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Transpupillary thermotherapy in the management of choroidal metastases

H. KIRATLI, S. BILGIÇ

Ocular Oncology Service, Hacettepe University School of Medicine, Ankara - Turkey

PURPOSE. *To report the authors' experience in the use of infrared diode laser transpupillary thermotherapy in the management of selected posterior choroidal metastatic tumors.*
METHODS. *Seven eyes of seven patients were treated using 810 nm infrared diode laser. Spot sizes of 0.5 to 3 mm were selected, each lasting 1 minute. When necessary, the treatment was repeated at 8- to 10-week intervals. Disappearance of the tumor was the main outcome measure.*
RESULTS. *The primary sites of carcinomas were breast, prostate, and lungs. The largest basal diameters of ocular tumors varied between 5 mm and 10 mm and the thickness ranged between 2 mm and 4.5 mm. A mean power of 612 mW was used in one to four treatment sessions. In six eyes the tumors were reduced into flat scars whereas in one case the tumor continued to grow necessitating external beam radiotherapy. In three eyes the visual acuity decreased and in three eyes the vision became better. In one eye the vision was restored after external beam radiotherapy with the disappearance of extensive subretinal fluid. There were no immediate postoperative complications.*
CONCLUSIONS. *Transpupillary thermotherapy can be a reliable, convenient, and cost-cutting option in the management of small, solitary choroidal metastatic tumors with a thickness of less than 3.5 mm and which have minimal subretinal fluid. Although successful in terms of tumor control, treatment close to the fovea or optic nerve head may cause a permanent decrease in visual acuity. (Eur J Ophthalmol 2004; 14: 423-9)*

KEY WORDS. *Breast, Prostate, Lung, Carcinoma, Uvea, Choroid, Metastasis, Transpupillary thermotherapy*

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INTRODUCTION

The incidence of symptomatic choroidal metastasis is increasing mostly because patients with cancer are living longer. The prevalence of choroidal metastatic tumors ranges between 2.4% and 9.2% if based on clinical observations and is found between 4% and 10% if postmortem studies are taken into account (1-3). If left untreated, these tumors can cause blindness or lead to enucleation as a result of intractable pain (4).

Several therapeutic options are available for the management of choroidal metastases. These include radiotherapy in the form of external beam radiation (5-8), plaque brachytherapy (9), or proton beam irradiation (10), laser photocoagulation (11), and the recently introduced infrared diode laser transpupillary thermotherapy (TTT) (12-14). The role of chemother-

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apy or hormone therapy appears controversial in the management of choroidal metastases, illustrated by the experience gained from patients with breast carcinoma (15). Chemotherapy may induce choroidal tumor regression in 81% of patients but conversely, 53% of patients may develop ocular metastases while on chemotherapy for their systemic disease (15). External beam radiotherapy (EBR) continues to be the treatment of choice in the majority of cases by virtue of its proven efficacy and the radiosensitivity of most tumors. A study of 264 patients with breast carcinoma, which is by far the most frequent to metastasize to intraocular structures, showed that EBR was selected in 59% of cases with a tumor regression rate of 64% (15). Other recent large studies report tumor regression rates between 29% and 83% (5-8). Because 30% to 50% of patients usually die 5 to 7 months after the diagnosis of choroidal metastasis, serious side effects due to EBR are seldom encountered (5). Frequent hospital visits over a long period of time and relatively elevated costs constitute the drawbacks of EBR. Plaque brachytherapy provides tumor control in 94% of cases (9). However, the need for two minor operations, a mean hospital stay of 86 hours to achieve an adequate therapeutic dose, and the significant cost of plaques are disadvantages of this technique (9). Obviously, an effective, low-cost, and one-stop treatment would be welcomed by patients and physicians. We therefore assessed the efficacy of TTT in a subset of patients with a solitary choroidal metastatic tumor that probably would have otherwise been treated with EBR. We build on three previous reports (12-14) by providing the results of more patients with different histologic types of larger tumors and with longer follow-up information.

