Case Report

# Ameloblastic carcinoma: A rare case with diagnostic dilemma

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**Abstract**

Ameloblastic Carcinoma is a rare malignant Odontogenic tumour with characteristic histopathology and clinical features which requires aggressive surgical treatment and surveillance and therefore differs from ameloblastoma. It is possible that ameloblastoma shows a variety of histologic and biologic behaviour ranging from benign to frank malignancy. Cases of ameloblastoma should thus be studied carefully, correlating their histologic pattern with biologic behaviour to direct subtle changes in histology that may predict the aggressiveness of the tumor. Thus the identifying features of Ameloblastic Carcinoma must be carefully known and recognized by dental professionals. The purpose of this article is to report a rare case of Ameloblastic Carcinoma and to highlight the clinical, radiological and variable histological features with possible differential diagnosis.

**Keywords:** Ameloblastic carcinoma, ameloblastic differentiation, ameloblastoma, malignant odontogenic tumor, odontogenic carcinoma

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## INTRODUCTION

Ameloblastic carcinoma (AC) is a rare malignant odontogenic tumor that has the histopathological features of ameloblastoma with cytological atypia even in the absence of metastases.[1] The term AC was introduced by Elzay in the year 1982.[2] The clinical course of the disease includes its aggressiveness, local destruction and distant metastasis.[1] Differentiating AC from ameloblastoma and malignant ameloblastoma is a challenge due to its overlapping clinical features, histopathology and different management approaches.[3] In this article, we report a rare case of AC of mandible with clinical and histopathological features that represented a diagnostic challenge.

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## CASE REPORT

A 33-year-old male patient presented with a chief complaint of swelling in the right side of lower jaw for 6 months. Swelling was sudden in onset and gradually increased in size. Extraoral examination revealed that swelling was diffuse extending on the right side of mandible, superoinferiorly from ala-tragus line to the lower border of mandible and anterioposteriorly 1 inch behind corner of mouth to the angle of mandible [Figure 1]. Swelling was firm in consistency with no local rise in temperature. Right submandibular lymph nodes were palpable and were tender and mobile. Intraoral examination revealed obliteration of right lower buccal vestibule.



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Radiographic examination revealed a well-defined unilocular radiolucency with sclerotic borders on the right side of posterior body and ramus of mandible, extending superiorly till the sigmoid notch with the involvement of coronoid process and inferiorly thinning of lower border of mandible. Root resorption was evident in 46 and 47 [Figure 2].

Based on the patient history, clinical features and imaging findings a provisional diagnosis of ameloblastoma were considered. Odontogenic keratocyst, calcifying epithelial odontogenic tumor, primary intraosseous carcinoma and metastatic tumors were in the list of differentials.

Fine needle aspiration cytology was performed with no significant findings.

Patient underwent incisional biopsy procedure in a private clinic and presented with the histopathology report of Basaloid Squamous Cell Carcinoma (BSCC).

Considering the lesion as malignant, hemimandibulectomy was planned and Right submandibular gland along with lymphnodes were removed and the specimen was sent for histopathological examination [Figure 3].

Microscopic examination revealed odontogenic epithelium arranged in variegated pattern predominantly plexiform and with few areas of follicular pattern. Sheets and nests of basoloid cells with peripheral palisading was evident. The cells showed hyperchromatic nucleoli and stippling with lack of cytoplasm. Few follicles exhibited stellate reticulum like areas along with squamous metaplasia and microcystic change. Marked cellular atypia with increased mitotic activity was seen. Stroma was minimal with moderate fibrous tissue component. Submandibular glands and lymphnodes were free of tumor infiltration. Reactive changes like prominent germinal center and sinus histocytosis were seen in the lymphnodes [Figure 4a-d].

Based on the histopathological features a working diagnosis of Ameloblastic carcinoma was considered.

Periodic Acid Schiff (PAS) special stain was performed, showed negative expression for mucin in the microcystic space [Figure 5].

