Osteosarcoma is the most common primary bone malignancy. It typically originates in the long bones, with only 6 - 13% of patients presenting with a primary tumor of the head and neck. Osteosarcoma of this region has a peak incidence in the fourth decade of life, more than a decade older than osteosarcoma of the long bones [1]. The prognosis is more favorable than that for osteosarcomas of the extremities, with the mainstay of therapy being surgical resection. The mandible and maxilla are the predominant sites of head and neck osteosarcomas [2]; those that present in the orbit are extremely rare. We report the case of a primary orbital osteoblastic osteosarcoma that masqueraded as a hyperostotic sphenoorbital meningioma. The osteosarcoma was successfully resected via a modified orbitozygomatic approach, after preoperative planning with a team of neurosurgeons, radiologists, oncologists, and radio-oncologists.

**CASE REPORT**

A 35-year-old woman was admitted to our institution with a 1-month history of blurred right vision and increasing right proptosis. The patient reported neither pain nor other symptoms. She denied having previous head trauma or surgery. Eye examinations revealed decreased right visual acuity but no restricted ductions or visual field defects. Her progressive right proptosis had an insidious onset, and this was first noticed by her coworkers and family.

A magnetic resonance imaging (MRI) scan of her brain revealed a well-defined mass arising from the superior and lateral walls of the right orbit, lying extraconally and measuring 3 × 2 × 2 cm, causing medial displacement of the right lateral rectus muscle and the optic nerve. Most of the mass was isointense relative to the gray matter on both
T1- and T2-weighted images, but it showed internal hypointensity, indicative of a significant calcified component. The mass enhanced strongly after intravenous injection of a gadolinium-based contrast agent (Fig. 1). The initial diagnosis made by neuroradiologists was hyperostotic meningioma, but the significant mineralized component and bony involvement made primary bone tumor a possibility that needed to be excluded.

A computed tomography (CT) scan of her brain was subsequently performed, which revealed a hyperattenuating mass arising from the superior and lateral walls of the right orbit (Fig. 2). The mass consisted of largely mineralized as well as soft-tissue components, and it showed cortical destruction. The mineralized component was consistent
with extensive osseous matrix, whereas the soft-tissue components were enhanced strongly after intravenous administration of an iodinated contrast medium. These findings supported the diagnosis of an aggressive primary bone tumor, namely, osteosarcoma. Staging workup of the chest, abdomen, and bones was negative for any distant metastases.

A modified orbitozygomatic approach was chosen to gain access to the orbital tumor. After the orbitozygomatic bone flap was removed, a grayish-red tumor was identified comprising both stony-hard and soft components, arising from the greater wing of the right sphenoid bone. With careful dissection, the tumor could be separated from the adjacent periorbita. Gross total tumor excision was performed smoothly. Then, the orbitozygomatic bone flap was repositioned and fixedated with miniplates and screws, and the fascia and temporalis muscles were anatomically repaired. After the operation, the patient recovered normal right visual acuity and had satisfactory cosmetic results.

Histopathologic examination of the tumor revealed proliferations of atypical plump neoplastic stromal cells with copious osteoid matrix. The tumor cells contained moderate nuclear pleomorphism and distinct nucleoli, with focal sheet-like arrangements, scattered mitotic figures, and mono- or multinucleated giant cells. There was evident tumor involvement of the vascular spaces as well as tumor permeation in the marrow spaces of neighboring trabeculae. Immunohistochemical staining was negative for cytokeratin, epithelial membrane antigen, and HMB-45, which excluded metastatic carcinoma and melanoma. A high-grade osteoblastic osteosarcoma was diagnosed accordingly (Fig. 3).

