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Clinical Investigation

Imaging Changes in Pediatric Intracranial Ependymoma Patients Treated With Proton Beam Radiation Therapy Compared to Intensity Modulated Radiation Therapy

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Summary

Radiation therapy after resection of pediatric intracranial ependymoma is sometimes associated with magnetic resonance

Purpose: The clinical significance of magnetic resonance imaging (MRI) changes after radiation therapy (RT) in children with ependymoma is not well defined. We compared imaging changes following proton beam radiation therapy (PBRT) to those after photon-based intensity modulated RT (IMRT).

Methods and Materials: Seventy-two patients with nonmetastatic intracranial ependymoma who received postoperative RT (37 PBRT, 35 IMRT) were analyzed retrospectively. MRI images were reviewed by 2 neuroradiologists.

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imaging–based image changes, but the clinical significance of these changes is not well defined. In this retrospective study, imaging changes were more prevalent with proton therapy and in patients less than 3 years of age. Factors associated with the development of clinically significant imaging changes are difficult to determine. Imaging changes are usually self-limiting, but some require medical intervention, especially those involving the brainstem.

Results: Sixteen PBRT patients (43%) developed postradiation MRI changes at 3.8 months (median) with resolution by 6.1 months. Six IMRT patients (17%) developed changes at 5.3 months (median) with 8.3 months to resolution. Mean age at radiation was 4.4 and 6.9 years for PBRT and IMRT, respectively ($P = .06$). Age at diagnosis (>3 years) and time of radiation (≥3 years) was associated with fewer imaging changes on univariate analysis (odds ratio [OR]: 0.35, $P = .048$; OR: 0.36, $P = .05$). PBRT (compared to IMRT) was associated with more frequent imaging changes, both on univariate (OR: 3.68, $P = .019$) and multivariate (OR: 3.89, $P = .024$) analyses. Seven (3 IMRT, 4 PBRT) of 22 patients with changes had symptoms requiring intervention. Most patients were treated with steroids; some PBRT patients also received bevacizumab and hyperbaric oxygen therapy. None of the IMRT patients had lasting deficits, but 2 patients died from recurrent disease. Three PBRT patients had persistent neurological deficits, and 1 child died secondarily to complications from radiation necrosis.

Conclusions: Postradiation MRI changes are more common with PBRT and in patients less than 3 years of age at diagnosis and treatment. It is difficult to predict causes for development of imaging changes that progress to clinical significance. These changes are usually self-limiting, but some require medical intervention, especially those involving the brainstem.

Introduction

Ependymoma accounts for 6% to 10% of all intracranial tumors and 15% of posterior fossa tumors in the pediatric population (1). Treatment typically includes maximal safe resection followed by postoperative radiation therapy (RT). Three-year progression-free survival rates are estimated at 75% after treatment (2, 3).

As the utility of adjuvant RT has been established and the peak incidence of intracranial ependymoma ranges from birth to 4 years of age (1, 3), there is well-justified interest in decreasing the long-term side-effect profile of RT. Compared to photons, proton beam RT (PBRT) results in favorably low and intermediate dose distributions, with similar high-dose distributions (4, 5). As dose and volume of normal tissue irradiated have been correlated with both early and late effects of RT, PBRT can ameliorate the normal tissue toxicity profile (6). Thus, the implementation of PBRT for pediatric patients is well accepted.

Surveillance following treatment of pediatric central nervous system (CNS) malignancies can be challenging, as treatment effects from radiation and chemotherapy seen on post-therapy imaging can be difficult to distinguish from tumor recurrence. Several studies have identified treatment-related transient brain lesions and recommended imaging features, location, and temporal course that clearly separates them from recurrence or necrosis (7-9).

Because the posterior fossa is a common location of ependymoma, brainstem toxicity is a major concern, and dose constraints have been published (10, 11). Incomplete recovery of brainstem function after RT for infratentorial ependymoma has been related to surgical morbidity and the volume/extent of tumor (12). These parameters are not as well defined for PBRT. Further studies are necessary to confirm that the existing brainstem dose-effect models are applicable due to the potential difference in radiobiological effects between photons and protons.

In this report, we aimed to identify risk factors for the development of imaging changes in pediatric ependymoma patients treated with postoperative RT. We closely examined patients who became symptomatic with changes to isolate features predisposing to poor outcomes. To accomplish this, we performed a retrospective analysis of intracranial pediatric ependymoma patients. After neuroradiology review of imaging, the presence and grade of imaging changes were correlated with clinical factors.

Methods and Materials

Patient data collection

After institutional review board approval, a retrospective chart review was conducted, including patients whose conditions were diagnosed at two institutions for nonmetastatic intracranial ependymoma (anaplastic and well-differentiated) between 2000 and 2013. Patients had at least 1 MRI performed at least 6 months after RT. Any previous intracranial radiation led to exclusion.

Imaging review

All available MRIs were reviewed by 2 neuroradiologists to determine grade and location of imaging changes. Changes were scored according to a previously published scale, where grade 1 = abnormal signal intensity on T2; grade 2 = increased signal intensity on T2 and contrast