. Positive reactivity was seen for S-100 (Figure 3), GFAP (Figure 4) and vimentin (Figure 5). The tumour cells were negative for cytokeratins AE1/AE3, SMA, desmin, EMA, and CD57 (Leu-7).

Discussion

ECT is a rare benign neoplasm. To date, 37 cases of this tumour have been described, all of them involving the tongue, generally the anterior tongue. One single palatal case has been reported as an ECT (3); however, since the immunohistochemical profile was not presented, we exclude it from this review.

Given the rarity of this neoplasm, differential diagnosis for ECT from the histological standpoint is not straightforward. The first two disease entities to be included in differential diagnosis are myoepithelioma and myxoid neurofibroma. Although myoepithelioma and ECT share some common features, the anatomical localization, as well as the clinical and microscopic absence of salivary glands adjacent to ECT, are useful to distinguish these two lesions (10). Myoepithelioma also usually presents several different cellular patterns within the same tumour, including plasmacytoid cells, which have never been described in ECT, and moreover it rarely shows muscle fibres infiltrated by the

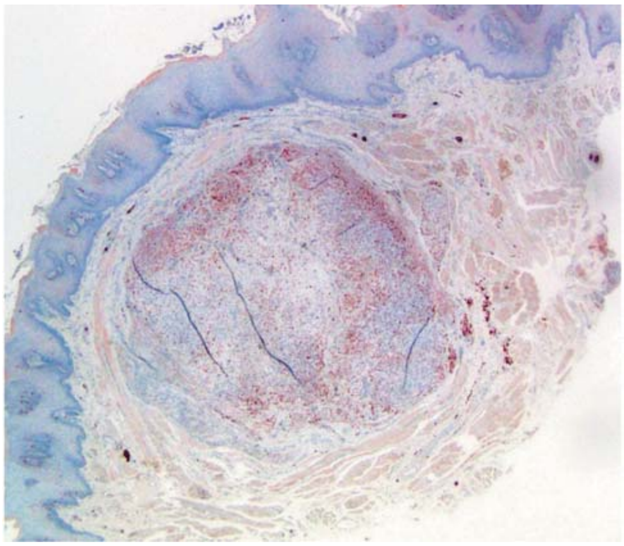

Figure 3. *Immunohistochemical expression of S-100 shows strong positivity of the lesional cells (original magnification ×20).*

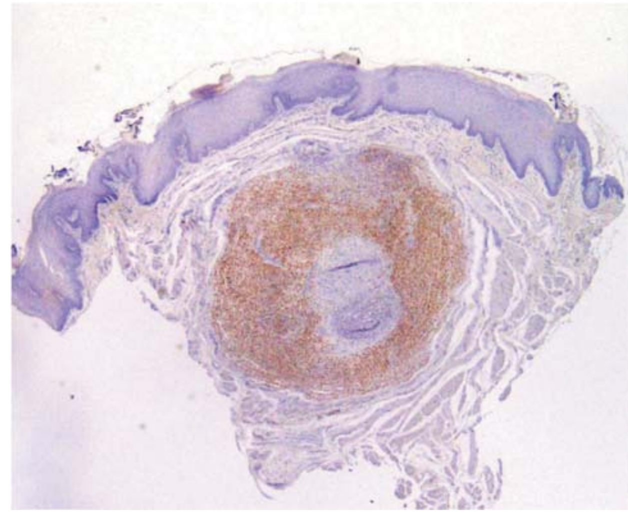

Figure 4. *Immunohistochemical expression shows positivity of the lesional cells for antibodies directed against glial fibrillary acidic protein (GFAP) (original magnification ×20).*

tumour cells, whereas this has been reported in some cases of ECT. Additionally, myoepithelioma is commonly positive for α-smooth muscle actin, which is expressed in only about 30% of ECT (1, 10, 14). Myxoid neurofibroma is the other main differential diagnosis tumour type, even though the cytomorphology of cells, with wavy nuclei in the neurofibroma, as well as the atypia or chondroid areas, are not found in myxoid neurofibromas; however, both lesions express vimentin, S100 protein, and GFAP (1, 4, 9, 15). Soft-tissue myxoma also enters into the differential diagnosis, but does not present chondroid areas. Ossifying fibromyxoid tumour can also show myxoid but not chondroid areas, and presents peripheral deposition of bone that is not seen in ECT. Another differentiation to be made is *versus* that of extraskeletal myxoid chondrosarcoma, which usually shows more evident areas of cellular atypia. Glial choristoma, though sometimes manifesting in the same anatomical region, has a glial component not seen in ECT. Chondroid choristoma possesses an abundant chondroid component that, unlike ECT, is mature and well-formed, with no atypia or myxoid areas, eventually showing trabecular bone deposition (9). Peripheral nerve sheath myxoma (neurotekeoma) does not present the chondroid pattern seen in ECT (1, 4, 9) In all cases, the histological and immunohistochemical profile is of considerable help in clarifying the differential diagnosis.

The histological appearance of our case is similar to those of other case reports, the tumour being composed of small, well-circumscribed nodules of spindle cells in a chondromyxoid stroma. While the immunohistochemical profiles of the published cases show some variation (Table 1), most cases demonstrate consistent positivity for S100, desmin and AE1/AE3.

