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Case Report

Short course palliative radiotherapy in the management of choroidal metastasis: An effective technique since ages

Soumyajit Roy [a,*], Renu Madan [a], Ajay Gogia [b], Koushik Tripathy [c], Dayanand Sharma [a], Pramod Kumar Julka [a], Goura Kishore Rath [a]

[a] *Department of Radiation Oncology, Dr. B.R. Ambedkar Institute Rotary Cancer Hospital, All India Institute of Medical Sciences, New Delhi 110029, India*
[b] *Department of Medical Oncology, Dr. B.R. Ambedkar Institute Rotary Cancer Hospital, All India Institute of Medical Sciences, New Delhi 110029, India*
[c] *Department of Ophthalmology, Dr. Rajendra Prasad Centre for Ophthalmic Sciences, All India Institute of Medical Sciences, New Delhi 110029, India*

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KEYWORDS

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Abstract *Purpose:* Uveal tract is the most common site of intra-ocular metastasis. Overall, the reported prevalence of clinically evident uveal metastases in patients with cancer ranges from 2% to 9%, with the majority of the cases being due to breast cancer. We aimed at evaluating the role of palliative radiotherapy in the management of choroidal metastasis from carcinoma breast.
Materials and methods: We describe the clinico-pathologic features, treatment and outcome of ten patients of carcinoma breast who presented to the ophthalmology department at our institution with ocular symptoms attributable to choroidal metastasis.
Results: Nine of the patients were female while one was male. All of them presented with painless progressive diminution of vision. Median duration of symptoms was 2.25 months. Five patients had associated lung metastasis while bone and brain metastases were seen in three and two patients respectively. All of them received palliative radiotherapy (RT) to the involved eye (or eye + brain) by 3D-CRT ($n = 7$), or 2 Dimensional technique ($n = 2$) or electron therapy ($n = 1$). Doses prescribed were 30 Gy/10#/2 weeks ($n = 8$); 20 Gy/5 #/1 week ($n = 2$). Simultaneously they received hormonal therapy ($n = 6$) or systemic chemotherapy ($n = 3$). After a median follow up of 18 months seven patients had complete resolution and two patients had partial resolution of the metastases.
Conclusion: Short course palliative radiation therapy is an effective modality for the management of choroidal metastasis in patients of carcinoma breast. In the current report it led to formidable local control with acceptable radiation induced toxicity.

* Corresponding author.
E-mail address: soumyajitroy8@gmail.com (S. Roy).

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Introduction

Uveal tract is the most common site for intraocular metastasis. The potential reason for such metastasis is the high vascular supply of the uveal tract. Choroidal metastasis accounts for 88% of cases followed by iris and ciliary body. Breast (37–41%), lung (7%) and colon carcinomas [1,2] are common malignancies which throw choroidal secondaries. Multiple treatment modalities exist for the management of choroidal metastasis; the choice depends on the primary, the associated systemic disease burden and the available resources. Palliative radiation therapy has been established as a successful local treatment for uveal metastasis. However no consensus about the adequate dose and technique of radiation therapy has been reached yet. We explored the option of short course palliative radiation therapy in the management of choroidal metastasis in patients with carcinoma breast.

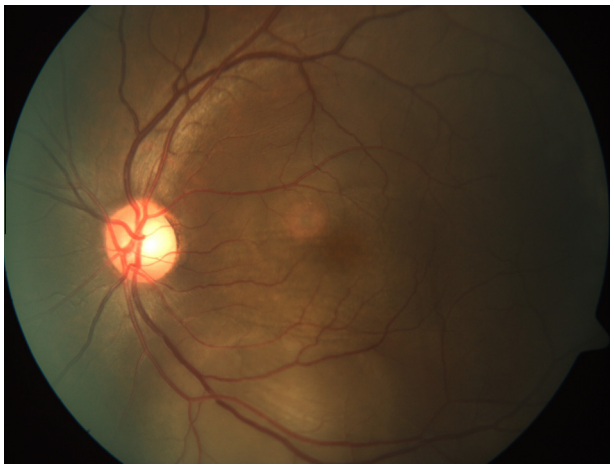

Figure 1 Left eye fundus photograph shows one yellowish lesion at the macula and another along the infero-temporal arcade with surrounding sub-retinal fluid accumulation.