METHODS

The medical records of patients with choroidal metastatic tumors treated with TTT between 1998 and 2002 were retrospectively reviewed. The data evaluated include the age of the patient, the eye involved, the origin of the metastatic tumor, tumor thickness and largest basal diameter, distance to the fovea and optic disc, pretreatment and final visual acuities, the laser power used, number of sessions, the tumor outcome, the final state of the patient, and length of follow-up. TTT was offered to non-randomly selected patients with an established diagnosis of systemic cancer if the tumor was solitary and located at the posterior pole, was less than 4.5 mm in thickness, was associated with minimal or no subretinal fluid, and if the patient was not receiving concurrent chemotherapy and did not receive any prior ocular treatment. The recommendations of the Declaration of Helsinki were followed.

TTT was performed using a slit-lamp mounted 810 nm infrared diode laser (Oculight, Iridex, Mountain View, CA). Spot sizes of 0.5 mm to 3 mm were used and each spot lasted 1 minute. The desired immediate response was faint whitening and a transient and momentary contractile and shrinking movement of the inner surface of the tumor and the retina. A 2 mm strip of presumably normal choroid bordering the tumor was also treated. In Patient 4, in whom the tumor involved the fovea, the spots were so placed that the edges of the final whitening spots were kept approximately 500 microns away from the foveola. Tumor response was assessed by fundus photographs, fluorescein angiograms, and B-mode ultrasonographic thickness measurements at the follow-up visits. When deemed necessary, TTT sessions were repeated at 2-month intervals.

RESULTS

Seven eyes of seven patients were treated with TTT. Table I summarizes the salient features of each patient. Patient 1 was previously reported (12). All patients were symptomatic when the decision to treat was made and none had any other identifiable extraocular metastatic sites. The origin of malignancy was lung in three patients, and breast and prostate in two patients each. There was no ocular involvement other than the choroid. Table II shows further details on each eye that received TTT. The ultrasonographic tumor thickness ranged between 2 mm and 4.5 mm and the largest basal diameter ranged between 5 mm and 10 mm. A mean power of 612 mW (range: 530 to 700 mW) was used in one to four treatment sessions. No immediate post-treatment complications occurred. In six eyes, which had metastatic prostate carcinoma (Fig. 1), breast carcinoma (Fig. 2), and pulmonary small cell carcinoma (Fig. 3), the posterior choroidal

TABLE I - CLINICAL AND THERAPEUTIC DATA OF PATIENTS WITH POSTERIOR CHOROIDAL METASTASES TREATED WITH TRANSPUPILLARY THERMOTHERAPY

Patient	Age, yr	Primary malignancy	Preop VA	Final VA	Power, mW	Number of sessions	Tumor outcome	Follow-up, months	Status
1	46	Breast	20/40	20/20	500	1	Flat	16	Died of metastasis
2	48	Breast	20/40	20/60	700	2	Flat	21	Died of metastasis
3	64	Prostate	CF	20/100	530	1	Flat	12	Alive, well
4	57	Prostate	20/25	20/200	700	2	Flat	48	Alive, well
5	36	Lung adenocarcinoma	CF	HM	600	4	Flat	12	Died of metastasis
6	44	Lung mixed small and large cell carcinoma	20/20	20/200	700	2	Growth	24	Alive, chemotherapy
7	43	Lung small cell carcinoma	20/100	20/40	550	2	Flat	12	Alive, chemotherapy

Preop = Preoperative; VA = Visual acuity; CF = Counting fingers; HM = Hand motions

TABLE II - SELECTED DATA ON METASTATIC CHOROIDAL TUMORS TREATED WITH TRANSPUPILLARY THERMOTHERAPY

Patient	Laterality	Location	Distance to fovea, mm	Distance to optic disc, mm	Largest diameter, mm	Thickness, mm	SRF
1	OD	Temporal	4	7	6.5	2.2	+
2	OS	Superior JP	1.5	0	5	2.5	++
3	OS	Temporal	2.5	5	6	2.0	-
4	OD	Macula	0	2.5	6.5	2.5	++
5	OD	Inferior JP	2.5	0	10	3.5	++
6	OD	Inferotemporal	4.5	7	8	4.5	4+
7	OD	Inferotemporal	2.5	5	7	2.4	+

