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ORIGINAL RESEARCH

Giant myxomas of the maxillofacial skeleton and skull base

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OBJECTIVES: To review our experience with patients diagnosed with giant myxomas of the maxillofacial skeleton.

STUDY DESIGN: All patients undergoing excision of myxomas of the head and neck from September 1998 through September 2003 with a minimum follow-up of 1 year by the senior author (YD) were included in the study.

METHODS: A retrospective chart review was conducted to select all patients who met the inclusion criteria. Clinical presentation, preoperative radiology findings, excisions performed, reconstruction, and follow-up were recorded and reported.

RESULTS: Four patients were identified who met the inclusion criteria. All underwent wide en bloc excision of the tumor with various reconstructions. Complete resection was achieved in each case, and no patients have had evidence of recurrence.

CONCLUSIONS: Giant myxomas of the maxillofacial skeleton have been reported to have significant rates of recurrence. Wide en bloc resection with appropriate reconstruction can result in excellent quality of life postoperatively and minimize the risk of recurrence. Lesser resections may not be appropriate especially in giant myxomas because of the potential morbidity that would be associated with a multifocal recurrence.

EBM rating: C-4

In 1871, Virchow used the term myxoma to describe tumors with histology similar to mucinous tissue of the umbilical cord. However, it was not until 1948 that Stout[1] established the generally accepted diagnostic criteria of this tumor. His original description was that of a mesenchymal neoplasm that did not metastasize and consisted of a loose mucoid stroma with undifferentiated stellate cells.

Myxomas are rare, benign tumors of connective tissue origin that are locally invasive and have been noted to arise within soft tissue and bone throughout the body. The left ventricle of the heart is the most frequent location overall, with the thigh and shoulder comprising other frequent soft-tissue sites.[2] Although the mandible and maxilla are the 2 most common sites of head and neck myxomas, only 3 instances of bony involvement have been documented outside the head and neck. These include the femur, clavicle, and metatarsus. Other less frequent head and neck sites include facial soft tissues, parotid gland, nasal cavity, paranasal sinuses, nasopharynx, and the eyelid.

The most common presentation is that of an otherwise asymptomatic swelling of the mandible or maxilla. In fact, many cases are found as an incidental finding on routine dental examination. Myxomas of the mandible often cause bony expansion that leads to loosening of teeth, root resorption, malocclusion, ill-fitting dentures, and facial deformity. In rare occurrences, patients with advanced tumors may have symptomatic pain, paresthesia of the trigeminal nerve, and anesthesia over the affected area. Because most myxomas are slow growing, generally painless lesions, most maxillary lesions cause bony expansion or extension into the maxillary sinus before the patient seeks medical attention.[3] Proptosis and infraorbital paresthesia are rare findings caused by advanced tumors. Although myxomas are normally slow-growing neoplasms, local trauma has been shown

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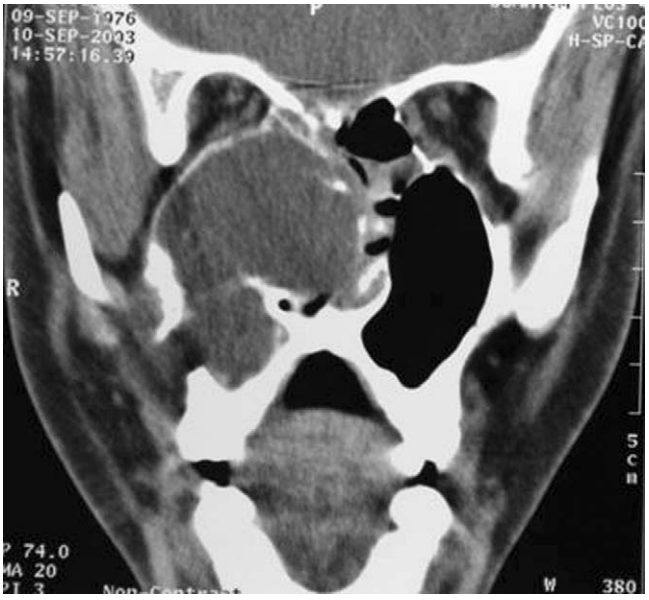

Figure 1 Preoperative coronal CT scan showing massive myxoma of right maxillary sinus with extension to the orbital apex and base of anterior cranial fossa.

to increase their rate of growth. Examples of this observation include tooth extraction, blunt injury, and as a complication of a Le Fort I osteotomy during secondary cleft palate repair.