Description of patients

Patient demographics

We documented the demographics and treatment details of ten patients of carcinoma breast with choroidal metastasis from our departmental archive. The median age of the patients was 50 years (range: 48–64 years). The female: male ratio

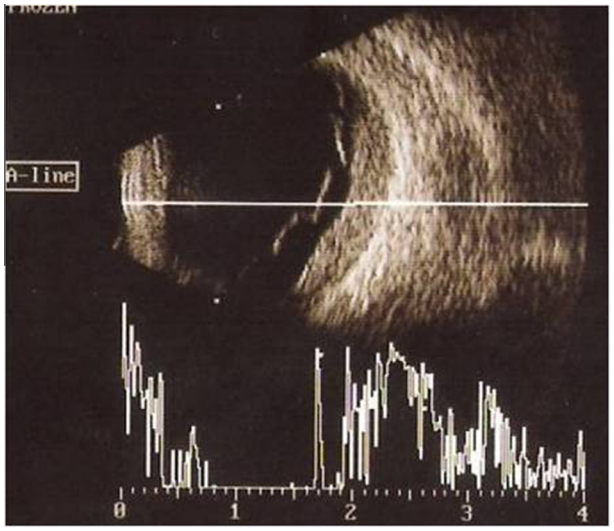

Figure 3 B-scan ultrasonography of a globe with choroidal metastasis shows an echogenic choroidal mass with diffuse ill defined borders and overlying retinal detachment. A-scan shows a 100% spike suggestive of retinal detachment along with moderate to high internal acoustic reflectivity of the choroidal mass.

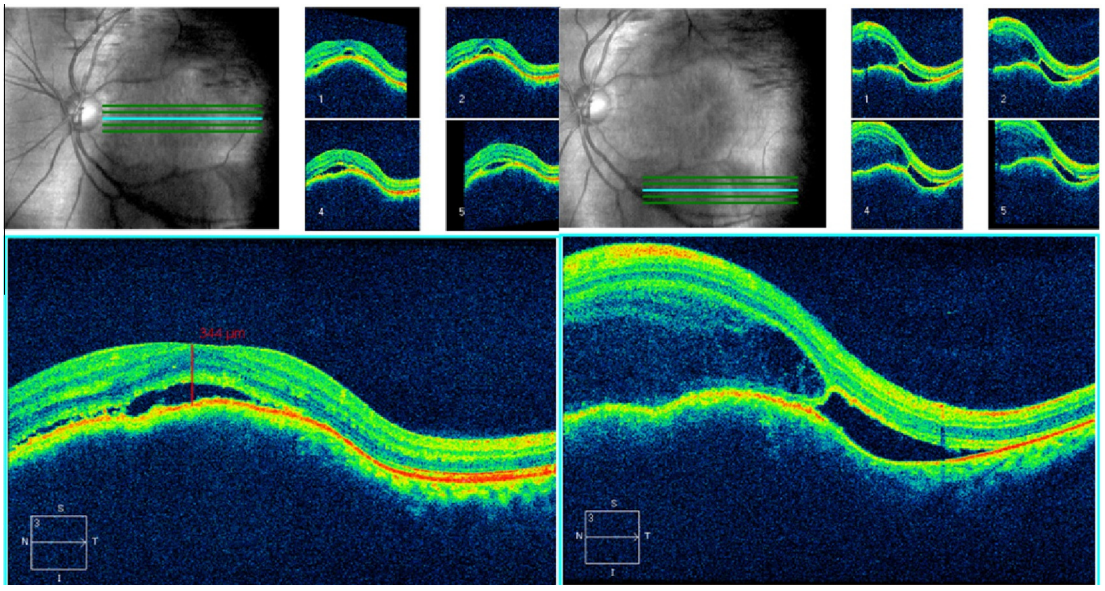

Figure 2 Optical coherence tomography shows a choroidal mass at the macula with sub-retinal fluid (Left) and another sub-retinal mass at the infero-temporal arcade with surrounding sub-retinal fluid (right).

Table 1 Showing the different histopathological features of the primary in ten patients.

Tumour characteristics	Number of patients
Size	> 10 cm: 2
	5–10 cm: 6
	< 5 cm: 2
Nodes	N0: 1
	N + ve: 9
ER status	Positive: 7
	Negative: 3
PR status	Positive: 6
	Negative: 4
HER2neu	Positive: 6
	Negative: 3
	Unknown: 1
Ki 67 index	> 15: 7
	< 15: 3

was 9:1. All of them presented with painless progressive diminution of vision. Median duration of symptoms was 2.25 months (range: 15 days–3 months).

Investigations

Fluorescein fundal angiography (FFA) ($n = 8$) (Fig. 1) was the most commonly done investigation to establish the diagnosis. In FFA the most common finding was multiple pin-point leaks ($n = 7$). Contrast enhanced magnetic resonance imaging of the brain and orbits and F-18 fluoro-deoxyglucose positron emission tomography of the whole body were done in two patients each. Optical coherence tomography (OCT) was the most common adjunct investigation ($n = 7$) (Fig. 2). In 5 patients B mode ultrasonography was done. The common finding on B mode ultrasonography was echogenic choroidal mass with diffuse ill-defined borders ($n = 2$) (Fig. 3). None of these patients had metastasis in any other intra-ocular or intra-orbital sites. Synchronous metastases were found in other organs like lung ($n = 5$); brain ($n = 2$); and bone ($n = 3$).

