

CASE REPORT

Acinic cell carcinoma of minor salivary gland showing features of high-grade transformation

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ABSTRACT

Introduction: Acinic cell carcinoma (AciCC) of salivary gland is a relatively infrequent tumor. Though known for its low-grade behavior, its unpredictable element of recurrence and malignancy should never be ignored. **Case Report:** A male patient with complaints of pain and swelling in the left jaw region since a year was operated based on the computed tomography (CT) and incisional biopsy report. Histopathology (routine staining, special staining, immunostaining and electron microscopy) of the excised specimen revealed it to be a variant of AciCC from minor salivary gland. **Discussion:** To the best of our knowledge, this is the first case of AciCC showing propensity for high-grade transformation (HGT), arising from minor salivary gland, being reported. The rarity of such variants and the importance of various investigative techniques in the diagnosis of such cases are discussed.

Key words: Acinic cell carcinoma, dedifferentiation, high-grade transformation, minor salivary gland

INTRODUCTION

Acinic cell carcinoma (AciCC) of salivary gland is a relatively infrequent tumor.^[1] Though identified as a separate entity since a century ago, its malignant potential was ascribed only in 1953.^[2,3] This low-grade malignant tumor commonly involves the parotid gland followed by the minor salivary gland, exhibiting a predilection for young age and female sex.^[4] The multidirectional differentiation of the neoplastic cells together with a scarcity in morphological hallmark of serous acinar cell differentiation, as evidenced in some cases, pose a real diagnostic challenge. Though the conventional AciCC is a low-grade tumor, poorly differentiated and high-grade transformed variants exhibit a propensity for metastasis and an unpredictable malignant behavior.^[5] This article reports a case of AciCC arising from minor salivary gland, portraying features suggestive of high-grade transformation (HGT).

CASE REPORT

A 69-year-old gentleman, presented with complaints of pain and swelling in left side of the lower jaw since 1 year. Extraorally

a diffuse ovoid swelling was present on the left cheek region, measuring about 6 × 2 cm in size, extending anteroposteriorly from left commissure of the lip to 3 cm in front of left ear lobe and supero-inferiorly from infraorbital margin to 1.5 cm below the lower border of mandible. There was another well-circumscribed swelling in the neck on the same side measuring about 6 × 3.5 cm in size. Skin over the swellings was stretched without any secondary changes but was tender on palpation [Figure 1]. Intraorally an ulceroproliferative lesion in the buccal mucosa of 36 region that readily bled, was seen extending anteroposteriorly from distal aspect of 34 to retromolar area and superoinferiorly obliterating the upper and lower gingivobuccal sulci.

Soft tissue window of the computed tomography (CT) scan revealed an ill-defined mass involving the gingiva, buccal mucosa and gingivo-buccal sulcus in the 36 region, extending into the retromolar trigone. Multiple enlarged nodes were evident (levels 1-4) with involvement of the submandibular region. Bony window revealed lesion infiltrating the mandible. Erosion of the alveolar ridge in 36 and 37 region with tooth displacement was also seen [Figure 2].

Based on the CT findings and incisional biopsy done elsewhere (reported as poorly differentiated squamous cell carcinoma of mandible), surgical intervention was done. The excised radical neck dissection specimen was submitted to us for histopathological evaluation [Figure 3].

Histopathological evaluation of the hematoxylin and eosin (H and E)-stained sections from the lesional tissue

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revealed tumor cells arranged in multiple patterns. Among the various patterns observed like microcystic, follicular, organoid and papillary cystic; the organoid pattern predominated [Figure 4]. Intercalated duct-like cells, identified by their amphophilic cytoplasm and large hyperchromatic nuclei and vacuolated cells, with clear cytoplasm and vesicular nuclei, were evident. However, majority of the cells were those arranged in syncytial sheets with ill-defined cell boundaries, large vesicular nuclei and occasional mitotic figures, identified as nonspecific glandular cells. Section showed several such areas with low-grade features; however, serous acinar cells were almost absent. Few areas showed frequent mitosis and tumor necrosis and tumor cells invading the vessels [Figure 5a-c].

