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Clinical Investigation: Central Nervous System Tumor

Challenges in Linear Accelerator Radiotherapy for Chordomas and Chondrosarcomas of the Skull Base: Focus on Complications

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Summary

Intracranial chordomas and chondrosarcomas are often difficult to treat due to their proximity to sensitive brain structures. This study reviewed a single institution's experience using linac-based stereotactic radiosurgery and radiotherapy to treat 15 patients. With an average follow-up of 4.5 years radiation-related complications were few. Photon therapy, judiciously given, represents a reasonable alternative to proton beam in those centers where proton technology is unavailable.

Purpose: Intracranial chordomas and chondrosarcomas are histologically low-grade, locally invasive tumors that infiltrate the skull base. Currently, consensus therapy includes surgical resection and adjuvant radiotherapy. Radiation delivery is typically limited by the proximity of these tumors to critical skull base structures.

Methods: This is a retrospective review of 13 cases of chordomas and 2 cases of chondroid chondrosarcomas of the skull based treated with linear accelerator stereotactic radiotherapy (SRT, $n = 10$) or stereotactic radiosurgery (SRS, $n = 5$). The average time to the most recent follow-up visit was 4.5 years. The tumor characteristics, treatment details, and outcomes were recorded. Each radiation plan was reviewed, and the dosage received by the brainstem, optic apparatus, and pituitary was calculated.

Results: Of the 10 patients treated with SRT, 6 were found to have unchanged or decreased tumor size as determined from radiographic follow-up. Of the 5 patients treated with SRS, 3 were found to have stable or unchanged tumors at follow-up. The complications included 1 SRT patient who developed endocrinopathy, 2 patients (1 treated with SRS and the other with SRT), who developed cranial neuropathy, and 1 SRS patient who developed visual deficits. Additionally, 1 patient who received both SRS and SRT within 2 years for recurrence experienced transient medial temporal lobe radiation changes that resolved.

Conclusions: Where proton beam therapy is unavailable, linear accelerator-based SRT or radiosurgery remains a safe option for adjuvant therapy of chordomas and chondrosarcomas of the skull base. The exposure of the optic apparatus, pituitary stalk, and brainstem must be considered during planning to minimize complications. If the optic apparatus is included in the 80% isodose line, it might be best to fractionate therapy. Exposure of the pituitary stalk should be kept to <30 Gy to minimize endocrine dysfunction. Brainstem exposure should be limited to <60 Gy in fractions. © 2012 Elsevier Inc.

Keywords: Linear accelerator, Stereotactic radiotherapy, Stereotactic radiosurgery, Chordoma, Skull base tumors

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Introduction

Chordomas are a rare group of slow-growing tumors arising from the notochord that can involve the cranial base, vertebrae, or sacrococcygeal regions (1). Chondrosarcomas are radiographically similar tumors derived from primitive mesenchymal cells within the cartilaginous matrix of the skull base (1, 2). Clinically, these tumors tend to present in a similar fashion (3). However, chordomas frequently arise from the clivus and tend to compress the brainstem, and chondrosarcomas commonly originate at the occipitotemporal bone synchondrosis and cause lower cranial nerve deficits (4). The definitive diagnosis can be made by histologic analysis. Although skull base chordomas and chondrosarcomas share similar radiographic features, clinical course, and locations, chondrosarcomas are associated with greater recurrence-free survival and responsiveness to therapy (3, 5). The therapeutic options for both chordomas and chondrosarcomas include surgical resection, fractionated radiotherapy, stereotactic radiosurgery (SRS), and proton beam radiotherapy. Complicating the treatment of these skull base tumors include the following: surgical therapy is rarely curative owing to their propensity to grow adjacent to and envelop critical structures and their propensity to recur (particularly chordomas); and radiation planning is frequently limited by their proximity to radiosensitive brain regions.

Surgical resection is considered the best first-line treatment, with greater degrees of resection associated with improved outcomes (2, 3, 6–8). Linear accelerator (LINAC) radiosurgery is widely available and has produced excellent tumor control rates, particularly when used as an adjuvant to surgical resection (9–12). LINAC radiosurgery has the inherent advantage of allowing a surgeon to target tumors with either single-dose radiosurgery or fractionated radiotherapy for a series of treatments. Gamma knife radiosurgery is another reasonable adjuvant therapy, with smaller tumors more likely candidates for SRS alone (13–16). More recently, proton beam radiotherapy has demonstrated tremendous promise, with excellent local tumor control and overall survival compared with conventional photon radiotherapy (17).

