Giant cell tumor of the skull in pediatric patients

Report of two cases

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✓ Giant cell tumors of the bone are rare, locally aggressive lesions that primarily affect the epiphyses of long bones. These tumors can occur in the skull, principally in the sphenoid and temporal bones. Symptoms of these tumors depend on their site of origin but typically include headache, pain, visual field defects, and conductive hearing loss. Histologically, these tumors consist of three cell types: osteoclast-like multinucleated giant cells; round mononuclear cells resembling monocytes; and spindle-shaped, fibroblast-like stromal cells. Radiographically, the tumors appear osteolytic and radiolucent without a sclerotic border. These tumors typically present in the third to fourth decades of life and rarely occur in patients under 20 years of age. The small number of studies of giant cell tumors of the skull has focused on the adolescent and adult populations.

The authors report two cases of giant cell tumors of the skull in pediatric patients. In the first case, a 2-year-old girl presented with swelling behind the right ear. In the second case, a 7-week-old girl presented with a mass within the external auditory canal. Both patients underwent metastatic workup and biopsy procedures before resection of the tumor. Both case reports contribute to the literature of giant cell tumors of the skull by describing this condition in pediatric patients. To the authors’ knowledge, these cases represent the youngest two patients with giant cell tumors of the skull yet described. (DOI: 10.3171/PED-07/07/069)

KEY WORDS • external auditory canal • giant cell tumor • osteoclastoma • pediatric neurosurgery • temporal bone

GIANT cell tumors of the bone (or osteoclastomas) are rare primary bone neoplasms, representing approximately 5% of all bone tumors. These tumors occur primarily in the epiphyses of long bones, especially in the distal femur, proximal tibia, and distal radius; however, they may also occur in the skull, most commonly in the sphenoid and temporal bones. Histologically, these tumors consist of three cell types: osteoclast-like multinucleated giant cells; round mononuclear cells resembling monocytes; and spindle-shaped, fibroblast-like stromal cells. Radiographically, the tumors appear osteolytic and radiolucent without a sclerotic border. Giant cell tumors have a low potential for metastasis, but are locally aggressive with a high rate of recurrence (40–60%). Resection is the preferred treatment for giant cell tumors of the skull, with local recurrence rates and prognosis for these tumors both correlate with the extent of resection. In this report, we describe two cases of giant cell tumors of the temporal bone in patients younger than 3 years of age, with an emphasis on neuroimaging features and management of these tumors.

Case Reports

Case 1

History and Examination. This 2-year-old girl presented with a 5-month history of an enlarging mass located behind her right ear. The mother stated that the patient occasionally cried and scratched at the mass in a manner indicating it was causing discomfort. The mother denied any evidence of nausea, vomiting, weight loss, fever, or changes in the child’s neurological function. During examination the child was awake, alert, and acting appropriately for her age. The results of her neurological examination were normal. Behind the girl’s right ear, a firm lesion (3 cm in diameter) was present that protruded approximately 2 cm. Skin and hair of a normal appearance covered the minimally tender mass.

Magnetic resonance images with and without Gd enhancement (Fig. 1) revealed a 5 × 7 × 7-cm mass centered...
in the posterior aspect of the right temporal bone, which caused expansion of the temporal bone and displaced the dura mater. This extradural lesion caused mass effect on the temporal lobe and cerebellum. The MR images revealed an intermediate signal on T1-weighted images; heterogeneous, but in general, low signal intensity on T2-weighted images; low signal intensity on diffusion-weighted images; and heterogeneous enhancement after the administration of Gd. The radiographic differential diagnosis included sarcoma, hemangiopericytoma, fibrosarcoma, or primitive neuroectodermal tumor. A nuclear medicine bone scan and a CT of the chest and abdomen showed no metastatic disease.

Operation and Postoperative Course. A biopsy specimen of the lesion was then obtained. Frozen section and permanent slides of the specimen showed histological features consistent with those of a giant cell tumor (Fig. 2).

