CLINICAL STUDY

Proton beam therapy for posterior pole circumscribed choroidal haemangioma

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Abstract

Background **Macular and juxtapapillary circumscribed choroidal haemangiomas (CCH) have always posed a diagnostic and therapeutic challenge. Proton beam therapy has been advocated by Zografos and associates as optimal for treating these tumours in this critical region as charged particles have a highly localised and uniform dose distribution.**

Patients **We present 3 cases of CCH treated with proton beam therapy. Two patients developed radiation optic neuropathy and maculopathy, and one had a persistent exudative macular detachment following treatment.**

Conclusion **Our experience with proton therapy of these tumours has been disappointing in preventing radiation optic neuropathy and maculopathy and offers little advantage over external irradiation. The majority of our patients with this condition are now treated with low-dose lens-sparing external beam radiotherapy or brachytherapy, which has encouraging visual results and is a far more cost-effective option.**

Key words Charged particle therapy, Choroidal haemangioma, Proton beam therapy, Proton therapy

Circumscribed choroidal haemangiomas (CCH) are rare discrete vascular harmatomas. They are classically unilateral and not associated with the encephalotrigeminal malformations of Sturge–Weber syndrome. They are thought to be present from birth but only become symptomatic when nodular thickening of a critical size develops causing exudation of subretinal fluid.[1] The peak incidence of presentation is in the fourth and fifth decades.[2]

Many treatment modalities have been tried for CCH including photocoagulation,[3–5] cryotherapy,[6] external irradiation[7,18] and brachytherapy.[9,10] Proton beam therapy has been extensively used for the treatment of choroidal melanomas[11–13] and should theoretically minimise the exposure of uninvolved tissues in the treatment of CCH.

We present 3 cases of CCH at the posterior pole treated with proton beam therapy at the Douglas Cyclotron, Clatterbridge. All patients received a dose of 1800 cGy (1980 cGy cobalt equivalent) in 4 fractions (Table 1).

Case reports

Patient 1

A 52-year-old man presented with blurred vision and metamorphopsia in his left eye with a Snellen acuity of 6/6. A diagnosis of juxtapapillary circumscribed choroidal haemangioma was made and conservative follow-up ensued. Two years later, the patient developed a serous retinal detachment over the tumour with a drop in visual acuity to 6/18. Scatter argon laser photocoagulation was performed with poor resolution of the detachment and the visual acuity deteriorated further to 6/60. Proton beam therapy was administered 3 months after the onset of visual impairment. At 1 month after treatment the visual acuity had returned to 6/24 and continued to improve to 6/18 over the next 2 year period with complete resolution of subretinal fluid with pigmentary macular changes. However, at follow-up 32 months after irradiation visual acuity had declined to 6/60 and fundoscopy revealed a swollen optic disc with telangiectatic vessels with lipid exudates and oedema at the macula (Fig. 1). A diagnosis of radiation optic neuropathy was made. No further treatment was undertaken.

Patient 2

A 48-year-old woman was referred with a diagnosis of left amelanotic choroidal melanoma with secondary exudative retinal detachment. Visual acuity was hand movements in the affected eye and had been poor for 2 years. The diagnosis of juxtapapillary CCH was made and confirmed by Doppler ultrasound and fluorescein angiography. There were no signs of neovascular glaucoma. The visual

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Table 1. *Physical characteristics of circumscribed choroidal haemangioma and response to proton beam therapy (PBT) in our 3 patients*

Tumour data	Patient 1	Patient 2	Patient 3
Max. width (mm)	9.3	12	13.6
Min. width (mm)	7.5	10.7	11.6
Height (mm)	3.3	5.2	6.3
% disc involved	33	50	
% macula involved		75	100
Distance from disc (mm)	0	0	2.3
Distance from macula (mm)	2.0		
Volume (cm^3)	0.13	0.34	0.58
Distance from equator (mm)	7.2	7.5	6
Timing of PBT after symptom onset (months)	3	2	72
Resolution of subretinal fluid after PBT (months)	32	11	N/A
Onset of radiation changes after PBT (months)	32	11	N/A

acuity remained at hand movements after proton beam therapy and there was slow resolution of subretinal fluid. The tumour continued to show shrinkage documented by serial ultrasound. At 1 year follow-up there was marked radiation optic neuropathy and maculopathy. At 3 year follow-up the macula was noted to be dry and atrophic.

Patient 3

A 39-year-old man was referred with a CCH just temporal to the fovea in his right eye. His left eye was amblyopic. Visual acuity was 6/12 and 6/24 in the right and left eyes respectively. He underwent four sessions of argon laser photocoagulation with initial resolution of fluid and improvement of the visual acuity to 6/9 (Fig. 2). The vision deteriorated again within 6 months of stopping treatment, with extensive exudative retinal detachment and cystoid macular oedema. Six years later there was concern over progressive increase in tumour thickness. The decision was taken to treat the tumour with proton beam therapy in the hope of shrinking the tumour and preventing further extensive bullous detachment. At 1 year after proton therapy there was still significant subretinal fluid over the macula. Visual acuity both before and after treatment was 3/60.

