Successful Treatment of Intraocularly Invasive Conjunctival Squamous Cell Carcinoma With Proton Beam Therapy

Due to an increase in UV light exposure, conjunctival squamous cell carcinoma has become increasingly more prevalent throughout the world. However, primary intraocular invasion from conjunctival squamous cell carcinoma still remains rare and is therefore often misdiagnosed. Larger, more aggressive lesions that invade the eye are frequently not amenable to standard excision and cryotherapy. For the treatment of such lesions, most authors advocate enucleation or exenteration if there is evidence of orbital invasion. The present case suggests that proton beam therapy may be a reasonable alternative to enucleation for the treatment of squamous cell carcinoma with intraocular invasion. To our knowledge, this is the first report of the treatment of invasive conjunctival squamous cell carcinoma using proton beam therapy.

Report of a Case. A 91-year-old woman from El Salvador was referred for evaluation of a suspicious conjunctival lesion in the right eye. She had been previously followed for a diagnosis of uveitis in the right eye that was treated with topical steroids. Ocular history was significant for pseudophakia in both eyes and primary open-angle glaucoma for which she was treated with 0.005% latanoprost (Xalatan; Pfizer, Inc, New York, NY) in each eye every night. Due to the risk of development of cystoid macular edema in patients with pseudophakia, this was changed to 2.0% dorzolamide hydrochloride (Trusopt; Merck and Co, Inc, Whitehouse Station, NJ) in each eye every night by our institution. The patient had no medical history of chronic illness or malignancy, and she received no medications other than the previously mentioned eyedrops.

On our initial evaluation, the patient described increased pain and decreased vision in the right eye. Visual acuity in the right eye was counting fingers at 4 ft with pinhole to 20/200, and best-corrected visual acuity in the left eye was 20/50 due to glaucoma. Slitlamp examination revealed an amelanotic, highly vascularized conjunctival mass arising from the limbus and extending onto the cornea from the 1-o’clock to 5:30 meridian in the right eye (Figure, A). On gonioscopy, a contiguous, white, fluffy mass was noted in the same meridian as the previously described conjunctival lesion (Figure, B). The mass could be seen extending onto the iris and into the chamber angle by slitlamp examination as well. Ultrasound biomicroscopy was performed, which further delineated and confirmed invasion of the conjunctival lesion into the anterior chamber angle from the 1-o’clock to 5:30 position. On slitlamp examination, no neovascularization of the iris was noted in either eye. There was trace cell and flare in the anterior chamber and vitreous cavity in the right eye. Applanation pressure was 19 mm Hg OD and 14 mm Hg OS. A dilated fundus examination revealed a cup-to-disc ratio of 0.9 in the right eye. On our initial evaluation, this revealed a moderate-to-well-differentiated squamous cell carcinoma. The specimen demonstrated malignant epithelial cells in the substantia propria of the conjunctiva forming keratin pearls with evidence of deep invasion (Figure, C). A histochemical stain for mucin was performed to rule out mucoepidermoid carcinoma, and it was negative. Due to the patient’s advanced age and refusal to undergo enucleation, a decision was made to treat her with proton beam radiation. The patient underwent debulking of the conjunctival component of the squamous cell carcinoma with simultaneous placement of tantalum marker clips to guide proton beam therapy (Figure, D). A vault conformer lens was placed within the palpebral fissure at the time of the surgical procedure, and it was left in place for approximately 1 month to prevent adhesion of the eyelids and the formation of conjunctival symblepharon.

The dose of proton beam radiotherapy used for treatment was 3200 cGy, or 800 cGy divided over 4 treatments on 4 consecutive days. The Crocker cyclotron (University of California, Davis) has an energy of 67.5 MeV, with a range of 30 mm and a width of the spread-out Bragg peak of 10 mm. This allows for a depth of penetration of 8 mm inside the eye. A 2-mm margin is allowed on the aperture. A thermoplastic head mask and bite block were used to immobilize the patient. A fixation light was used to specify the gaze angle. To plan the treatment, EYEPLAN software (distributed by Massachusetts General Hospital, Boston) was used. Individualized treatment plans are developed for each gaze direction, customized apertures are fabricated, and dose distributions are calculated for each patient. These modifications allow for a relative sparing of vital anterior segment structures that the tumor does not involve.

