CASE REPORT

Case Report: Odontogenic carcinosarcoma arising from ameloblastic fibrodentinoma with immunohistochemical profile [version 1; peer review: awaiting peer review]

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Abstract
Odontogenic carcinosarcoma is an extremely rare mixed malignant odontogenic neoplasm in which both the epithelial and the ectomesenchymal components are cytologically malignant. Owing to the scarcity of the reported cases, the clinical behavior of odontogenic carcinosarcoma remains unexplored. The present work reports a case of odontogenic carcinosarcoma of the mandible with the detailed immuno-histochemical profile. A 28-year-old male presented with a left painless swelling, which recurred after hemimandiblectomy of the lesion. Complete excision of the lesion with a wide safety margin was performed. The histopathological examination revealed cytological malignant features in the follicles as well as in the ectomesenchyme. The immuno-histochemistry demonstrated evidence of epithelial mesenchymal transition. After nine months, the patient demonstrated recurrence in the infra-temporal fossa. Odontogenic carcinosarcoma is a rare highly aggressive malignant odontogenic tumor. Positive expression of smooth muscle actin and vimentin in the epithelial component is a useful aid in the diagnosis of odontogenic carcinosarcoma.

Keywords
Odontogenic carcinosarcoma, α-smooth muscle actin, vimentin, epithelial mesenchymal transition, Ki-67.
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Introduction
Malignant odontogenic tumors are rare group of malignant neoplasms that arise from odontogenic remnants\(^1\). One of these neoplasms is odontogenic carcinosarcoma (OCS), an extremely rare mixed malignant odontogenic neoplasm in which both the epithelial and the ectomesenchymal components are cytologically malignant\(^1\). In the 1992 World Health Organization (WHO) classification of tumors, OCS was included in the malignant odontogenic tumors after Tanaka and co-workers (1991) first reported an odontogenic tumor with a mixture of malignant epithelial and ectomesenchymal components\(^3\). In the 2005 WHO classification, the tumor was removed due to an absence of current diagnostic criteria\(^4\). OCS has been added again in the 2017 edition because of the availability of cases with adequate diagnostic immunohistochemical and molecular criteria\(^5,6\). Owing to the scarcity of reported cases in the English literature - OCS clinical behavior remains unexplored\(^7,8\). In the current work, we report a case of OCS with the detailed clinical, radiographic, histopathological and immunohistochemical description.

Case report
A 28-year-old Egyptian male patient working as an accountant was referred to the Department of Oral and Maxillofacial Surgery, Faculty of Dentistry, Cairo University, with a complaint of painless swelling of six months duration in the left side of his face measuring 7 × 6 cm. The patient had a pathological report of an incisional biopsy, performed outside our institute, which was diagnosed as ameloblastoma. There were no palpable lymph nodes. Intra-oral examination revealed an absence of the lower left molars with a fistula opening on the alveolar crest with no oozing pus.

A cone beam computed tomography examination revealed an ill-defined multilocular osteolytic lesion with fine radiopacities extending from the lower left second premolar up to the ramus (Figure 1). A hemi-mandibulectomy was performed based on the incisional biopsy diagnosis and the pathological fracture of the mandible. The ramus was totally destructed and the tumor was invading the masseter muscle (Figure 2).

Figure 1. Cone beam computed tomography of odontogenic carcinosarcoma, axial view showing the multilocular lesion extending from the left lower second premolar to the condyle involving the whole ramus with buccal perforation. There was scattered radiopacities closely related to the impacted first molar. The second molar was displaced against the angle of the mandible.

Figure 2. Gross examination: (A) Hemi-mandibulectomy with safety margin including the masseter muscle. (B) Cross-section of the resected specimen showing the fleshy neoplasm and the impacted first molar. (C) Top view of the resected specimen showing the necrotic fistula on the alveolar ridge. (D) The excisional specimen of the recurred lesion.
Differential diagnosis was made based on the clinical examination, radiographic appearance and gross examination as: ghost cell odontogenic carcinoma, ameloblastic carcinoma, ameloblastic fibrosarcoma, ameloblastic carcinosarcoma, calcifying epithelial odontogenic tumor, atypical type of ameloblastic fibrodentinoma and ameloblastoma.

Histopathological examination revealed follicles of odontogenic epithelium that were compressed by highly cellular hyalinized primitive connective tissue resembling dental papilla. The epithelial cells showed little pleomorphism and hyperchromatism. In some fields, dentinoid matrix was detected around the epithelial strands (Figure 3). Based on the histopathological examination, a diagnosis was made of ameloblastic fibrodentinoma (atypical type).

After nine months, the patient returned with another large painless swelling in the left temporal and infra-temporal fossa that had appeared three months previously. An oral and maxillofacial surgeon used local anesthesia and an intra-oral approach to completely excise the recurrent lesion (Figure 2D). Augmentin 1gm tablet/12 hours for five days and anti-inflammatory medication were prescribed for the patient after the surgery. Histopathological examination revealed highly cellular neoplasm, which showed cellular atypia and increased mitosis in both epithelial and ectomesenchymal components (Figure 4).

