



# Clinical management of primary odontogenic sarcoma in the mandible: a case report after WHO nomination

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## Abstract

Ameloblastic fibro-odontosarcoma (AFOS) now designated as odontogenic sarcoma is an extremely rare odontogenic tumor, which histologically presents as a biphasic neoplasm with a malignant mesenchymal component plus ameloblastic epithelium. Here we report a 27-year-old Chinese female with the complaint of a painful swelling for half a month in the right mandible. A segmental mandibulectomy, with an immediate mandibular reconstruction using a free vascularized osteocutaneous fibular flap was performed using surgical guide models. Histological analysis revealed a primary odontogenic sarcoma. The postoperative period was uneventful, and no clinical indication of recurrence or metastasis was observed during the 3-year follow-up. No adjuvant therapy was proposed. This is the first odontogenic sarcoma case reported in China after the new World Health Organization classification of odontogenic lesions.

**Keywords:** odontogenic sarcoma, ameloblastic fibrosarcoma, ameloblastic fibro-odontosarcoma, mandibular reconstruction

## Introduction

Malignant odontogenic tumors (MOTs) account for an extremely small percentage of all odontogenic tumors (OTs), and can occur as either carcinomas or sarcomas. Odontogenic sarcomas are mixed tumors, histologically characterized by a benign ameloblastic epithelium within a sarcomatous mesenchymal component, with or without dentine and enamel<sup>[1-2]</sup>. The 2005 World Health Organization (WHO) category of odontogenic sarcomas lists 3

subcategories: ameloblastic fibrosarcoma (AFS) and ameloblastic fibrodentinosarcoma (AFDS) and/or fibro-odontosarcoma (AFOS)<sup>[3]</sup>. All are now termed as odontogenic sarcomas since the publication of the 2017 WHO classification of OTs and ameloblastic fibrosarcoma is clarified as the most common type<sup>[4]</sup>.

Odontogenic sarcomas can arise in a pre-existing ameloblastic fibroma (AF) or present as a primary one, whereas most cases have been diagnosed as in *de novo* process<sup>[5]</sup>. Odontogenic sarcoma is termed as AFOS when AFS shows deposition of dentin and

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enamel. Here, we report the first case of primary odontogenic sarcoma in China after the new WHO nomenclature, on whom a segmental mandibulectomy was performed, followed by a vascularized fibular flap with the histological analysis revealing as odontogenic sarcoma.

The study was approved by the Research Ethics Committee of Nanjing Medical University, China. Informed consent was obtained from this patient. Written patient consent was obtained for the publication of the clinical photographs.

### Case report

In June 2018, a 27-year-old Chinese female patient was referred to the Department of Oral and Maxillofacial Surgery, Stomatological Hospital of Nanjing Medical University due to painful swelling in the right mandible. The patient had visited the local clinic two weeks before. The radiographic examination revealed a radiolucent lesion in the right mandible and no treatment was performed. Since no clinical improvement was seen, the patient came for maxillofacial consultation out of concern over deteriorating symptoms.

The patient was generally healthy and physical examination revealed that the right mandibular mass

contributed to facial deformation, and the right facial overlying skin was normal (**Fig. 1A**). Intraorally, a fixed sizable mass measuring about 5 cm×5 cm×3 cm occupied the right side of the mandible from the pre- to post-molar area. There was vestibular mucosa tenderness to palpation associated with a ping-pong feeling in the position of teeth #45 to #47 (**Fig. 1B**). Furthermore, the patient had slight numbness in the right lower lip, accompanied by slightly limited mouth opening. No evidence of lymph nodes or metastasis was discovered.

The cone beam computed tomography (CT) examination showed an irregular, ill-defined osteolysis (a multilocular radiolucent lesion) in the right mandible. The neoplasm was from the right first pre- to post-molar area, in which the radiopaque foci and the serrated absorption of the root of tooth #46 were observed, with no perforation of the external cortical bone (**Fig. 1C**). Needle biopsy found yellow granules with blood clot in blood.

