*Original Article*

# Choroidal Melanoma: Our Experience

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## Abstract

**Background:** Choroidal melanomas are diagnosed in approximately 6 out of one million Americans per year, and although their incidence is low, they are the most common primary intraocular tumor in adults.
**Methods:** Choroidal melanoma is rare tumors and till date no such reports with scleral involvement has been reported from Nepal. It is a prospective case series. The aim of this study is for awareness of the severity of the Choroidal melanoma and it's management. Besides, it is also to study the demography, presentation, histopathological variations and management of cases of choroidal melanoma. All the consecutive cases of Choroidal melanoma presenting between Jan 2017 to May 2018 and those who were within the inclusion criteria were included in this study.
**Results:** There were eight patients, five male and three female, within age range of 18-73, median age was 47. All patients presented with decreased vision ranging from 6/24 to PL of less then three months to 2 years duration. Fundus showed choroidal mass associated with Vitreous hemorrhage (VH), and retinal detachment (RD). Two patients were managed with enucleation with External beam radiotherapy (EBRT). Four underwent only enucleation. One patient with lesion size less then 10mm underwent plaque brachytherapy. One patient underwent initially Plaque brachytherapy but later had to undergo Enucleation. Histopathological examination (HPE) of enucleated patient revealed epitheloid cell melanoma grade three in four and Spindle cell melanoma in three patients. Each one patient of epitheloid cell melanoma and spindle cell melanoma had scleral involvement. Indication for radiotherapy was scleral involvement.
**Conclusion:** With 8 cases of Choroidal melanoma in a single year in a single hospital gives us a clue that there may be much more undiagnosed cases of Choroidal melanoma in Nepal that should be taken seriously. Going for annual eye examination with routine dilated fundus exams can help in prevention and early diagnosis of this life and sight threatening condition and to reduce the mortality rate.

**Key words:** Choroidal melanoma, Enucleation, Plaque brachytherapy.

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## Introduction

Choroidal melanoma is the most common primary malignant intraocular tumor accounting for 80% of all melanomas of the uveal tract (Denniston AKO et al, 2009). They represent 5% of all melanomas, but because of high rate of metastasis & poor response to treatment they account for about 13% of melanoma death. They are diagnosed in approximately 6 out of one million Americans per year (Seddon JM et al, 1989). Although Choroidal melanoma is commonest primary intraocular tumor, it is rare and even rarer in the Asian population (Duke-Elder S et al, 1966; Kuo PK et al, 1982; Margo CE et al, 1984; Manohar S et al, 1984; Egan KM et al, 1988). It usually occurs in elderly patients but in Asian it has been found in young and middle-aged people too (Egan KM et al 1988). Choroidal melanoma may arise from melanocytes within the choroid. It is thought to develop from preexisting melanocytic naevi. The colour varies from darkly pigmented to amelanotic. It is usually dome shaped if it breaks through Bruch's membrane. It can be bilobular, multilobular & diffuse in shape. Occasionally there may be number of small lesions in one or both eyes, although bilateral involvement is generally rare. Malignant melanoma can be said to have an intermediate prognosis, mortality being close to 50%, 15 years after enucleation (Mc Lean IW et al, 1982). We would like to share our experience with choroidal melanoma that we have managed.

## Methodology

Choroidal melanoma is rare tumors and till date no such reports with scleral involvement has been reported from Nepal. It is a prospective case series. The aim of this study is for awareness of the severity of the Choroidal melanoma and it's management. To study the demography, clinical presentation and histopathological patterns of presentation of choroidal melanoma at tertiary eye hospital from 2017 Jan- to 2018 May.

The study was conducted with the clearance from Institutional review committee (IRC). All consecutive patients presented at Tilganga eye hospital, Oculoplasty department that were clinically, radiologically and histopathologically diagnosed as Choroidal melanoma were included in the study. Written consent for study was taken from the patients. Patients refusing to take part in the study, refused for management, enucleated for melanoma somewhere else and not under regular follow up were excluded from the study.

## Result

Total of eight cases within the age range of 18-73 years, median age of 47 years were included in the study. All cases were unilateral, four were involving right eye (RE) and four left eye (LE). The demography of the patients is classified in the table1.

