Primary central carcinoma ex pleomorphic adenoma of the mandible: report of a rare case and literature review

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We report a rare case of primary carcinoma ex pleomorphic adenoma (CXPA) of the mandible. A 13-year-old girl presented with a large mass, measuring about 30 cm in its greatest dimension, involving the mandible. She was referred to our department for surgery, and her postoperative course was uneventful; she is currently free from the disease 48 months after surgery. Primary CXPAs located centrally within the jawbones are rare with only 10 cases reported in the English and Chinese literature. This case illustrates 2 key facts regarding the diagnosis and therapy of CXPA. First, clinicians should be aware of this possibility and should emphasize the need for submission of so-called cystic lytic lesions for histopathologic analysis. Second, tumors should be excised en bloc with adjuvant postoperative radiotherapy when local recurrence and regional metastasis are suspected clinically. (Oral Surg Oral Med Oral Pathol Oral Radiol Endod 2011;112:e24-e28)

Pleomorphic adenoma (PA) is the most common benign neoplasm involving both major and minor salivary glands. Malignant PA refers to 3 different entities: (1) carcinoma ex pleomorphic adenoma (CXPA), which is defined by the 2005 World Health Organization’s histologic classification1 as a pleomorphic adenoma in which an epithelial malignancy develops; (2) carcinosarcoma (true malignant mixed tumor); and (3) metastasizing pleomorphic adenoma. CXPA, which develops in primary or recurrent PA, is by far the most common subtype. The incidence of CXPA in all salivary tumors is approximately 3.6% (range 0.9% to 14.0%) and about 12.0% in all salivary malignancies (range 2.8% to 42.4%)1. Primary CXPA located within the jawbones is rare, comprising fewer than 4.34% (range 2.7% to 4.34%)2-4 of all primary central salivary gland carcinomas. In a review of 138 cases of central salivary gland tumors, Brookstone and Huvos2 noted only 6 (4.34%) intraosseous CXPAs. In contrast, intraosseous mucoepidermoid carcinoma, the most common histologic subtype of malignant salivary gland tumors of the jawbones, accounts for 89 of 138 cases. Bouquot et al.3 summarized 224 patients with primary central salivary gland tumors of the jawbones; 6 (2.7%) of these lesions were CXPA. In another review of 197 cases of intraosseous salivary gland tumors from the English and Chinese literature, Li et al.4 reported 8 cases (4.1%) of CXPA. The aim of this article was to report a rare case of central CXPA, which was extremely infiltrative and had a huge gross (30 × 25 cm), primarily involving the mandible. The clinical and radiographical presentation, and microscopic appearance, and treatment of central CXPA are briefly discussed.

CASE REPORT

A 13-year-old girl presented with an expansile asymptomatic mandibular mass of 6 months’ duration involving the mandible. In September 2005, she underwent a dental extraction in a local hospital because of 3 loose teeth. Following the dental extraction, the mass grew rapidly and became large with bleeding. One month later, she underwent an initial excision of the mass in a local hospital, but the details of the findings at the primary operation are not clear. The biopsy was interpreted as ameloblastoma. In November 2005, she was referred to the Department of Oral Pathology at the West China College of Stomatology. Clinical examination showed a poorly circumscribed, nontender mass (30 × 25 cm) in the mandible body. The mass shifted the lower lip outward, and she was not able to open her mouth because of the large mass. No lymph node was palpable. A radiograph (Fig. 1) showed an expansile lytic lesion with irregular margins in the body of the mandible, suggesting a malignant lesion with aggressive and destructive behavior. A large soft tissue mass also occupied the body of the mandible with 3 floating teeth. During the surgery, another mass was found (10 × 10 × 10 cm) connecting to the mandibular mass. Intraoperative frozen section of the node showed a malignant epithelial tumor. Wide surgical excision of the tumor was carried out, with an
en bloc partial resection of the mandible followed by reconstruction with a titanium plate.

Pathologic examination of the resected specimen revealed a firm, gray-white unencapsulated tumor mass with a nodular ill-defined border (Figs. 2, 3, and 4). Frank destruction of the capsule, was evident on examination of serial sections. In addition to the presence of benign pleomorphic adenoma areas that exhibited ductlike structures with a benign appearance, a myoepithelial carcinoma area also existed, occupying more than 80% of the tumor, in which clear myoepithelial cells were arranged in cords and nests with few mitoses and atypical nuclei. Microscopically, this tumor was diagnosed as invasive carcinoma ex pleomorphic adenoma.

