

Case of the Season: Gnathic Osteosarcoma



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A case of chondroblastic osteosarcoma of the mandible, followed by a discussion of this entity and other pathology of the masticator space.

Case Report

A 42-year-old male with no significant prior medical history presented with gradually progressive symptoms involving the left jaw. The patient reported mild discomfort and soreness of the temporomandibular joint (TMJ), and following ENT referral, was initially treated for presumed TMJ dysfunction using conservative methods such as a mouth guard. The patient's symptoms continued to progress however, and an associated mass eventually became apparent prompting imaging.

Maxillofacial noncontrast computed tomography (CT) was performed for the initial imaging evaluation, which revealed a mass within the left masticator space. The bulk of the mass appeared to be centered on and medial to the left mandibular ramus, which was markedly irregular in appearance with areas of severe cortical thinning and destruction, other areas of cortical thickening, as well as extensive periosteal reaction, some of which showed a “sunburst” appearance (Fig. 1). The mass was fairly well-circumscribed, predominantly soft tissue and fluid in attenuation with scattered central calcifications, and expansile resulting in mass effect on the adjacent maxillary sinus and parapharyngeal space. There was visible bowing and cortical thinning of the adjacent lateral maxillary wall and lateral pterygoid plate (Fig. 2). Thinning was additionally noted involving the greater wing of the sphenoid at the superior aspect of the mass.

Open biopsy of the mass was performed, and pathology revealed a high-grade tumor containing osteoid and cartilaginous differentiation, which following an initial diagnosis of chondrosarcoma was revised to chondroblastic osteosarcoma.

Subsequent magnetic resonance imaging (MRI) was performed and demonstrated a fairly well-circumscribed mass within the left masticator space which appeared hyperintense on T2 with predominantly peripheral as well as a few scattered areas of central enhancement (Figs. 3-4). Initial PET/CT revealed a predominantly photopenic mass with peripheral FDG uptake. No areas of definite metastatic involvement were identified.

The patient underwent surgical resection of the mass with free-flap reconstruction. Surgical pathology at that time was again suggestive of a chondroblastic type of high-grade conventional osteosarcoma.

Over the following months the patient underwent several alternative treatments abroad, after which time he began to develop worsening symptoms including increased facial swelling, difficulty with mastication, left-sided headaches, tongue paralysis/paresthesia, dysphagia, and hoarseness. MRI performed at that time was concerning for residual/recurrent tumor as well as a small area of perineural spread into the middle cranial fossa via foramen ovale.

Over the course of the next 6 months the patient was treated with chemoradiation. Shortly thereafter the patient's condition continued to worsen, and repeat imaging showed increased intracranial extension (Fig. 5) with progressive signal abnormality and enhancement within the left temporal lobe. The patient's mental status continued to deteriorate, and he was eventually discharged home with hospice where he passed approximately 18 months after his initial CT (Fig. 6).

Discussion

The masticator space, centered on the mandibular ramus, additionally contains the muscles of mastication and mandibular division of the trigeminal nerve (V3). Masticator space pathology can extend into the middle cranial fossa via perineural spread along the mandibular nerve through foramen ovale, as seen in our case of osteosarcoma. Secondary invasion into the masticator space can also occur. Because malignant tumors may appear well defined and confined to the masticator space, biopsy should be performed when a mass is identified. When imaging the masticator space CT

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Figure 1 Initial evaluation with CT demonstrates a mass within the left masticator space with destruction of the left mandibular ramus and aggressive periosteal reaction.