Immunohistochemistry showed an immunoreactivity for cytokeratin (CK) 19 [Figure 6].

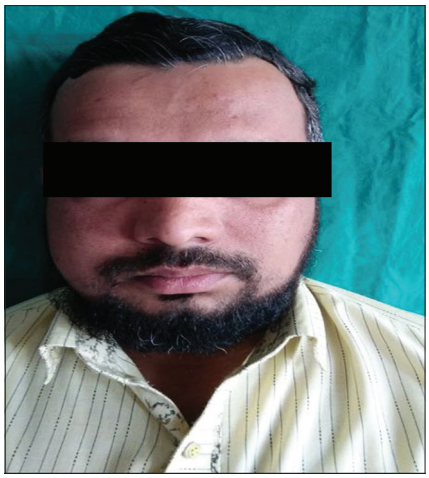

**Figure 1:** Swelling over the right side of the mandible

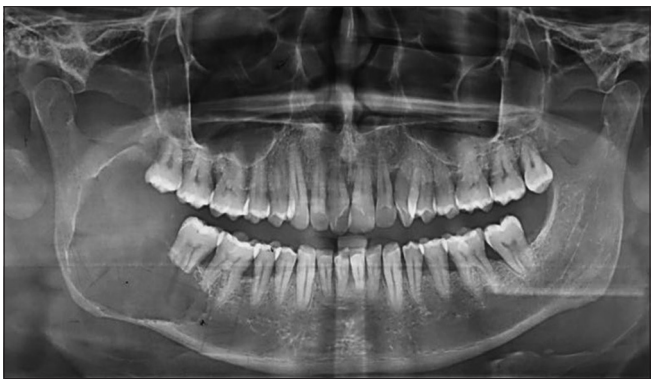

**Figure 2:** Unilocular radiolucency with well-defined sclerotic borders on the right side of the mandible

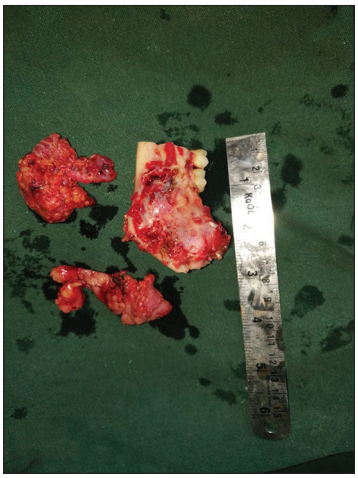

**Figure 3:** Segmental hemimandibulectomy specimen, along with right submandibular gland and lymph nodes

Thus, the histopathology and immunohistochemistry confirmed the diagnosis of AC of right mandible.

The patient was followed up and was free of recurrence for a period of 6 months.

