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Case Report

Cribriform Adenocarcinoma of Minor Salivary Gland Origin: A Case Report with Emphasis on Differential Diagnosis

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Abstract: Cribriform adenocarcinoma of minor salivary glands [CAMSG] is a recently defined neoplasm mostly, but not exclusively involving the base of the tongue. Other sites involved are minorsalivary glands present in the oral cavity. CAMSG histopathologically resembles papillarycarcinoma of the thyroid gland because of the characteristic nuclear appearance but, is consistently negative with both thyroglobulin and TTF-1. It is a distinct tumor entity that can also be differentiated from polymorphous low-grade adenocarcinoma by its location, cytology, histological architecture, and behavior, with frequent metastases at the time of presentation. It also holds a record of having a better prognosis amongst salivary gland tumors. All the factsadds up the uniqueness of CAMSG among the low-grade salivary gland tumors.
Keywords: papillarycarcinoma, salivary gland, thyroglobulin

INTRODUCTION

Michal et al in 1999, described a low grade salivary gland tumour as “Cribriform adenocarcinoma of the tongue” based on a small series of eight tumours, all involving the tongue[1]. World Health Organization[WHO] in 2005 had recognized this lesion as a possible variant of polymorphous low-grade adenocarcinoma.[2] Soon case reports with a similar pattern of presentation started to be described at sites other than tongue. Skálová et al. in 2011, published alarge case series, comprising 23 new such cases among more than 5000 salivary gland tumours from their archives.[3] Their study proved this lesion to be a distinct tumor entity that differs from polymorphous low-grade adenocarcinoma by location, cytology, histologic architecture, and behaviour, and they had proposed the term, Cribriform adenocarcinoma of minor salivary gland origin, CAMSG. This tumor mostly occurs in the posterior tongue, and the frequency of cervical lymph node metastasis at presentation is very high [74%].[4] However, despite frequent positive nodal status, the prognosis of CAMSG appears favourable. Morphologically, they are low-grade salivary gland tumors strikingly characterized by the optically clear nuclei resembling those of papillary thyroid carcinoma. The tumours exhibit diverse histologic architecture, often dominated by cribriform and solid growth patterns. Immunohistochemically, CAMSG shows strong expression of cytokeratin, vimentin, and S-100 protein, and variable expression of basal ormyoepithelial cell markers such as smooth muscle actin, calponin, and p63 protein. Many earlier cases of CAMSG had been previously reported as polymorphous low-grade adenocarcinoma. Mucoepidermoid carcinoma, adenoid cystic carcinoma, cystadenocarcinoma, low-grademyoepithelial carcinoma, and adenocarcinoma not otherwise specified.[3] Recognition of CAMSG is important because of its clinical course, which differs from that of other salivary gland tumours.

This case report is another one such example, where the lesion was initially diagnosed as sclerosing mucoepidermoid carcinoma. But later investigations, proved it to be CAMSG, further adding to the few reported cases of this unique and rare presentation.

CASE REPORT

A 43 year old diabetic female patient reported with a complaint of swelling in the left retromolar trigone area, since 2 months. It had started as a small growth which rapidly grew into the then current size. Other than diabetes she had a history of myotonic dystrophy for which she was under treatment for about 5 years. On her family side, she had a paternal aunt, who had diedof oral cancer. On examination there was an ulcero proliferative growth on the left retromolar trigone area of size 3.5* 3cm extending to anterior faucial pillar and soft palate. figure 1.There was also the presence of lesions on dorsal aspect of tongue, suggestive of geographic tongue. An MRI examination revealed a heterogenous post contrast enhancement in left retromolar trigone region, along with a single peripherally enhancing necrotic level 2 cervical lymphnode. A previous incisional biopsy had been done and a diagnosis of sclerosing mucoepidermoid carcinoma was given. A wide excision of the lesion was carried out at our surgery department under local anaesthesia. The lymph node was excluded from surgery due to expected complications associated with patient's history of myotonic dystrophy.

Microscopy

The gross examination showed a firm soft tissue mass. Figure 2 Cut section showing a white tan unencapsulated proliferative mass devoid of hemorrhage and necrosis. Histopathological examination showed an infiltrating tumor composed of minimally pleomorphic basaloid cells with a prominent papillary and solid growth patterns, and areas with tubular [ductal] differentiation. Cytologically the tumor was composed of a single cell type. The cytoplasm showing oxyphilic property, containing pale, vesicular nuclei with a ground-glassquality. The nuclei showed overlapping and grooving, similar to papillary carcinoma of the thyroid. Necrosis and hemorrhage were not appreciated; mitotic figures and psammoma bodies were also not found. Figure 3, 4The characteristic nuclear appearance and lack of histological diversity helped us exclude polymorphous low grade adenocarcinoma and consider cribriform adenocarcinoma of minor salivary gland origin or metastatic papillary thyroid carcinoma as differential diagnosis.

