

Experiences of two different modalities in the management of choroidal melanoma in the Asian Indian population

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Abstract

Background: Choroidal malignant melanoma is a rare intraocular cancer in Asian Indian population. There is a paucity of data from our population comparing iodine 125 (I-125) brachytherapy and enucleation. **Aim:** This study aims to compare two groups of choroidal melanoma patients treated with either I-125 brachytherapy or enucleation in the Asian Indian population. **Objectives:** To evaluate the long-term morbidity and mortality rates in choroidal melanoma patients treated with either I-125 brachytherapy or enucleation. **Methods:** It is a retrospective study involving forty four eyes, diagnosed with choroidal melanoma from May 2008 to February 2015. All were evaluated preoperatively for metastasis. Twenty-two underwent globe salvaging I-125 brachytherapy surgery whereas remaining 22 underwent globe destructive primary enucleation procedure. **Results:** At a mean follow-up 39 months, 2 of 22 cases (9%) died in the brachytherapy group. One was secondary to metastasis in the liver while the other case died of a natural cause. In the enucleation group also, there were two deaths (9%) secondary to metastasis. The metastasis free survival was 95% in the brachytherapy group and 91% in the enucleation group, which was not statistically significant ($P = 0.3577$). Kaplan–Meier survival at 3 years and 5 years was 95% and 89% for brachytherapy group and 94% and 89% for enucleation group. **Conclusion:** This study found no difference in the long-term survival of choroidal melanoma patients treated with either brachytherapy or enucleation in the Asian Indian eyes.

Key words: Choroidal melanoma, enucleation, India, iodine 125 brachytherapy

Introduction

Choroidal melanoma is the most common primary malignant intraocular tumor in adults.^[1,2] It is more prevalent in the Caucasian population with an incidence of about 5.1 cases per million population per year in the United States.^[3] Studies done across Europe and the Americas have also confirmed this incidence pattern establishing white race as a risk factor.^[4-6] This tumor is relatively rare among the pigmented population. In India, it is considered a rare diagnosis with very few published reports about this entity.^[7,8] Even though it is rare, it assumes significance in that it is the leading primary intraocular disease which can cause mortality in adults.

The management of this condition assumes specific challenges in the Indian context. Since the incidence is quite low, clinical suspicion is not routinely aroused. Indirect ophthalmoscopy is not a routinely performed diagnostic protocol in the primary and most of the secondary eye care centers in the region. Added to this, the innocuous and slow growing nature of this condition in the early stages contributes to the delay in the diagnosis. Very often, it is recognized after the tumor has caused a retinal detachment.^[9] All these factors may result in the tumor progressing to a very advanced stage, at which time, the only treatment of choice would be surgical enucleation.

Globally, the treatment protocols for uveal malignant melanoma have largely been influenced by the results of the Collaborative Ocular Melanoma Study (COMS).^[10,11] This randomized study compared the efficacy of two treatment modalities, namely, iodine 125 (I-125) brachytherapy and surgical enucleation in the treatment of medium-sized uveal melanoma. The end point of this study was to assess cancer free survival among the individuals randomized to both these groups. Interestingly, this study found the two treatment modalities to be comparable. These results may not be entirely applicable to a developing country situation, typified by the Indian

subcontinent. Enucleation is the most commonly performed surgical procedure, while brachytherapy is not extensively practiced. I-125 brachytherapy using indigenously manufactured Bhabha Atomic Research Center I-125 Ocu-Prosta seeds in the treatment of choroidal melanoma has been recently reported.^[9] In this study, it was found that the eyes subjected to this treatment protocol demonstrated excellent tumor control. There are significant advantages of brachytherapy like the anatomic preservation of the eye and vision. However, this modality may also require the patients to come for regular follow-up and there is every likelihood that this treatment modality may have challenges in implementation in the Indian context. There are no studies comparing brachytherapy versus primary enucleation for choroidal melanomas in the Indian population, because of its rarity. This comparative study may provide valuable insights into the preferred treatment modality in our population and probably pave a way for establishing a preferred practice pattern for treating this rare condition in India.