**DISCUSSION**

Traditional criteria for diagnosing central CXPAs involving the jaw include the following: 1) absence of a primary salivary gland tumor combine with evi-

Fig. 1. Preoperative orthopantomogram (OPG) showing an expansile lytic lesion with irregular margins in the body of the mandible.

Fig. 2. Photomicrograph showing tumor within the bone matrix. Both benign pleomorphic adenoma areas composed of ductlike structures (right) and carcinomatous components are seen (left) (hematoxylin and eosin [H&E], ×200).

Fig. 3. Photomicrograph of the extensive area showing myoepithelial carcinoma-like changes (H&E, ×200).

Fig. 4. The area of prominent cellularity in which the clear myoepithelial cells are arranged in nodules separated by thin fibrous septa. Focally, the tumor exhibits necrosis (in the center) (H&E, ×100).
dence of a lesion in the maxilla or mandible; (2) radiographic evidence of distinct osteolysis with integrity of cortical bones; (3) absence of any oral mucosal ulceration; (4) clinical and histological, exclusion of an odontogenic or a metastatic lesion; and (5) histologic confirmation of CXPA. However, in our case, penetration of the cortical plate and invasion of nearby tissue had occurred. We diagnosed this case as intraosseous tumor because of primary presentation of mandibular swelling and absence of any primary salivary gland tumors and distinct osteolysis.

In this case the histologic subtype of the malignant component was mainly myoepithelial carcinoma. Generally, the benign component of the CXPA may be minor and is easily ignored, whereas the malignant component is often difficult to classify. As in this case, extensive sampling and careful assessment of the resected lesion may be necessary to identify the PA component.

Primary central CXPAs of the jawbones are uncommon neoplasms, with only 10 cases previously reported to the best of our knowledge. There were detailed records on the tumors in 8 cases. In the 2 cases in which no detailed information was provided, both were located within the maxilla. Following surgery, 1 patient died without definite reason 1 year later, and the other patient was alive for 4 years. Combined with our current case, this represents a total of 11 reported cases. In the 9 cases described in detail (Table I), bony swelling (8/9) was the most common clinical finding, which was followed by spontaneous pain, bleeding, loosening of teeth, and numbness. There were 5 male and 4 female patients, with a mean age of 40 years (range 9 to 68 years). The median age of CXPA in the jawbones is 61 years (range 34 to 95 years) in the study of Olsen and Lewis and 67 years (range 33 to 93 years) in the study of Zbären et al. Both children and adults can be affected by the central CXPA. Fleitz et al. hold the opinion that the tumors in children tended to cause more destruction and deformity than those in adults. In the 8 cases in which the information is known, the duration of symptoms ranged from 1 to 15 months with an average duration of 6 months. Five tumors arose in the maxilla and 6 in the mandible. The most common site was the body of the mandible. Most cases in the literature reported expansion of the involved area; however, in our case it was extremely infiltrative and extruded into the oral cavity. Radiographic imaging in all cases revealed poorly defined and infiltrative margins. All cases were clinically misdiagnosed as ameloblastoma, sarcoma, fibroma, chon-

| Table I. Summary of clinical records of 9 patients with primary central carcinoma ex pleomorphic adenomas of the jawbones from the Chinese and English literature (not serial epidemiologic reports) |
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| Author | Age, y/sex | Site | Complain | Size, cm | Radiography | Clinical diagnosis | Treatment (times) | Radiotherapy | Follow-up, mo |
| Freedman et al. | 36/F | Mandible | Numbness | 9 × 5 × 1 | Well-circumscribed radiolucent | Uncertain | Surgery (4) | Y | At least 16 |
| Fleitz et al. | 9/M | Maxilla | Swelling | 3 × 2 × 1.5 | Well-circumscribed radiolucent | Uncertain | Surgery (2) | NA | Meta |
| Stoll et al. | 33/F | Maxilla | Pain, swelling | 2.5 × 2 × 2.5 | Chondrosarcoma | Chondromyxosarcoma | Surgery (2) | NA | At least 16 |
| Stoll et al. | 34/F | Mandible | NA | 5 | Chondromyxosarcoma | Fibroma | Surgery (4) | NA | Lost |
| Morgan et al. | 52/M | Mandible | Swelling | 6 × 3.5 × 1 | Extensive destruction | Fibroma | Surgery (2) | 0.5 | Loss |
| Zhang et al. | 50/M | Maxilla | Swelling | 4 × 2.5 | Malignant tumor | Malignant tumor | Surgery (1) | NA | 8 |
| Wang et al. | 68/M | Mandible | Swelling | 4 × 3 | Malignant tumor | Malignant tumor | Surgery (1) | NA | 38 |
| Li et al. | 63/M | Mandible | Swelling | 10 × 4 | Malignant tumor | Ameloblastoma | Surgery (1) | NA | 48 |
| Present | 13/F | Mandible | Swelling | 30 × 25 | Ameloblastoma | Ameloblastoma | Surgery (1) | NA | 48 |