Immunohistochemistry

Tumor showed strong immunoreactivity to cytokeratin marker CK 7 and S-100 protein and negative to thyroglobulin antibodies. Thereby ruling out papillary thyroid carcinoma and reach conclusive diagnosis of cribriform adenocarcinoma of minor salivary gland origin. Fig 5, 6

Discussion

Cribriform adenocarcinoma of the tongue was described first in 1999 by Michal et al.[1]Though the earlier WHO classification had considered this lesion as a possible variant of PLGA, subsequent case reports describing lesions affecting minor salivary glands at multiple oral sites, has prompted authors to consider it as a distinct tumor. Currently it is known as Cribriform adenocarcinoma of minor salivary gland, CAMSG and considered a strong candidate to be included in the next WHO salivary gland tumor classification.[5] All the cases reported so far have been seen in adults, within quite a broad age range of 25 to 70 years. Recently the lesions has been consistently described in reviews of new salivary gland tumors, but the number of reports remains still low.[6]

A total of 43 cases have been previously reported as CAMSG. Amongst these 23 cases occurred in females, 16 in males and the rest were not specified. The neoplasm most commonly involved the tongue [32 cases] but other sites were also reported including soft palate, retromolar trigone, upper lip, floor of the mouth, the epiglottis and lingual tonsils. A total of 32 of the 43 cases reported in the literature [74%] showed cervical lymph node metastasis. Interestingly, distant metastatic disease has never been reported. [7,8]Grossly, the tumors are unencapsulated, white-tan to grey in color, and hard inconsistency with no areas of necrosis and hemorrhage.[9]The histological structure is quite characteristic with cribriform, tubular, glomeruloid or solid areas in variable proportions, separated by fibrous tissue. The most prominent feature of the tumors, however, is the appearance of the nuclei. These often overlap one another, and are pale, optically clear and vesicular. Rarely, solid areas composed of these cells with ground glass appearance nuclei may be present. Cellular atypia is mild and mitotic figures are in most cases are. Generally, there are one to three small inconspicuous nucleoli. The cytoplasm may be clear to eosinophilic. Cytologically, all the tumors are composed of one cell type. The overall morphology of the tumor, particularly with focal papillary growth and with overlapping clear, "Orphan Annie eye–like nuclei", is remarkably similar to various variants of papillary thyroidcarcinoma. The cervical lymph node metastases have usually identical appearances to theprimary tumors. Presence of mucinous-spindle cell myfibroblastic stromal septa composed of mucinous matrix and rare spindle cell myofibroblasts, seen mostly in early infiltrative foci has also been reported. Psammoma bodies, however, are not a typical feature[9]. The distinction from both metastatic and ectopic thyroid carcinoma is important exacerbating the potential for misdiagnosis as metastatic papillary thyroid carcinoma [PTC], which has led to unnecessary thyroidectomies. It has been suggested that the Cribriform adenocarcinoma might originate from thyroid tissue remnants, which are frequent in this location. However, CAMSG lacks the cysts and deeply eosinophilic colloid associated with PTC and reliably stains negative for TTF-1 and thyroglobulin markers and positive for cytokeratin, smooth muscle actin, and S-100 protein.[6, 10]Another lesion to be included in

the differential diagnosis is adenoid cystic carcinoma, which rarely, has been reported in the tongue.[11, 12] Adenoid cystic carcinoma may be even morecribriform than seen in CAMSG, and the cytological features are altogether unalike, displaying smaller cells and dark nuclei. Due to highly aggressive nature of this lesion, an attentive differential diagnosis is required. The lesion also bears histological similarity to polymorphous low-grade adenocarcinoma[PLGA] of the salivary gland, complicated with the immunohistochemical profile with expression of epithelial markers, vimentin, and S-100 protein in both lesions. But PLGA has characteristic target-like concentric whorls and single-file columns of cells, and the diverse histological pattern can be differentiating features. The authors of the WHO classification, earlier had felt cribriform adenocarcinoma insufficiently separated from polymorphous low-grade adenocarcinoma to merit a separate rubric.[2,13] also the frequency of lymph node metastases is higher in cribriform adenocarcinoma. On the other hand, distant spread was not described, and the long-term prognosis seems to be good, in any case not worse than in polymorphous low-grade adenocarcinoma[14, 15].

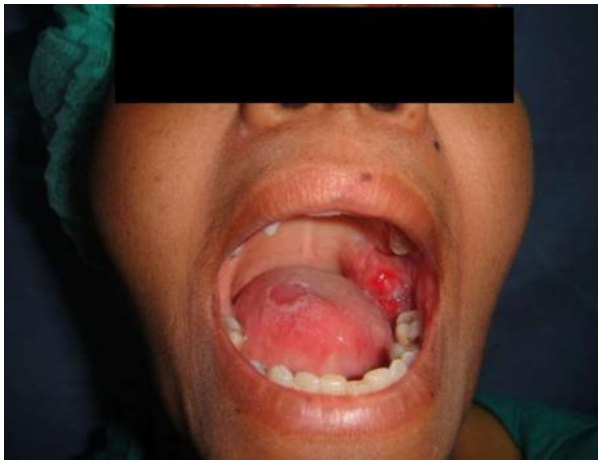

Fig-1: Showing the ulceroproliferative growth in the left retromolar trigone area, extending to anterior faucial pillar and soft palate