Because of high tumor grading and vascular space involvement, this patient received adjuvant CT-guided intensity-modulated radiation therapy (total dose, 60 Gy) in the tumor bed, followed by 2 cycles of systemic chemotherapy consisting of doxorubicin, ifosfamide, high-dose methotrexate, and cisplatin. She developed uncomplicated neutropenia during chemotherapy; otherwise, no notable adverse effects were reported. Serial CT scans followed in the outpatient setting, and she remained tumor free 1 year after surgery.
Orbital osteosarcoma masqueraded as hyperostotic meningioma

**DISCUSSION**

Osteosarcoma is a primary malignant neoplasm that arises from the metaphysis of long bones, most frequently at the distal femur and proximal tibia. Tumors of the craniofacial bones occur infrequently, constituting only 6% to 13% of all osteosarcomas. The majority of head and neck osteosarcomas occur in the mandible and maxilla of patients in the fourth decade of life, a decade older than when they trend to occur in the extremities [1]. Head and neck osteosarcomas that arise in the extragnathic bones are infrequent, those in the orbit are exceedingly rare and seldom present with complete illustration. When they mimic the appearance of hyperostotic meningiomas, as in this case, they complicate the diagnosis and the surgical planning.

The clinical manifestation of head and neck osteosarcomas depends on the location of the tumor, with focal pain and swelling being the most frequent symptoms of mandibular lesions. Osteosarcomas that involve the maxilla, paranasal sinuses, and orbit are less likely to present with pain, but symptoms typically relate to the site of the tumor [3]. For example, as in this case, it can present with ocular symptoms including proptosis, diplopia, ophthalmoplegia, and others comparable to retrobulbar masses.

Radiographically, osteosarcoma of the long bones demonstrates a mixed osteoblastic and osteolytic pattern, but pure osteoblastic and osteolytic types are also seen [4]. Most tumors show a variable amount of intraleisonal fluffy, cloudlike opacities, characteristic of osseous matrix production. The higher-grade osteosarcomas are associated with aggressive periosteal reactions (Codman’s triangle, laminated, hair-on-end, or sunburst patterns) and soft-tissue masses, in most cases [4]. Osteosarcomas of the head and neck have distinctly different radiographic appearances. While most mandibular lesions are osteoblastic or mixed in appearance, most lesions of the other craniofacial bones tend to be osteolytic. Periosteal reaction is observed infrequently, and only in mandibular lesions [5].

Conventional radiographs have limited value in the diagnosis of head and neck osteosarcomas because of superimposed bone structures. CT, on the other hand, provides excellent characterization of tumor matrix mineralization and cortical involvement. It shows an expansile bony lesion with increased density and aggressive periosteal reaction in pre-contrast study and enhancement of the solid component after contrast administration. Although inferior to CT in the detection of calcification, MRI provides a better demonstration of the intramedullary and extraosseous tumor components. MRI shows heterogeneous findings: the mineralized part of the tumor shows low signal intensity on both T1 and T2 images, while the solid non-mineralized part of the tumor shows intermediate signal intensity on T1WI and hyperintensity on T2WI. A variable degree of enhancement of the solid, non-mineralized part is observed.
on enhanced T1WI.

In our case, the patient initially presented with blurred right vision followed by progressive right proptosis, which suggested a mass effect on the optic nerve at the level of the orbital apex. Imaging studies showed a well-defined mass with calcification and enhancement arising from the superior and lateral walls of the right orbit, causing medial displacement of the lateral rectus muscle and the optic nerve. The differential diagnosis would have included hyperostotic meningioma, osteosarcoma, hemangiopericytoma, angiosarcoma, malignant fibrous histiocytoma, or osteoblastic metastasis. The presence of hyperostosis of the bone and calcification (mineralized part) of the tumor excluded the possibility of hemangiopericytoma and angiosarcoma. The osseous matrix of the tumor, revealed by the CT scan, made the diagnosis of malignant fibrous histiocytoma less likely. The lack of primary tumors also excluded metastasis. Thus, hyperostotic meningioma and osteosarcoma were the 2 possible diagnoses, which might have similar pattern features on MRI scans.

