# Case report: Choroidal melanoma: experience from a tertiary referral centre in Malaysia.

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***Background****: Choroidal melanoma is known as the most common primary intraocular malignancy in adults. Nevertheless, it is more commonly found in Caucasians and rarely found in Malaysian population.*

***Objective****: We present eight cases of choroidal melanoma referred to Hospital Selayang, a tertiary centre for medical retinal cases, from year 2012 to 2016.*

***Method****s: Retrospective case series.*

***Results****: There were seven females and one male with a mean age was 53.9 years old. Five patients were Chinese and three were Malay. The presenting complaints were visual field defect (n=3), distorted vision (n=2), photopsiae (n=2) and decreased vision (n=1). The tumour thickness ranged from 3.00 to 13.94 mm (mean=8.93mm). One case had exudative retinal detachment while the remaining had adjacent sub-retinal fluid. Three patients had undergone globe-preserving therapy (plaque brachytherapy and stereotactic radiotherapy) while the remaining had undergone enucleation or exenteration. The histopathological examinations showed three cases of spindle B cells, one with epitheliod cells and one with mixed features. One patient died due to tumour recurrence and complications of multiple distant metastasis while the rest were well under regular follow-up.*

***Conclusions****: Although choroidal melanoma is very rare among Malaysian population, it is a crucial diagnosis to make in view of its metastatic risks. Early presentation and diagnosis of choroidal melanoma is significant to save lives.*

***Keywords****: Choroidal melanoma, case series, melanoma, Malaysia, primary, uvea*

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## Introduction

Choroidal melanoma is known as the most common primary intraocular malignancy in adults. The incidence of primary choroidal melanoma is approximately 6 cases per million population in United States and 7.5 cases per million per year in Denmark and other Scandinavian countries.[1] However, it is commonly found in Caucasians and rarely found in Malaysian population. The risk factors for choroidal melanoma includes fair skin, lighter iris color, ultraviolet light exposure and smoking.

## Materials and Methods

A retrospective analysis of patients referred to the Medical Retinal Clinic, Department of Ophthalmology, Hospital Selayang from year 2012 to 2016 and diagnosed with choroidal melanoma were identified. Patients' demographic data, tumour characteristics, treatment, outcome and complications were reviewed and tabulated.

The diagnosis of choroidal melanoma was made by thorough clinical evaluation, ophthalmic examination, supported by ultrasound, fundus fluorescein angiograph, optical coherence tomography and reviewed by ophthalmic oncology subspecialist.

## Results

A total of eight cases diagnosed with choroidal melanoma were identified and analysed. Among the eight patients, there were seven females and one male. The mean age was 53.9 years old which ranged from 33 to 66 years old. Five patients (62.5%) were Chinese and another three (37.5%) were Malay. The presenting complaints include visual field defect (n=3, 37.5%), distorted vision (n=2, 25%), photopsiae (n=2, 25%) and blurring of vision (n=1, 12.5%). Three of them had family history of malignancy in first-line relatives, but none of them had family history of ocular malignancy. One of the patients was an ex-smoker who smoked 40 packs/ year but quit smoking 10 years ago and the rest were non-smokers. Their occupations did not involve prolonged sunlight exposure. None of them had other pre-existing ocular comorbidity prior to presentation. Table 1 summarized the demographic data including age, gender, ethnicity, occupation, ocular presentation, presenting visual acuity, co-morbidity, family history of cancer and smoking history.

Table 2 showed tumour characteristics of the eight cases which were analysed based on the mnemonic device "To find small ocular melanoma using helpful hints daily'', representing thickness, fluid, symptoms, orange pigment, margin, ultrasonographic hollowness, halo absence and drusen absence.[2] The tumour thickness ranged from 3.0 to 13.94 mm (mean=8.93mm). One case had exudative retinal detachment while the remaining were associated with adjacent sub-retinal fluid. Three out of eight cases had orange pigment on the tumour. All of the tumours were more than 3 milimeter or 2 disc diameter (DD) away from the optic disc and were not associated with halo or drusen.