The lesional tissue was subjected to periodic acid-Schiff and mucicarmine staining. Demonstration of the diastase-resistant periodic acid-Schiff-positive serous cells in the sections was subtle [Figure 6a]. No positivity to mucicarmine was noticed. Following this, sections were submitted for transmission electron microscopy (TEM) (Philips-Christian Medical College, (CMC) Vellore). Though negligible in number, the electron microscopy

picture could clearly reveal the serous acinar cells with electron dense secretory granules [Figure 6b]. Immunostaining of the lesional tissue with cyclin D1, p53, Ki 67, neuron-specific enolase (NSE) and the nodal tissue with thyroglobulin was done. Focal areas with few cells showing positivity to cyclin D1 [Figure 5e], p53 and Ki 67 was noticed

Histopathological typing of the submandibular lymph nodes revealed replacement of the normal tissue by intercalated duct-like cells, few arranged in solid pattern and majority in follicular pattern [Figure 5d]. Lymph nodes from level 1 to level 4 were involved. Invasion of the tumor cells into the bone was also evident [Figure 5f].

Based on these findings, it was diagnosed as a variant of AcicCC from minor salivary gland with increased propensity for HGT. However, our patient died 2 months after the surgery from cardiac failure.



Figure 1: Extraoral photograph showing swellings in the left cheek and neck region



Figure 3: Macroscopic photograph of the submitted excised specimen. Inset showing cut surface of submandibular gland

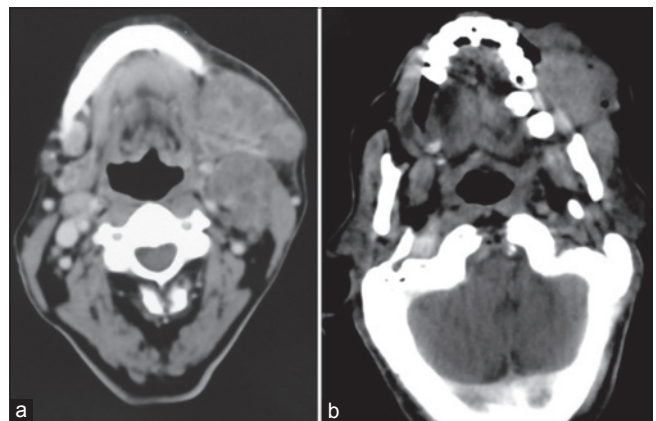


Figure 2: (a) Computed tomography scan image showing a mass from the left buccal mucosa extending to the retromolar trigone and involving the submandibular region of the same side. (b) Computed tomography scan picture showing lesion infiltrating mandible

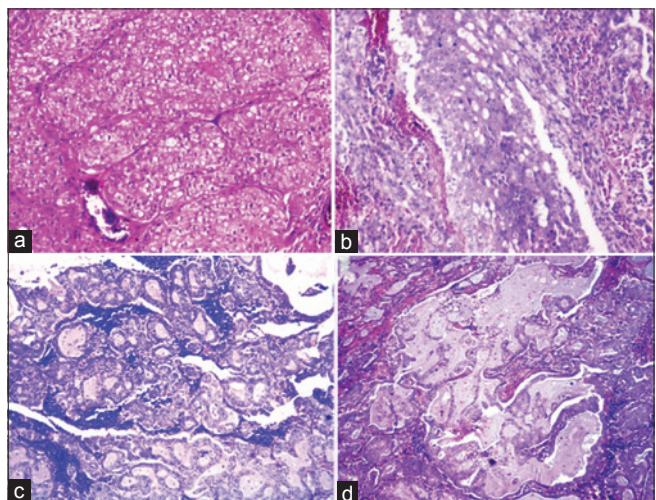


Figure 4: Photomicrograph showing various patterns. (a) Organoid (H&E stain, x100), (b) microcystic (H&E stain, x40), (c) follicular (H&E stain, x40) and (d) papillary cystic (H&E stain, x40)