Resection of the lesion was then planned. Prior to surgery, the patient underwent cerebral angiography with embolization of the vessels supplying the tumor. Branches to the tumor were supplied by the right occipital artery, right middle meningeal artery (anterior and posterior divisions), and right superficial temporal artery. The interventional radiologist reported greater than 90% occlusion of the tumor vascular bed with embolization.

The tumor was initially debulked. The skull adjacent to the tumor was removed until the margin of the tumor was exposed. Using microsurgical techniques, the tumor was re-moved from the surface of the dura. All bone involved by tumor, including the apex of the petrous bone, was removed. Gross-total resection of the tumor was achieved and confirmed by postoperative MR imaging, leaving a 9 × 9–cm skull defect (Fig. 1C and D). The patient has had no neurological deficits either before or after the surgery. A follow-up MR image obtained 13 months postoperatively showed no evidence of recurrence. To date, the patient has not required cranioplasty.

Case 2

History and Examination. This 7-week-old infant presented with a 3-week history of a rapidly enlarging mass in her left EAC. A biopsy procedure, performed when she was an outpatient prior to admission, showed only keratin debris. At the time of her admission, the patient was noted to have drainage from a friable, fungating mass in the EAC and fullness in the left parotid region. A CT scan of the head and neck with and without contrast enhancement demonstrated a heterogeneously enhancing mass within the left temporal bone causing opacification of the middle ear. The lesion involved the EAC and extended inferiorly to the parotid gland, internal auditory canal, confluence of sinuses, and cerebellopontine angle. The radiographic differential diagnosis included rhabdomyosarcoma, eosinophilic granuloma, and metastatic neuroblastoma. Otolaryngologists then performed a biopsy procedure of the mass in the EAC followed by a biopsy procedure of that portion of the tumor extending to the parotid region. Examination of the specimens revealed giant cell tumor in these locations (Fig. 3).

Magnetic resonance images of the brain and neck with and without contrast enhancement (Fig. 4) showed a mass centered within the left temporal bone that appeared extradural. The mass had a low signal intensity on T2-weighted images and enhanced on T1-weighted images after contrast agent administration. The lesion extended inferiorly into the left parotid gland.
A nuclear medicine bone study and a CT scan of the chest revealed no areas of metastasis. The patient underwent angiography for potential embolization of arteries feeding the tumor. Branches of the ascending pharyngeal and posterior auricular arteries were noted to feed the tumor; however, these arteries were deemed too small for embolization by the interventional radiologist.

**Operation and Postoperative Course.** The patient was taken to the operating room where a gross-total resection of the mass was accomplished and confirmed by postoperative MR imaging. Postoperative deficits in the patient included a persistent left facial palsy. A follow-up MR image obtained 11 months postoperatively revealed some lymphadenopathy and surgical changes, but clearly no intracranial tumor. Cranioplasty was not required for this patient.

**Discussion**

Giant cell tumors, originating from connective tissue within bone marrow, are benign, locally aggressive lesions with the potential to metastasize to the lung. Giant cell tumors constitute 3 to 7% of all primary bone tumors; 90% involve the epiphysis of long bones, and less than 2% involve the skull. Although rare, cranial giant cell tumors occur most frequently in the endochondral bone of the middle fossa floor with a specific tendency to occur in the sphenoid and temporal bones. In 1969, Pitkethly and Kempe reported that, of 429 tumors of the skull, five were giant cell tumors: one in the temporal bone, one in the mastoid bone, and three in the sphenoid bone. In 1981, Schajowicz and coworkers noted that of 350 cases of giant cell tumors, five were in the skull, specifically in the sphenoid and temporal bones. In 1987, Findlay et al. recorded 23 cases of giant cell tumor of the skull in the literature: 12 tumors in the sphenoid bone, six in the petrous temporal bone, one in the middle fossa, and four elsewhere within the cranial vault. The series of 546 cases of giant cell tumors described by Bertoni and colleagues at the Mayo Clinic confirmed these earlier findings, as only three cases involved the sphenoid bone and one the temporal bone.