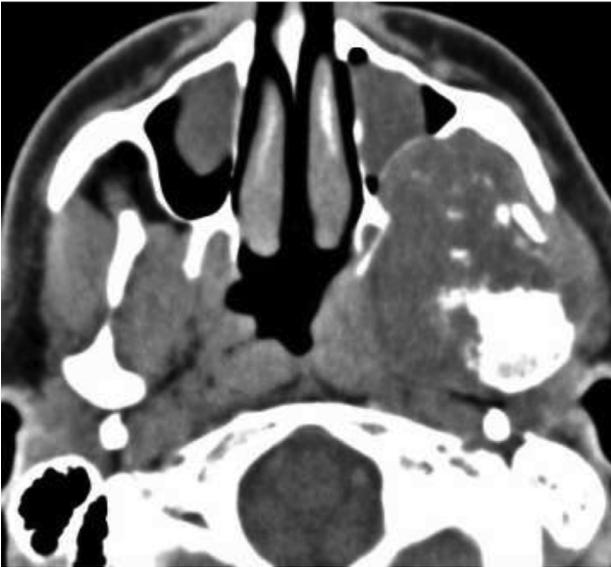


Figure 2 Soft tissue windows again demonstrate osseous destruction with soft tissue involvement containing matrix calcifications, as well as bowing of the lateral maxillary wall and pterygoid plate.

and MRI act in a complimentary fashion, with CT superior for the detection of subtle osseous erosion and tumor matrix mineralization, whereas MRI better demonstrates soft tissue extension and perineural tumor spread.¹

The most commonly encountered pathology within the masticator space represents extension of odontogenic infection/abscess, which is often seen in patients with poor dental hygiene and dental caries or following tooth extraction. Patients often present with infectious signs and symptoms, absent from our case, as well as trismus. Imaging demonstrates inflammatory

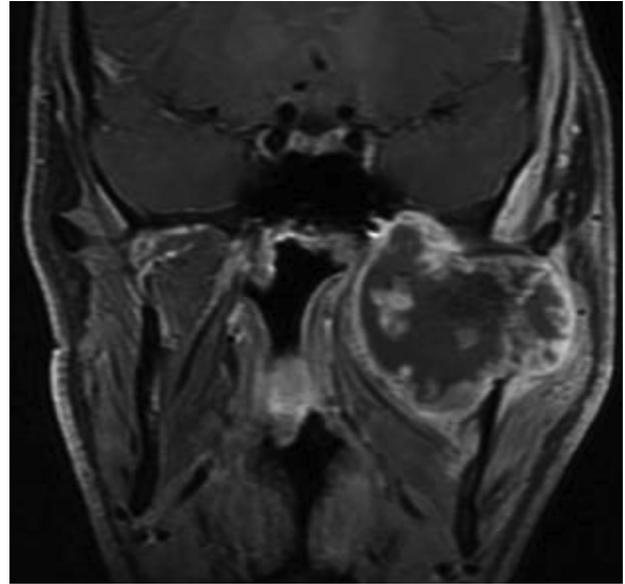


Figure 3 Contrast-enhanced T1-weighted MRI demonstrates a well-circumscribed expansile mass centered on the left mandibular ramus. Peripheral as well as scattered central enhancement is seen.

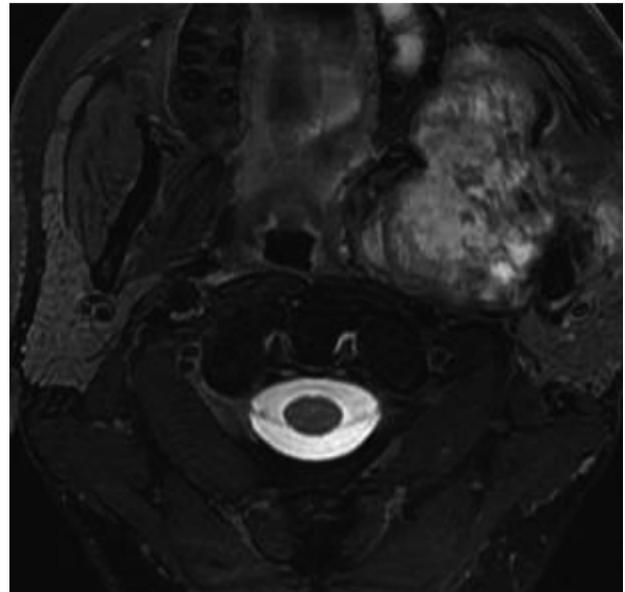


Figure 4 Fat-suppressed T2-weighted MRI shows a T2 hyperintense mass containing scattered central areas of T2 hypointensity corresponding with matrix mineralization.