Treatment with plaque brachytherapy was not available in Malaysia. Two patients

deemed suitable for plaque brachytherapy were referred to centres offering the above treatment. One patient underwent stereotactic radiotherapy. Five patients required more radical treatments like enucleation or

**Table 1**: Patients' demographic data

| No. | Age | Gender | Ethnicity | Occupation | Ocular presentation | Presenting vision | Co-morbidity | Family history of cancer | Smoking history |
|---|---|---|---|---|---|---|---|---|---|
| 1 | 60 | Female | Chinese | Housewife | Visual field defect for 1 month | 6/9 | Nil | No | No |
| 2 | 52 | Female | Chinese | Housewife | Visual field defect with floaters for 3 months | 6/18 PH:6/12 | Hypertension | Yes | No |
| 3 | 53 | Female | Chinese | Waitress | Decreased vision with floaters for 2 months | 6/18 | Diabetes, hypertension, dyslipidemia | Yes | No |
| 4 | 33 | Female | Chinese | Pharmacist | Decreased vision with distortion for 2 weeks | 6/12 PH:6/9 | Nil | No | No |
| 5 | 58 | Female | Malay | Teacher | Decreased vision with visual field defect for 2 months | 6/18 | Left tentorium cerebelli meningioma | No | No |
| 6 | 44 | Female | Malay | Housewife | Distorted vision for 2 weeks | 6/60 | Nil | Yes | No |
| 7 | 66 | Male | Malay | Computer manager | Decreased vision for 1 year | HM | Diabetes, hypertension, treated renal carcinoma | No | Ex-smoker |
| 8 | 65 | Female | Chinese | Housewife | Flashes for 6 months | 6/18 PH:6/9 | Dyslipidemia, left deep vein thrombosis | No | No |

exenteration. Lid-sparing exenteration was performed in case no. 3 due to radiological evidence of lateral rectus and lateral orbital wall involvement. The histopathological examinations showed three cases of spindle cells type B, one with epitheliod cells and one with mixed features.

The two patients that underwent plaque brachytherapy developed foveal atrophy and cystoid macular edema. The cystoid macula edema did not respond very well to treatment with orbital floor triamcinolone. Intravitreal Anti-Vascular Endothelial Growth Factor (anti-VEGF) was not performed in this patient due to presence of significant macular ischaemia found in fundus fluorescein angiography. The patient who had stereotactic radiotherapy developed radiation retinopathy which was treated with laser retinal photocoagulation and intravitreal anti-VEGF injection. The visual outcome of all these patients were poor.

One patient had tumor recurrence with multiple distant metastasis to the brain and liver which was diagnosed at eight months after enucleation. This patient died two weeks after the diagnosis of metastasis. Otherwise, other patients were well under regular follow-up without recurrence or distant metastasis. The mean duration of follow-up till date was 26.5 months (ranged from 8 months to 50 months). Table 3 summarized the treatment, histopathological findings, complications, final vision outcome, duration of follow-up and current general status.

**Table 2**: Tumor characteristics

| No. | Tumour thickness (mm) | Subretinal fluid | Symptoms | Orange pigment | Margin from optic disc | Ultrasono-graphic hollowness | Halo | Drusen |
|---|---|---|---|---|---|---|---|---|
| 1 | 6.1 | Yes | Yes | No | 4DD | Yes | No | No |
| 2 | 5.87 | Yes | Yes | No | 5DD | Yes | No | No |
| 3 | 13.07 | Yes | Yes | No | Unable to visualise | Yes | No | No |
| 4 | 3.0 | Yes | Yes | Yes | 4DD | Yes | No | No |
| 5 | 11.4 | Yes | Yes | Yes | 3DD | Yes | No | No |
| 6 | 13.94 | Yes | Yes | No | Unable to visualize | No | Unable to visualize | No |
| 7 | 9.36 | Yes | Yes | No | - | Yes | No | No |
| 8 | 8.69 | Yes | Yes | Yes | 4DD | Yes | No | No |