Considering the clinical syndrome of numbness, we performed a biopsy to validate the malignancy neoplasm. Unexpectedly, the preoperative biopsy fast frozen pathology showed that the neoplasm was composed of hypercellular spindle to pleomorphic cells, in which the constituent of odontogenic



**Fig. 1** Photos of facial landscape and oral cavity and the preoperative or postoperative image manifestation. A: Clinical facial landscape shows a mass in the right mandible, contributing to the facial asymmetry. B: Photo of oral cavity performance shows an inconspicuous vestibular. C: Cone beam computed tomography examination images of the patient. The computed tomography revealed the lesion had occupied the half right mandible. D: Postoperative panoramic examination (3 years after surgery).



epithelial cells was found. In addition, some eosinophilic dentine-like substances were observed. Based on the medical history, clinical presentation, and histological examination, the diagnosis of odontogenic sarcoma in the right mandible was made. A segmental mandibulectomy, with an immediate mandibular reconstruction using a free vascularized osteocutaneous fibular flap, accompanied by a right supraomohyoid neck dissection, was proposed by oral and maxillofacial surgeons (**Fig. 1D**). A stereolithographic model was made to guide the bending of the titanium plate and the surgical procedure (**Supplementary Fig. 1**, available online).

The postoperative histopathological examination showed a biphasic neoplasm with sarcomatous mesenchyme consisting of benign odontogenic epithelial and spindle cells, with deposition of dentin and enamel. The tumor displayed a large number of benign-looking cords or islands in the epithelial component with spindle cells located beside it. The dentine matrix materials were in red (eosinophilic) areas. The epithelial cord structure mimicked the cytological characteristics of ameloblastoma whereas the sarcomatous mesenchymal component exhibited the typical cytological characteristics of malignancy (**Fig. 2**). All the margins were tumor-free. Immunohistochemical (IHC) assays were performed for vimentin, Ki-67, SATB2, CD34, AE1/AE3, CKH, smooth muscle actin (SMA), and S-100. The mesenchymal spindle cells were positive for vimentin, Ki-67, SATB2, AE1/AE3, CKH, S-100, and SMA, but negative for CD34 (**Fig. 3**). The Ki-67 positive area in the mesenchyme was approximately 30% (**Fig. 3B**), which was higher than the epithelium. These results confirmed the diagnosis of odontogenic sarcoma. Considering the patient had no history of odontogenic tumor, the mandibular tumor was considered a primary odontogenic sarcoma.

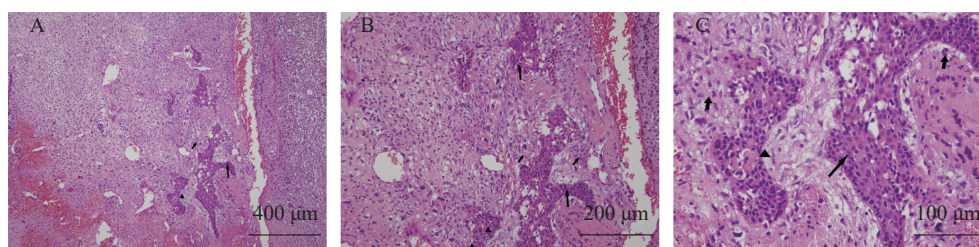
## Discussion

MOTs account for less than 10% of OTs and odontogenic sarcomas constitute about 1% of OTs. AFS is the most common type of odontogenic sarcomas<sup>[5]</sup>. Odontogenic sarcoma can arise *de novo* or emerge from a sarcomatous change in AF and approximately one-third of AFS cases stem from a recrudescence AF<sup>[6]</sup>. The case presented in this paper is diagnosed as a primary odontogenic sarcoma because there is no previous medical history of AF.

