Ameloblastic Carcinoma with Diverse Histological Features: A Case Report

Srinivas R Ponnam, Gautam Srivastava, Sudhakar G

Abstract
Ameloblastic carcinoma is a rare tumor of jaws associated with aggressive behavior and poor prognosis. This lesion may develop directly from the remnants of odontogenic epithelium in the jaws (primary type) or may arise from malignant transformation of a benign odontogenic cyst or ameloblastoma (secondary type). The diagnosis of ameloblastic carcinoma is based on the demonstration of cytological atypia on microscopic examination. In the current case report, we present a case of ameloblastic carcinoma showing diverse histopathological features in the epithelial component of the lesion.

Key-words: Odontogenic Tumors; Ameloblastoma; Carcinoma; Neoplasms; Dental Tissue; Anaplasia.

Introduction
Ameloblastic carcinoma (AC) is a rare, malignant odontogenic tumor associated with poor prognosis. AC is considered to have histopathological features of ameloblastoma in addition to cytological atypia with or without metastasis.1

Malignancy in ameloblastoma’s has been subjected to controversies and confusion for number of years. World Health Organization (WHO) published the first classification of odontogenic carcinomas in the year 1971 (table 1).1 Later, WHO had updated the classification which included metastasizing ameloblastoma, ameloblastic carcinoma, primary intraosseous carcinoma (PIOC), ghost cell odontogenic carcinoma (GCOC), and clear cell odontogenic carcinoma. Elzay in 1982 modified the WHO classification by separating tumors that are histologically identical to classic ameloblastoma and metastasize from ameloblastoma-like lesions that are histologically malignant before metastasizing (table 2). Slootweg and Muller further modified the classification based on the characteristics of malignancy in the year 1984 (table 3).2,3 They defined ameloblastic carcinoma as a tumor combining morphologic features of both ameloblastoma and carcinoma, which can arise de novo, ex ameloblastoma, or ex odontogenic cyst.3

AC is seen in wide range of age groups with no sex or race predilection. Majority of these lesions are reported in the mandible showing aggressive clinical behavior associated with poor prognosis.1,4 The most common form of its clinical presentation is a rapidly progressing and painful swelling. Histologically, ameloblastic carcinoma is considered to be a form of ameloblastoma that has lost most of its recognizable microscopic features.5 AC most commonly metastasizes to the regional lymph nodes followed by lungs. Since the lesion is associated with aggressive clinical behavior it is usually treated by wide surgical excision with or without radiotherapy.6

Case report
A 65 year old male patient came to the Department of Oral Medicine and Radiology with a chief complaint of swelling on the right side of the face since three months. Case history revealed that the swelling had gradually increased to the present size and is slightly associated with pain. Patient underwent extraction of posterior tooth due to mobility in the area of lesion. On extraoral examination, swelling was seen on the right side of face extending from corner of the mouth to the tragus of the ear. The swelling over the face revealed sinus tracts that were undergoing resolution (Fig 1). On palpation the right submandibular lymph nodes were enlarged, painless and fixed. On intraoral examination, the right buccal vestibule was found to be obliterated by the swelling which was seen extending from first molar to the retromolar area. The swelling was approximately measuring a...
size of 3 x 2 cm in size and the mucosa over the lesion was slightly erythematous. On palpation the swelling was hard, firm, and non-tender without any purulent discharge (Fig 2).

<table>
<thead>
<tr>
<th>Type</th>
<th>Features</th>
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<tbody>
<tr>
<td>1</td>
<td>Malignant ameloblastoma</td>
</tr>
<tr>
<td>2</td>
<td>Primary intraosseous carcinoma</td>
</tr>
<tr>
<td>3</td>
<td>Other carcinomas arising from odontogenic epithelium, including those arising from odontogenic cysts.</td>
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</table>

Table 1: WHO classification of odontogenic carcinoma (1971).