Although the most frequent age at presentation is during the second to fourth decades,[4] myxomas can occur at any age. However, rarely does this tumor occur before 10 years of age or after the age of 50. Because this is a benign tumor with a slowly progressive course but is highly infiltrative locally, there are many treatment options. All include some form of surgical intervention with adequate margins. Options range from conservative resections, including enucleation or curettage,[5] whereas more aggressive surgeries include wide local resection[6] or en bloc resection (hemimaxillectomy or hemimandibulectomy).[7] Myxomas are known for their frequent recurrences. Recurrence rates vary depending on the method of treatment, with the highest rates occurring after the "conservative" techniques.

In this case series, we will review our experience with 4 cases of giant myxomas of the maxillofacial skeleton, including method of surgical excision, reconstruction, and postoperative follow-up.

A 27-year-old black woman presented to our clinic complaining of maxillary sinus pain, nasal airway obstruction, and hyposmia. She had no visual complaints. A computed tomography (CT) scan (Fig 1) of the sinuses was performed that revealed a unilateral right maxillary sinus mass displacing the floor of the orbit superiorly and obstructing the nasal airway medially. It also abutted the floor of the anterior cranial fossa. A Caldwell-Luc biopsy was performed and was consistent with a myxoid tumor. The patient subsequently underwent a subtotal maxillectomy, orbital resection with reconstruction of the orbital floor, and anterolateral maxilla with split-thickness calvarial bone grafts. Eighteen months postoperatively, the patient has had no visual complaints or evidence of disease recurrence based on radiographic and clinical examination.

A 68-year-old woman presented for evaluation of an enlarging mandibular mass (Fig 2). A biopsy was taken and a diagnosis of myxoma made. The patient subsequently underwent a hemimandibulectomy with fibula free flap reconstruction. Seven years postoperatively, the patient is eating normally, the flap remains viable, and she has no evidence of disease recurrence.

A 30-year-old white man presented with a maxillary sinus tumor, which he reported was partially resected 6 years previously. He reported progressive disfigurement of his face with loosening of his dentition, dysphagia, and nasal obstruction over the previous 15 years. Physical examination revealed a massive lesion occupying the right hard and soft palate with contiguous extension from the right maxillary sinus into the nasal cavity and infratemporal fossa. A CT scan showed a large 6×7 cm expansive mass of relatively low attenuation and central bony component involving the right maxilla (Fig 3). The mass extended into the soft tissues of the cheek, the hard palate, and the oral cavity. A magnetic resonance imaging (MRI) scan showed a large multiloculated tumor measuring $7 \times 7 \times 10$ cm involving the right maxillary sinus (Fig 4). The tumor showed increased signal on T2-weighted images, intermediate and low-signal intensity on T1-weighted images, and patchy central and mild partial peripheral contrast enhancement with gadolinium. Bone scan showed increased uptake in the maxillary sinus but was otherwise negative. The patient underwent endoscopic biopsy of the lesion. Pathologic examination revealed fragments of nonkeratinizing stratified squamous epithelium showing marked acanthosis and some parakeratosis and hyperkeratosis. The underlying connective tissue was expanded by a lesion composed of delicate stellate cells with regular oval nuclei and moderate amounts of elongated ciliated cytoplasm set in a myxoid stroma. A diagnosis of myxoma was made. The patient underwent right total maxillectomy and resection of tumor at the skull base and orbital apex with obturator reconstruc-

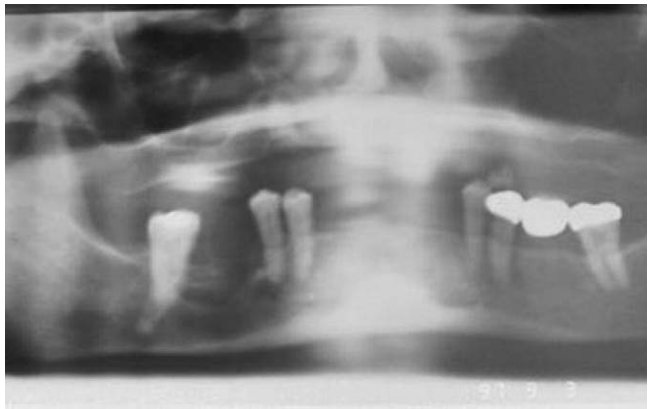

Figure 2 Preoperative panorex showing lytic destruction of right mandibular body with root involvement.