changes within the soft tissues, such as enlargement, inhomogeneous enhancement, and T2 hyperintensity of the muscles of mastication, as well as a well-defined gas and fluid-containing collection in the case of abscess.^{1,2} Similarly, osteomyelitis of the mandible can occur separately or as a complication, and shows lytic changes with cortical thinning/disruption on CT in the acute phase, or with enhancing T1 hypointensity and T2 hyperintensity of the bone marrow on MRI.² Osteonecrosis of the mandible is a well-described entity that can mimic acute osteomyelitis on imaging, and should be considered in patients with a history of radiation therapy or bisphosphonate use. Imaging

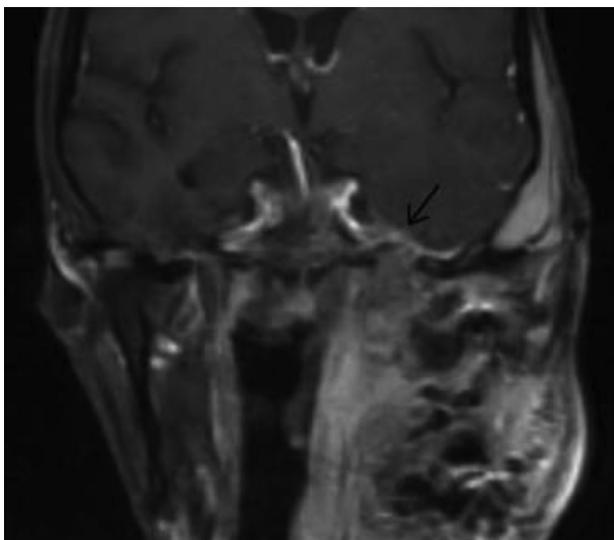


Figure 5 Repeat contrast-enhanced MRI at the time of recurrence demonstrates marked enlargement of the heterogeneously enhancing mass with extension into the middle cranial fossa via foramen ovale and associated dural thickening/enhancement.



Figure 6 Extensive involvement within the left neck at the time of recurrence with characteristic matrix mineralization.

findings can make this a difficult entity to distinguish from tumor recurrence in patients with a history of radiation.² In the case of chronic osteomyelitis, sclerosis and periosteal thickening is seen.

Additional odontogenic pathology such as ameloblastoma, which shows a characteristic expansile “soap bubble” appearance on CT, more commonly involves the mandibular body around the crown of a tooth, with secondary extension into the mandibular ramus. The mandibular third molar is most commonly involved. Ameloblastomas, unlike odontogenic cysts such as dentigerous cysts or odontogenic keratocysts, may demonstrate an enhancing soft tissue component. The

appearance of both entities can otherwise be highly variable on MRI. Aneurysmal bone cysts (ABCs), as well as simple bone cysts (including post-traumatic) are other classically described lucent lesions that can affect the mandible. ABCs usually occur in children and are suggested by the presence of a fluid-fluid level on CT or MRI.¹

Fibro-osseous lesions have additionally been known to affect the mandible. Fibrous dysplasia typically appears as osseous expansion with “ground-glass” density on CT. Ossifying fibromas appear as well-circumscribed lesions with variable radiodense/radiolucent appearance, with a possible characteristic “halo” of less ossified fibrous tissue.¹

Osteomas and tori are benign outgrowths that can involve the mandible, commonly appearing as densely mineralized, well-circumscribed masses, typically without a medullary cavity. Mandibular tori typically arise from the inner surface of the mandible above the level of the mylohyoid, and are often seen bilaterally.

