Diagnosis and treatment of primary synovial cell sarcoma that occurred in the left mandible body: a case report and literature review

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Objective. The authors describe a case of synovial sarcoma in the left mandible body.

Study design. The primary tumor was investigated morphologically and immunohistochemically. The patient was treated with mandibulectomy and lymph node dissection, which was followed by an immediate reconstruction of the left mandible with a revascularized osteomyocutaneous fibula free flap.

Results. The primary tumor was described as gingival sarcoma. The initial preoperative biopsy showed positive staining for cytokeratin, vimentin, smooth muscle actin, and desmin by immunohistochemistry. The definitive diagnosis of monophasic synovial sarcoma was established following postoperative excision biopsy. Antigens of S-100 and CD99 displayed positive staining but epithelial membrane antigen, Bcl-2, and CD34 were negative. Also, no metastasis or other bone swelling was observed by radionuclide survey suggesting the left mandible was the primary lesion of occurrence.

Conclusions. Synovial sarcoma is an uncommon soft tissue malignant neoplasm. This is the sixth case of primary synovial sarcoma occurring in the jaw. (Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2011;111:e12-e20)

A cancer diagnosis between 15 and 30 years of age is 2.7 times more common than a diagnosis during the first 15 years of life, and yet it is still relatively rare compared with malignant neoplasms occurring in older age groups.1 The distribution of such malignant neoplasms in persons 15 to 30 years of age is unique depending on the types that occur. Hodgkin lymphoma, for example, has the highest incidence within this age group. Soft tissue sarcoma is also reported frequently in adolescents; however, its international incidence rate is only between 1.8 and 5.0 cases per 100,000 per year.2

Synovial cell sarcoma is a malignant mesenchymal neoplasm that has been reported frequently in 15- to 30-year-old patients without gender imbalance.3 It accounts for up to 10% of all histologic types of soft tissue sarcoma.4 The final incidence of synovial cell sarcoma, therefore, ranges only between 1.8 and 5.0 cases per 1 million per year.

Most synovial cell sarcoma is reported in the extremities, typically in a periarticular location or close to a bursa or tendon sheath.5 The head and neck has been regarded as an extremely rare location of synovial cell sarcoma with the hypopharynx being the most commonly affected site. The other reported sites are the masticator space, parapharyngeal space, sinonasal space, and infratemporal fossa.6

In this study, we describe a rare case of synovial cell sarcoma occurring primarily in the left mandible body in a young Chinese woman. We also summarize the clinicopathological features of previously reported cases in the relative regions of synovial cell sarcoma.

CASE PRESENTATION

The patient, a 20-year-old woman, complained of a recurring swelling in the region of the left posterior teeth, without pain, but she felt alveodental suppuration. Three years prior she underwent a local excision of tumor in the same intraoral region at an outside hospital. The tumor was diagnosed as benign epulis. For 4 months before enrolling in our hospital, she found a recurrence of the swelling, augmenting quickly, and accompanied by teeth motility. No history of trauma was mentioned in her presentation. Facial asymmetry and left facial swelling were observed. Physical examination revealed a 6 × 4-cm, firm, tender, nonmobile mass in the left mental foramen region. No restriction of mouth opening or lymph node enlargement was observed. X-ray indi-
cated a large area of bone absorption (Fig. 1, A). A computed tomography (CT) scan revealed a continuity fragment of the normal structure of left mandible body (Fig. 1, B, C), whereas a 3-dimensional reconstructive CT disclosed a soft mass invading in the bone (Fig. 1, D). The patient underwent pathologic biopsy before the operation, which showed positive staining for the proteins cytokeratin (CK), vimentin (Vim), smooth muscle actin (SMA), and desmin (Des); a diagnosis of gingival sarcoma was given (Fig. 2).

Preliminary diagnosis and operative designation

The preliminary diagnosis of gingival sarcoma was based on the following considerations. First, the clinical symptoms suggested that the tumor could be malignant rather than benign because of the properties of its speed of augmentation, alveodental suppuration, and the bone destruction. Although a few benign mandible neoplasms also possess the phenotype of bone invasion, such as ameloblastoma and odontogenic keratocyst, their growth speed is limited and the symptom of alveodental suppuration is unusual. Second, the pathologic biopsy diagnosis demonstrated that the tumor originated from mesenchymal tissues rather than epithelia because the spindle-shaped cells were observed predominantly with the positive markers of mesenchyma (Vim, SMA, Des). Although fibroblastlike cells are also observed in some cases of gingival squamous cell carcinoma, epithelial cells are, however, the majority rather than stromal cells, and the epithelial cells often constitute “cancer nests.” Third, abnormal aggregation of radionuclide occurred in the left mandible (Fig. 3), suggesting that the enhanced metabolism of bone was a result of the invading mass. In summary, we made the preliminary diagnosis that this lesion occurring in the left mandible body was gingival sarcoma. This was consistent with the preoperative diagnosis by pathologic biopsy.