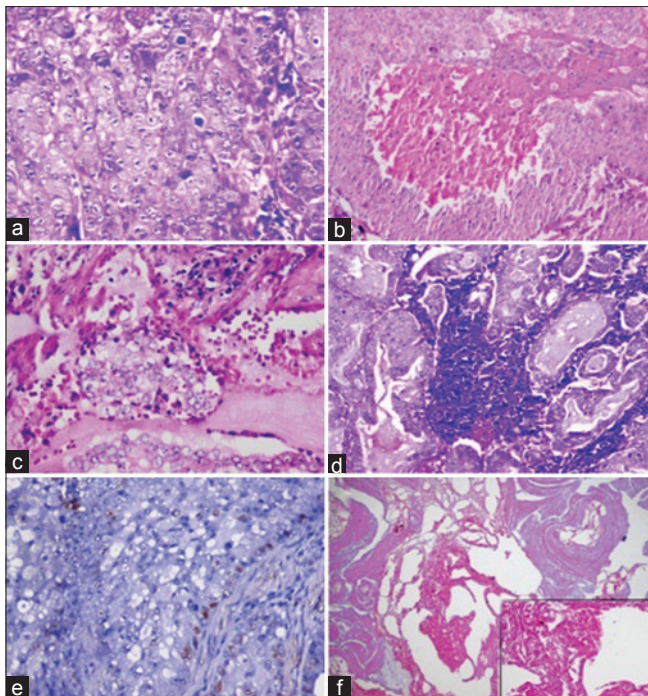


Figure 5: Photomicrograph showing features of High grade transformation. (a) Increased typical and atypical mitosis (H&E stain, $\times 400$), (b) Comedonecrosis (H&E stain, $\times 200$), (c) Tumor invasion into the vessels (H&E stain, $\times 400$), (d) Nodal tissue replaced by tumor cells (H&E stain, $\times 200$), (e) Photomicrograph showing few cells positive to cyclin D1 (IHC stain, $\times 400$) and (f) Tumor invasion into the bone (H&E stain, $\times 100$). Inset showing tumor cells at higher magnification (H&E stain, $\times 400$)

DISCUSSION

AciCC is histologically defined as a tumor with predominant differentiation toward serous acinar cells, admixed with ductal and myoepithelial elements. Though known for its low-grade behavior, its unpredictable element of recurrence and malignancy should never be ignored.^[5]

A total of 83% of the cases arise in parotid gland. However, in minor salivary glands, it develops most frequently in the buccal mucosa, which was also the site involved in our case. The average age of occurrence is 42 years and male to female ratio is 1:3 according to different studies.^[6] However, here the patient was a male whose age was slightly above the usual range. Lei quoted that in contrast to its conventional counterpart, AciCC showing high-grade transformation shows a male predilection.^[5]

Histologically the tumor is usually characterized by well-differentiated serous acinar cells rich in granules along with intercalated duct-like cells, vacuolated cells, nonspecific glandular cells and occasionally, clear cells, which are arranged in solid/organoid, microcystic, papillary cystic and follicular patterns.^[6]

Though all the above-mentioned patterns were present in our case, the organoid pattern, often termed as the classic pattern

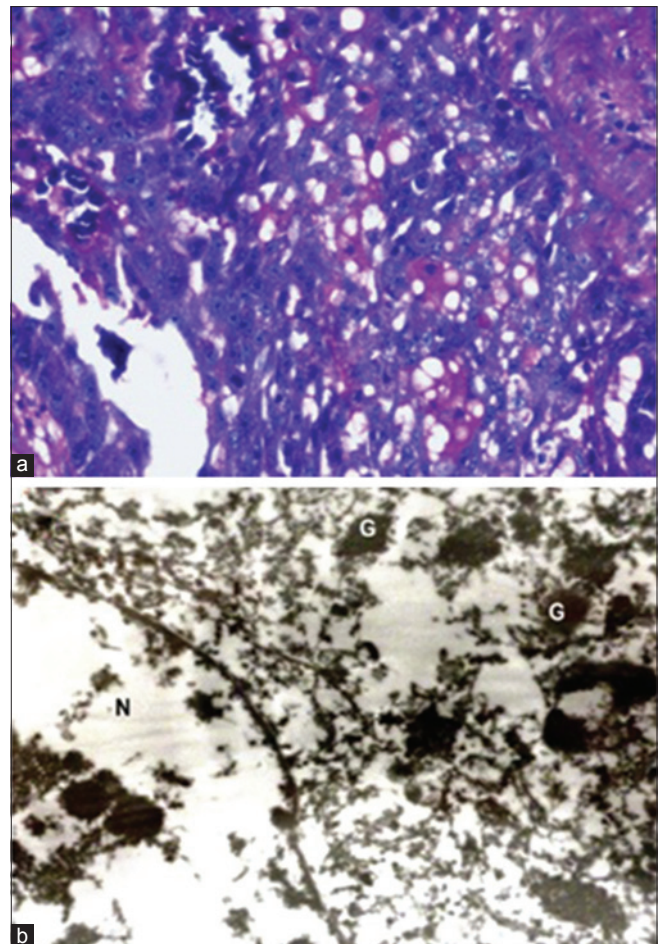


Figure 6: (a) Photomicrograph showing section stained with periodic acid-Schiff and treated with diastase (PAS with diastase digestion stain, $\times 200$). (b) Electron microscopic picture showing electron dense secretory granules (G) adjacent to the nucleus (N) of serous acinar cell

of AciCC predominated. The predominance of nonspecific glandular cells in solid areas was also atypical because usually the solid areas are seen predominated by serous acinar or intercalated duct-like cells.

