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 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 involve the sphenoid and petrous temporal bone and more rarely in the ethmoid, frontal, parietal, and occipital bones. The increased incidence in the sphenoid bone is due to the endonasal 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 8/18/11 with a 1 month history of right orbital headache, neck pain, nasal obstruction, and blurred vision. CT head showed a 5 cm mass involving the sphenoid sinuses with invasion into the sphenoid, posterior ethmoid sinuses and clivus. She was taken for endoscopic endonasal biopsy on 8/22 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 VI palsy. MRI showed invasion into the cavernous sinus with encroachment on the optic chiasm and internal carotid arteries bilaterally. Patient underwent endoscopic endonasal transphenoidal resection of the mass the following day with final pathology consistent with giant cell tumor. Post operatively her symptoms improved. Her cranial nerve VI palsy slowly improved over the course of several months following surgical resection. The patient received 125 mg of subcutaneous denosumab every 4 weeks, with additional doses on Days 8 and 15 of therapy. 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 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 Presentation:

A 27 year old female presented to our institution with a one month history of right orbital headache, neck pain, nasal obstruction, and blurred vision. CT head showed a 5 cm mass involving the sphenoid sinuses with invasion into the sphenoid, posterior ethmoid sinuses and clivus. She was taken for endoscopic endonasal biopsy on 8/22 which was consistent with giant cell tumor. Post operatively her symptoms improved. Her cranial nerve VI palsy slowly improved over the course of several months following surgical resection. The patient received 125 mg of subcutaneous denosumab every 4 weeks, with additional doses on Days 8 and 15 of therapy. Three month post-treatment MRI showed no evidence of residual disease.

Treatment

Surgical Procedure

An endoscopic endonasal approach was initiated by Otolaryngology. The endonasal biopsy was performed with pathology consistent with giant cell tumor. Post operatively the patient's symptoms slowly improved, including her cranial nerve VI 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.

Discussion

Giant cell tumor is a benign yet aggressive tumor that consists of both osteoclast-like giant cells and osteoblast precursor cells. Research has identified chromosomal instability secondary to centrosome alterations as a potential mechanism for its aggressive nature. The incidence of giant cell tumors is highest in the skull base and surgical resection is the treatment of choice. The primary method of mid skull base access remains the minimally-invasive endonasal/ethmoidal endoscopic 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 more challenging due to tumor 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.

Adjunctive therapies, particularly for recurrent, partially-removed, or multifocal tumors, 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%, 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 tumor cell number and underlying stromal 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 appealing as both neoadjuvant and adjuvant treatment for skull base giant cell tumors. Neoadjuvant denosumab therapy for preoperative tumor downsizing has shown to decrease patient morbidity and frequency of surgical management. Various case reports have identified resolution 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 but the possibility of incomplete resection and high recurrence rates, adjuvant therapy is considered necessary for local control.

References

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