Giant Cell Tumor of the Sphenoid Sinus Presenting with Nasal Obstruction and Cranial Neuropathies.

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Abstract

Introduction
Giant cell tumor of bone are rare, usually benign but locally aggressive neoplasms that primarily occur in the epiphyses of long bones. Less than 2% of all giant cell tumors occur in the head and neck. Skull base giant cell tumors most frequently involve the sphenoid and petrous temporal bone and very rarely in the ethmoid, frontal, parietal, and occipital bones. The occurrence in the sphenoid bone is due to the endochondral ossification during development as compared to membranous ossification of other bones of the skull. Giant cell tumors have high recurrence rates after incomplete surgical excision. Even with advances in endoscopic surgical techniques, complete resection in skull base tumors is not possible without functional compromise.

Case:
We present a 27 year old female who presented to our institution on 9/30/18 with a 1 month history of retro orbital headache, neck pain, nasal obstruction, and blurred vision. CT head showed a 5 cm mass involving the sphenoid sinuses with invasion into the sella, posterior ethmoid sinuses and clivus. She was taken for endoscopic endonasal biopsy on 10/2 which was consistent with giant cell tumor. Patient presented to the emergency department 5 days later with new onset diplopia of the right eye and worsening headache. She was found to have a right sided cranial nerve 6 palsy. MRI showed invasion into the cavernous sinus with encroachment on the optic chiasm and internal carotid arteries bilaterally. Patient underwent endoscopic endonasal transsphenoidal resection of the mass the following day with final pathology consistent with giant cell tumor. Post operatively her symptoms improved. Her cranial nerve 6 palsy slowly improved over the course of several months following surgical resection. The patient received 120 mg of subcutaneous denosumab every 4 weeks, with additional doses on Days 8 and 15 during the first month of therapy to treat any residual disease and prevent recurrence of the tumor. Three month post treatment MRI showed no evidence of residual disease.

Conclusion:
Giant cell tumors of the skull base are rare benign locally aggressive with high recurrence rates. The age of presentation is usually between 20 and 40 years with a predominance in females. The presenting clinical symptoms vary widely depending on tumor location. Hearing loss, headache, tinnitus and dysfunction of the cranial nerves are the usual modes of presentation in skull base involvement. Surgical excision remains the treatment of choice but the possibility of incomplete resection and high recurrence rates, adjuvant therapy is considered necessary for local control.

Introduction

Giant cell tumor of bone are often benign, locally aggressive neoplasms that occur in the epiphyses of long bones. Giant cell tumors account for 3-5% of primary bone tumors with less than 2% occurring in the head and neck. Due to the rarity of primary skull-base giant cell tumors, standard treatment regimens remain unclear. Such tumors frequently present in the second and third decade of life and have a female predominance. Symptoms vary depending on tumor size and location and may include headache, cranial nerve palsy, proptosis, and diplopia. Skull base giant cell tumors most frequently involves the sphenoid and petrous temporal bone and more rarely in the ethmoid, frontal, parietal, and occipital bones. The increased occurrence in the sphenoid bone is due to the endochondral ossification during development as compared to membranous ossification of other skull bones. Even with advances in endoscopic surgical techniques, complete resection of skull base tumors is often not possible without functional compromise. Additionally, these tumors have high recurrence rates with incomplete surgical excision. Recent utilization of the NF-kappa B ligand (RANKL) inhibitor Denosumab shows utility in decreasing tumor burden and preventing tumor recurrence.

Case Presentation:

A 27 year old female presented to our institution with a one month history of retro-orbital headache, neck pain, nasal obstruction, and blurred vision. CT head identified a sphenoid mass with extension into the sella, clivus, and ethmoid sinuses. MRI showed a clival mass extending into the sphenoid sinus and cavernous sinus with a mass effect on the contents of the sella turcica. An endoscopic endonasal biopsy was performed with pathology consistent with giant cell tumor. The patient was discharged with plans to resect the mass using a two team approach at a later date.

The patient then presented to the emergency department five days later with new onset diplopia of the right eye, nasal drainage, and worsening headache. She was found to have a right sided cranial nerve six palsy. MRI showed invasion into the cavernous sinus with encroachment on the optic chiasm and internal carotid arteries bilaterally. The patient was admitted to the hospital with plans for urgent surgical resection of the mass. She underwent combined resection of the mass the following day in a combined procedure performed by Otolaryngology and neurosurgery.

Treatment

Surgical Procedure
An endoscopic endonasal approach was initiated by Otolaryngology. The nasal cavity and ethmoids sinuses were opened bilaterally. The face of the sphenoid was taken down bilaterally. The left ethmoid and sphenoid bones were noticed to be grossly destroyed by infiltrating tumor. Due to size of the mass and high likelihood for a CSF leak a large nasal septal flap was elevated. The posterior nasal septum was then removed, creating a common cavity for the subsequent bimanual approach. A significant amount of tumor was then removed from the nasal cavity. The Neurosurgical team continued removal of tumor within the sphenoid sinus and overlying the carotid arteries bilaterally. The tumor capsule was scarred to the clival and sellar dura, requiring meticulous dissection to avoid injury to the pituitary and carotid arteries. An abdominal fat graft was utilized for closure due to a grade 1 CSF leak and bony dehiscence over the sella and carotid arteries. The nasal septal flap was subsequently positioned over the fat graft.