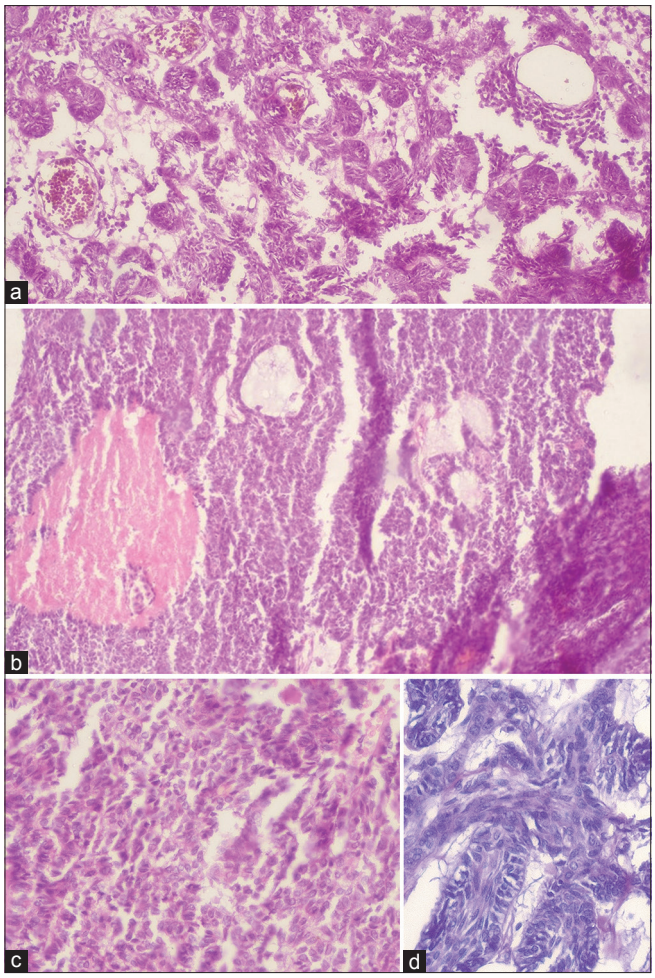


**Figure 4:** (a and b) Nests of basaloid cells with peripheral palisading with microcyst formation (H&E X10). (c) Sheets of bizarre basaloid cells with cellular pleomorphism, nuclear hyperchromatism and increased mitotic figures (H&E X10). (d) Ameloblastic differentiation of tumor cells (H&E X10)

## DISCUSSION

AC is a rare, aggressive malignant epithelial odontogenic tumor of the maxillofacial skeleton with a distinct predilection in the mandible.[4] In the WHO 2005 classification, AC was divided into three categories: Primary type (a), secondary type (dedifferentiated) intraosseous (b) and secondary type (dedifferentiated), peripheral (c). These tumors were classified under "AC" in the WHO 2017 classification based on the morphologic features and similar behavior between these entities.[5]

AC occurs more frequently in men and involves more often the mandible.[1] According to Dhir *et al*., the age range of appearance of AC is 51–84 years with a mean age of 53.5 years.[6]

Most cases of AC arise spontaneously (*de novo*) with few cases arising from a malignant transformation of an existing ameloblastoma or a benign odontogenic cyst.[7] Hypermethylation of p16 tumor suppressor gene has been found to be involved in the malignant transformation of ameloblastoma to AC.[8] AC shares the same BRAF mutation like ameloblastoma.[5]

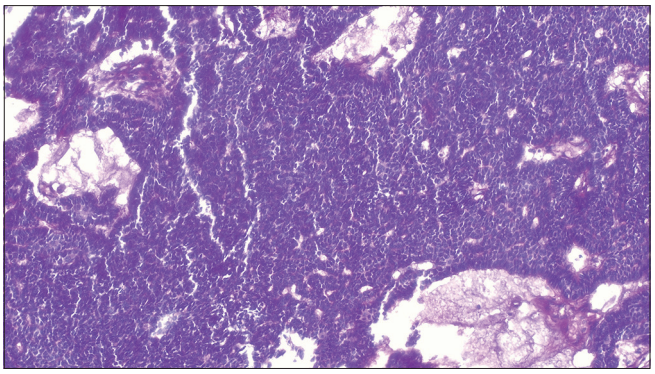

**Figure 5:** Negative for mucin expression (PAS X10)

The clinical symptoms of AC is more aggressive than ameloblastoma. Distinct features from ameloblastoma are swelling with rapid growth, perforation of the cortex, pain, tooth mobility, a nonhealing extraction site, ulcer or fistula, facial asymmetry, trismus and paresthesia.[9]

Radiologically, ameloblastoma and AC can be unilocular or multilocular with distinct borders in ameloblastoma and ill-defined borders in AC. Loss of lamina dura and root resorption is evident. In case of AC, there is often the presence of local radiopacity, reflecting dystrophic calcifications.[10,11]