Odontogenic sarcoma mostly occurs in the second and third decades of life (mean age, 30 years), about one decade later than AF and AFO (mean age, 14.8 years)<sup>[5,7]</sup>. The age of our case at diagnosis is in line with previous reports. Clinically, most patients have a complaint of painful swelling, with the symptom lasting from 2 months to 10 years<sup>[8]</sup>. Odontogenic sarcoma seems more prevalent in mandibles than in maxillae, and a major proportion is in the retromolar to ramus region with no gender difference noted. Among the cases reported to date, all have shown bone expansion and a high rate of cortical bone perforation or tooth displacement. Radiological examination shows that odontogenic sarcoma usually presents as a multilocular expansile radiolucent lesion, although sometimes unilocular, with ill-defined confines and radiopaque dense foci<sup>[5,9]</sup>.

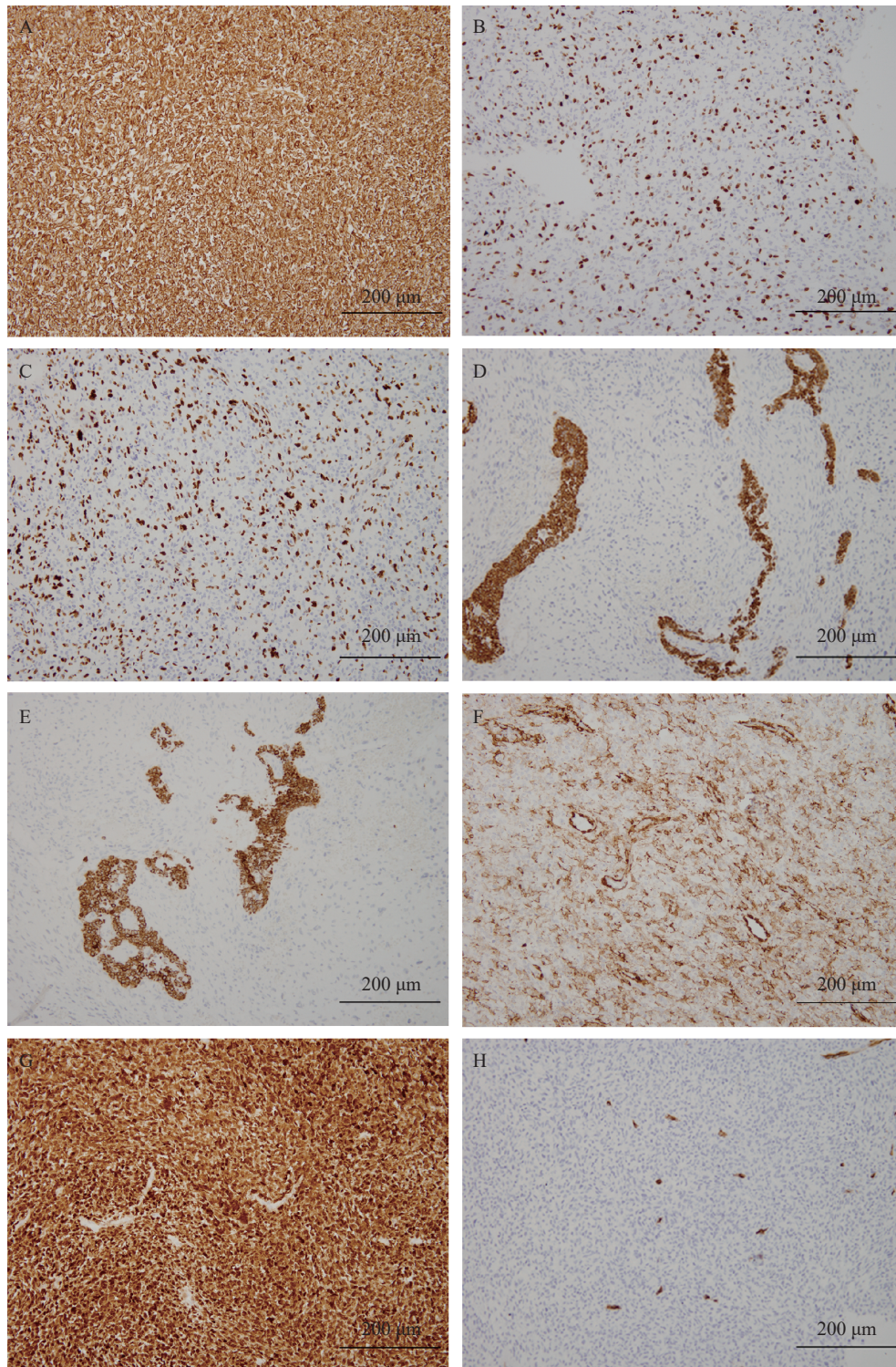
Histologically, most odontogenic sarcomas are of low or intermediate grade. In this case, the tumor showed a proliferation of spindle malignant mesenchymal cells, presenting various degrees of anaplasia, and containing islands or cords of ameloblastic epithelium with some dentin deposition. As the anaplasia is not always regularly distributed throughout the tumor, misdiagnosis like AF could be made from the surgically resected pieces.