<table>
<thead>
<tr>
<th>Type</th>
<th>Features</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type 1</td>
<td>Arising from an odontogenic cyst</td>
</tr>
</tbody>
</table>
| Type 2 | Arising from an ameloblastoma  
  a. Well differentiated  
  (malignant ameloblastoma)  
  b. Poorly differentiated  
  (ameloblastic carcinoma) |
| Type 3 | Arising de novo  
  a. Nonkeratinizing  
  b. Keratinizing. |

Table 2: Modified WHO classification by Elzay (1982).

<table>
<thead>
<tr>
<th>Type</th>
<th>Features</th>
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<tbody>
<tr>
<td>Type 1</td>
<td>PIOC ex odontogenic cyst</td>
</tr>
</tbody>
</table>
| Type 2 | malignant ameloblastoma  
  b. ameloblastic carcinoma, arising de novo, ex ameloblastoma or ex odontogenic cyst |
| Type 3 | PIOC arising de novo  
  a. nonkeratinizing  
  b. keratinizing. |

Table 3: Modified WHO classification by Slootweg and Muller (1984).

The orthopantomograph revealed a scooped-out unilocular radiolucency extending from posterior aspect of the right second molar into the ramus of the mandible. Inferiorly the radiolucency was seen extending slightly below the mandibular canal. Superiorly the radiolucency had completely eroded the alveolar bone and anterior part of the ramus of mandible. The periphery of the radiolucency showed notching, which is suggestive of a moth-eaten appearance (Fig 3). Patient's chest radiograph did not reveal any evidence of metastasis.

The clinical differential diagnosis for this lesion includes osteomyelitis, odontogenic tumors and other non odontogenic tumors of connective tissue origin. Chronic osteomyelitis was ruled out as there were no decayed or periodontally compromised teeth in the area of lesion, and radiographically there was no evidence of sequestra and ill defined margins of radiolucent area. A provisional diagnosis of malignant tumor of jaw was made based on the clinical and radiographic features and the patient was advised for biopsy.

On histopathological examination, hematoxylin and eosin sections revealed islands and strands of odontogenic epithelium in the connective tissue stroma with moderate inflammatory cell infiltrate (Fig 4). The periphery of these islands and strands were lined by columnar ameloblast-like cells and the central cells were round to ovoid in shape (Fig 4 & 5). The cells in the epithelial islands revealed marked cytological atypia, with features of cellular and nuclear pleomorphism, hyperchromatism and abnormal mitotic figures (Fig 4, 5, & 6). The cells in the epithelial islands showed acanthomatous changes with attempts of keratin pearl formation mimicking primary intraosseous carcinoma (Fig 5). It is interesting to note the columnar ameloblast like cells attempting to form rosette like structure is also noticed in the epithelial islands as seen in adenomatoid odontogenic tumor (Fig 6).

Based on the clinical, radiographic and histopathological features such as ameloblastomatous islands with severe atypia, attempts of keratin pearl formation and rosette like structures, the lesion was diagnosed as ameloblastic carcinoma.

Discussion
The term ameloblastic carcinoma was first introduced by Shafer et al, to describe an ameloblastoma with histopathological features of malignant transformation. AC is classified into two types, a primary odontogenic malignancy arising de novo and a secondary type resulting from the malignant transformation of pre-existing ameloblastoma. In this case report, we present a case of primary ameloblastic carcinoma that aroused de novo at the time of its presentation.

The clinical presentation of ameloblastic carcinoma varies from case to case. It may arise in the form of a cystic lesion with benign clinical features, or as a large tissue mass with ulceration, bone resorption and
tooth mobility. In the present case, patient presented with a swelling on the right side of the face with healing sinuses. The duration of the lesion was short with a period of 3 months, indicating it to be a malignant lesion or chronic inflammatory condition.

Radiographically, AC may be seen as cup-shaped radiolucent lesion or as a unilocular radiolucency with ill-defined ragged borders. However, few lesions are reported to exhibit a well circumscribed radiolucency. Orthopantomograph in the present case showed a scooped-out unilocular radiolucency with moth-eaten borders in the third molar area (figure 3).