In this case, the morphological hallmark, i.e., the well-differentiated serous acinar cells were almost unidentified in the H and E sections and subtly demonstrated in the periodic acid-Schiff-stained diastase-treated sections. This necessitated additional diagnostic procedures to be performed to arrive at a definitive conclusion. Considering the overlapping histopathological features of such poorly differentiated AciCCs with many other salivary gland neoplasms and the fact that immunohistochemical analysis for such neoplasms may prove refractory,^[6] we decided to subject the tissue for TEM. Though very little in number, the TEM sections showed serous acinar cells with granules, few round endoplasmic reticulum (rER) and mitochondria adjacent to the nuclei. The intercalated duct-like cells, identified by their smaller size to acinar cells and absence of cytoplasmic granules, were also evident.

Another strikingly important feature displayed here that is of utmost diagnostic and prognostic relevance was the juxtaposition of the conventional low-grade areas with areas of HGT.

The term HGT implies that the dedifferentiated component in a tumor often maintains some form of the original tumor. Histologically it is characterized by features like anaplastic cells with abundant cytoplasm, large polymorphic nuclei, loss of acinar differentiation, necrosis and vascular and perineural invasion. Clinical parameters indicative of HGT include high recurrence rate and increased propensity for cervical lymph node metastasis. The various salivary gland carcinomas in which HGT have been reported are AciCC, mucoepidermoid carcinoma, adenoid cystic carcinoma, epithelial myoepithelial carcinoma, myoepithelial carcinoma, polymorphous low-grade adenocarcinoma and salivary duct carcinoma.^[7] Retrospective clinicopathological study of 12 AciCC cases by Munteanu showed that the frequency of regional lymph node involvement is 3.8 to 16%.^[8]

The first case of AciCC showing dedifferentiation was reported in 1988.^[9] Since then, 35 cases reported to date were all of parotid origin. For such tumors with no specific histological criteria to predict the clinical outcome, evaluation of the proliferative activity of tumor cells, is a suggested prognostic factor. Immunohistochemical markers used to analyze the HGT in various salivary gland tumors include beta catenin, E-cadherin, Bcl 2, Ki 67, cyclin D1 and p53.^[7] Immunostaining of the lesional tissue was performed for this case, based on the above-mentioned ideology and areas with few cells showing positivity to cyclin D1, p53 and Ki 67 were noticed.

The clinical parameters like large tumor size, extensive involvement of levels 1-4 nodes and histopathologic features like increased typical and atypical mitosis, necrosis, absence of acinar differentiation and observation of tumor cells within the vascular spaces and bone invasion displayed by this case satisfactorily categorizes it as an entity for HGT.

Though our case displayed most of the clinical and histological criteria for HGT, the immunotyped picture did not characteristically reveal the transformed areas. This was similar to the inconsistent results observed in the studies by Henley *et al.*, and Fonseca *et al.* Based on this it can be suggested that the reliability of evaluating the expression of these proliferation markers in such poorly differentiated salivary gland tumors is yet to be explored. The exact mechanism of the expression of these markers in the transformed areas is not fully established.^[7,10] To the best of our knowledge, based on our search using the PubMed engine with the key words 'acinic cell carcinoma of salivary gland', 'dedifferentiation' and 'metastasis' and the Google search engine with the key words 'acinic cell carcinoma' and 'high grade transformation'; this is the first case of AciCC showing propensity for HGT originating from minor salivary gland.

Lei quoted that for anatomic sites outside of the parotid glands, broader differential diagnoses should be considered before accepting morphologic variants of AciCC as the final diagnosis.^[11] Presence of vacuolated cells, microcystic pattern and mucicarmine negativity observed here convincingly differentiated it from cystadenocarcinoma, mucoepidermoid carcinoma and polymorphous low-grade adenocarcinoma. Presence of the papillary cystic and follicular pattern with coexisting nodal metastasis necessitated a differentiation from follicular thyroid carcinoma. With this background, immunostaining for thyroglobulin was done that turned out to be negative. Neuroendocrine differentiation in AciCC was ruled out based on negativity to NSE.