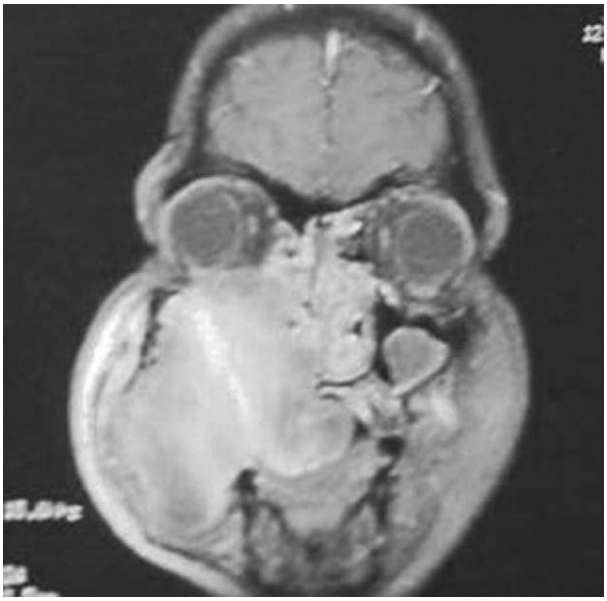

Figure 3 Coronal MRI scan showing expansion of the right maxillary sinus with involvement of the orbital floor.

tion. Three years postoperatively, the patient is eating normally and has no evidence of disease recurrence.

A 37-year-old white man presented after having 3 limited surgeries for an odontogenic myxoma of the mandible. The patient's previous surgeries included a narrow-field segmental mandibulectomy and free iliac crest bone graft, and his last surgery was 1 year previous to presentation. On presentation, the patient reported progressive enlargement and distortion of his left face with nasal airway obstruction and enlargement of his left neck. CT scan showed a 4.5 × 3 cm septated mass originating from the posterior two thirds of the previously resected mandible and extending into the left neck and base of skull (Fig 5). An MRI scan showed extension along the nasopharynx to the anterior skull base without intracranial extension (Fig 6). The patient was taken to the operating room and underwent left mandibulectomy, left maxillectomy, excision of tumor from the skull base and nasopharynx, and tracheotomy with a planned return for secondary reconstruction. Pathologic examination revealed multinodular profileration of bland spindles to stellate cells set within a myxomatous chondroid matrix punctuated by small-caliber bland nonanastomosing vessels and occasional collagenous strands. At the time of the planned reconstruction, the patient underwent further resection that was negative for tumor and underwent fibular free flap reconstruction. Three years postoperatively, the patient is eating a regular diet and has no evidence of recurrence.

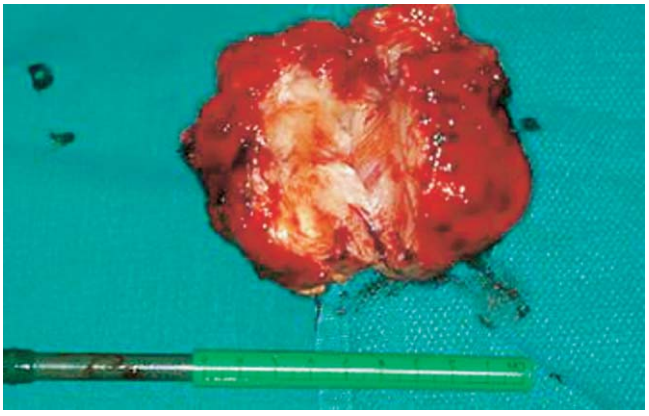

Figure 4 Cut section of gross specimen showing jelly-like amorphous nature of resected myxoma of patient in Figure 3.

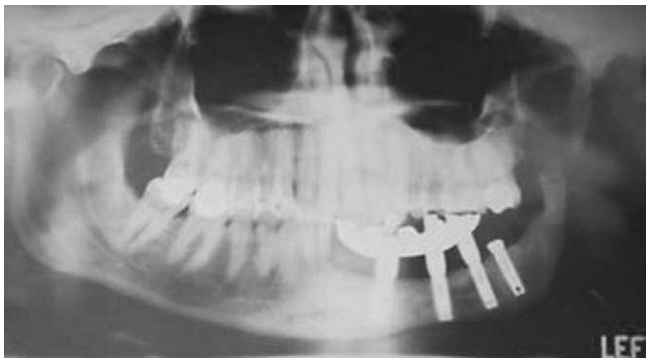

Figure 5 Preoperative panorex of patient with massive recurrent myxoma destroying left hemimandible and temporomandibular joint.