Characteristics of the primary tumour

The histopathological and immunohistochemical features of the primary tumour have been shown in Table 1. The median time to develop choroidal metastasis was 41.25 months (range 18–72 months).

Treatment details

Seven out of ten patients received palliative RT by three dimensional conformal RT (3D-CRT) ($n = 7$). Two dimensional fluoroscopic simulator based technique and electron beam therapy were used in two and one patient respectively. The commonly prescribed radiation dose regime was 30 Gy in 10 fractions over 2 weeks ($n = 8$) followed by 20 Gy in 5 fractions over 1 week ($n = 2$). The target volume for radiation planning consisted of the involved globe + 5 mm isotropic margin (Fig. 4). Whole brain was included in the portal when brain metastasis was present simultaneously. Concomitant hormone therapy included exemestane alone ($n = 1$), anastrozole ($n = 3$), and a combination of exemestane and everolimus

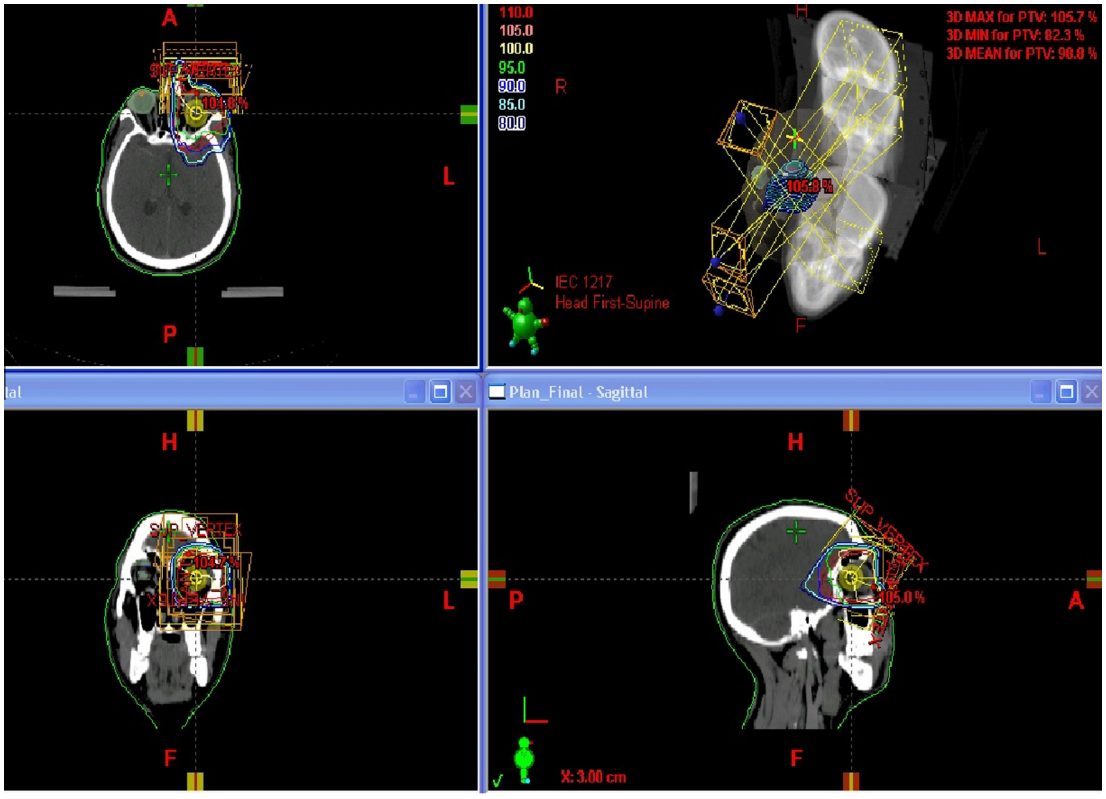

Figure 4 The target volume delineation and three dimensional radiation beam placement in a patient of choroidal metastasis are shown.

Table 2 Showing the improvement in visual acuity in eight patients.

Patient serial no.	At baseline	1 month after radiation completion	6 months after completion of radiation
1	6/60	6/24	6/18
2	Finger counting at 3 metres distance	6/36	6/24
3	Finger counting at 3 metres distance	6/60	6/36
4	6/18	6/9	6/6
5	Only light perception	Finger counting at 3 metre distance	Finger counting at 1 metres distance
6	6/18	6/9	6/6
7	Only light perception	6/60	6/60
8	6/18	6/12	6/6
9	6/36	6/36	6/36
10	Only light perception	Only light perception	Only light perception

Table 3 A comparative analysis of dose, fraction, local control and toxicity profile of different techniques of radiotherapy.