There were five male and three female patients from province number 3, 4, 6 and one patient was from outside Nepal. All patients presented with diminution of vision for 2months to 2 years. Slit lamp examination, Indirect ophthalmoscopy, Ultrasound (USG) A, B scan, orbital Imaging done in all cases are mentioned in table 2.

All patients were diagnosed as Choroidal melanoma clinically. Six patients underwent enucleation with implant and the eyeball was sent for histopathological examination. One patient underwent plaque brachytherapy followed by Enucleation, One patient underwent Plaque brachytherapy alone. A detail of management of the patients is in table 3.

Among the six enucleated patient the HPE showed scleral involvement in two patients that underwent EBRT explained in table 4.

Patient number 4, 40 years male presented with diminution of vision in his right eye for 3 months. On examination his VA was perception

of light and projection of rays accurate in right eye and in left eye it was 6/6. After examination and investigations he was diagnosed as a case of Choroidal melanoma RE. He had enlarged periocular lymph nodes. CT head, orbit, neck, & chest showed small enhancing lymph node in right level Ib & II cervical chains, probably reactive lymphnodes. Cervical LN FNAC showed reactive changes. CT Abdomen was normal. He underwent RE Enucleation with implant. His HPE report showed Choroidal melanoma, spindle cell variant with scleral involvement. He was advised for radiotherapy and referred to oncologist for further management where he was given radiotherapy for 25 days and is now asymptomatic.

These were the first two cases of choroidal melanoma with scleral involvement that received radiotherapy in Nepal case number1 and 4.

Patient number 7 was a 43 years female presented with diminution of vision for 2 months in her RE. Her BCVA RE was 3/60 and LE was 6/6. After examination and investigation (table 2) she was diagnosed as a case of choroidal melanoma RE and was advised for plaque brachytherapy RE. After 9months of brachytherapy she developed recurrent uveitis that troubled her persistently and insisted on enucleation.

There was no complication related to enucleation surgery, prosthesis or radiotherapy in any of the patients. There was no recurrence or metastasis in any of the patients until last follow up. Their chest x ray, USG abdomen, LFT were normal. All patients are under regular follow up.

**Table 1: Demography of patients with choroidal melanoma.**

| Patient No | Age | Gender | Laterality | Presenting BCVA | Province No | Presenting complain |
|---|---|---|---|---|---|---|
| 1 | 18 | F | RE | 6/36 | 3, Dhading | Diminution of vision 3 months |
| 2 | 73 | M | LE | 6/18 | 3, KTM | Diminution of vision for 2months |
| 3 | 61 | M | LE | 6/18 | 3, KTM | Diminution of vision for 2 years |
| 4 | 40 | M | RE | PL | 4, Gorkha | Diminution of vision for 3 months |
| 5 | 70 | M | RE | 6/9 | Outside Nepal | Diminution of vision for 2 months. |
| 6 | 29 | M | LE | 6/6 | 3, KTM | Diminution of vision for 2 months. |
| 7 | 43 | F | RE | 3/60 | 6, Surkhet | Diminution of vision for 2 months |
| 8 | 45 | F | LE | 6/18 | 3, KTM | Diminution of vision of her LE for 3 months. |

**Table 2: Fundus, USG and radiological details of patients.**

| Patient No | Fundoscopy of the involved eye | USG | Imaging |
|---|---|---|---|
| 1 | RE serous RD with diffuse pigmented elevated choroidal mass lesion with orange pigmentation. | RE Solid elevated mass with scleral thickening with superotemporal RD. | Sub retinal intraocular mass compromising with vitreous. $T_1$ high & $T_2$ low signal intensity were in subretinal location of right globe of the eye. |