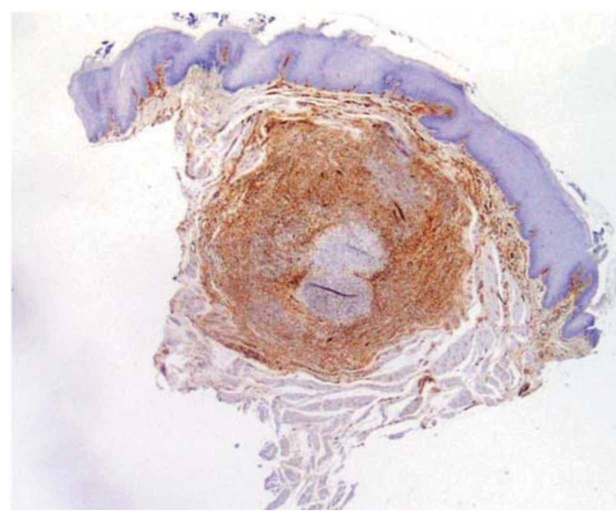

Figure 5. *Immunohistochemical expression shows strong immunoreactivity of the lesional cells for antibodies directed against vimentin (original magnification ×20).*

The present case showed strong GFAP, S-100, and vimentin positivity. We observed immunoreactivity for GFAP, in line with other studies (1, 5, 7, 9, 13). Seckin *et al.* reported that expression of GFAP was detected in a few tumour cells in their case (11), but without widespread or strong staining, as indicated in many other case reports, for instance those by Smith *et al.* (1), Kaplan *et al.* (5), and Goevas *et al.* (1). Smith *et al.* Reported that the reactivity with polyclonal anti-GFAP antibody was intense in all tumours in their series; however, monoclonal anti-GFAP antibody reacted in only 73%. From the

Table II. *Immunohistochemical features of ectomesenchymal chondromyxoid tumour.*

Authors (ref.)	n	S100	GFAP	CKs	Vimentin	SMA	LEU-7	Desmin	EMA
Smith *et al*. (1) n=19	19	9	13	12	NP	7	8	0	0
Kannan *et al*. (9) n=3	3	3	3	0	3	0	3	1	0
Van der Wal and van der Waal (10) n=1	1	1	1	0	1	0	0	0	0
Carlos *et al*. (8) n=1	1	1	1	NP	NP	NP	NP	NP	NP
De Visscher *et al*. (7) n=2	2	2	2	0	2	0	NP	1	NP
Ide *et al*. (6) n=1	1	1	1	0	1	0	1	NP	NP
Kaplan *et al*. (5) n=1	1	2	2	0	0	0	0	0	0
Woo *et al*. (4) n=1	1	1	0	1	1	0	1	0	0
Goveas *et al*. (2) n=1	1	1	1	0	1	0	0	0	0
Nigam *et al*. (3) n=1	1	NP	NP	NP	NP	NP	NP	NP	NP
Seckin *et al*. (11) n=1	1	1	1	0	1	0	1	NP	NP
Portnof *et al*. (12) n=1	1	1	1	0	1	1	0	NP	0
Pires *et al*. (13) n=3	3	3	3	2	3	1	NP	0	NP
Present case. n=1	1	1	1	0	1	0	0	0	0
Total	37	36	36	35	16	35	30	32	28
Total positive		27	30	15	15	9	14	2	0
% (Total positive/Total n)		75.0%	83.3%	42.9%	93.8%	25.7%	46.7%	6.3%	0.0%

NP, Not performed; CKs, cytokeratins; EMA, epithelial membrane antigen; SMA, smooth muscle actin; GFAP, glial fibrillar acid protein.

data reported in Table II, it appears that there was 75% positivity of cases to S100, 83.3% to GFAP and 93.8% to vimentin.

Since its initial identification, some controversy has surrounded the histogenesis of ECT. Smith *et al*. (1), proposed two possible histogenetic origins: from the minor salivary glands, or from pluripotent ectomesenchymal cells of neural crest origin. This latter hypothesis proposes that pluripotential ectomesenchymal cells are capable of differentiating into either cartilaginous or peripheral nerve structures. Others have suggested that the origin is from the minor salivary glands, although this hypothesis has generally been rejected on the grounds that the commonest location of the tumour, the dorsal anterior part of the tongue, is generally devoid of salivary glands (14).

Other reports point to the clinical, histological, and immunohistochemical similarities between ECT and soft-tissue myoepithelioma (4), supporting the theory that myoepithelioma and ECT are variations of the same entity. Others have proposed a myogenic origin of ECT, since many of the lesions reported have been found to spread among muscle fibres. However, the immunohistochemical features of these lesions do not support this theory. To date there is still no consensus regarding the histogenesis of ECT.

Treatment consists of conservative surgical excision, and while recurrence is possible, it has only been noted in <10% of reported cases (14). Recurrence of the tumour has been reported to occur up to 19 months after the original resection (9). Our patient is symptom-free 10 months after surgery; she will continue to be monitored closely with follow-up visits every 6 months.

In conclusion, ECT is an uncommon intraoral asymptomatic mesenchymal soft tissue neoplasm located on the dorsum of the tongue. Thirty-seven cases have been reported to date, including the present one. ECT is characterized microscopically by a biphasic myxoid and chondroid pattern. Immunohistochemical expression of S100, GFAP and vimentin is very helpful in confirming diagnosis, suggesting a probable mesenchymal and neural origin of this rare entity.

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