

# Cribriform adenocarcinoma of minor salivary gland: A mimic of polymorphous low-grade adenocarcinoma

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## INTRODUCTION

Cribriform adenocarcinoma of the tongue is a rare entity described in the literature and has been renamed as cribriform adenocarcinoma of minor salivary glands (CAMSG).

Adenocarcinoma is relatively less common on the tongue.<sup>[1]</sup> Polymorphous low-grade adenocarcinoma (PLGA) is a malignant tumor of minor salivary glands which is slow growing and carries a low metastatic potential. Histologically, PLGA exhibits a spectrum of growth patterns such as cribriform, tubular, trabecular, fascicular and solid structures. Concentric whorls forming target-like patterns are noted as prominent finding. The nuclear features appear to be bland. Invasion of the perineural spaces and other adjacent tissues is typical. Despite this invasive growth pattern of PLGA, the overall prognosis remains to be favorable.<sup>[2,3]</sup>

Regional lymph node metastases have been observed in the reported case series on PLGA. In addition, papillary growth pattern was prominent in those cases which show nodal metastases.<sup>[4,5]</sup>

In 1999, a series of adenocarcinoma of posterior tongue and retromolar region were reported. These adenocarcinoma cases were characterized by synchronous metastases to the lateral neck lymph nodes, but there was no distant spread; these cases were then designated as cribriform adenocarcinoma of the tongue (CAT).<sup>[6]</sup> CAT was recognized as a variant of PLGA by the latest issue of the WHO classification (2005);<sup>[3]</sup> at the

same time; it was not clear whether CAT represented a genuine separate entity.

Subsequently, over the years, new series of such cases (CAT) arising from minor salivary glands other than in the tongue were reported.<sup>[6]</sup> Thus, CAT was renamed as cribriform adenocarcinoma of the minor salivary gland (CAMSG).<sup>[7]</sup>

At present, CAMSG is considered to be a distinct entity that differs from PLGA by location, histologic architecture, cytology and behavior, with frequent metastases at initial presentation of the primary tumor. A total of 33 cases have been reported in English literature.<sup>[1,6-10]</sup> Here, we present a case of CAMSG arising from lateral tongue, which was a mimic of PLGA.

## CASE REPORT

A 55-year-old female reported to the Outpatient Department with a chief complaint of a swelling on the right lateral border of the tongue, which she noticed 15 days before. The swelling was of primary incidence and sudden in onset. There was no history of biting the tongue. Furthermore, the swelling was neither associated with pain nor showed any bleeding tendency. There was no difficulty in eating, speaking or swallowing. The history included hypertension for which she was on medication since 2 years. Regional lymph nodes were not positive.

Intraoral examination revealed the presence of a soft tissue growth, measuring 2 cm in greatest dimension

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with multilobular appearance [Figure 1]. A provisional diagnosis of irritational fibroma was given. The lesion was completely excised and submitted for pathological evaluation.

Histopathology of the surgical sample revealed a partially encapsulated lesion with lobular configuration of cribriform nests separated by fibrous septa [Figure 2]. Solid mass of tumor cells was a feature at places. The cribriform pattern and solid areas of tumor cells were in variable proportions. Intermingled tubular pattern was noticed. The glands were found to be fused back to back, and focal papillary and pseudopapillary projections were observed [Figure 3]. The glands of the lesional tissue showed cuboidal cells. The cytoplasm was eosinophilic with focal vacuolation. The nuclei were found to be oval, with granular chromatin. In addition, the overlap of the nuclei was noticed [Figure 3]. Cytologic atypia was mild, and mitotic activity was minimal.



**Figure 1:** Clinical photograph showing lobulated lesion on right lateral border of the tongue

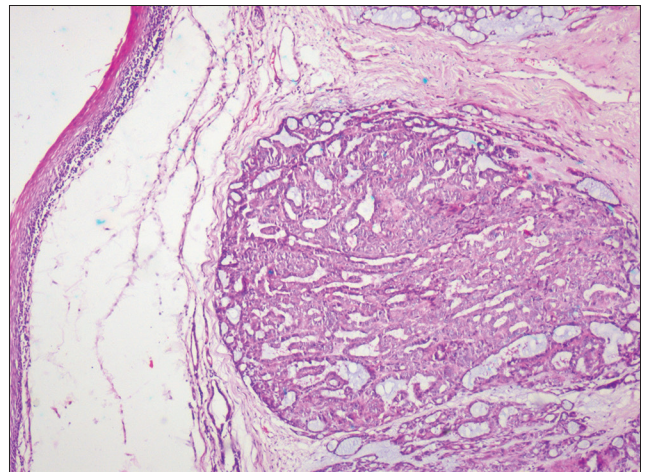
The background was filled with mucoid matrix [Figure 4]. Invasive growth pattern with infiltration of muscle was seen at places, but lymphovascular invasion was not evident. The tumor was covered by intact squamous epithelium devoid of dysplasia and ulceration.