The difficulty in diagnosing our case was, in part, due to choosing MRI study over CT scan as the first-hand examination. While MRI offered excellent resolution of the tumor extent in the right orbit, it was unable to reveal any information on the matrix calcification, and hyperostotic meningioma was the initial diagnosis made by neuroradiologists on the basis of its location, strong enhancement, and suspicion of a dural tail sign. CT enabled better characterization of the osseous matrix and cortical destruction, both highly indicative signs of osteosarcoma. Moreover, the lack of inner table periosteal reaction, inward vault bulging of the lesion, surface irregularity of the hyperostotic bone, and intracranial change also did not support the diagnosis of hyperostotic meningioma. After reviews by several experienced musculoskeletal pathologists as well as interdepartmental discussion with neurosurgeons and radiologists, we diagnosed the patient with a high-grade osteoblastic osteosarcoma was made. The three-dimensional volume-rendering of the craniofacial bones, provided by the multidetector CT scan, also provided invaluable information on preoperative planning.

Histologically, osteosarcoma arises from immature bone-forming cells or through neoplastic differentiation of other immature mesenchymal cells into the osteoblasts. By definition, these tumors have proliferating malignant cells that produce a characteristic osteoid matrix. Depending on the predominant differentiated element, osteosarcoma can be classified into osteoblastic, chondroblastic and fibroblastic subtypes. Although there is no significant association between the histological type and patient survival, osteoblastic cases have been shown by Smith et al. to have a lower 5-year survival rate compared to the chondroblastic cases [6]. In addition to histological typing, the tumors can be graded from I to IV, according to the degree of anaplasia of the stromal content. The higher-grade osteosarcomas have been reported to show a negative correlation with survival [1, 6].

Complete surgical excision is the mainstay of treatment for head and neck osteosarcomas [6, 7]. The prognosis for extragnathic tumors is poorer than that for those arising from the mandible and maxilla because tumors at these locations are more difficult to resect and to achieve negative surgical margin. Since negative surgical margin has been reported to be the only significant predictor of overall and disease-specific survival, meticulous preoperative planning, with the goal of complete surgical excision, is important for these patients. With advances in neuroimaging and microsurgical techniques, previously inaccessible tumors at difficult locations can now be resected readily.

For osteosarcomas that are unresectable, the use of chemotherapy and radiation therapy is straightforward, but there is a controversy regarding their use in the adjuvant and neoadjuvant settings to curative surgery. Two recent meta-analyses, by Kassir et al. and Smeele et al., have reported conflicting conclusions on the impact of adjuvant chemotherapy on survival [8, 9]. This discrepancy may be due to flaws inherent to retrospective analyses of multi-institutional patient populations treated with different treatment protocols. Despite the absence of a universally accepted guideline, the prevailing trend in the literature is to treat head and neck osteosarcomas in a multidisciplinary manner (neoadjuvant or adjuvant chemotherapy and postoperative radiation therapy) [7].

Because of the posterior location of the tumor in the right orbit, our neurosurgical team performed a gross total excision of the tumor via a modified orbitozygomatic approach, similar to the one-piece supraorbital modified orbitozygomatic craniotomy described by Lemole et al. [10]. This approach enabled better exposure and reduced brain retraction, while leaving the malar eminence and zygoma root unexposed, thus preserving the frontal branch of facial nerve. It also permitted good exposure of the tumor at the superolateral orbit, with minimal bone loss. Because of evident vascular space involvement by tumor cells, our multidisciplinary team reached a consensus to perform radiation therapy and chemotherapy after surgery. This patient was followed regularly at our oncology clinic, with no tumor recurrence found at 1 year after surgery.

In summary, orbital osteosarcomas are very rare tumors that may masquerade as the more commonly seen sphenoorbital meningiomas. Obtaining the correct preoperative diagnosis may prove crucial in this highly malignant disease that requires aggressive treatment and planning from a multidisciplinary team of neurosurgeons, radiologists, oncologists and radio-oncologists. Complete surgical excision is critical to successful outcomes for these patients. Chemotherapy and radiation therapy may be of survival benefit in high risk patients in an interdisciplinary combination with surgical resection.
REFERENCES