| | | | |
|---|---|---|---|
| 2 | RE retinoschisis with outer retinal breaks, RPE changes with ERM. LE juxtapapillary choroidal mass with sub hyaloid hemorrhage. | LE Solid elevated mass, scleral thickening. | T1 hyperintense & T2 hypointense lesion in left globe of eye. |
| 3 | LE exudative RD with mild vitritis due to choroidal mass lesion | LE Dome shaped elevated mass with RD | T1 high & T2 low signal complex lesion in posteromedial wall of left globe. |
| 4 | RE superotemporal elevated choroidal mass with hemorrhage & inferior RD. | RE Dome shaped elevated mass with scleral thickening with RD. | T1 high & T2 low signal intensity mass in superotemporal right globe. |
| 5 | RE ciliochoroidal melanoma | RE Cilio choroidal mass of vertical height of 9.3mm, width was 12.95x12mm, basal diameter was 14.4mm size | Not done |
| 6 | LE mass lesion in superonasal quadrant with brownish pigmented boarder and surrounding subretinal fluid. | LE Elevated dome shaped mass with apical height of 10.4mm and basal diameter of 11.4mm. | T1 intermediate to high and T2 low signal intensity intraocular mass with homogenous enhancement in superomedial aspect of left globe of eye attached to the posterior wall. |
| 7 | RE Elevated subretinal mass with large RD in inferior retina. | RE Elevated diffuse mass. | T1 hyperintense & T2 hypointense mass in inferior right globe. |
| 8 | LE mass lesion in superotemporal quadrant of retina. | LE Dome shaped mass with thickness 12mm. | CT orbit showed hyperdense mushroom shaped mass in superotemporal quadrant of left globe. |

**Table 3: Management of choroidal melanoma**

| Patient No | Management |
|---|---|
| 1 | RE Enucleation with implant followed by EBR |
| 2 | LE Enucleation with implant |
| 3 | LE Enucleation with implant |
| 4 | RE Enucleation with implant followed by EBR |
| 5 | RE Ruthonium 106 radioactive plaque brachytherapy 10,000 c Gy at 6mm thickness for 5 days |
| 6 | LE Enucleation with implant |
| 7 | RE Plaque brachytherapy followed by Enucleation with implant |
| 8 | LE Enucleation with implant |

**Table 4: Histopathological examination of the patients**

| Patient No | Histopathological examinations of enucleated eye |
|---|---|
| 1 | Epitheloid cell melanoma grade 3, basal dimension 2.8cm, maximum thickness 0.7cm, sclera was involved by the tumor, ciliary body was free of tumor. AJCCpTNM stage-p T2aNx. |
| 2 | Epitheloid cell melanoma, grade 3, maximum tumour dimention 1cm, tumor thickness 0.7cm, retinal tissue involved by tumour, ciliary body, optic nerve margin free of tumor. AJCC p TNM stage pT1aNx. |
| 3 | Epitheloid cell melanoma grade 3, maximum tumor dimension-1.2cm, maximum tumor thickness 0.8cm, optic nerve margin was not involved with tumor, ciliary body & sclera free of tumor. AJCC p TNM stage-pT2aNx. |
| 4 | Spindle cell melanoma, max basal diameter 1.5cm, maximum thickness 1.5cm, sclera was involved by the tumor, ciliary body & optic nerve margin free. |
| 6 | Epitheloid cell melanoma, Epitheloid cell melanoma grade 3, Basal diameter is 1.2cm, maximum tumor thickness 1.2cm. Ciliary body, sclera, optic nerve all were free of tumor. AJCCp TNM stage p T3a Nx. |
| 7 | Spindle cell B, limited to choroid with thickness of 12mm. Ciliary body, sclera, optic nerve all were free of tumor. |
| 8 | Spindle cell B, choroidal melanoma with 12mm apical height. Ciliary body, sclera, optic nerve all were free of tumor. |