Giant cell tumors of the skull typically present in the third and fourth decades of life with a slightly higher predominance in women and a high rate of recurrence (40–60%). These tumors are exceptionally rare in individuals younger than 20 years of age. Their characteristic presentation depends on their site of origin and local anatomy. Temporal bone giant cell tumors present with pain (usually behind the ear on the affected side), conductive hearing loss resulting from the tumor invading the infratemporal fossa and obstructing the Eustachian tube, and facial weakness. Giant cell tumors involving the sphenoid bone present with symptoms including headache, ophthalmoparesis, trigeminal hypesthesia, and vision failure. Giant cell tumors within the sellar region present with symptoms including headache, visual field defect, blindness, diplopia, dysfunction of the second through eighth cranial nerves, neck pain, endocrinopathy, and mental status changes.

Radiographic features of giant cell tumors typically include a radiolucent, osteolytic lesion causing bone erosion without a sclerotic rim, but with sharp margins on CT. Magnetic resonance imaging of giant cell tumors demonstrates a well-circumscribed lesion that is isointense on T1-weighted images and hypointense on both T2-weighted...
and diffusion weighted images. The mass typically enhances heterogeneously. Digital subtraction angiography may show significant vessels feeding the tumor. In one of the cases presented here, the configuration of the vessels was amenable to preoperative embolization.

Other lesions that must be considered in the differential diagnosis include giant-cell reparative granuloma, aneurysmal bone cyst, chondrolysisplasia, eosinophilic granuloma, plasmacytoma, metastatic lesions, fibrous dysplasia, Ewing sarcoma, and “brown tumor” of hyperparathyroidism. Of these other lesions, giant-cell reparative granuloma must be differentiated from giant cell tumor because their prognosis and treatment differ.2

Ewing sarcoma of the skull may present with clinical and radiographic findings similar to giant cell tumor, although primary Ewing sarcoma of the skull is extremely rare. The lesion may present as a painful mass of the skull or with lateralizing neurological signs. The tumors typically enhance on T1-weighted MR images after intravenous Gd administration.3 Ewing sarcoma may be distinguished from giant cell tumor in that histopathological examination shows sheets of periodic acid–Schiff positive cells with scant cytoplasm, indistinct cell borders, and uniform small, oval nuclei when stained with H & E.4 Accurate identification of Ewing sarcoma is imperative because postoperative adjuvant chemotherapy and radiation therapy are standard practice.

Giant-cell reparative granuloma is a nonneoplastic proliferative lesion that occurs in response to hemorrhage or trauma. It is typically found in the mandible and maxilla but has been reported to occur in the frontal bone.9,16,17 Giant-cell reparative granuloma is distinguished from giant cell tumor histologically by the fibrogenic quality of the stroma in the former. The stroma is composed of proliferating fibroblasts found palisading around areas of osseous metaplasia or foci of hemorrhage.42 Excision of giant-cell reparative granuloma is effectively a cure.

According to Wulling et al.,43 the histologic features of giant cell tumors consist of three cell types: osteoclast-like multinucleated giant cells; round mononuclear cells resembling monocytes; and spindle-shaped, fibroblast-like stromal cells. Wulling et al.43 further postulate that stromal cells secrete monocyte chemotactic proteins that stimulate monocyte migration to bone and their subsequent fusion into osteoclast-like, multinucleated giant cells. Thus, the stromal cell component may be of neoplastic origin and the multinucleated giant cells may be a reactive component. Histological types of tumors wherein giant cells may be found include osteogenic sarcoma, chondrosarcoma, malignant fibrous histiocytoma, chondromyxoid fibroma, or eosinophilic granuloma.

Immunohistochemistry may help distinguish giant cell tumors from other lesions, such as chondroblastoma and osteosarcoma. Tumor giant cells are CD68 positive, indicating a monocyte or macrophage origin.11,18 Both stromal cells and tumor giant cells are negative for Mac-387 (another monocyte/macrophage marker) and S100 protein. Negative S100 staining eliminates the possibility of a chondroblastoma. The authors of one study showed stromal cells and giant cells to be vimentin and MIB-1 positive,18 whereas another group found negative reactivity of tumor stromal cells to vimentin.11 The patterns of mononuclear tumor cell lysozyme staining and proliferating cell nuclear antigen staining are variable, but may help distinguish the giant cell tumor from osteosarcoma and chondroblastoma.11

Surgical excision is the preferred treatment for giant cell tumors of the skull.2,26,37,38 Local recurrence rates and prognosis both correlate with the extent of resection. Giant cell tumors are considered locally aggressive and may recur at or near the site of resection. Tumor growth or recurrence may compromise vital neurological or vascular structures, particularly in the parasellar region.17 Invasion of the tumors into the dura26 and cortex11 has been reported. In addition, the location of giant cell tumors is not always amenable to complete resection; therefore, some authors have reported their experience with adjuvant therapy.