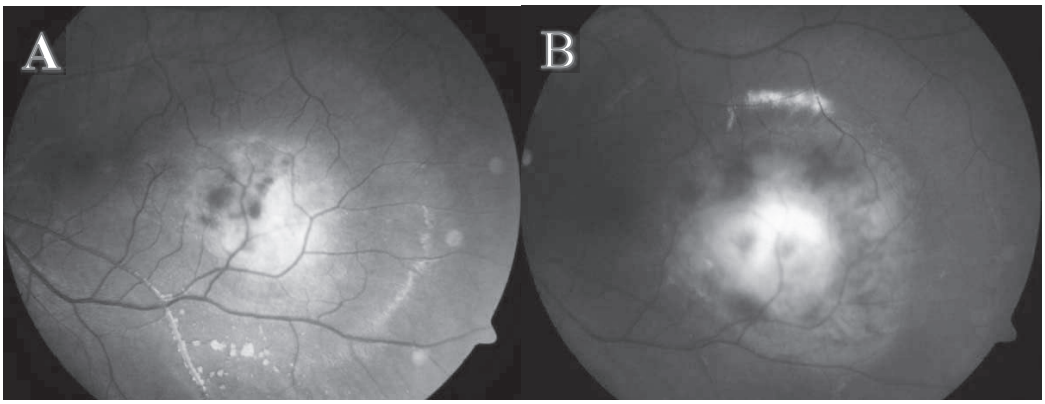


**Figure 1:** Case 4: left eye fundus. (**A**) Dome-shaped pigmented mass temporal to macula measuring 2DD with sub-retinal fluid. Patient underwent 5 sessions of stereotactic radiotherapy. (**B**) Post-treatment photo showing shrinkage of tumour size.

**Table 3**: Treatment, outcome and complication

| No. | Treatment | HPE | Complication | Final vison | Duration of follow-up (months) | Current status |
|---|---|---|---|---|---|---|
| 1 | Plaque brachytherapy | - | Foveal atrophy | CF 2 feet | 22 | Well |
| 2 | Plaque brachytherapy | - | Cystoid macular oedema | 6/60 PH:6/36 | 18 | Well |
| 3 | Lid-sparing exenteration | Spindle B cells | Wound breakdown | - | 21 | Well |
| 4 | Stereotactic radiotherapy | - | Radiation retinopathy | CF 2 feet | 50 | Well |
| 5 | Enucleation | Spindle B cells | Nil | - | 42 | Well |
| 6 | Enucleation | Epitheloid cells | Recurrence with metastasis to brain and liver | - | 8 | Dead |
| 7 | Enucleation | Mixed cells | Nil | - | 24 | Well |
| 8 | Enucleation | Spindle B cells | Nil | - | 27 | Well |

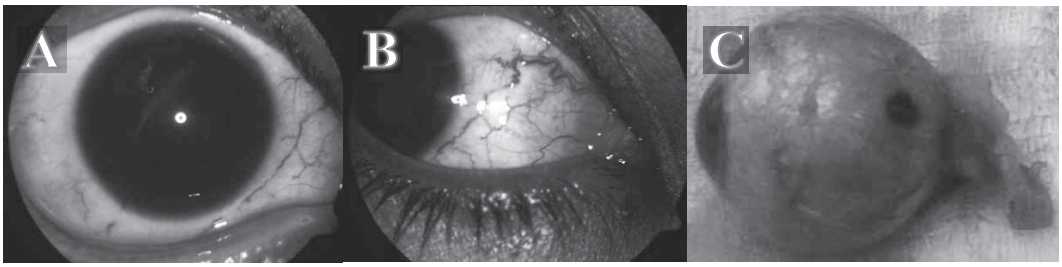


**Figure 2:** Case 6

Fast growing choroidal melanoma with sentinel vessel (**A & B**). Enucleation was performed which showed pigmented lesion on posterior sclera (**C**). Optic nerve and rectus muscles margin were free of tumour cells. Unfortunately, patient had recurrence eight months later and died due to complications of distant metastasis to brain and liver.

**Discussion**

Melanoma appears as a unifocal mass with variable pigmentation arising from melanocytes of choroid, ciliary body or iris. Choroidal melanoma accounts for about 80% of all uveal melanoma. In this case series review, majority of cases involve the Chinese population. This is likely related to host factor that Chinese has fairer skin color and inability to tan. Shah et al.[3] found that chronic ultraviolet exposure and occupational sunlight exposure were borderline factors.