To consider the characteristics of malignancy and bone invasion of the tumor, we designed the operation in 3 parts: extensive neoplasm resection, extensive left mandibulectomy and lymph node dissection, and the preparation of a revascularized osteomyocutaneous fibula free flap for the reconstruction of the left mandible.

Definitive diagnosis and postoperative care

During the process of the operation, we found that the cortex of the bone was destroyed completely by tumor cells invading the medulla of bone down to the level of the mandibular canal. The tumor, the subtotal of the left mandible, and the regional lymph nodes were excised successfully. The final size of the tumor was $8 \times 6 \times 5$ cm (Fig. 4), and it was soft and without a capsule. Frozen section microscopy showed no metastatic tumor cells in the lymph nodes. Following the assessment of the primary lesion by immunohistochemistry, we found not only the proteins of CK, Vim, SMA, and Des, but also S-100 and CD99 showed positive staining (Fig. 2). Epithelial membrane antigen, Bcl-2 and CD34 were also studied but did not show positive staining (Fig. 2), which was not consistent with the properties of gingival sarcoma. Because gingival sarcomas, including angiosarcoma, malignant fibrous histiocytoma, and liposarcoma, are often associated with the negative expression of CD99 but positive expression of CD34, it was suggested that the hematopoietic and vascular-associated tissues should not be involved in this lesion, but that immunocytes were. This diagnosis was adjusted from gingival sarcoma to synovial cell sarcoma because of the pre- and postoperative immunohistochemistry assays.

After tumor resection, the patient underwent adjuvant radiation treatment (4000 cGy), for 1 month. When the radiotherapy finished, the patient was asked to return for several check-ups over 6 months. At present, the patient is free of recurrence without functional disturbances of mastication, swallowing, and speech (Fig. 5).

DISCUSSION

The term synovial cell sarcoma was first proposed by Knox in 1936. It was nominated because in histology the cases reported in the early period showed some resemblance of the tumor to normal synovial tissues. This tumor, however, can be found anywhere in the human body without restriction to synovial cells. The origin of the tumor from synovial tissue therefore has not been fully elucidated.

Most of these tumors are reported in the extremities. It is suspected that because of misdiagnosis in the oral and maxillofacial region only about 100 cases have been published in head and neck sites to date. Notably, intraoral cases are extremely rare, in fact, only 31 patients had been reported in English language journals by the end of 2003. This number increased to 37 in 2009 with the tongue being the common site of the intraoral cases. The others are cheek, soft palate, gingivobuccal sulcus, retromolar area, submental, floor of mouth, and jaw bone. Interestingly, in these 37 cases only 7 subjects are reported in jaws, including 2 cases occurring in the mandible metastatic from calf and foot, respectively (Table 1). So far it is known that only 5 cases have existed that are the primary synovial cell sarcomas occurring in jaws (tumors found in temporomandibular joint are excluded). Here, we report a
Fig. 1. The swelling is captured by radiology assay. Panoramic radiograph shows that the bone of the left mandible body is destroyed (A). Axial CT image shows an inhomogeneous enhanced round mass in the left lower gingiva (B). CT image reveals extension of the soft tissue mass toward the bone. There is an alveolar bone resorption and continuity fragment with unclear border and irregular margin (C). The image of 3-dimensional CT shows that the swelling invades the medulla of bone down to the level of mandibular canal (arrow). The image of high density on the soft mass is the filler of resection of epulis at an outside hospital (D).
Fig. 2. The biopsy specimen of the tumor is illustrated by immunohistochemistry assay. All are at the magnification of ×200. The subtype of this neoplasm is monophasic, with predominant spindle cell component by hematoxylin and eosin staining (A). It showed that antigens of cytokeratin (B), vimentin (C), smooth muscle actin (D), desmin (E), S-100, (F) and CD99 (G) are all positive, but epithelial membrane antigen (H), Bcl-2 (I), and CD34 (J) are negative. The arrows in J are positive endothelial cells but not tumor cells.
rare case of a local recurrence in the left mandible body, and then summarize the properties of synovial cell sarcoma in origin, diagnosis, and treatment.