SRF = Subretinal fluid; OD = Right eye; OS = Left eye; JP = Juxtapapillary; + = Present, – = Not detected clinically and angiographically

tumors regressed into flat scars. In Patient 6, further tumor growth with a rapid increase in serous retinal detachment was observed. This patient was then managed with EBR, which successfully eradicated the tumor and the subretinal fluid. The visual acuity of the affected eyes before treatment ranged from light perception to 20/20. Three eyes had improved visual acuity following TTT. In three eyes that had a slight but permanent visual loss, the tumors were juxtapapillary (Patients 2 and 5) and macular (Case 4, Fig. 1) in location. In Patient 6, the visual acuity reached 20/20 level with the reattachment of the retina following radiotherapy. During a mean follow-up of 20.7 months (range: 12 to 48 months), three patients died of cancer-related causes, two patients were alive and healthy, and two patients were undergoing chemotherapy for systemic recurrence.

DISCUSSION

The ophthalmologist charged with the management of intraocular metastatic tumors will usually face a dilemma. The treatment strategy, which is almost always palliative, has to be based on the overall status of the patient, the degree of tumor activity, the size

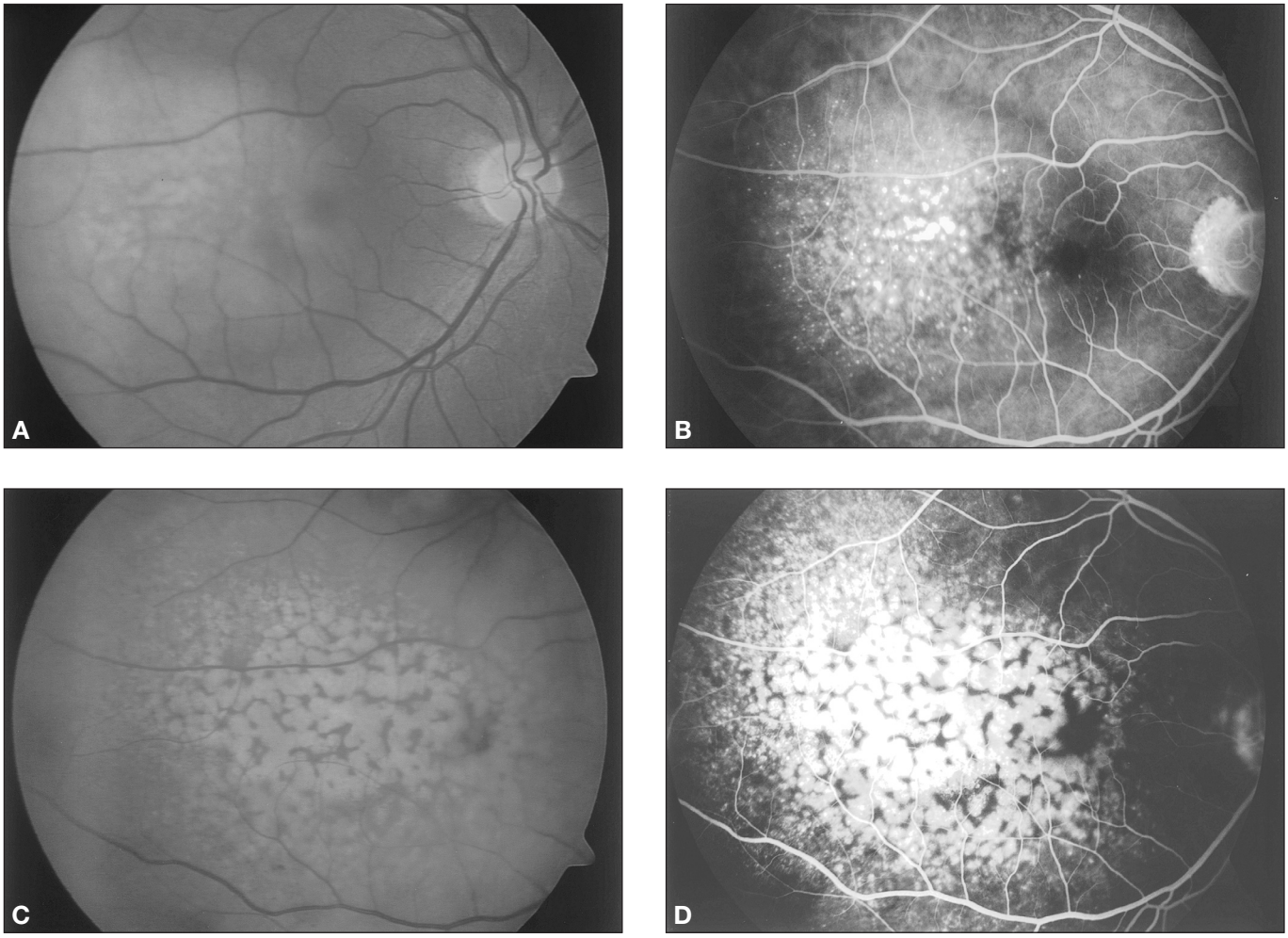

Fig. 1 - *Patient 4 with metastatic prostate carcinoma. (A) Pretreatment right fundus view showing the dark-cream colored tumor occupying the macula. (B) Pretreatment recirculation phase fluorescein angiogram showing pinpoint hyperfluorescence over the tumor. (C) Six months later with two sessions of transpupillary thermotherapy (TTT) performed, the tumor is flat with widespread retinal pigment epithelial alterations. (D) Post-treatment late phase fluorescein angiogram demonstrates the changes induced by TTT.*

and location of the tumor, the visual acuity, and the status of the fellow eye. The median survival is 7.4 to 8 months after the diagnosis and treatment of intraocular metastasis (1). Therefore any prolonged treatment will compromise the quality of life of the patient. On the other hand, modern daily life requires good visual function, which should be provided during the final months of the patients. Laser treatment of choroidal metastasis, which seems most convenient for the patient, has never become popular. In the early days of light coagulation, a number of peripheral tumors were treated successfully by xenon photocoagulator, whereas failure was reported for a tumor near the optic disk (16). Later, the use of laser was recommended only for delimiting serous retinal detachment causing visual loss accompanying an otherwise controlled tumor (17). More recently, Levinger et al (11) published their results on the use of krypton red/argon green lasers in 10 eyes with metastatic breast carcinoma. These authors observed tumor regression days after treatment, disappearance of subretinal fluid within 14 days, and a marked improvement in visual acuity (11).

TTT has earned a solid place within the past decade in the management of some choroidal melanomas and hemangiomas, which encouraged clinicians to test this modality in choroidal metastatic tumors as well. The