The epithelial nests showed strong membranous positivity with AE1/AE3, while vimentin stained the ectomesenchyme diffusely and the epithelial nests patchily. Alpha-smooth muscle actin (α-SMA) showed positivity in the endothelial cells as well as in scattered epithelial and ectomesenchymal cells. Ki-67 index was around 40% in the epithelial component, while in the ectomesenchymal component it was around 12% (Figure 5).

Based on the histopathological and immunohistochemical findings, the case was diagnosed as OCS arising from ameloblastic fibrodentinoma. The patient was missed for the follow-up appointment after the last excision of the lesion and could not be reached for further follow-up.

**Discussion**

OCS is a rare biphasic malignant odontogenic neoplasm that has the same architecture of ameloblastic fibroma, in which the epithelial and the ectomesenchymal components are cytologically malignant. It can develop de novo from odontogenic remnants or as a transformation from a preexisting odontogenic benign or malignant neoplasm. This transformation may be attributed to multiple surgical procedures or recurrences of the neoplasm. The present case arose from a preexisting ameloblastic fibrodentinoma. To the best of our knowledge, this is the first reported case of OCS to arise from ameloblastic fibrodentinoma. Kunkel et al. (2004), DeLair et al. (2007) and Chikosi et al. (2011) reported cases aroused from ameloblastic fibrosarcoma, ameloblastic fibroma and ameloblastoma, respectively.

Our case was a 28-year-old male with the lesion affecting the posterior mandible. In the English literature, there was only one case that occurred in maxilla. The most common radiographic picture of OCS is ill-defined multilocular radiolucency with cortical perforation. The current case showed multiple radiopacities owing to the preexisting ameloblastic fibrodentinoma.

OCS must be distinguished from ameloblastic fibrosarcoma, in which the ectomesenchymal component only shows cellular atypia, and spindle cell variant of ameloblastic carcinoma, which lacks the ectomesenchymal component. In the present case, there was a patchy positive expression of vimentin in the

![Figure 3. Histopathological examination of the resected specimen (hematoxylin and eosin stain, X100). (A) Microscopic image showing odontogenic epithelial follicles formed of ameloblast-like cells on the periphery and stellate-reticulum like cells on the center, which were surrounded by primitive ectomesenchyme resembling dental papilla. Dentinoid material was detected in contact with the epithelial follicles. (B) Microscopic image showing another field which was hypercellular in both components with mild pleomorphism and hyperchromatism.](image-url)
Figure 4. Histopathological examination of the recurred lesion (hematoxylin and eosin stain). (A) Microscopic image showing hypercellular epithelial follicles along with hypercellular ectomesenchyme (X100). (B) Microscopic image showing pleomorphism, hyperchromatism, increased mitosis and increased nuclear-cytoplasmic ratio (X400). (C) Microscopic image showing atypia in ectomesenchymal component with increased mitosis and abnormal mitotic figures (X400).

Figure 5. Immunohistochemical staining (X200). (A) Microscopic image showing strong membranous expression of AE1/AE3 in the epithelial component. (B) Microscopic image showing strong diffuse cytoplasmic expression of vimentin in ectomesenchymal component along with patchy expression in the epithelial component. (C) Microscopic image showing cytoplasmic expression of α-SMA in the endothelial cells and scattered epithelial and ectomesenchymal cells. (D) Microscopic image showing high nuclear expression of Ki-67 in both epithelial and ectomesenchymal components.
epithelial component. This could be explained as OCS undergoes epithelial mesenchymal transition, a process in which the polarized immotile epithelial cell changes to gain the mesenchymal phenotype and indicates more aggressive behavior of the neoplasm12,13.

In accordance with Dos Santos et al. (2018), α-SMA staining in the current case showed scattered cytoplasmatic staining in both the ectomesenchymal and epithelial cells7. Its expression in the ectomesenchymal cells could be attributed to the emergence of cancer associated myofibroblasts, which play a significant role in tumor progression and the epithelial mesenchymal transition process, explaining α-SMA expression in the epithelial cells14.

The proliferative index Ki-67 in our case was around 40% in the epithelial component and 12% in the ectomesenchymal component. This is in accordance with the work of Dos Santos et al. (2018) and Soares et al. (2019), who found that Ki-67 index was higher in the epithelial component than the ectomesenchymal component7,12.

The principle line of treatment, as with other malignant odontogenic neoplasms, is surgical resection with a wide safety margin along with neck dissection. However, adjunctive radiotherapy is still a matter of question, and it may be helpful in cases with soft tissue invasion7.

**Conclusion**

OCS is an extremely rare odontogenic malignant neoplasm that shows very aggressive clinical behavior with multiple recurrences and possible metastasis. Immunohistochemical staining with vimentin, α-SMA and Ki-67 is helpful in the diagnosis of OCS.

**Data availability**

All data underlying the results are available as part of the article and no additional source data are required.

**Consent**

Written informed consent for publication of their clinical details or clinical images was obtained from the patient.

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**References**


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