Given the location of these tumors and the difficulty in maintaining conformality because of the proximity of radiosensitive structures, any form of radiotherapy has met (at best) moderate success. A detailed analysis of treatment failures and complications is necessary to discern the limitations of LINAC radiotherapy and radiosurgery and additional future approaches to improve strategies for radiation delivery to these tumors. In the present series, we report 15 patients with cranial base chordomas and chondrosarcomas treated with LINAC radiosurgery, with particular regard to the potential reasons for failure or complications. To facilitate the present investigation, a detailed analysis of the radiotherapy treatment plans was conducted to provide the dosage received by critical brain structures.

Methods and Materials

Patient selection

The Institutional Review Board and Office for the Protection of Human Subjects at University of California, Los Angeles, approved the present retrospective review. The senior author (A.A.F.D.) performed 15 cases of postoperative adjuvant stereotactic radiotherapy (SRT, $n = 10$) and SRS ($n = 5$) for chordoma and chondrosarcoma between 1998 and 2006 using LINAC. All patients had undergone at least one surgical resection before receiving radiotherapy. The decision between performing SRS and SRT was reached through consensus of the neurosurgeon and radiation oncologist, mainly according to the tumor volume and the proximity to radiosensitive structures. In general, SRS was performed in patients with smaller volume tumors. In the SRT group, 6 patients were men and 4 were women. Two patients in this group were diagnosed with low-grade chondrosarcoma. The mean age at treatment was 48.9 ± 4.3 years. Six of these patients (60%) had tumors primarily located in the clivus, 3 (30%) had tumors growing out of the cavernous sinus, and 1 (10%) had a tumor predominantly located in the cerebellopontine angle. In the SRS group, 2 were men and 3 were women. One patient in this group received SRS 2 years after failing SRT. The mean age at treatment was 63.5 ± 3.6 years. Two patients (40%) had tumor predominantly involving the clivus, and three (60%) had tumor of the cavernous sinuses.

LINAC radiotherapy/radiosurgery

All radiosurgical procedures were targeted using 1.5T magnetic resonance imaging (MRI) scans fused to computed tomography scans of the brain, allowing for correction of magnetic resonance distortion. The magnetic resonance images were obtained using a Signa 1.5-Tesla MRI unit from General Electric Medical Systems (Milwaukee, WI). The computed tomography images were obtained using an MxTwin computed tomography scanner from Marconi Medical Systems (Mission Viejo, CA). The tumors were contoured using Brainlab iPlan software (Westchester, IL). During planning, three additional structures were contoured according to the magnetic resonance T_1-weighted and fluid-attenuated inversion recovery sequence images: the optic apparatus (nerves, chiasm, and tract), pituitary (gland and stalk), and brainstem (Fig.). This allowed for calculations of the dosage received by these structures at the 50%, 80%, and 90% isodose lines (IDLs). The neurosurgeon, radiation oncologist, and medical physicist formulated the final SRS plans. Radiation was delivered using the 6-MV Novalis LINAC equipped with multileaf collimator (Novalis, Heimstetten, Germany). SRT was delivered with the patient in a custom-fitted thermoplastic facemask. For SRS, patients received radiation while wearing the Brainlab stereotactic frame. The patients were discharged the same day as their radiation treatment.

Outcome and follow-up

All patients, except for 1, were followed up with sequential MRI and clinical visits. All patients were screened for new symptoms, including visual acuity or field deficits, cranial neuropathy, and endocrinopathy at scheduled postradiation visits. Endocrinopathy was defined as any evidence of new onset or worsening of existing endocrine dysfunction, including (but not limited to) diabetes insipidus, thyroid dysfunction, or panhypopituitarism after radiotherapy. The MRI scans were reviewed for evidence of radiation changes or tumor progression. Treatment failure was defined as evidence of tumor progression on neuroimaging after completion of SRT/SRS. This usually resulted in the patient being referred for further surgical resection or being considered for additional