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Clinical Investigation

Outcomes of Proton Therapy for the Treatment of Uveal Metastases

Sophia C. Kamran, MD,* John M. Collier, PhD,† Anne Marie Lane, MPH,‡ Ivana Kim, MD,‡ Andrzej Niemierko, PhD,§ Yen-Lin E. Chen, MD,† Shannon M. MacDonald, MD,† John E. Munzenrider, MD,† Evangelos Gragoudas, MD,‡ and Helen A. Shih, MD†

**Harvard Medical School; †Department of Radiation Oncology, Massachusetts General Hospital; ‡Retina Service, Massachusetts Eye and Ear Infirmary; and §Division of Biostatistics, Department of Radiation Oncology, Massachusetts General Hospital, Boston, Massachusetts*

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Summary

This retrospective review investigated the use of proton therapy in providing local control of uveal metastases with minimization of normal tissue injury. Proton therapy was found to be an effective treatment, with modest localized symptoms. Visual function declined over time, but the high rate of local control, prevention of morbid disease symptom progression, and an efficient and cost-effective delivery system support proton therapy as a favorable option for palliation of uveal metastases.

Purpose/Objective(s): Radiation therapy can be used to treat uveal metastases with the goal of local control and improvement of quality of life. Proton therapy can be used to treat uveal tumors efficiently and with expectant minimization of normal tissue injury. Here, we report the use of proton beam therapy for the management of uveal metastases.
Methods and Materials: A retrospective chart review was made of all patients with uveal metastases treated at our institution with proton therapy between June 2002 and June 2012. Patient and tumor characteristics, fractionation and dose schemes, local control, and toxicities are reported.
Results: Ninety patients were identified. Of those, 13 were excluded because of missing information. We report on 77 patients with 99 affected eyes with available data. Patients were 68% female, and the most common primary tumor was breast carcinoma (49%). The median age at diagnosis of uveal metastasis was 57.9 years. Serous retinal detachment was seen in 38% of treated eyes. The median follow-up time was 7.7 months. The median dose delivered to either eye was 20 Gy(relative biological effectiveness [RBE]) in 2 fractions. Local control was 94%. The median survival after diagnosis of uveal metastases was 12.3 months (95% confidence interval, 7.7-16.8). Death in all cases was secondary to systemic disease. Radiation vasculopathy, measured decreased visual acuity, or both was observed in 50% of evaluable treated eyes. The actuarial rate of radiation vasculopathy, measured decreased visual acuity, or both was 46% at 6 months and 73% at 1 year. The 6 eyes with documented local failure were successfully salvaged with retreatment.
Conclusions: Proton therapy is an effective and efficient means of treating uveal metastases. Acutely, the majority of patients experience minor adverse effects. For

Reprint requests to: Helen A. Shih, MD, Department of Radiation Oncology, Massachusetts General Hospital, 30 Fruit St, Boston, MA 02114. Tel: (617) 724-9627; E-mail: hshih@partners.org

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longer-term survivors, the risk of retinal injury with vision loss increases significantly over the first year. © 2014 Elsevier Inc.

Introduction

Uveal metastases are the most common intraocular tumor (1, 2), with the choroid as the most common site of involvement (3). Autopsy studies reveal an incidence of 4% to 12% of choroidal metastases in asymptomatic individuals with solid primary tumors (4). Typical symptoms include vision loss or visual field deficits, photophobia, and floaters (5). The most common primary tumors to give rise to intraocular metastases are lung and breast carcinoma (5). Untreated uveal metastases will cause gradual vision loss (6), and with continued progression, they will grow into the orbit, causing significant morbidity of pain, proptosis of the affected eye, and complete vision loss (7). Although uveal metastases are not typically fatal, they can be a source of significant morbidity if untreated, and therefore the goals of therapy include local control and improvement of quality of life.

The use of proton beam radiation for uveal metastases has been in practice at Massachusetts General Hospital in collaboration with Massachusetts Eye and Ear Infirmary since 1975. Over time, the practice has evolved with dose reduction from 28 Gy(relative biological effectiveness [RBE]) to 20 Gy(RBE) divided in 2 fractions. To date, there is limited published literature on the outcomes of uveal metastases treated with proton beam therapy, specifically with evaluation of treatment details such as dose and target volume effects. Here, we present our results in patients with uveal metastases treated with proton beam therapy.

Methods and Materials

This institutional review board—approved retrospective study reviewed all records of patients treated with proton beam therapy for uveal metastases between June 2002 and June 2012. Patients included in the study were >18 years with a diagnosis of uveal metastasis from any primary site.

A detailed review of electronic medical records and chart records was completed. Data collected included patient characteristics, primary tumor characteristics, primary tumor treatment, uveal metastasis information, uveal metastasis treatment information, and ophthalmologic follow-up data including tumor response and adverse events as defined by visual acuity and radiation vasculopathy, other new adverse effects or worsening of existing symptoms, and other potential findings on direct examination. Adverse effects were based on patient report and clinical documentation. Adverse effects were classified for their lack of presence before treatment and arising after treatment to differentiate potential radiation treatment effect from symptoms related to disease. Treatment adverse events were defined as toxicity or deficit determined by formal evaluation, namely radiation vasculopathy, radiation papillopathy, and resulting decrease in visual acuity at any point after treatment, not to be scored more than once per patient. Follow-up was defined from the completion of treatment. The diagnosis of choroidal metastasis was based on ophthalmic examination, including fundoscopy and ultrasonography. Biopsy was not routinely performed, and it was assumed that the choroidal metastasis originated from the known primary tumor.

Planning and treatment

All patients were treated definitively for their uveal metastases with proton radiation therapy. This involved creating a model of the patient's eye using software that was initially developed at our center and subsequently further advanced by others (8) (Eyeplan, Clatterbridge Cancer Center, NHS Foundation Trust, UK). Integrated data into the eye model included the tumor location, shape, and size, based on clinical examination, fundus photographs, and ultrasound measurements of both eye and tumor. Beam selection and patient gaze direction were determined by use of Eyeplan with both ophthalmologist and radiation oncologist working collaboratively with the medical physicist. Patients were positioned for treatment sitting upright with a thermoplastic mask and dental mold used for immobilization of the head. The patient's eye was positioned for treatment by the patient's voluntary fixation on a spot positioned to achieve the desired eye gaze position, typically in such a manner that the proton beam was directed on the sclera to avoid the anteriormost eye structures as much as possible without compromising target coverage. If the patient was not able to fixate on the light source with the eye being treated, setup was achieved by use of the contralateral eye for achieving the desired placement of the eye being treated. Optimal gaze direction was selected based on providing full-dose coverage to the tumor while minimizing dose to critical normal tissues, including the macula, optic disc, retina, lens, ciliary body, limbus, lacrimal gland, canthi, and eyelids. Treatment planning used 4-mm lateral margins to the field edge. Beam modulation delivered dose with 3-mm proximal and 4-mm distal margins. The net target coverage was by the 90% isodose. Dose prescription was typically in 2 fractions, most commonly 14 Gy(RBE) or 10 Gy(RBE) per fraction for a total of 28 or 20 Gy(RBE), respectively. There was some dose variation, as detailed in Table 1. Each treatment required a radiation oncologist present to verify the setup based on incident light field on the eye to be treated.

Statistical analyses

The Kaplan-Meier method was used for actuarial analysis of overall survival and time to tumor progression. Survival