Typically starts as dome-shaped lesion, choroidal melanoma acquires a mushroom or collar-button shape as it grows and breaks through the Bruch membrane. It often associates with subretinal fluid and causes retinal detachment. It can also develop vitreous haemorrhage and secondary glaucoma. Choroidal melanoma can be grouped into three sizes based on the tumour thickness, including small (0-3.0 mm), medium (3.1-8.0 mm) and large (8.1 mm or greater).[4]

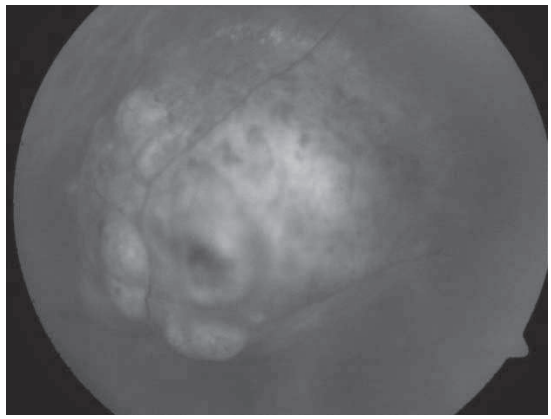

**Figure 3**: Case 2 Dome shaped raised mass at superotemporal retina measuring 5DD associated with sub-retinal fluid.

The management of choroidal melanoma depends on patient's age, general health, preference, status of fellow eye, tumour size and location. Options of management including eye-preserving techniques such as transpupillary thermotherapy, plaque brachytherapy,proton-beam radiotherapy, transcleral resection and endoresection, and radical treatment such as enucleation or orbital exenteration.

The use of focal radiotherapy such as proton beam irradiation or plaque brachytherapy can generally achieve good local tumour control, but it may be associated with poor visual outcome. Gunduz et al studied 1,300 eyes with posterior uveal melanoma treated with plaque brachytherapy, showed that 42% patients subsequently developed radiation retinopathy by 5 years after treatment.[4] Sagoo et al analysed 650 consecutive eyes with juxtapapillary choroidal melanoma (≤1mm to optic disc) treated with plaque brachytherapy and found that this treatment modality commonly leads to retinopathy and papillopathy, and visual loss should be anticipated in 45% by 5 years. Nevertheless, they concluded that plaque brachytherapy remains a suitable treatment of juxtapapillary melanoma in view of high globe retention rate, which was 84% at 5 years.[5]

The Collaborative Ocular Melanoma Study (COMS) was a prospective study designed to evaluate the management of choroidal melanoma. COMS consists of three substudies including the large, medium and small choroidal melanoma trials. The large tumor trial showed no difference in patient's survival when comparing enucleation and preenucleation radiation groups.[6] The medium tumor trial showed no difference in patient's survival when comparing enucleation and plaque brachytherapy up to 12 years follow-up.[7] The cumulative all- cause mortality at 12 years was 43% in the plaque brachytherapy group and 41% in the enucleation group.

According to American Joint Committee on Cancer (AJCC) TNM Staging, the clinical features that is associated with poor prognosis is usually related to tumor size of more than 15mm, tumor location in ciliary body, extrascleral tumor extension, older age at diagnosis and regrowth after globe-conserving therapy. Histopathological and cytogenic factors associated with poorer prognosis includes epithelioid cell type, increased mitotic activity, infiltrating lymphocytes, tumor vascular networks and chromosomal mutations (monosomy 3 and trisomy 8).[8] Shield et al. found that each milimeter increase in tumor thickness is related to 5% increased rate of metastasis.[9]

Distant metastasis usually occurs hematogenously by penetration into vortex veins and at risk of spreading to liver, lungs, bone, skin or brain.[8] Lymphatic spread is usually rare. Subsequent follow-up are required to watch out for recurrence and monitoring of metastasis. Thorough physical examination, twice yearly liver function tests, yearly chest radiograph and liver imaging are advisable.

## Conclusion

Choroidal melanoma has a very low incident in Malaysia. Nevertheless, it is an important diagnosis to make as it leads to life-threatening consequences. Early presentation and diagnosis of choroidal melanoma is significant to save lives.


## Acknowledgements and conflict of interest

None.


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