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Basic Original Report

The role of proton beam therapy in central neurocytoma: A single-institution experience

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Abstract

Purpose: Central neurocytomas (CNs) are rare World Health Organization grade II tumors managed with surgery and radiation therapy. We report our experience in managing CN with proton beam therapy (PBT) when radiation therapy was used.

Methods and materials: We identified 61 patients with pathologically diagnosed CN treated at our institution between 1996 and 2016, of which 24 met inclusion criteria. Patient, tumor, and treatment characteristics are reported in context of progression-free survival and treatment-related adverse events.

Results: Of 24 patients identified, median age at diagnosis was 21 years (range, 14-60). Median maximal tumor diameter was 4.5 cm (range, 1.4-6.8). Eighteen (75%) patients underwent upfront surgery alone. Sixteen (67%) patients received adjuvant or salvage PBT at a median dose of 54 Gy (relative biological effectiveness). Median follow-up was 56 months. Median progression-free survival (PFS) was 61 months. Eleven patients had disease progression with median time to progression of 22 months. Of the 5 patients with gross total resection, 4 experienced local recurrence and had MIB-1 >4% (range, 4.5-30). There was improved PFS with addition of PBT to definitive surgery (log-rank, P = .06); there was no disease progression to date. In patients who experienced disease recurrence/progression, MIB-1 <4% was associated with improved PFS (log-rank, P = .007). All patients tolerated PBT well with toxicities typical for cranial irradiation and with no grade 3+ toxicities.

Conclusion: In our cohort, CN with elevated MIB-1 index were at increased risk for disease progression. However, adjuvant radiation therapy appears to effectively prevent failure. PBT toxicities appear to be comparable to if not less than published photon experiences.

Preliminary findings were presented at the 2017 American Society for Radiation Oncology 59th Annual Meeting on September 24-27, 2017 in San Diego, CA.

Conflicts of interest: T.Y: NCI/Protom/IBA (research funding), MimCloud (inkind donation). The remaining authors declare no conflicts of interest.

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Introduction

Central neurocytomas (CNs) are rare, well-differentiated World Health Organization grade II tumors of neuronal/neuroglial origin, usually within the cerebral ventricular system.[1,2] They account for ~0.1% to 0.5% of all intracranial tumors and typically have indolent natural histories.[3,4] Gross total resection (GTR) is an important prognostic indicator[5]; however, because these tumors have a rich blood supply and develop close to critical structures, resection is limited in up to one-half of cases,[6,7] which can negatively affect local control and overall survival.[8-12] Furthermore, even after GTR, local recurrence is possible.[13-15] Adjuvant radiation therapy (RT) can improve local control rates in patients with incompletely resected[9,10,16] or atypical CN.[9,17-19] In recurrent disease, salvage RT has been shown to improve disease outcomes.[16,20]

Here, we present a first experience with proton beam therapy (PBT) in CN. The unique physical properties of PBT permit reduced irradiation of normal tissue, mitigating late RT effects.[21,22] Our study aims to investigate the outcomes of CN patients treated with surgery, stratified by receipt of PBT, and to explore the optimal timing, efficacy, and tolerability of PBT.

Methods and materials

Patient selection

This single-institution retrospective study included all patients diagnosed with pathologically confirmed CN between 1996 and 2016 who received either surgery alone or surgery with adjuvant PBT. A clinical data query tool was searched for patients with mention of "neurocytoma" in their electronic medical record (EMR). This query resulted in 61 potential cases. Study inclusion was based on: (1) confirmed histopathologic diagnosis, (2) receipt of curative treatment at our institution, and (3) at least 1 imaging study and/or disease-related clinic visit following treatment completion. After manual EMR review, 24 patients met all inclusion criteria. Each EMR was reviewed for patient and tumor characteristics, clinical presentation, diagnostic details, and outcomes. The institutional review board approved this study.

Treatment and follow-up

The extent of surgical intervention was determined from intraoperative observation and/or follow-up magnetic resonance imaging (MRI) scan and was classified as GTR or non-GTR. Non-GTR included subtotal resection, unspecified resection extent, ventriculostomy with biopsy, and biopsy alone. Eleven (46%) patients received surgery at an outside institution and subsequently received PBT and long-term care at our institution and were thus included for progression/recurrence. Details of PBT plans were reviewed in MIM software (version 6.6; MIM Software Inc., Cleveland, OH) for assessment of target and prescription volumes, dose distribution, and conformity index (prescription volume divided by target volume). For 1 patient with multiple intraventricular sites of disease, a combined target volume was reported. Follow-up time was calculated from date of first surgical intervention to date of last clinical evaluation/imaging. The primary endpoint was progression-free survival (PFS), as measured from date of first surgical intervention to date of first radiographic recurrence/progression. The secondary endpoint was treatment-related morbidity, which was retrospectively rated according to the National Cancer Institute's Common Terminology Criteria for Adverse Events, version 4.0.[23] Duration of events was categorized as transient (resolution before/by last follow-up) or permanent (still present at last follow-up).

Statistical analysis

All statistical analyses were conducted using Stata software (release 15; StataCorp LLC, College Station, TX). Kaplan-Meier product-limit estimator and log-rank test were used to plot and compare PFS for subgroups. Univariate Cox regression analysis was performed to determine the influence of patient and disease characteristics on PFS. For all analyses, $P < .05$ indicated statistical significance.

Results

Patient and disease characteristics

The median age at diagnosis was 21 years (range, 14-60) (Table 1). More than one-half (58%) of the cohort was female, and 67% were Caucasian. Of the 24 included patients, 22 (92%) presented with symptoms including headache (79%), nausea/vomiting (46%), and visual disturbances (33%), mostly of acute (<1 month before presentation) to subacute (1-6 months before presentation) duration. Hydrocephalus was noted in 17 (71%) patients. The median maximal tumor diameter on preoperative MRI scan was 4.5 cm (range, 1.4-6.8); the median MIB-1 index was 4.25% (range, 0.5-30). All tumors originated in the ventricular system.

Treatment

The majority (18; 75%) of patients underwent surgical intervention alone (Table 1). None of the 5 GTR cases received postoperative RT. Nineteen (79%) patients received non-GTR, including 2 who received either biopsy with ventriculostomy or biopsy alone. Sixteen (67%) patients received adjuvant or salvage PBT (Table 2). Adjuvant (n = 6) and salvage (n = 10) PBT were delivered at median total doses of 52.2 Gy (relative biological effectiveness [RBE]) and 54 Gy (RBE), respectively. All