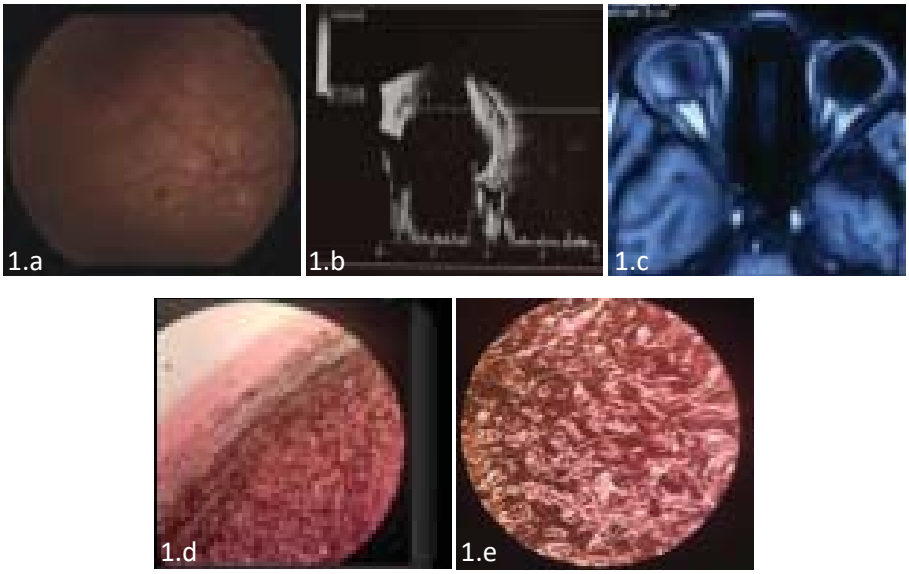


**Figure 1:** Case 1, 18 years female, (a) Fundus picture showing RE serous RD with diffuse pigmented elevated choroidal mass lesion with orange pigmentation. (b) USG image Of RE, A scan showing low internal reflectivity with reduction in amplitude, B- scan showing solid elevated mass, scleral thickening with superotemporal RD. (c) MRI orbit showing Sub retinal intraocular mass compromising with vitreous. $T_1$ high & $T_2$ low signal intensity in subretinal location of right globe of the eye. (d, e) HPE slides showing epitheloid cell melanoma, grade 3, basal dimension-2.8 cm, maximum thickness- 0.7cm, sclera involved by tumor, ciliary body free of tumor.

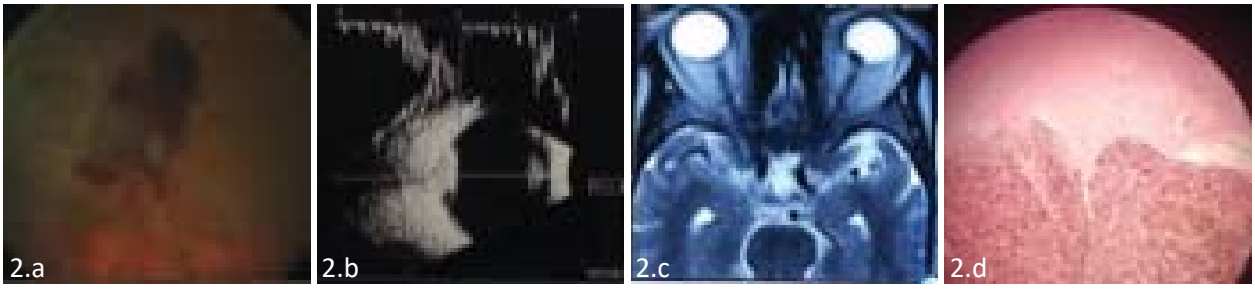


**Figure 2:** Case 2, 73 years male, (a) Fundus picture showing LE junxtapapillary choroidal melanoma with subhyaloid hemorrhage. (b) USG LE showing Solid elevated mass with scleral thickening. (c) MRI orbit showing T1 hyperintense & T2 hypointense lesion in left globe of eye. (d) HPE slide showing Epitheloid cell melanoma, Grade 3, Maximum tumour dimention 1cm, Tumor thickness 0.7cm, retinal tissue involved by tumour, ciliary body, optic nerve margin free of tumor.

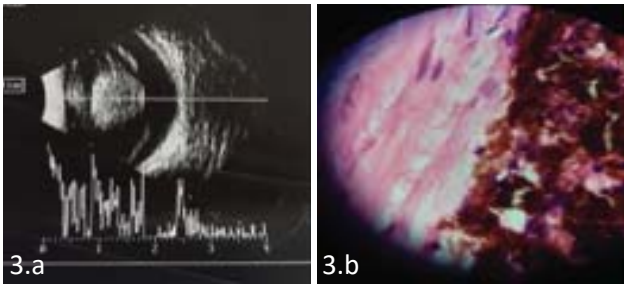


**Figure 3:** Case 4, 40 years male, (a) RE Dome shaped elevated mass with scleral thickening with RD in USG B Scan. (b) HPE showing malignant melanoma, spindle cell variant max basal diameter 1.5cm, maximum thickness 1.5cm, sclera was involved, ciliary body & optic nerve margin free of tumor.