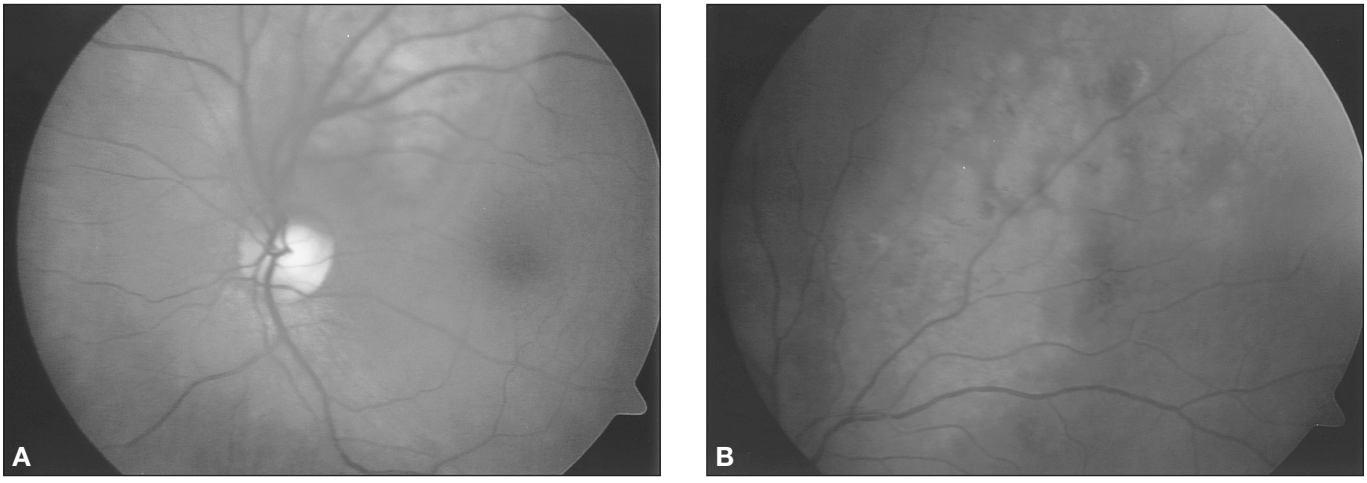

Fig. 2 - *Left fundus view of Patient 2 with metastatic breast carcinoma. (A) The tumor lies superotemporal to the disk separated by a narrow band of normal appearing choroid. (B) Eight months after two sessions of transpupillary thermotherapy, 10 weeks apart, the tumor is completely flat, showing areas of chorioretinal atrophy.*

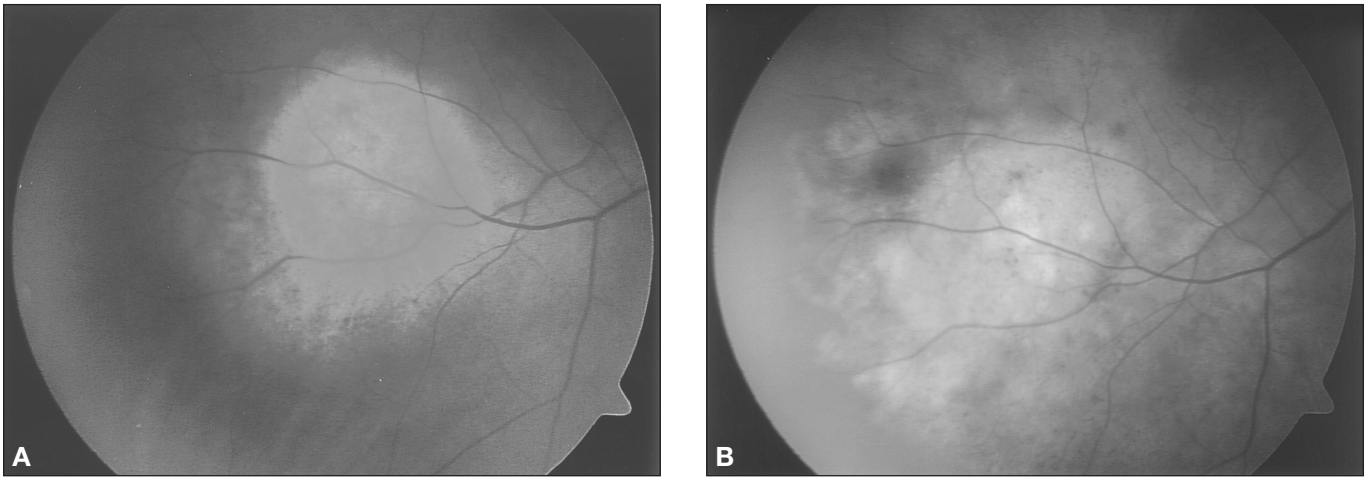

Fig. 3 - *Right fundus view of Patient 7 with metastatic small cell carcinoma of the lung. (A) Before treatment; (B) 6 months after transpupillary thermotherapy.*