Methods

This is a retrospective case series of forty-four patients who presented with choroidal melanoma at our institute from May 2008 to February 2015. The initial diagnosis and assessment was done after detailed history taking and a comprehensive ocular examination by an ophthalmologist, which included visual acuity assessment, slit lamp biomicroscopy, indirect ophthalmoscopy, and ocular ultrasonography. These tumors were classified into small, medium, and large according to the COMS criteria.^[11] The patients also underwent a chest X-ray, abdominal ultrasonography, and a clinical examination by an oncologist to screen for tumor metastasis. The treatment options were explained to all the patients and based on mutual decision they were treated with either brachytherapy or enucleation. Brachytherapy was preferred for all medium-sized melanoma cases while enucleation was preferred for the large-sized

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tumors. Informed consent was taken from all the patients and this study was approved by the ethics committee.

Brachytherapy procedure using the I-125 indigenous seeds was done using gold plaques.^[9] The plaque was placed over the sclera, just below the tumor. A total dose of 85 Gy was calculated till the tumor apex. After removing the plaque, the patient was reviewed periodically to monitor for tumor regression.^[9] In case of enucleation, after surgically removing the whole globe, a silicon implant was placed immediately followed by a prosthetic eye placement after 1 month. All enucleated specimens were sent for histopathology. Postoperative metastatic workup was done on a yearly basis for all the cases. Statistical analysis was done using student *t*-test for quantitative variables. Chi-square test was used for evaluation of differences in proportions. $P < 0.5$ was considered statistically significant. All analyses were performed using SPSS 12.0 software (vesion 12.0, IBM, USA).

Results

Forty-four patients were diagnosed with choroidal melanoma. Of these, 22 patients (50%) were treated with brachytherapy, while the rest 22 (50%) were treated by enucleation. The baseline characteristics of both groups of patients are given in Table 1.

There was one case in the enucleation group which initially presented with a small melanoma and was lost to follow-up. He came back after 7 months with secondary angle closure glaucoma with total retinal detachment and large intraocular mass and the eye was enucleated after that. Histopathology of this patient revealed epithelioid subtype.

Patients who underwent brachytherapy received a mean dose of 0.55 Gy/h. The average height of the tumor was reduced to 4.8 mm after treatment. There was a statistically significant decrease in the mean basal diameter of the tumors ($P = 0.0413$) after brachytherapy. In 3 cases (14%), the tumor completely regressed. 3 eyes were pseudophakic before brachytherapy. At the mean follow-up period of 39 months (range 6-86 months), 13 patients (59%) developed brachytherapy-related complications. The median follow-up was 30 months. Cataract was seen in 4 (18%) cases, radiation retinopathy in 7 cases (32%), radiation neuropathy in 4 (18%), secondary glaucoma in one case (4.6%), and corneal epithelial defect in one case (4.6%). Three eyes were secondarily enucleated in the brachytherapy group. Of these, two were enucleated because of suspected tumor recurrence (both of which showed mixed cell type on histopathology), and one because the patient complained of severe pain. Thus, the globe salvage rate was 86% (19/22 eyes) and the tumor control rate was 91% (20/22 eyes). Prebrachytherapy, 13 eyes (59%) had visual acuity $>20/40$ compared to only 5 (23%) cases, postbrachytherapy.

In the enucleation group, the histological subtypes were, 9 (41%) with spindle cells, two (9%) with epithelioid and 9 (41%) with mixed subtype. Histopathology of one eye showed a melanocytoma. All were fitted with silicone implants and customized prosthesis.

Two (9%) cases died in the brachytherapy group. One was secondary to metastasis in the liver while the other case

died of a natural cause. In the enucleation group also, there were two deaths (9%) secondary to metastasis [Table 2]. Both these cases had delayed enucleation from the time of diagnosis. The metastasis free survival was 95% in the brachytherapy group and 91% in the enucleation group, which was not statistically significant ($P = 1$). A subgroup analysis comparing only medium-sized tumors with similar follow-up from both groups (six from enucleation group and nine from brachytherapy group) did not show any significant difference in metastasis and survival.

Kaplan–Meier survival at 3 years and 5 years for the brachytherapy group was 95% and 89%, and for the enucleation group, it was 94% and 89%, respectively.