AC is composed of islands and chords of ameloblastomatous odontogenic epithelium in an infiltrative pattern. The epithelium may reveal a single outer layer of ameloblastic cells of columnar or cuboidal shape which may or may not exhibit a tendency for palisading and reverse nuclear polarity. The stellate reticulum within the islands is often condensed and hypercellular. The characteristic features of ameloblastic carcinoma are nuclear enlargement with granular stippled nucleus, nuclear hyperchromatism, mild pleomorphism, an increased mitotic activity with abnormal forms of mitosis. Dyskeratosis, keratin pearl formation, necrosis and dystrophic calcifications may be observed in some cases. Different histopathologic patterns like highly differentiated squamous cell or a more basaloid and poorly differentiated variety may be noted in the malignant counterpart. Seldom, AC may reveal clear cell differentiation.[12]

Yoon *et al*. compared the immunohistochemical markers and found that the significant expression of CK18,

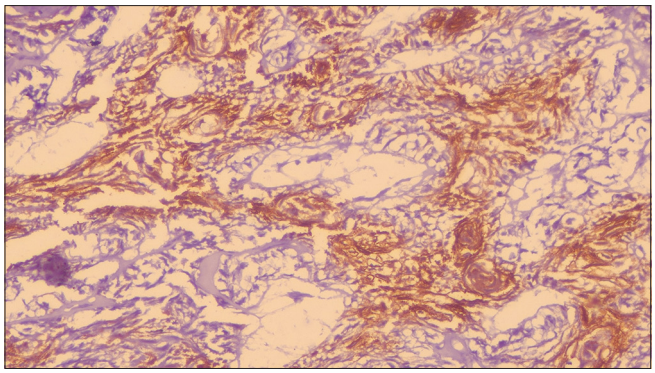

**Figure 6:** CK19 positivity (immunohistochemistry)

parenchymal matrix metalloproteinases-2 (MMP-2), stromal MMP-9 and Ki-67 differentiated AC from ameloblastoma.[13]

In the differential diagnosis of AC, acanthomatous ameloblastoma, squamous odontogenic tumor, primary intraosseous carcinoma (PIOC), clear cell odontogenic carcinoma, BSCC have to be considered.[14]

In our case, BSCC and PIOC were in the differentials that caused a dilemma in the diagnosis of this case as AC.

Solid nests and strands of tumour cells with peripheral palisading along with micro cystic space are the characteristic feature in BSCC.[14] In our case mucin in the microcystic spaces were PAS negative which ruled out BSCC.

The presence of sheets/islands of cells which have undergone metaplastic change with high amount of mitotic activity in AC can be mistaken for PIOC. In PIOC, there is absence of ameloblastic differentiation which is always seen in AC.[14]

According to Hall *et al*., four points in the clinical criteria can be helpful for diagnosis of ameloblastic carcinoma such as rapid growth, propensity to perforate the cortex, pain, and paresthesia that are distinct from their benign counterpart.[15]

Surgical resection along with prophylactic and therapeutic excision of involved lymph nodes is the treatment of choice for AC. *En bloc* removal with 1–2 cm of normal bone margin is the safest surgical modality to ensure disease-free survival. This surgical method has resulted in local recurrence rates <15%. ACs can recur locally 0.5–11 years after definitive therapy. Distant metastasis is usually fatal and may appear as early as 4 months or as late as 12 years postoperatively.[16] The lung is the common site for distant metastasis, followed by bone, liver and brain.[16,17]

The major prognostic factor of AC is the clinical course of the disease which includes its aggressiveness, local destruction and distant metastatic spread.[18] The location of AC also contributes to its prognosis as maxillary AC has an unfavorable prognosis than mandibular AC.[19]

## CONCLUSION

AC is an uncommon odontogenic tumour that exhibits malignant histologic features in the primary site. It is important to consider AC as a differential when in patients presents with pain, rapid growth and paresthesia. It is important to look for the evidence of metastasis to rule out the possibility of malignant ameloblastoma. The present article reinforces upon the rarity of AC and its spectrum.

### Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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### Conflicts of interest

There are no conflicts of interest.

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