The presence of healing sinuses together with enlarged painful lymph nodes favors the diagnosis of chronic osteomyelitis. However, absence of decayed or periodontally compromised teeth in the area of lesion rules out osteomyelitis in the present case. Based on the location and radiographic features a provisionally diagnosis of malignant odontogenic tumor or a malignant non odontogenic connective tissue tumor was made.

Histopathologically, AC is considered by some authors to be a form of ameloblastoma that has lost most of its recognizable histopathological features. It has also been suggested that the presence of sheets, islands, or trabeculae of epithelium with minimum or lack of stellate reticulum-like areas should alert the pathologist of the possibility of AC. Round to spindle-shaped epithelial cells with little or no differentiation toward the columnar cells of ameloblastoma further suggest the malignant process.

On microscopic examination, the present case showed anastomosing strands and nests of odontogenic epithelium in the connective tissue stroma (Fig 4). The epithelial islands and strands revealed areas of peripheral palisading columnar cells with a vacuolated cytoplasm and reverse polarized nuclei away from the basement
membrane (Fig 5). In few areas the central squamous cells were loosely arranged in an acanthomatous pattern attempting to form keratin pearls (Fig 5). In other areas, the epithelial component showed cytological malignancy, characterized by nuclear pleomorphism, altered nucleus-to-cytoplasm ratio, hyperchromatic nuclei and a high degree of mitotic rate (Fig 4-6). The histopathological differential diagnosis for the current lesion includes ameloblastoma, primary intraosseous carcinoma and ameloblastic carcinoma. Ameloblastoma was ruled out based on the presence of marked cellular atypia with minimal features showing ameloblastomatous differentiation.

PIOC on microscopy varies from well-differentiated tumors exhibiting significant keratinization to nonkeratinizing poorly differentiated carcinomas. The main diagnostic criterion for PIOC is the presence of ulcerative lesion in the oral cavity along with the radiographic evidence of bone involvement. In the present case, lesion showed acanthomatous changes with attempts of keratin pearl formation mimicking PIOC. However, PIOC was ruled out based on the absence of lesion involving oral mucosa (Fig 2) and also due to the presence of ameloblastomatous differentiation of tumor cells (Fig 5).

The Hematoxylin and Eosin stained photomicrograph showing Islands and strands of odontogenic epithelium with ameloblastomatous differentiation (arrow-a) and neural invasion (arrow-b) (Figure 4). The columnar ameloblast-like cells (arrow-a) showing acanthomatous changes (arrow-b) (Figure 5). Under high power view the epithelial island showing rosette-like area (arrow-a) with clear cell (arrow-b) changes (Figure 6) may be noted.
Diagnostic criteria for ameloblastic carcinoma include the presence of tumor cells as seen in ameloblastoma along with marked cytological atypia. Other features of malignancy that should be searched for include hyperchromatism, large or atypical nuclei, increased mitotic index, necrosis, neural, and vascular invasion. Presence of many clear cells (>15% of tumor cells) is also suggested to favor the diagnosis of ameloblastic carcinoma. Finally, the lesion was diagnosed as ameloblastic carcinoma based on the histological features of ameloblastomatous differentiation of epithelial islands and strands showing marked cytological atypia which include cellular and nuclear pleomorphism, increased mitotic index and neural invasion.

The treatment for AC includes resection with wide surgical margins with or without radiotherapy. Recurrence rates for AC ranges from 15 to 25% after wide surgical excision. Recurrence rates are as high as 90% with local curettage without surgical excision. Early surgical intervention has the best prognosis reducing the chances for metastasis. The present case was treated by hemimandibulectomy together with the removal of the involved submandibular lymph nodes.

To conclude, we report a rare case of ameloblastic carcinoma showing diverse histological features which include, ameloblastomatous islands with acanthomatous changes and attempts of keratin pearl formation, islands showing marked cytological atypia with clear cells and an area showing the attempt of rosette-like area formation, which was treated by hemimandibulectomy together with the removal of the involved lymph nodes.

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**References**


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