first cases treated accordingly were metastatic breast (12) and renal cell carcinomas (13). The latter tumor measuring 1.5 mm in base and 1 mm in height received three shots of 600-850 mW energy that caused substantial regression in 4 weeks (13). Concurrently, Puri et al (14) reported the outcome of four patients with metastatic solitary breast carcinoma treated with TTT. A gradual tumor regression was induced by indocyanine green augmented TTT, using power settings greater than 1000-1250 mW (14). That study concluded that comparable results to radiotherapy with minimal complications and retention of good visual acuity could be obtained with TTT (14). While our results largely support these conclusions, we achieved satisfactory tumor control at lower power levels (530 to 700 mW) and without the use of indocyanine green dye. The spectrum of tumors that we treated ranges from the most common breast carcinoma to prostate carcinoma, which rarely metastasizes to uvea, and three different histopathologic subtypes of lung cancer. All tumors except the pulmonary mixed small and large cell carcinoma metastasis responded favorably

to TTT and we believe that failure in Patient 6 was due mainly to the large size of the tumor. Three of our patients with mild visual loss after TTT deserve further attention. All three eyes had more subretinal fluid compared to eyes that recovered visual acuity. Although the fovea was not directly targeted in Patient 4, subfoveal tumor infiltration, further compromise of vascular supply by encircling the fovea, and the slow scarring process could have contributed to final visual loss. In Patients 2 and 5 with juxtapapillary tumors, direct nerve fiber damage and treating an additional 2 mm strip of presumed normal neighboring choroid within the macula might be among the possible causes of decline in visual acuity.

The short-term benefits of EBR as an effective palliative measure by improving visual acuity outweigh the small risk of radiation-related complications (7). Rudoler et al (7) found that 57% of patients had improved visual acuity or maintained navigational vision and 36% of legally blind eyes regained useful vision following a median total radiation dose of 36 Gy. In a prospective study using a standard total dose of 40 Gy, visual acuity improved in 36% of eyes and remained stable in 50% of eyes (3). Patient age less than 55 years, tumor base diameter less than 15 mm, and a preoperative visual acuity higher than 20/40 are significant predictive factors for maintaining or improving visual acuity (8, 15). Also, eyes with smaller tumors without retinal detachment have better visual acuity after EBR than larger tumors with retinal detachment (18). Persistent retinal detachment and tumor related structural damage are the most common causes of poor vision (8). In contrast to TTT, macular location does not significantly correlate with poor visual outcome (7). With the limited preliminary data on TTT currently available, it is still premature to make any meaningful comparison with the vast experience on EBR accumulated over many years.

Our experience with this small number of patients may nevertheless allow us to suggest a framework for the use of TTT in choroidal metastatic tumors. For the TTT to be effective, the ocular media should be clear and only a minimal amount of subretinal fluid should exist on or around the tumor if at all. Since almost two thirds of choroidal metastases are associated with serous retinal detachment, this may limit the use of TTT (19). The thickness of the tumor appears important as tumors having less than 3.5 mm of height responded favorably. Also, tumor infiltration of the choroid is usually more extensive than can be appreciated ophthalmoscopically (1). For this reason, treatment should cover at least 2 mm of apparently healthy choroid surrounding the tumor.

The results of this study suggest that TTT may be used for small, solitary choroidal metastatic tumors with minimal or no subretinal fluid in selected patients with satisfactory outcomes in terms of tumor control. This technique will not only help to lower the costs but obviate the use of radiotherapy as well in this special subset of patients. However, patients with tumors close to the fovea or in contact with the optic disc may experience a decreased final visual acuity.

Reprint requests to:
Hayyam Kiratli, MD
Associate Professor of Ophthalmology
Hacettepe Hastanesi Goz ABD
Sıhhiye 06100 Ankara, Turkey
hkiratli@hacettepe.edu.tr

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