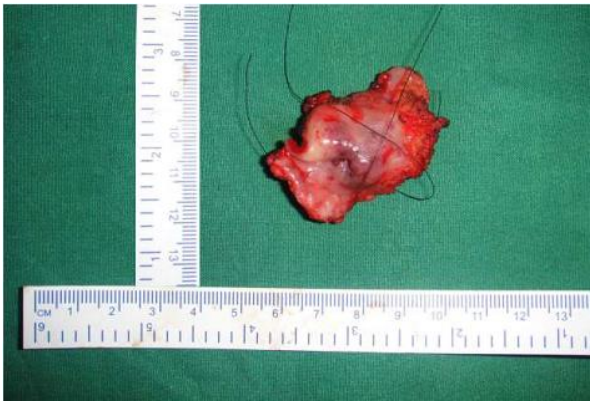

Fig-2: Surgical specimen

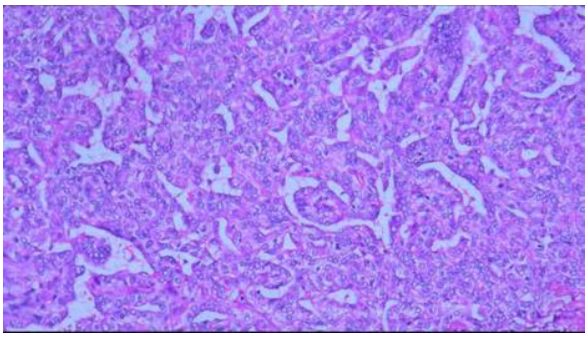

Fig-3: H & E stained section showing infiltrating tumor composed of minimally pleomorphic cells with a prominent papillary growth pattern [10x]

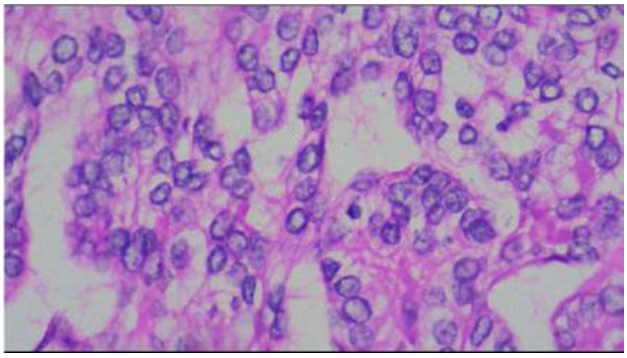

Fig-4: Cytologically similar cells showing characteristic ground glass nuclei [H&E40x]

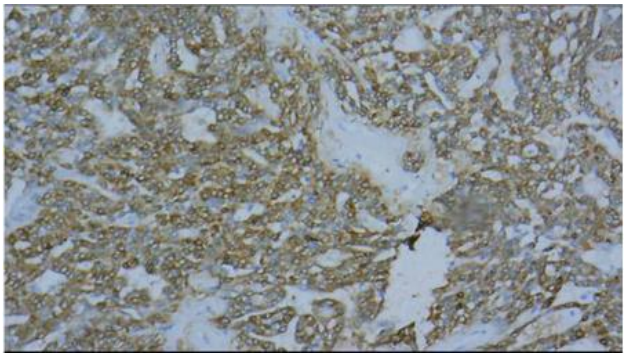

Fig-5: Tumor cells showing strong positivity for S-100 [10x]

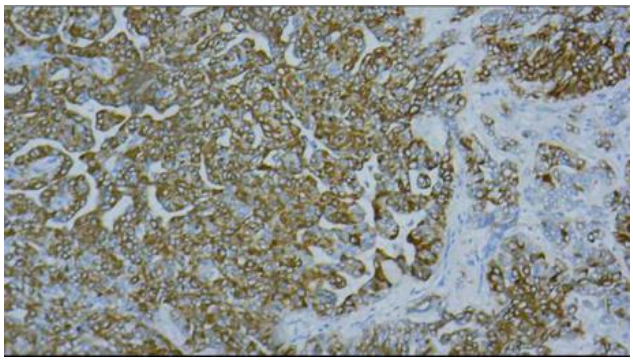

Fig-6: Tumor cells showing strong positivity for CK-7[10x]

CONCLUSION

CAMSG is a rare and unique low grade salivary gland neoplasm which is currently identified as separate entity. This case report is intended to increase the understanding of this particular unique low grade salivary gland neoplasm, in particular when there are only still a few cases reported in the current scientific literature. The present case is unique for its many reasons including:-

- For its site of presentation, i.e. retromolar trigone area, where only two previous cases have been reported.
- Prominence of papillary growth pattern rather than a cribriform pattern
- And the rarity of the lesion itself.

Recognition of CAMSG is important because of its clinical course, which differs from that of other salivary gland tumors and so does the prognosis.

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