Skull Base Chondrosarcoma
Evidence-Based Treatment Paradigms

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KEYWORDS

• Chondrosarcoma • Skull base • Microsurgery • Radiotherapy

KEY POINTS

- Cranial chondrosarcomas are generally low-grade, indolent malignancies of bone that cause morbidity through compression of neurovascular structures at the skull base.
- The mainstay of treatment for chondrosarcoma is surgical resection followed by adjuvant radiation therapy. Although proton beam radiotherapy is often considered optimal management, multiple radiotherapy modalities demonstrate equivalent efficacy in long-term studies.
- Surgical approaches should be selected based on pattern of tumor growth and attachment, as well as preexisting neurologic deficits.
- Although chemotherapy is not currently part of the standard treatment regimen for chondrosarcoma, emerging molecular-targeted therapies may contribute to tumor control in the future.

INTRODUCTION

Chondrosarcoma is the second most common primary malignancy of bone, arising from cells of chondroid (cartilage) origin throughout the axial and appendicular skeleton.[1] Only 1% of chondrosarcomas arise in the skull base, and account for 6% of all skull-base tumors.[2] The vast majority of cranial tumors are low to intermediate grade with indolent growth and low metastatic potential.[3] However, their intimate association with critical neural and vascular structures at the skull base often results in significant morbidity from tumor growth and surgical intervention. The mainstay of therapy for chondrosarcoma is surgical resection, with fractionated radiation therapy used to limit recurrence. Recently, radiosurgery has been investigated as an alternative to fractionated radiotherapy. There has been little role for chemotherapy in the treatment of this disease.

This review examines the published literature on the management of cranial chondrosarcoma, including the importance of the extent of microsurgical resection and the multiple modalities of adjuvant radiation including radiosurgery, proton beam, and heavy-particle radiotherapy. The goal is to provide an evidence-based guideline for the management of this rare and complicated disease. In addition, laboratory evidence is presented for new molecular targets to improve emerging chemotherapies for chondrosarcoma.

PATHOLOGY

Cranial chondrosarcoma occurs primarily at the base of the skull, arising from rests of chondrocytes within the synchondroses of the basilar skull bones.[4] Tumors are found most often in the paraclival region arising from sphenopetrosal, petro-occipital, or spheno-occipital synchondroses.[5] The vast majority of lesions involve the bone of the clivus, and extend anteriorly into the parasellar sinuses or middle cranial fossa (30%–50%), or posteriorly into the posterior fossa (50%).[6] Although invasion through the dura is uncommon, compression of the brainstem or temporal lobe is frequent at presentation (**Fig. 1**).[6] Cranial chondrosarcoma occurs preferentially at the skull base,

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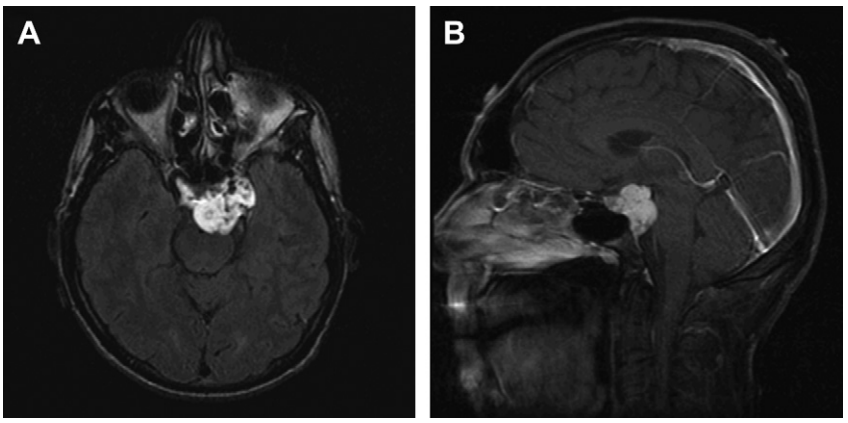

Fig. 1. T2-weighted axial FLAIR (*A*) and T1-weighted contrast enhanced sagittal (*B*) images of a patient with a skull-base chondrosarcoma centered at the left petroclival junction.

owing to differences in bone development between the cranial vault and the basilar structures. The cranial vault grows primarily by intramembranous ossification, whereas the basilar skull bones develop by endochondral ossification and retain rests of chondrocytes into maturity, which can undergo malignant degeneration.[7,8] Most chondrosarcomas develop sporadically, although tumor formation has been associated with diseases of endochondroma formation including Ollier disease and Maffucci syndrome.[9]

Chondrosarcoma manifests grossly as a destructive, mineralized mass that invades bone and extends into soft tissues. Lesions typically grow in bone with an infiltrative pattern, replacing normal marrow elements and spreading through Haversian canals.[10] Eventually lesions break through the cortex and invade surrounding soft tissue. Histopathologically, chondrosarcomas can be of the conventional, mesenchymal, clear-cell, or dedifferentiated type. Almost all skull-base tumors are the conventional type, with rare (<10%) mesenchymal lesions reported.[11] The clear cell and dedifferentiated types do not occur in the axial skeleton. Conventional chondrosarcoma can be composed of hyaline or myxoid cartilage, or a combination of the two (**Fig. 2**). Conventional lesions are graded according to the degree of cellularity, cytologic atypia, and mitotic activity on a 3- or 4-tiered scale, with the lowest grade representing well-differentiated tumors. In the 2 largest case series of skull-base chondrosarcoma reported in the literature, 50% of the lesions were low grade (grade 1) and nearly 90% were low to intermediate grade (grade 1–2).[11,12] High-grade, poorly differentiated lesions of the conventional subtype are rare in all anatomic locations, and identification of aggressively invasive, poorly differentiated cartilage should raise the possibility of chondroblastic osteosarcoma.

Chondrosarcomas, especially low-grade tumors, have relatively indolent growth compared with other sarcomas. Nonetheless, they are highly invasive and have the potential for distant metastasis. Approximately 7% of patients have distant metastasis, which is most commonly seen with high-grade conventional tumors and the mesenchymal subtype.[11]

CLINICAL PRESENTATION

Data from the national cancer database indicates that the median age at presentation for cranial chondrosarcoma is 51 years, with a slight male predominance (55% of cases).[11] Most cases (85%) occur in non-Hispanic white patients. As indicated previously, most cases demonstrate a conventional histologic subtype with low-grade pathology. Fewer than 10% of cases are of the mesenchymal subtype, and these patients tend

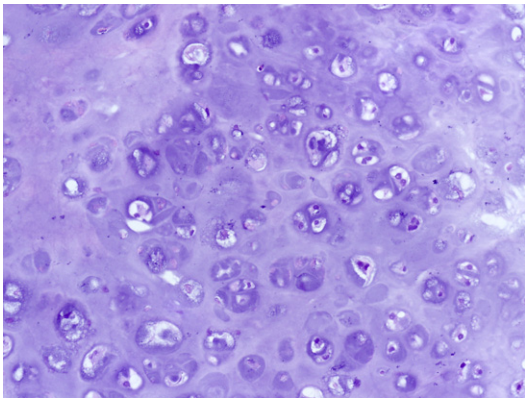

Fig. 2. Conventional chondrosarcoma, grade 1, demonstrating hyaline architecture (hematoxylin and eosin; original magnification ×200).