There are few data supporting a role for chemotherapy in the treatment of these lesions. Although giant cell tumors are locally aggressive, malignancy develops in only 5 to 10% of cases.35 When these tumors do metastasize, the usual location is the lung.3,20 Tumors that may benefit from chemotherapy are those that are incompletely resectable or those that recur and are not considered suitable for reoperation. Recurrence rates, reported to be 40 to 60%, correlate with the extent of resection and develop within 2 years.7 According to Yamamoto44 and Maloney27 and their colleagues, no standard protocol exists for the treatment of giant cell tumors with chemotherapy. Patients have, however, been treated with interferon-alpha and chemotherapeutic regimens consisting of methotrexate, cyclophosphamide, and doxorubicin with limited success.14,44

Anract et al.1 treated 11 patients with malignant giant cell tumor of the bone using combined chemotherapy and surgery. Two patients underwent preoperative chemotherapy followed by surgery. The first patient died of pulmonary metastatic disease after 66 months; the second patient remained alive without recurrence after 5 years of follow-up. In evaluating all 11 patients, Anract and colleagues1 found the 1-year survival rate to be statistically higher for patients treated with combined surgery and chemotherapy than for those treated by surgery alone. The 5-year survival rates and actuarial survival curves were not statistically different between the groups, however.

Osaka and coworkers60 evaluated six patients with giant cell tumors of bone and pulmonary metastases. All six patients received chemotherapy: cyclophosphamide 100 mg/day for 3 to 6 years in three cases; and doxorubicin 50 mg/m², cisplatin 120 mg/m², and vincristine 2 mg administered three to four times in three cases. In two cases, the pulmonary metastases were decreased in size either because of the chemotherapy or because of spontaneous regression. In two other cases, the metastases were slow-growing with chemotherapy. In the final two patients, chemotherapy was not effective, according to the authors, because the patients died early.

Because there is not a well-defined, accepted protocol for treatment of giant cell tumors with chemotherapy, Maloney et al.27 recommend against the use of chemotherapy in view of the unproven benefit and potentially significant morbidity of this adjuvant therapy.

Like chemotherapy, the use of postoperative radiation therapy for incompletely resected tumors is controversial. Some authors believe that giant cell tumors are not radiosensitive and that radiation may cause a sarcomatous transformation in the residual tumor tissue. Distinguishing whether a malignant transformation represents the natural course of
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the disease or the development of true postirradiation sarcomas is difficult. Thus, other authors recommend a single course of a moderate dose, megavoltage radiation therapy to decrease the likelihood of malignant transformation. According to Yamamoto and colleagues, in the past two decades radiation therapy using newly developed megavoltage equipment has been utilized as adjuvant treatment for giant cell tumors and has resulted in excellent local control of the disease.

Conclusions

Giant cell tumors are benign, locally aggressive lesions of bone with the potential to metastasize. Although typically found at the epiphyses of long bones, giant cell tumors may occur in the skull, most commonly in the sphenoid and temporal bones. These tumors typically present in the third to fourth decades of life and rarely occur in patients under 20 years of age. Surgical excision is the treatment of choice for giant cell tumors of the skull. Local recurrence rates and prognosis both correlate with the extent of resection. This report contributes two cases of giant cell tumor of the skull, specifically of the temporal bone, to the literature. More important, the cases reported here represent the youngest two patients harboring giant cell tumors of the skull yet described. One must, therefore, include giant cell tumor as a possible diagnosis in neonates and infants presenting with enlarging skull lesions.

References


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