As described previously, although the tendency is to arise near large joints,24 it seems that the origin of synovial cell sarcoma is not related to synovial tissues, and the name synovial sarcoma may be a misnomer. Recently, a novel nomenclature of “carcinosarcoma” has been discussed based on frequent coexpression of epithelial and mesenchymal markers, such as CK and Vim. In fact, the feature of “uncertain differentiation” of this neoplasm is currently regarded as part of the nature of this kind of tumor.25 It has been reported that myoblasts could be targeted as a potential source of synovial cell sarcoma.26 In one study, a conditional mouse model over-expressing the oncoprotein of SYT-SSX2 in immature myoblasts within the skeletal muscle lineage, led to the induction of synovial cell sarcoma with 100% penetrance. However, when its expression was transfected into more differentiated myoblasts, the induction of myopathy appeared without tumor formation.26 This new discovery provided a novel insight that undifferentiated cells of skeletal muscle lineage were the origin of synovial cell sarcoma as well as illustrating a clinical phenomenon of frequent occurrence within or in proximity to skeletal muscles of this neoplasm.27

The diagnosis of synovial cell sarcoma is a tough task at present. It is the fourth most common type of sarcoma following malignant fibrous histiocytoma, liposarcoma, and rhabdomyosarcoma.28 Misdiagnosis often occurs among these types of sarcoma, especially at the oral and maxillofacial region. The optimal diagnosis of synovial cell sarcoma is composed of a multispecialty approach. CT is the key indicator and initial staging of a lesion, as it is helpful in identifying subtle soft tissue calcifications and local bony changes, particularly in regions of complex anatomy.29 Because CT images of all types of sarcoma reveal similar extension of the soft tissue mass, the definitive diagnosis of tumor could not be made except for at the border and margin of the neoplasm. For example, on the image of gingival angiosarcoma, bone window settings show a regular margin and clear border of bone resorption, which might illustrate that angiosarcoma is less aggressive than other malignant tumors.30 Compared with the images of synovial cell sarcoma on which the margins of bone invasion are often irregular and unclear,31 it is suggested that angiosarcoma and synovial cell sarcoma could be discerned only by CT scan. It has been shown, however, that a CT scan could not distinguish osteogenic sarcoma, such as osteosarcoma from synovial cell sarcoma of primary bone origin. Osteoid tumor matrix mineralization is the typical feature of osteosarcoma on the images of CT, while they show soft tissue extension component usually beyond the area of bone destruction.32 Similarly, soft tissue synovial cell sarcoma may be calcified in 15% to 20% of cases.33 Hence, if the mass of synovial cell sarcoma primarily originates from bone, it is more difficult to make a correct diagnosis by CT scan alone, even if the osteoblastic changes are found with a bone window.

Although histopathologic diagnosis is more persuasive than radiology for a synovial cell sarcoma, the differential diagnosis of mesenchymal tumors and those with mesenchymal-like features, still can be difficult.34 Synovial cell sarcoma tumors are uniquely composed of 2 morphologically distinct cell types: spindle cells and epithelioid cells. Three histologic subtypes, coming

Fig. 3. Metastasis is detected by radionuclide survey. 99mTechnetium scintigraphic scans show increased uptake of isotope in the left mandible. No other sites of abnormal aggregation of radionuclide are shown in this assay. A, anterior view. B, posterior view.
from the presence of the 2 cell types, exist along a continuous spectrum: biphasic, monophasic (predominant fibrous or rare epithelial), and poorly differenti-ed.\textsuperscript{35} Monophasic epithelial synovial cell sarcoma or the gland predominant biphasic synovial cell sarcoma is similar to adenocarcinoma leading to potential misiden-
tification as adenocarcinoma. The poorly differentiated type poses a diagnostic challenge and demonstrates structures that resemble high-grade small round cell tumors: high cellularity, frequent mitosis, and necrosis. The common diagnosis of synovial cell sarcoma is the biphasic pattern or monophasic fibrous type, but also can be easily confused with spindle cell carcinoma, myofibromatosis, leiomyosarcoma, primitive neuroectodermal tumors, malignant peripheral nerve sheath tumors, and malignant fibrous histiocytoma. It has been advised that a panel of antibodies in an immunohistochemistry assay must be assessed together with other observations. For example, unlike other spindle cell sarcomas, synovial cell sarcoma expresses CK7 and 19, which can help to distinguish it from neurogenic tumors. Also, CD34, the vascular-associated marker is often not expressed in synovial cell sarcoma, which can help to distinguish it from vascular tumors. More importantly, synovial cell sarcoma demonstrates a specific t(X;18) (p11.2;q11.2) translocation, which is a more significantly useful diagnostic tool, especially when histologic features are equivocal.