DISCUSSION

Although myxomas are rare, benign tumors that are locally invasive and arise in both soft tissue and bone throughout the body, their etiology remains uncertain. In 1940, Ewing[8] presented evidence suggesting their origin was from remnants of embryonal mesenchyme. In 1948, Willis[9] postulated that myxomas were derived from degenerative changes in fibroblasts, whereas Stout was the first to de-

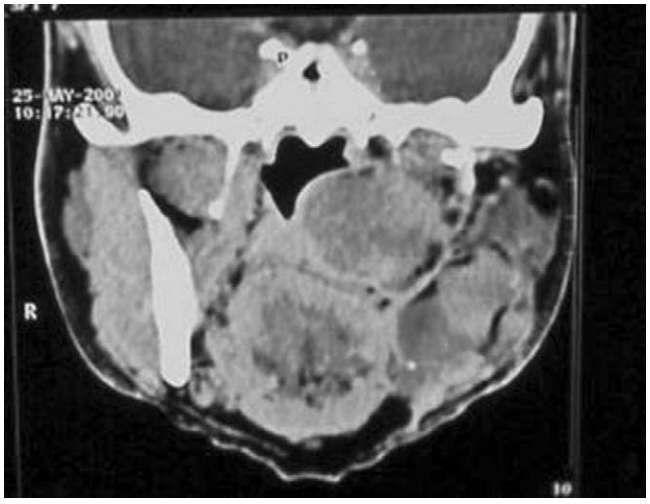

Figure 6 Preoperative coronal CT scan showing destruction of left hemimandible and extension to base of middle cranial fossa.

scribe them as a true mesenchymal neoplasm.[2] The discovery of inclusion bodies in intramuscular myxomas by Glazunov and Puchkov[10] in 1960 led them to postulate an infectious origin. In addition, evidence has been presented suggesting local trauma as a cause. Today, it is generally accepted that myxomas arise from primitive embryonic mesenchymal cells or fibroblasts with the propensity to produce copious mucopolysacharides.

Greater than 60% of myxomas in the head and neck occur in the facial bones, of which, over 75% arise in either the mandible or the maxilla at a 3:1 ratio.[11] Although 74% of the maxillary myxomas cause bony expansion, only half ultimately extend into the maxillary sinus. Nearly 75% of head and neck myxomas occur in adults, with the vast majority diagnosed between the second and fourth decades.[3] However, they can occur at any age, as evidenced by a maxillary myxoma occurring in an 11-month old.[12] Patients' most common complaint is that of a slow-growing, painless mass, which ranged from 1 month to 24 years before medical attention was sought.[11] This finding is supported by the slow progression of myxomas. Finally, there is a slight female predominance.[3]

On plain films and CT scans, myxomas appear similar to other benign, slow-growing lesions by prominent bony destruction and remodeling. Early in their growth, the bony cortex appears thinned and expanded, which can ultimately result in a perforation from the continuous growth. Of note, these lesions vary significantly in their radiographic appearance. Although the majority appear as well circumscribed, radiolucent masses, they can also appear as radiopaque or even mixed tumors. In addition, although myxomas can appear either as a unilocular or multilocular mass, the latter are much more common in myxomas greater than 4 cm in diameter.[3] Although the central radiolucent compartments commonly have a soap-bubble, trabeculae appearance, they less frequently have a honeycomb or tennis-racquet appearance because of the formation of septa.[11]

As with the other radiographic modalities, there is significant variability in the intensity of myxomas using MRI. This variability has been postulated to be related to either the mucoid substance viscosity or the protein density of the tumor.[13] Therefore, radiographic plain films, CT scans, and MRI are used primarily to aid in determining the extent of the lesion before surgical resection instead of as a diagnostic modality.