Nonosseous tumors can be encountered within the masticator space, such as nerve sheath tumors (Schwannomas or neurofibromas), which typically arise from the mandibular nerve. Schwannomas appear as oval or fusiform masses that are soft tissue density on CT and homogeneously T2 hyperintense and enhancing on MRI, though may be heterogeneous when large. Neurofibromas may demonstrate the characteristic “target sign” on T2-weighted imaging with central hypointensity and peripheral hyperintensity, and when multiple or plexiform should raise suspicion for neurofibromatosis type 1. Vascular malformations can also be seen in the masticator space, as well as soft tissue tumors such as rhabdomyosarcoma.¹ The presence of matrix calcifications makes primary soft tissue sarcoma less likely.²

Metastatic involvement of the mandible, which is more common than primary mandibular tumors, as well as multiple myeloma are worthwhile differential considerations in the adult population.¹

Gnathic osteosarcoma, unlike chondrosarcoma and Ewing's sarcoma of the mandible, occurs fairly commonly, comprising approximately 4%-8% of all osteosarcomas.⁵ Gnathic osteosarcoma more commonly affects the mandible, particularly the mandibular body, however can also be seen in the maxilla, where the alveolar ridge is most commonly involved. Patients often present 10-20 years later than the typical appendicular osteosarcoma with a peak incidence of 30-40 years of age (although may be seen in a much wider range), and with a slight male predilection. Risk factors include a history of Paget's disease or prior radiation therapy, particularly in patients over the age of 40. Patients are often asymptomatic however may present with a mild dull/gnawing pain and swelling. Lack of symptoms, initial misdiagnosis, or inadequate initial biopsy often results in delayed diagnosis at an advanced stage. Lack of signs and symptoms of inflammation should raise suspicion for neoplastic conditions. Rapid growth may occur as a result of hemorrhage, secondary infection, or dedifferentiation.³

Histopathology demonstrates malignant mesenchymal cells that invariably produce bone matrix (referred to as “osteoblastic

osteosarcoma” when the predominant feature), although this may be present in minimal amounts and missed on initial biopsy, particularly with superficial samples. Superficial biopsy and resultant lack of osteoid/bone matrix may lead to misdiagnosis as pyogenic granuloma (PG) due to presence of granulation tissue or other nonmatrix producing lesion such as fibrosarcoma. Well-differentiated osteosarcoma may also be confused with an ossifying fibroma or other benign reactive osseous lesion at biopsy. Variable amounts of cartilaginous matrix can also be produced, and is the predominant feature in the “chondroblastic osteosarcoma” subtype. In the third subtype, “fibroblastic osteosarcoma”, neither of these features predominates. The appearance at initial biopsy is key due to possible presurgical chemotherapy-related changes at the time of surgical resection.³

Initial imaging evaluation may be performed with panoramic radiographs at the patient's oral health care provider. On radiographic and CT imaging gnathic osteosarcoma classically appears as an osseous-based tumor with cortical expansion, osseous destruction, and soft tissue invasion. Imaging classically progresses from initially radiolucent to mixed radiolucent-radiopaque containing an osteoid pattern of matrix mineralization in later stages. A “sunburst” radiopaque pattern may be seen arising from the cortical bone.³ Differentiation from chondrosarcoma and Ewing's sarcoma can be difficult based on imaging findings alone, although osteosarcoma is far more common.¹ Appearance on MRI varies depending on the degree of matrix mineralization, which appears hypointense on both T1 and T2, with solid nonmineralized tumor typically appearing intermediate on T1 and hyperintense on T2. Contrast enhancement is variable and heterogeneous.⁶ Soft tissue extension is better seen on MRI as is perineural tumor spread, which appears as widening or destruction of the neural foramen and excessive enhancement of the nerve. Resultant

denervation may lead initially to enlargement and increased enhancement of the muscles of mastication with eventual muscle atrophy and weakness.¹

Tumors are often treated with preoperative chemotherapy followed by complete surgical excision and postoperative chemotherapy and/or radiation.³ The overall prognosis for gnathic osteosarcomas is favorable when compared to osteosarcoma of the long bones, with reported 5-year survival rates in the range of 52%-77%. However, a higher grade at presentation and the presence of disease recurrence, both of which were seen in our patient, are associated with decreased overall survival.⁴ Additional negative prognostic factors include secondary presentation (history of prior radiation), maxillary location, larger size, positive surgical margins, and lower degree of necrosis at the time of surgical resection.^{4,5}

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