Subsequent to treatment, the patient has been followed at monthly intervals for approximately 9 months. To date, there has been stable regression and no recurrence of this intraocularly invasive...
Figure. Squamous cell carcinoma invading the anterior chamber. A, Slitlamp photograph of the right eye. Squamous cell carcinoma involving the nasal conjunctiva with invasion onto the cornea as well as into the anterior chamber is noted. B, Gonioscopic photograph of the right eye. A cream-colored fluffy lesion is situated in the anterior chamber and involves the anterior chamber angle from the 1-o’clock to the 5:30 position. Satellite tumor nodules are present on the iris surface. C, Histopathologic specimen of the right eye. Tumor cells display atypia with variable keratin pearl formation. The lesion is consistent with a moderate-to-well–differentiated squamous cell carcinoma with evidence of deep invasion (hematoxylin-eosin, original magnification ×50). D, Slitlamp photograph of the right eye immediately following radiation. The superior and inferior tantalum marker clips are visible. A vault conformer lens is in place to prevent adhesion during healing. E, Slitlamp photograph of the right eye 4 months following radiation, demonstrating complete tumor regression. There is a small stromal scar involving the nasal cornea. F, Gonioscopic photograph of the right eye 4 months after radiation. The intraocular component shows complete regression. The small pale iris nodule is consistent with a residual scar.
squamouso cell carcinoma both on the bulbar conjunctiva (Figure, E) as well as in the anterior chamber angle and iris (Figure, F). The best-corrected visual acuity remains stable at 20/200 in the treated eye.

Comment. Intraocular invasion of conjunctival squamous cell carcinoma is rare. The Bowman membrane is a thick acellular layer composed largely of collagenous tissue. Due to its structure, it often acts as an impenetrable barrier to the intraocular spread of conjunctival melanoma. More aggressive histologic variants that have a greater potential for invasion include spindle cell and mucoepidermoid carcinomas. It is of note that although the lesion in our patient did not fall within this subtype, it still demonstrated invasive behavior. Although squamous cell carcinoma generally exhibits slow growth and has a low likelihood of metastasis, this case highlights the need for accurate diagnosis and early intervention.

This patient received successful treatment of invasive squamous cell carcinoma of the conjunctiva with proton beam therapy. Recently, the therapeutic options available to the clinician for the treatment of superficial conjunctival and corneal squamous cell carcinoma have expanded. Promising reports in the literature describe the use of photodynamic therapy and topical mitomycin C for the treatment of more extensive and recurrent lesions. However, previous to this article, the options that were suggested for the treatment of intraocularly invasive squamous cell carcinoma were limited to enucleation. This article suggests proton beam therapy as a potential alternative to enucleation.

On review of the literature, some authors describe visually limiting complications with the use of external beam radiation for the treatment of conjunctival malignancy. Compared with other forms of irradiation, proton beam therapy can be delivered precisely to the superficial tissues and anterior chamber structures without significant deeper tissue penetration, thus minimizing unnecessary irradiation of the lens, ciliary body, and retina. Such a treatment approach is particularly suited to elderly patients who may be limited in surgical options by other medical comorbidities. Proton beam therapy was extremely well tolerated by our patient, who experienced no adverse effects from the radiation. Adverse effects may include dry eye, intraocular inflammation, conjunctival scarring, or glaucoma.

Our knowledge of the efficacy of proton beam therapy is limited by the fact that we have only treated 1 patient and that we have relatively short-term follow-up data. The regression of tumor and lack of recurrence in this patient does, however, suggest that proton beam therapy should be considered as a possible alternative to enucleation for the treatment of invasive conjunctival squamous cell carcinoma.

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Unilateral Retinal Nerve Fiber Myelination With Contralateral Amblyopia

During normal prenatal development, retinal ganglion axon myelination starts centrally in the lateral geniculate body and proceeds anteriorly to the optic tracts, chiasm, and nerves. This process of myelination normally terminates shortly after birth at the level of the lamina cribrosa; however, occasionally myelination occurs in the retinal nerve fiber layer. Although generally considered to be a benign funduscopic finding, myelinated nerves have been associated with visual field defects, severe myopia, amblyopia, and strabismus. To our knowledge, all of the reported cases of amblyopia have occurred in the eye affected with myelinated fibers. In this article, we describe 2 patients with unilateral myelinated nerve fibers who had amblyopia in the eye not affected with nerve fiber layer myelination. We believe that these cases shed light on the causes of reduced visual acuity in patients with retinal nerve fiber layer myelination.

Report of Cases. Case 1. A 5-year-old boy was referred for evaluation of a “wandering eye” that was first noted in infancy. He had received no previous eye treatment. Visual acuity without correction was 20/125 OD and 20/300 OS. Cycloplegic refraction revealed −2.50 diopters (D) OD and +7.50 D OS, correcting visual acuity to 20/40 OD and 20/160 OS. A 23–prism diopter, left-sided...