Authors	Technique	No of patients	Dose	Local control	Symptomatic improvement	Toxicity rate
Shields et al. [4]	Plaque brachytherapy	36	Tumour apex: 69 Gy; Tumour base: 236 Gy.	94%	Improvement: 19% Stable: 39%	8%
Bellmann et al. [5]	SRT/SRS	10	10–20 Gy in single fraction or 30 Gy in 10 fraction	80%	N/A	No persistent toxicity
Tsina et al. [6]	Proton beam therapy	63	28 CGE in two fractions	84%	47%	56%
Wiegel et al. [7]	Conventional radiatherapy	50	40 Gy in 20 fractions	N/A	36%	5%
Present study	Conformal radiation technique ($n = 7$) Electron therapy ($n = 1$) Conventional technique ($n = 2$)	10	30 Gy/10 Fractions ($n = 8$) 20 Gy/5 fractions ($n = 2$)	90%	70%	No persistent toxicity

($n = 2$). Systemic agents included combined bio-chemotherapy with lapatinib and capecitabine ($n = 1$), gemcitabine, paclitaxel and bevacizumab ($n = 1$) or multi-agent chemotherapy with cyclophosphamide and vinorelbine ($n = 1$).

Follow-up and outcome

All patients were followed up with serial FFA and OCT done at 3 monthly intervals. After a median follow-up of 18 months (range: 6 months–37 months) seven patients had complete resolution (CR) and two patients had partial resolution of the metastases while one patient (with associated brain metastasis) expired after 4.3 months. The objective response rate (ORR) (summation of CR and PR) was 90% in our series. Serial charting of visual acuity revealed improvement in vision in 8 patients. In the other two patients no objective improvement was discernible in visual acuity (Table 2). We observed acute radiation induced conjunctivitis in 4 patients (grade II: 3 patients; grade III: 1 patient). Two patients developed epiphora after 7 months and 9 months respectively. Three patients developed cataract (posterior subcapsular cataract), two in the same eye, and one in the opposite eye. The median latent period for cataract formation after completion of radiation was 17.8 months (range: 16–24 months). All of them were treated successfully using the phacoemulsification technique.

Discussion

Perls was the first person who described the first case of choroidal metastasis. In the next six decades only 230 cases were described in the literature.

External beam radiation (EBRT) has been traditionally used for treatment of choroidal metastasis when they fail to regress after systemic therapies. Disappearance or regression of lesions occurs in 85–93% of patients. The prescription dose ranges from 30 Gy to 50 Gy [3–7]. The main disadvantages of using radiotherapy were its side effects which may be acute or late. The common morbidities include acute conjunctivitis, keratitis, cataracts, exposure keratopathy, iris neovascularization, radiation induced retinopathy and papillopathy. These side effects have been seen in 12% of patients in the reported series [3]. Currently various modern techniques of EBRT have been deployed for managing choroidal metastasis like stereotactic radiosurgery or fractionated stereotactic radiotherapy or proton beam therapy. Plaque brachytherapy has also been applied in some series. The result we observed in our study is comparable to other series in terms of response and toxicity though our cohort size was smaller than others (Table 3). Use of conformal technique and electron beam radiation precluded emergence of any late toxicities.

Multiple other local treatment modalities have emerged in the present era. Four case reports have described the use of

intravitreal bevacizumab in patients with choroidal metastasis despite systemic therapy. In all four case reports, lesions regressed and retinal detachments resolved after one injection of bevacizumab [8].

Laser photocoagulation, photodynamic therapy, transpupillary thermotherapy, cryotherapy, local excision and even enucleation have been used as other local treatment modalities [9,10]. But some of these patients needed multiple treatment sessions or further radiation therapy [10] to achieve adequate local control. Complete loss of vision in a substantial number of patients has been another cause of worry for these modalities. Finally external beam radiation is still a cost effective regimen with respect to these emerging techniques.

The current study has its own limitations. The underlying bias owing to the heterogeneity of treatment regimens cannot be neglected. However one must accept the difficulties of carrying out a uniform prospective trial for such a rare disease entity. In a resource limited developing country like ours, palliative radiotherapy is still an acceptable and feasible option. It yields commendable treatment compliance and good response rate at the cost of acceptable morbidities. The overall cost effectiveness of this short course palliative EBRT regimen makes it worthwhile to use in such a resource constrained set-up.

Conclusion

Palliative radiation stands tall in spite of emergence of other local treatment techniques and advancement of systemic therapies in the management of choroidal metastasis. It provides superior local control and symptomatic improvement with minimal toxicity. It is non-invasive, cost-effective, and has better compliance. This option merits more judicious expedition in a developing nation like ours.

Financial disclosure

None.

Conflicts of interest

None.

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