Taking into consideration that synovial cell sarcoma is a somatic genetic disease and tumorigenesis is dependent on a permissive microenvironment, prevention of local recurrence and distant metastasis of this tumor are the pivotal tasks of treatment. Depending on the extent of the lesion, the surgical intervention includes complete resection together with affiliated organ dissection and regional lymph node dissection. In the oral and maxillofacial region, however, the integrity of personal appearance is a big challenge for surgeons after ablative resection of malignant and aggressive tumors. Today, ensuring good morphology and function are primary goals in the reconstruction of oral cavity. Loss of mandible continuity results in alteration in speech, swallowing, and mastication. A variety of free vascularized flaps have been suggested as useful treatment of mandibular discontinuity defects, including the iliac crest, radius, scapula, and fibula. Although vascularized fibula transfer has become the preferred method of mandibular reconstruction following oncological ablative surgery, when it should be operated on is still a controversy. Primary reconstruction following tumor ablation seems to be mandatory in most of the cases within the oral cavity. This offers several advantages compared with the secondary reconstruction. It avoids fibrosis in the surgical bed and minimizes significant functional disability. In the process of tumor ablation, however, the “safety boundary” of malignant and aggressive tumors is difficult to define, so an unexpected seed of risk of recurrence would be buried in the immediate reconstruction, which could finally result in failure of treatment.

In light of the disadvantages mentioned previously, it has been advised that radiation therapy and chemotherapy must be added following primary reconstruction to help kill potentially migratory cells of synovial cell sarcoma. In a retrospective study, however, it was shown that there was no significant difference in outcome between patients treated with or without chemotherapy at this stage even though the use of radiation therapy proved to be a significant factor in reducing mortality. In that research, the authors also confirmed a conventional viewpoint that tumor size was an important prognostic factor for both overall survival and event-free survival. Tumor size of 5 cm or greater and the presence of bone and neurovascular invasion were independent adverse predictors of distant recurrence and mortality. It was documented that lesions ranging from 2 to 14 cm were observed; however, most tend to be large—more than 85% were larger than 5 cm.

### Table 1. Clinicopathological features of reported and current cases of synovial cell sarcoma in jaws

<table>
<thead>
<tr>
<th>Case</th>
<th>Reference</th>
<th>Site</th>
<th>Age</th>
<th>Gender</th>
<th>Size, cm</th>
<th>Type</th>
<th>Treatment</th>
<th>Follow-Up</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Maxymiw (1990)</td>
<td>Maxilla R</td>
<td>32</td>
<td>Female</td>
<td>10</td>
<td>B</td>
<td>C/R/S</td>
<td>Dead: multiple metastases</td>
</tr>
<tr>
<td>2</td>
<td>Karr (1991)</td>
<td>Mandible L premolar area metatstatic from L calf</td>
<td>41</td>
<td>Female</td>
<td>5 × 5</td>
<td>M</td>
<td>Late R/C</td>
<td>Dead: multiple metastases</td>
</tr>
<tr>
<td>3</td>
<td>Karr (1991)</td>
<td>Mandible R metastatic from L foot</td>
<td>63</td>
<td>Female</td>
<td>Unknown</td>
<td>M</td>
<td>R</td>
<td>Dead: metastases to lung, liver, and bone</td>
</tr>
<tr>
<td>5</td>
<td>Captier (1999)</td>
<td>Mandible in premolar area</td>
<td>10</td>
<td>Male</td>
<td>5</td>
<td>B</td>
<td>C/S/R</td>
<td>A/W: 1 y</td>
</tr>
<tr>
<td>8</td>
<td>Tao (2010)</td>
<td>Mandible body L</td>
<td>20</td>
<td>Female</td>
<td>8 × 6 × 5</td>
<td>M</td>
<td>S/R</td>
<td>A/W: 1 y</td>
</tr>
</tbody>
</table>

A/W, alive and well; B, biphasic; L, left; M, monophasic; R, right; C, chemotherapy; R, radiation; S, surgery.
in 1 series of deeper lesions. In this case report, the final size of the neoplasm was $8 \times 6 \times 5$ cm. Although the tumor was quite large, the prognosis of the patient was good at 6 months postsurgery, and at present the patient is free of recurrence.

CONCLUSIONS

To the best of our knowledge, this is the sixth case of primary synovial cell sarcoma occurring in the jaw. The definitive diagnosis was made by CT scan and immunohistochemistry. Given that jaws are circumvoluted by masseter muscle, temporalis, buccinator, medial pterygoid muscle, and lateral pterygoid muscle, we suspect the true origin of the reported 6 cases of synovial cell sarcoma is undifferentiated myoblasts but is not osteogenic. Exploring this hypothesis is the subject of further work.

The treatment of this tumor was complete surgical resection supplemented with radiation therapy, without chemotherapy. Although the patient currently is free of recurrence, long-term observation is advised, as it has been calculated that tumor size larger than 5 cm associates with poor outcomes.

Consent

Written informed consent was obtained from the patient for publication of this case report and all accompanying images.

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REFERENCES


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