The mammary analog secretory carcinoma is now identified as a distinct salivary gland neoplasm.^[12] The suggested histologic resemblance of this neoplasm with the intercalated duct-like cell-rich AciCC and the proposal by Lei regarding a male sex predilection with submandibular gland involvement of this neoplasm,^[11] as seen in our case, undoubtedly required a differentiation. However, though infrequent, the presence of serous acinar cells, intracytoplasmic and intraluminal mucicarmine negativity observed in our case supports the diagnosis of AciCC.

Surgical resection is the treatment of choice for AciCC.^[13] If the tumor was well encapsulated without extracapsular spread, Gomez *et al.*, suggested that surgery alone was satisfactory in the control of AciCC.^[14] However, in contrast with its conventional counterpart, for AciCC showing features of high-grade transformation, the treatment proposed is surgical resection followed by radiotherapy. Neck dissection is exclusively reserved when clinically positive nodes are detected.^[15]

CONCLUSION

High-grade transformation occurring in AciCC could actually be a complex process than simple progression through histological grades. Owing to the poor prognostic value evidenced in such cases, early appropriate diagnosis is important. A combination of clinical and morphological criteria together with modern diagnostic aids like gene mutation analysis should serve as a useful tool in identifying the transformed component.

REFERENCES

1. Clarke JS, Hentz EC, Mahoney WD. Bilateral acinic cell carcinoma of the parotid gland. *Ann Surg* 1969;170:866-9.
2. Buxton RW, Maxwell JH, French AJ. Surgical treatment of epithelial tumours of the parotid gland. *Surg Gynecol Obstet* 1953;97:401-16.
3. Foote FW Jr, Frazell EL. Tumours of major salivary glands. *Cancer* 1953;6:1065-133.
4. Spiro RH, Huvos AG, Strong EW. Acinic cell carcinoma of salivary origin. A clinicopathological study of 67 cases. *Cancer* 1978;41:924-35.

5. Di Palma S, Corletto V, Lavarino C, Birindelli S, Pilotti S. Unilateral aneuploidy dedifferentiated acinic cell carcinoma of the parotid gland. *Virchows Arch* 1999;434:361-5.
6. Ellis GL, Auclair PL. Acinic cell adenocarcinoma. In: Ellis GL, Auclair PL, Gnepp DR, editors. *Surgical Pathology of the Salivary Glands*. 1st ed. Philadelphia: W B Saunders; 1991. p. 299-317.
7. Costa AF, Altemani A, Hermsen M. Current concepts on dedifferentiation/high grade transformation in salivary gland tumors. *Patholog Res Int* 2011. Article ID 325965. doi: 10.4061/2011/325965.
8. Munteanu MC, Margaritescu C, Cionca L, Nitulescu NC, Daguci L, Ciuca EM. Acinic cell carcinoma of the salivary glands: A retrospective clinicopathologic study of 12 cases. *Rom J Morphol Embryol* 2012;53:313-20.
9. Stanley RJ, Weiland LH, Oslen KD, Pearson BW. Dedifferentiated acinic cell (acinous) carcinoma of the parotid gland. *Otolaryngol Head Neck Surg* 1988;98:155-61.
10. Henley JD, Geary WA, Jackson CL, Wu CD, Gnepp DR. Dedifferentiated acinic cell carcinoma of the parotid gland: A distinct rarely described entity. *Hum Pathol* 1997;28:869-73.
11. Lei Y, Chiose SI. Reevaluating historic cohort of salivary acinic cell carcinoma with new diagnostic tools. *Head Neck Pathol* 2012;6:166-70.
12. Skalova A, Vanecek T, Sima R, Laco J, Weinreb I, Perez-Ordóñez B, *et al.* Mammary analogue secretory carcinoma of salivary glands, containing ETV6 – NTRK3 fusion gene: A hitherto undescribed salivary gland tumour entity. *Am J Surg Pathol* 2010;34:599-608.
13. Ellis G, Simpson RH. Acinic cell carcinoma. In: Barnes L, Eveson JW, Reichart P, Sidransky D, editors. *World Health Organisation classification of Tumors Pathology and Genetics of Head and Neck Tumors*. Lyon: IARC Press; 2005. p. 216-8.
14. Gomez DR, Katabi N, Zhung J, Wolden SL, Zelefsky MJ, Kraus DH, *et al.* Clinical and prognostic features in acinic cell carcinoma of the parotid gland. *Cancer* 2009;115:2128-37.
15. Hirota SK, Modolo F, Portela de Albuquerque MA, Lehn CN, Sugaya NN, Machado de Sousa SO, *et al.* Recurring acinic cell carcinoma of the buccal mucosa: A case report. *Quintessence Int* 2007;38:289-94.

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