Immunostaining provides key information about tumor occurrence and development, which could help in the definitive diagnosis of complicated cases. The



**Fig. 2 H&E staining examination of lesions.** Histopathological examination by H&E staining shows a biphasic pattern with the benign odontogenic epithelium (long black arrow) resembling a cord or island, and sarcomatous mesenchymal elements (short arrow) combined with dentine matrix formation (the triangle icon). Magnifications: 100× (A), 200× (B), and 400× (C). Scale bars: 400 μm (A), 200 μm (B), and 100 μm (C). H&E: hematoxylin and eosin.





**Fig. 3 Immunohistochemical staining assay of lesions.** A–G: Vimentin(A), Ki-67 (B), SATB2 (C), AE1/AE3 (D), CKH (E), SMA (F), and S-100 (G) are positive for tumor cells. H: CD34 is negative for tumor cells. Scale bar, 200 µm.

immunohistochemical study revealed that the vimentin positivity in mesenchymal spindle cells was higher than the ameloblastic epithelial component of odontogenic sarcoma<sup>[8]</sup>. In addition, Ki-67, PCNA, and p53 were reported to overexpress in the sarcomatous component of the AFS, whereas they

were absent or lowly expressed in AF. In our case, Ki-67, S-100, AE1/AE3, SMA, and vimentin were positive and the positivity rate of Ki-67 in the malignant mesenchyme area was approximately 30%, which was consistent with previous studies, indicating that the proliferative factors, such as Ki-67, may be

potential markers for malignant tumors. In addition, the expression of SATB2 indicated the odontogenic epithelium.

Radical surgical excision with clear margins is the widely preferred treatment for odontogenic sarcoma. Neck dissection is not routinely suggested as few regional lymph node metastases are identified. Postoperative radiation therapy is an acceptable alternative for cases with positive surgical margins. Chemotherapy is seldom used, with unsatisfactory results. Saede *et al* presented a 32-year-old female patient diagnosed with AFOS receiving an *en bloc* resection. Three years after the surgery the patient suffered a recurrence. Then the patient underwent surgical treatment combined with chemotherapy, and a year later, there arose pulmonary, mediastinal, and axillary lymph node metastases<sup>[2]</sup>. Gatz *et al* reported an 8-year-old child with AFOS, who underwent adjuvant chemotherapy of ifosfamide and doxorubicin. However, 2 years after the radical resection and chemotherapy, lung metastasis was found<sup>[10]</sup>. In the present case, the patient was treated by segmental mandibulectomy combined with the reconstruction using a vascularized fibular flap, with no adjuvant therapy. No clinical indication of recurrence and metastasis was observed 3 years after the operation and the patient recovered well.

In conclusion, odontogenic sarcoma is rare and could arise from AF. Molecular mechanisms associated with its malignant evolution are unclear. Therefore, the diagnosis of odontogenic sarcoma is made microscopically, and the Ki-67 and SATB2 are potential immunohistochemical markers for the diagnosis. Though the optimal treatment strategies for odontogenic sarcoma are not yet defined, radical resection with no adjuvant therapy and with long-term follow-up seems to be effective.

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