Discussion

Nature of CCH

Choroidal haemangiomas are rare vascular harmatomas with an incidence 1/15 to that of choroidal melanomas.[4] Two distinct histological types have been described: the circumscribed and the diffuse (associated with Sturge–Weber syndrome). The cavernous element may make them more radiosensitive than the predominantly capillary structure of Von Hippel tumours.[2] There is also a subgroup of patients with CCH who have no apparent encephalotrigeminal involvement but who show diffuse choroidal thickening on ultrasound.[1] It is believed that the tumours may exist at birth[2] but do not give rise to symptoms until years later.

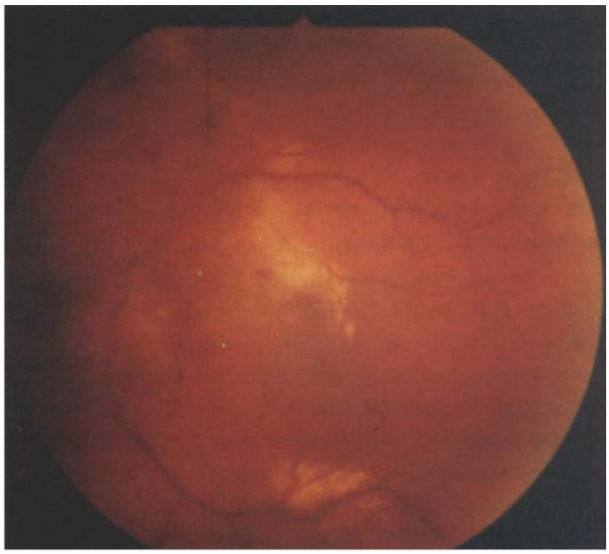

Fig. 1. *Patient 1. Radiation maculopathy and optic neuropathy at 32 month follow-up.*

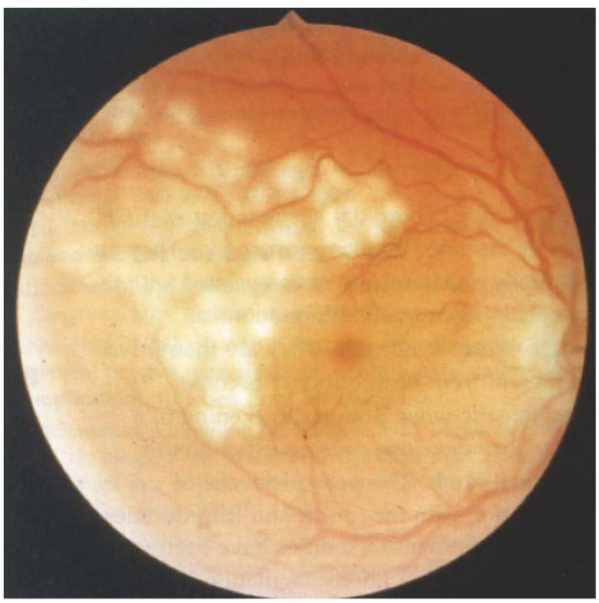

Fig. 2. *Patient 3. Initial improvement in vision with resolution of serous retinal detachment following grid argon laser photocoagulation.*

Diagnosis and treatment of CCH

In the past CCH have proved a diagnostic pitfall in many cases, with the diagnosis only made histologically after the eye has been enucleated for suspected amelanotic choroidal melanoma.[14] Fortunately with the routine use of fluorescein angiography and B-scan ultrasound the modern ophthalmologist should be able to distinguish a CCH with increased certainty.[15,16] It is rare to clinically observe growth in CCH as in case 3.[17]

However, even if the correct diagnosis is made in time, both the location and the natural history of these sight-threatening harmatomas make consensus in the choice and timing of treatment difficult.[1] They classically occur at the posterior pole and juxtapapillary area[2] and cause symptoms rapidly once subretinal fluid leakage occurs. The course of this visual deterioration may be relapsing and remitting and may lull the clinician into a false sense of security while missing the critical period for treatment when optimal visual outcome can be achieved. If unchecked, glaucoma may result from angle neovascularisation or angle closure.

Many authors recommend laser photocoagulation. Although this often results in a temporary resolution of the serous detachment, many reports have documented the re-accumulation of the subretinal fluid and poor final visual acuity.[3–5] This poor outcome is reflected in patients 1 and 3. Both brachytherapy[18] and external beam irradiation[7,18] have shown some promise in treating CCH.