Grossly, myxoma of the jaw is typically a poorly circumscribed mass with a white, gelatinous cut surface and occasional small fluid-filled cyst-like spaces. The tumor may expand but remain confined to the bone from which it arises or it may extend into the adjacent soft tissue. Histologically, the tumor is composed of sparse, cytologically bland stellate and spindled cells with ovoid hyperchromatic nuclei and scant cytoplasm, scattered within an abundant myxoid stroma with few collagen strands and a poorly developed vascular pattern. In general, the histologic appearance is similar to that of its more common counterpart in the soft tissue, although myxomas of the jaw tend to exhibit a slightly greater degree of cellularity, cellular pleomorphism, and a higher rate of mitosis. Additionally, in contrast to myxomas arising in soft tissue, myxomas of the jaw may contain strands of odontogenic epithelium, which are favored to represent fetal remnants. Other features that may occasionally be present include small foci of calcification, increased fibrous tissue, encapsulation, a prominent vascular pattern, and the presence of multinucleate tumor cells.

The spindled and stellate cells of myxoma are fibroblasts and myofibroblasts, which stain positively for vimentin and may show some positivity for S-100 protein and muscle-specific actin.[14,15] The myxoid matrix is composed of glycosaminoglycans rich in hyaluronic acid and stains positively with Alcian blue, mucicarmine, and colloidal iron.

Because myxoid areas may be present in a number of different lesions involving the head and neck, the differential diagnosis of myxoma of the jaw is broad and ranges from benign, nonneoplastic lesions to various malignant neoplasms. Some of the entities that may present a differential diagnostic dilemma include pleomorphic adenoma, nodular fasciitis, fibrous dysplasia, chondromyxoid fibroma, neurofibroma, and sarcomas with myxoid areas including myxofibrosarcoma, rhabdomyosarcoma, and liposarcoma. The histologic features of myxoma are sufficiently distinct such that a correct diagnosis should not be problematic when adequate material is available for examination. Because of the broad differential for myxoid lesions in the head and neck, however, myxoid lesions should be thoroughly sampled and diagnosis deferred on small biopsies or fine-needle aspiration specimens showing only myxoid material until the entire lesion can be examined.

The mainstay of treatment is surgery; however, the extent of resection varies between authors. Conservative resections include enucleation or curettage,[5] whereas more aggressive surgeries include wide local resection[6] or en bloc resection (hemimaxillectomy or hemimandibulectomy).[7] One major complication with conservative resections is a higher recurrence rate,[11,14] attributed to poorly defined tumor boundaries because of their incomplete capsules. Although conservative methods have a higher recurrence rate, they have been performed in an effort to minimize morbidity. Our favorable esthetic and functional outcomes in our series of giant myxomas with no evidence of recurrence would tend to support aggressive en bloc resections of these neoplasms whenever technically feasible. Furthermore, conservative treatment increases the likelihood of further surgical procedures, thereby risking greater facial morbidity or deformity.[16]

Recurrences have occurred as early as 3 months and as long as 15 years after primary resection; however, the most common time period for recurrence is 2 years.[14] Of note, although bony myxomas have a proclivity to recur, no matter the method of resection, intramuscular myxomas have never recurred. Radiation therapy has no role in the treatment of myxomas, which is supported by 2 studies

showing little to no response to radiotherapy.[17,18] However, in 1966, Attie et al[19] used preoperative radiation to shrink maxillary tumors encroaching on the orbital floor in 2 patients. Both patients responded well, allowing complete resection of the masses without sacrifice of the orbital floor.

Finally, before performing surgery on a patient with a myxomatous tumor, one must be cognizant of the myxosarcoma variant. Although these tumors grossly appear identical to myxomas, they have a very invasive growth pattern. Two examples of this malignant variant have resulted in infiltration and destruction of the skull base and intracranial extension, even after multiple aggressive resections.[14,20] Although they have the same appearance of stellate cells and a myxoid matrix, they also contain stellate cells with nuclear pleomorphism and atypical, bizarre mitotic figures. Karyotype analysis has also shown these tumors to contain chromosomal abnormalities.[14] In addition, although no individual has died from a myxoma, myxosarcoma has directly led to the death of 3 individuals.[14,20]

In conclusion, myxomas are rare, benign tumors of connective tissue origin that are locally invasive and destructive. They arise in soft tissue and bone throughout the body. Although they can occur in many different locations of the head and neck, the 2 most frequent sites are the mandible and the maxilla. Because the most common complaint at presentation is asymptomatic swelling of the mandible or maxilla, the treating physician must include myxomas in his or her differential. Wide en bloc resection with primary reconstruction appears to be associated with a favorable esthetic and functional outcome while minimizing risk of recurrence. We do not favor lesser resections because of high recurrence rates and the mutlifocal oftentimes difficult to treat nature of any recurrences that do occur.

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