Post-operative management and recovery
Final pathology was consistent with giant cell tumor. Post operatively the patient's symptoms slowly improved, including her cranial nerve 6 palsy. Due to concern for incomplete resection, adjuvant medical therapy was advised. The patient received 120 mg of subcutaneous denosumab every four weeks, with additional doses on Days 8 and 15 of therapy. Three month post-treatment MRI showed no evidence of residual disease

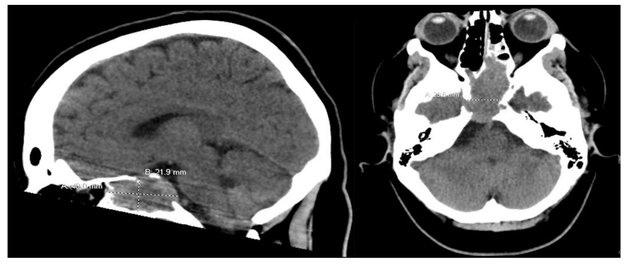


Figure 1. CT Head: Large mass filling and expanding the sphenoid sinuses with invasion into the adjacent sella, posterior ethmoid sinuses, and clivus.

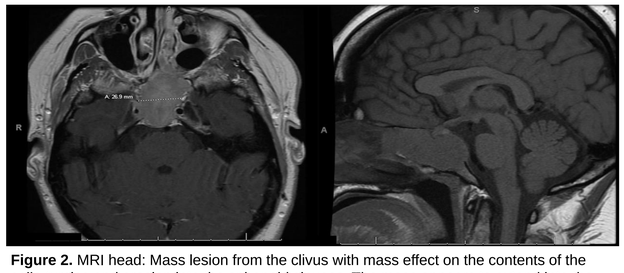
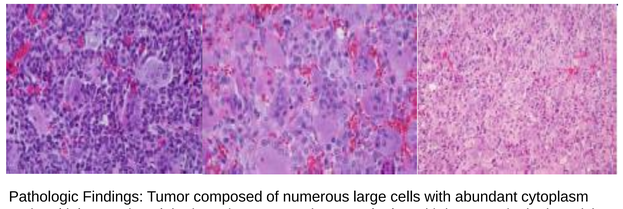


Figure 2. MRI head: Mass lesion from the clivus with mass effect on the contents of the sella turcica and erosion into the sphenoid sinuses. The mass appears to extend into the cavernous sinuses and is in close proximity with the internal carotid arteries bilaterally.



Pathologic Findings: Tumor composed of numerous large cells with abundant cytoplasm and multiple round nuclei. These have a prominent nucleolus with increased mitotic activity.

Discussion

Giant cell tumor is a benign yet aggressive tumor that consists of both osteoclast-like giant cells and osteoclast precursor cells. Research has identified chromosomal instability secondary to centrosome alterations as a potential mechanism for its aggressive nature. The incidence of giant cell tumor within the skull is rare and surgical resection is the treatment of choice. The primary method of mid skull-base access remains the minimally-invasive endoscopic endonasal approach. This approach allows for precise identification and resection of the tumor, decreasing overall morbidity. Due to a high local recurrence rate, complete resection is preferred. This is often made difficult by the tumor's proximity to essential structures. It is for this reason that adjuvant therapy is recommended after local resection, particularly if the entire mass is not excised.
Adjuvant therapies, particularly for recurrent, partially-resected, or multifocal disease, include medical therapy and radiation. Medications used in the past include standard chemotherapy and bisphosphonate agents. Radiation has also been utilized to reduce primary tumor recurrence, yet with a historical risk of malignant transformation and secondary malignancies. The recent approval and utilization of the human monoclonal RANKL inhibitor Denosumab for giant cell tumor has provided physicians an additional therapeutic option for neoadjuvant and adjuvant management of this aggressive neoplasm.
The RANK signaling cascade is essential for physiologic bone remodeling. The combination of RANKL (secreted by osteoblastic cells) and RANK (located on osteoclastic cells) stimulates osteoclastic bone resorption. In the early 2000's, the RANK pathway was identified to play a role in the pathogenesis of giant cell tumor. Denosumab has shown to significantly reduce the tumor burden of giant cell tumors by upwards of 90%, all while remaining safe with minimal adverse effects By binding to and inhibiting RANKL, Denosumab disrupts osteoclastic activity. The response to denosumab therapy can be seen both histologically and radiographically. Giant cell tumor tissue analysis after denosumab therapy has shown to decrease both giant cell tumor numbers and underlying stromal cell proliferation. Post-denosumab therapy radiographic findings include decreased tumor size, bone lysis, and standardized fluorodeoxyglucose (FDG) uptake.
Due to the difficulties associated with skull base surgery, denosumab is particularly interesting as both neoadjuvant and adjuvant treatment for skull base giant cell tumors. Neoadjuvant denosumab therapy for preoperative tumor downstaging has shown to decrease patient morbidity and frequency of surgical management. Various case reports have identified regression of sellar lesions and a decrease in associated symptoms after initiating denosumab therapy.

Conclusion

Giant cell tumors of the skull base are rare benign locally aggressive with high recurrence rates. The age of presentation is usually between 20 and 40 years with a predominance in females. The presenting clinical symptoms vary widely depending on tumor location. Hearing loss, headache, tinnitus and dysfunction of the cranial nerves are the usual modes of presentation in skull base involvement. Surgical excision remains the treatment of choice, yet due to the possibility of incomplete resection and high recurrence rates, adjuvant therapy is considered necessary for local control.

References

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