Characteristics of proton beam therapy

Charged particle irradiation was advocated as a treatment for haemangiomas in this critical region due to its attractive physical characteristics. In contrast to conventional radiotherapy with its collateral irradiation of surrounding tissues, especially at the entry site, the energy in proton beam therapy is deposited at the end of its path (Bragg peak of ionisation)[12] (Fig. 3). Because the precise depth of penetration can be controlled, the radiation can be targeted almost exclusively to the tumour volume with minimal irradiation of the surrounding tissue. Accurate localisation of the tumour is achieved by the insertion of at least four radio-opaque tantalum markers sutured to the sclera at known distances from the tumour edge. These are inert and left in situ after treatment. Localisation can be further improved for these posterior lesions by choosing an appropriate fixation angle which brings the tumour closer to the entrance of the beam. Precise targeting is further achieved with bite blocks and face and head masks of mouldable plastic mesh.[8] Similar to conventional radiotherapy, proton therapy uses dose fractionation and multiport beam entry.

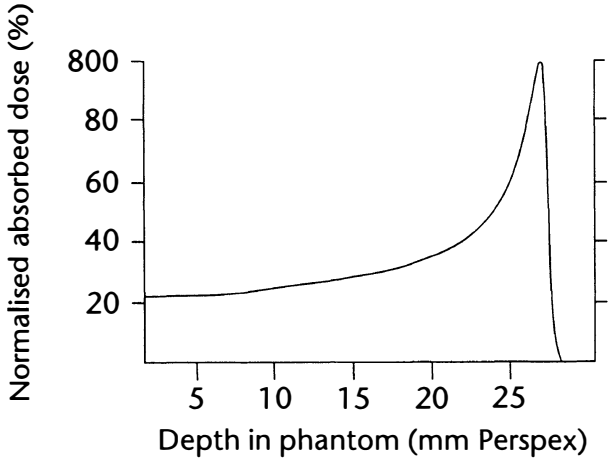

Fig. 3. *Bragg peak of ionisation.*

Proton beam treatment has been described for both CCH and diffuse choroidal haemangioma by Zografos *et al*. in three cases.[9,10] He observed no radiation complications except for subretinal fibrosis in one case of macular CCH. This case showed marked improvement of vision from 6/60 to 6/7.5 at 1 year follow-up.[10] This favourable outcome over a short follow-up period invites comparison with the initial improvement in case 1.

Visual outcomes, tumour shrinkage and subretinal fluid resolution

The visual outcome in our 3 cases reflects the response to external radiotherapy reported by Schilling *et al*.[7] (Berlin/Essen group) that the functional success of the treatment depended on the lag duration between first onset of symptoms and treatment. Patient 1, who presented early, had an initial impressive visual improvement after treatment. Both patients 2 and 3, who had symptoms and poor visual acuity of long duration, did not improve after treatment. None of our patients has yet developed the subretinal fibrosis described as being a prevalent cause of late visual deterioration.[7] None of our patients developed neovascular glaucoma. There was no radiation-induced cataract.

All the tumours treated with proton therapy showed marked shrinkage and in patients 1 and 2 were undetectable by ultrasound after 3 years of follow-up.

Radiation doses and side-effects

The radiation doses were chosen empirically as there is little precedence in using proton beam therapy to treat CCH. There is still no consensus as to the ideal radiation dose to treat this tumour. (The dose depends on the relative biological effectiveness of the source, so direct dose comparisons between different treatment modalities are not possible.) The choice hinges on whether one is aiming merely for resolution of the subretinal fluid or for actual shrinkage of the tumour volume. With external beam radiotherapy, the Berlin/Essen group aimed for the former and advocated using a lower radiation dose, whereas the London group[1] felt that a higher dose causing an effective decrease in tumour size decreases symptoms of metamorphopsia and prevents further recurrences. We currently prescribe a total dose of 1800–3000 cGy administered in 15–19 fractions with lens-sparing external beam radiotherapy.

Gragoudas *et al.*[13] described proton treatment of choroidal melanomas within 3 mm of the fovea and/or optic nerve area showing variable changes in visual acuity, but the majority of their patients had less than 2 years of follow-up. It is interesting to speculate why these radiation changes have developed given that the dose of 1800 cGy for CCH is significantly lower than the dose of 5200 cGy for choroidal melanomas.[19] This may be attributed to the vascularity of these lesions causing increased absorption leading to radiation changes. Also the dose fractionation may not be adequate compared with conventional radiotherapy that is administered in 20 or more fractions.

Current choice of CCH treatment

Since its discovery by Wilson in 1946, proton therapy has moved out of the physics research laboratory to costly purpose-built clinical facilities to treat a very specific subgroup of tumours.[20,21] The cost-benefit ratio is constantly being evaluated. In the field of ophthalmology there have been recent publications[19] questioning the justification of treating choroidal melanomas with proton beam therapy rather than other modes of treatment.[21]

In our experience, proton beam therapy for CCH causes effective tumour shrinkage but does not appear to be less likely to cause radiation-induced damage than does external beam lens-sparing radiotherapy or brachytherapy. Given the large cost difference between proton beam therapy and the other available treatments, the treatment of choice for CCH in the current climate of an increasingly cost-conscious health service appears to be obvious.

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