Considering all the above features and in correlation with the reported literature, a diagnosis of CAMSG was made.

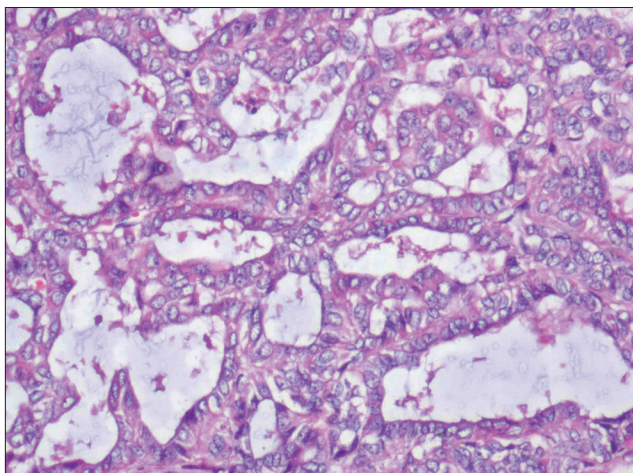
Immunohistochemical analysis was not performed as the patient could not afford for additional investigative procedures.

Margins of the excised lesion were resected to obtain clearance and microscopic examination of the same revealed to be clear and free of lesional tissue.

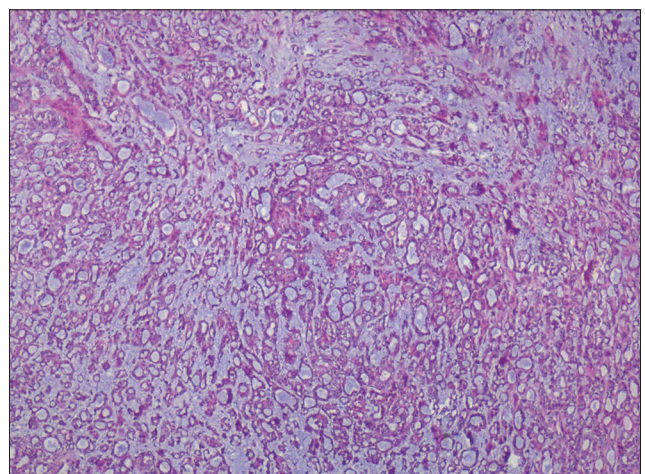
The patient is on follow-up. A follow-up of 10 months has shown neither recurrence of the tumor nor metastasis to the regional lymph nodes.



**Figure 2:** Tumor lobule exhibiting cribriform, tubular and solid growth patterns; partial encapsulation and fibrous septa are also observed. The lesion is surfaced by stratified squamous epithelium (H&E stain, x40)



**Figure 3:** Focal papillary and pseudopapillary projections with back to back fusion of the glandular components; there is overlap of nuclei and nuclei are showing ground-glass appearance (H&E stain, x100)



**Figure 4:** Tumor exhibiting cribriform pattern with abundant mucinous matrix (H&E stain, x40)

## DISCUSSION

CAMSG is a rare tumor of the salivary glands. It was thought to be a variant of PLGA under the WHO classification of salivary gland carcinomas (2005), even though the entity was not clearly described.<sup>[3,10]</sup>

The first description of this tumor was by Michal *et al.*, under the term CAT.<sup>[6]</sup> Later, it was renamed as CAMSG when a series of 23 new cases was reported by Skalova *et al.*<sup>[7]</sup> They had shown that CAMSG was a distinct tumor entity and differed from PLGA in location, cytology, histologic architecture and biologic behavior. In their report on case series of CAMSG, the tumors were unencapsulated, white tan to gray and hard in consistency. In the present case, the tumor was partially encapsulated and was firm in consistency.