F, female; M, male; Meta, metastasize; NA, not available; Re, recurrence; Y, yes.
dromyxosarcoma, or chondrosarcoma, based on preliminary clinical and radiologic findings.

Various theories regarding the origin of central salivary gland tumors have been proposed, including (1) neoplastic transformation of heterotopic entrapment of retromolar mucous glands or developmentally included embryonic remnants of submandibular glands within the mandible; (2) neoplastic transformation of the epithelial lining of odontogenic cysts, mainly dentigerous cysts; and (3) neoplastic transformation of the sinus epithelium. The microscopic presentation of our review of the literature demonstrated no evidence of a dental cyst or impacted tooth. Three cases in the maxilla did not show chronic sinusitis or embedded and entrapped sinus epithelium. Heterotopic salivary tissue gland has been reported in many sites throughout the head and neck region, including the maxilla and mandible. However, the pathogenesis of CXPA in salivary glands is still a matter for debate. Olsen and Lewis\textsuperscript{15} support 2 hypotheses: these tumors were malignant from the onset, or carcinoomatous transformation of a PA occurred. About 1.6% to 7.5% of PAs showed carcinoomatous transformation in long-standing cases.\textsuperscript{17} We favor the first hypothesis that proposes the presence of heterotopic salivary tissues within the jaw with subsequent neoplastic transformation.

Prognosis of the CXPA of the salivary glands is based on pathologic stage, proportion of carcinoma, proliferation index, and extent of invasion.\textsuperscript{1,15,16} Previous articles suggested the histologic subtype of the CXPA was an important prognostic factor and it appeared that the presence of myoepithelial carcinoma histology increased the risk of recurrence and distant metastasis in CXPA.\textsuperscript{18} However, this is in contradiction to in Olsen and Lewis\textsuperscript{15} study of 73 cases, in which the histologic subtype was found not to be a prognostic factor. It is also important that the status of the overlying jaw be considered for central salivary gland tumors. Brookstone and Huvos\textsuperscript{2} proposed a 3-stage classification of intraosseous salivary gland tumors: stage I, lesions without expansion or rupture of the cortical plates; stage II, lesions with some degree of expansion but with intact cortical plates; and stage III, lesions with perforation of the cortical plates or occurrence of regional metastasis. Stage I offers the best prognosis according to this classification; all 9 detailed cases presented here were classified as stage III tumor, which may have a poorer prognosis.

A tumor that is typically considered a high-grade carcinoma is locally recurrent and frequently metastasizes to regional nodes and causes tumor-related deaths. In the 11 described cases, 2 cases developed cervical metastasis after 1.5 years and 4 years, respectively, and were treated with sectional neck dissection. Two cases with local recurrence were treated with wide local excision with postoperative radiotherapy. Few series of central CXPA have reported on long follow-up, making it difficult to analyze prognosis and survival for these tumors. Reliable and proper treatment protocols have yet to be developed for management of central CXPA.

Wide local excision is the main treatment. Neck dissection is applied within the occurrence of regional cervical lymph node metastasis. Generally speaking, the follow-up of central CXPA was short. It will be invaluable to provide complete follow-up of future reports to assess local recurrence and distant metastasis.

Clinically and radiographically, CXPA, which may resemble lesions of odontogenic tumor and osteosarcoma, is characterized by progressive swelling of the jaw, spontaneous pain, loosening of teeth, numbness, and typically presents as a radiolucency with destruction of bone.

REFERENCES


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