Discussion

The management of choroidal melanoma is challenging in India for several reasons. First, the incidence is much less in the Indian population when compared with the Caucasian population.^[7,8] Second, due to its rarity, patients are very often misdiagnosed and the correct diagnosis is attained at a much later stage.^[12] Third, very few centers in India provide eye salvaging treatments such as brachytherapy. Thus, the most commonly performed treatment modality in India for this condition is enucleation.^[12-14] Very few reports about

Table 1: Baseline characteristics of both the brachytherapy and enucleation groups

| Variable | Brachytherapy (n=22) | Enucleation (n=22) | P |
|----------------------|-------------------------|-----------------------|--------|
| Mean age (years) | 53 | 50 | - |
| Gender | | | |
| Male | 14 (64) | 10 (45) | 0.364 |
| Female | 8 (36) | 12 (55) | |
| Tumor type | | | |
| Posterior | 21 (95) | 21 (95) | - |
| Ciliary body | 1 (5) | 1 (5) | |
| Tumor classification | | | |
| Small | - | 1 (5) | 0.0005 |
| Medium | 19 (86) | 7 (32) | |
| Large | 3 (14) | 14 (63) | |
| Tumor size (mm) | | | |
| Mean LBD | 12.0 | 13.7 | 0.035 |
| Mean AD | 6.5 | 9.4 | 0.0012 |
| Presenting VA | | | |
| $\geq 20/40$ | 13 (59) | 4 (18) | 0.0081 |
| $< 20/200$ | 6 (27) | 15 (68) | |
| Symptoms | | | |
| Defective vision | 17 (77) | 22 (100) | - |
| Floaters | 2 (9) | - | |
| Routine exam | 2 (9) | - | |
| Flashes | 1 (5) | - | |

LBD=Largest basal diameter, AD=Apical diameter, VA=Visual acuity

Table 2: Outcomes of brachytherapy and enucleation groups

| | Brachytherapy (n=22) | | Enucleation (n=22) | | P |
|----------------------------------|-------------------------|------------|-----------------------|------------|---|
| | n | Percentage | n | Percentage | |
| Metastasis | 1 | 4.5 | 2 | 9 | 1 |
| Number of deaths | 2 | 9 | 2 | 9 | 1 |
| Kaplan-Meier survival at 5 years | - | 89 | - | 89 | - |

the alternative treatment options available in India exist in the literature.^[9,15] There are no studies from India comparing these two treatment modalities for choroidal melanoma, due to the low incidence of this disease. This is the first study comparing long-term survival after brachytherapy and enucleation for choroidal melanomas in the Asian Indian population.

The COMS study, which was done mainly on Caucasian population, found that both the treatment modalities had comparable outcomes with regard to metastasis and mortality.^[10] After 5 years, the survival rate was 81% and 82% in the enucleation and the brachytherapy group, respectively. In this study, done on the Asian Indian population, only one patient in the brachytherapy group and two in the enucleation group developed metastasis. This difference was not statistically significant ($P = 1$). Another patient in the brachytherapy group died of a natural cause. Thus, the metastasis free survival in our study was 95% in the brachytherapy group and 91% in the enucleation group. The 5 years survival rate was 89% for both groups.

The recurrence rate following globe salvaging I-125 brachytherapy in the COMS was 10.3% and 12.5% required enucleation. Thus, the tumor salvage rate for the COMS study was 89.7% and the globe salvage rate was 87.5%.^[16] The tumor salvage rate in our study was 91% and the globe salvage rate was in 84%. In another study with large tumors,^[17] 80% of these eyes could be retained.

Our study showed radiation retinopathy as the most common complication encountered in 32% of the cases. Thirteen cases (59%) had presenting visual acuity better than 20/40 in the brachytherapy group which dropped to 5 (23%) post 3 years after brachytherapy. In the COMS trial, 70% had presenting visual acuity better than 20/40 and it dropped to 34% at the end of 3 years.^[18]

In the COMS,^[17] of the primary enucleated eyes, 9%, 5%, and 86% were spindle cell type, epithelioid type and mixed cell type respectively compared to 41%, 9%, and 41%, in our study. Other studies from India have found 25%, 10%, 63%,^[12] and 53.9%, 18.4%, 18.4%^[13] to be spindle cell type, epithelioid type, and mixed cell type, respectively. One case (4.5%) in our study was misdiagnosed and was found to have melanocytoma on histopathology. In the COMS, five eyes were misdiagnosed and they had a very high diagnostic accuracy of 99.7%^[19] compared to 95.5% in our study. Few authors have even tried intravitreal bevacizumab along with plaque therapy.^[20] However, it was not tried for any of our cases.

There are some definite limitations to this study. First, it is a retrospective study with a small sample size and second the brachytherapy group had more medium sized tumors compared to the enucleation group (86% vs 32%). However, a subgroup analysis of medium-sized melanomas in our study, showed no difference in metastasis and long-term survival between both groups.

Conclusion

Brachytherapy seems to be a promising eye preserving technique for eyes with choroidal melanomas in the Asian Indian population.

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Conflicts of interest

There are no conflicts of interest.

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