According to the study by Skalova *et al.*,<sup>[7]</sup> the salient microscopic features of CAMSG were:

1. The tumors were covered by intact squamous epithelium devoid of ulceration, but with varying degree of pseudoepitheliomatous hyperplasia
2. Invasive margins of the tumor with infiltration of the muscle and/or adjacent tissues
3. Presence of lymphovascular invasion
4. Predominance of cribriform and solid structures with intermingled tubular pattern
5. In solid areas, glomeruloid appearance due to detached tumor nests from the surrounding fibrous stroma by artifactual clefts
6. Overlapped nuclei, which appeared pale, optically clear and vesicular with a ground-glass appearance (cytologically resemble papillary carcinoma of the thyroid)
7. Mild cellular atypia and minimal mitoses
8. 1–3 small inconspicuous nucleoli
9. Cytoplasm - clear to eosinophilic
10. Cervical lymph node metastatic deposit resembling the primary tumor.

In the present case, features with Sl no. 1, 2, 4, 6, 7 and 9 were observed.

Metastasis may not be seen in all cases of CAMSG.<sup>[7]</sup>

In accordance with the literature, nodal metastasis was not evident in the present case.

Immunohistochemical analyses for CAMSG has shown diffuse expression of cytokeratin, vimentin, and S-100 protein, and variable expression of myoepithelial and basal cell markers such as calponin, smooth muscle actin and p63 protein.

Ultrastructural findings have shown the features of hybrid myoepithelial secretory cells.

Molecular genetic findings have revealed no mutations of c-kit, PDGFRa, BRAF and KRAS genes.<sup>[7]</sup>

### Differential diagnoses of cribriform adenocarcinoma of minor salivary gland

CAMSG is cytologically monomorphous tumor, composed of one cell type exhibiting a limited range of growth patterns. In contrast, PLGA shows a wide range of architectural appearances, with tubule, solid, cribriform and fascicle formation. The characteristic feature would be the presence of streaming columns of a single file or narrow trabeculae of cells forming concentric whorls, creating a target-like appearance. In addition, the perineural invasion is often seen. Clear cells and infrequently mucous cells are observed. 3%–5% cases have shown crystals simulating tyrosine-rich crystals as observed in some pleomorphic adenomas. Except cribriform and tubule formation, none of these features are seen in CAMSG. Another interesting feature of CAMSG is the nuclear similarity to papillary carcinoma of the thyroid. This feature is not observed to a greater extent in PLGA. Then, PLGA metastasizes only rarely.<sup>[3,7,11]</sup> The reported literature shows that good number of metastasizing PLGA could have actually been CAMSG.<sup>[7]</sup>

Another important differential diagnosis of CAMSG is metastatic papillary carcinoma of the thyroid, if nodal disease is the first presentation. The absence of colloid and negative expression of thyroglobulin and thyroid transcription factor 1, are the features of CAMSG.<sup>[7]</sup>

A third differential diagnosis would be an adenoid cystic carcinoma, attributed to its cribriform, tubular and solid growth patterns. The presence of isomorphic basaloid tumor cells, cellular pleomorphism and higher mitotic activity will distinguish adenoid cystic carcinoma from CAMSG.<sup>[12]</sup>

Morphologic diversity being the hallmark of pleomorphic adenoma, where it exhibits combinations of gland-like epithelium and mesenchyma-like tissue in varying proportions; chondromyxoid areas, squamous and osseous metaplasia and areas of hyalinization are a few to mention.<sup>[13]</sup> In contrast, CAMSG is cytologically monomorphous tumor with a limited range of growth patterns.

In a nutshell, for CAMSG:

- The tongue is the common location; other reported sites are tonsil, palate, retromolar area and upper lip. The extra-lingual location excludes the possibility of origin from the remnants of thyroglossal duct, (which was thought once) and points toward minor salivary glands
- The tumor is cytologically monomorphous with limited range of growth patterns

- Arising at any location, CAMSG can develop metastases, preferably to the regional lymph nodes, but not all reported cases have shown lymph node metastasis. On the contrary, nodal disease may be the initial presentation
- Despite metastatic spread, the prognosis remains very good.

## CONCLUSION

CAMSG is a rare malignancy of the salivary glands, which is a distinct tumor, differing from PLGA. CAMSG may be kept in mind when there are features of low-grade adenocarcinoma of salivary gland with or without nodal disease.

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## Conflicts of interest

There are no conflicts of interest.

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