## Discussion

Five out of 7 Nepali patients are from province number 3 and out of that 4 are from Kathmandu. This may show many patients of Choroidal melanoma remains undiagnosed or are ignored by family members due to long distance travel for cancer management. Enucleation is the only treatment done even in the well facilitated eye care centers outside Kathmandu. Having 4 centers for radiotherapy across the country, patient still has to travel across the country for plaque brachytherapy and further management.

In most cases, the median age at diagnosis is about 55 years, and there is slight preponderance of males (Seddon JM et al, 1989). In New England, rates were uniformly higher in males, except among those aged 20-39 years, whose rates were 2.3 times higher in females (Egan KM et al, 1987). In our series we have male preponderance with 5 male and 3 female within the age range of 18-73 years with median age of 47 years. The youngest patient was an 18 years female where as the eldest patient was 73 years male. In a study among 113 patients histopathologically diagnosed with choroidal melanoma over 10 years, most were males. In a study 33.6% of patients were below 40 years of age, of among which 6 (5.3%) patients were less than 20 years (Dhupper M et al, 2012). This is in contrast to the collaborative ocular melanoma study (COMS) where mean age of eligible patients was 60 years (Shields CL et al, 1991; COMS 9,1989). Melanomas are nearly always unilateral but rarely can be multicentric (Volcker HE et al, 1978). In our series all Choroidal melanoma were unilateral.

Choroidal melanoma may remain asymptomatic for prolonged period of time so they are diagnosed lately. Tumors can be asymptomatic and detected incidentally on fundus exam or symptomatic with decreased visual acuity, blurring, metamorphopsia, flashes, floaters or visual field loss (Egan KM et al, 1988). Severe pain may be experienced with impingement of

tumor mass on ciliary nerves or due to acute angle closure glaucoma. They are asymptomatic until the tumor has grown sufficiently to become necrotic and produce complications such as endophthalmitis, massive intraocular haemorrhage, and/or secondary glaucoma. Choroidal layer being devoid of lymphatics majority of the choroidal melanomas spread by haemotogenous route mainly to the liver (Kath Ret al, 1993). If the tumor originates anteriorly it takes longer duration for diagnosis due to delay in any symptoms. As in our patient with ciliochoroidal melanoma, who presented at the age of 70 and underwent plaque brachytherapy out side Nepal. In this series all patients presented with diminution of vision with BCVA of 6/6 to 3/60 in seven patients and only one patient with near total RD presented with perception of light besides this there was no other complain. They were incidentally diagnosed on examination by dilated indirect ophthalmoscopy and ultrasonography.

Diagnosis of choroidal melanomas is usually clinical, with fundoscopy and ancillary tests, including B-scan ultrasonography and in some cases fluorescein angiography. (Shields CL et al, 2004). Ultrasound is the most easily available imaging modality for evaluation of choroidal melanoma. Tumors less than 3mm size are better evaluated on ultrasound as they might not be seen in CT or MRI and may be easily ignored. On Ultrasound melanomas appear spherical mass deeply embedded in or arising from choroid. Tumor is moderately reflective with some acoustic shadowing; mushroom appearance suggests broken Bruch's membrane. Retinal detachment is well seen in ultrasound. Dynamic scanning is useful in presence of hemorrhage as with rapid eye movements tumor is fixed to the wall while hemorrhage shows movements. In our series the USG B scan showed diffuse elevated mass to collar stud appearance, with RD. A Scan showed initial high spike followed by low to medium intensity spike followed by high spike. For extra ocular invasion CT scan and MRI are more sensitive (Fielding JA, 2001). In our series there were no radiological evidence of extra ocular involvement by the tumor.

Melanotic melanomas appear markedly hyperintense to normal vitreous on T1 WI and mildly hypointense on T2WI. Heterogenous signal intensities suggest mixed pigmentation (Lemke AJ et al, 1999). Amelanotic melanoma is slightly hyperintense or isointense on T1WI. Major differential diagnosis of intraocular melanoma is metastasis. Both are seen posterior to the equator of eyeball. Metastasis extends in the plane of choroid with relatively little increase in thickness unlike protuberant melanoma. Retinal detachment and bilaterality favors metastasis while hemorrhagic mass favours melanoma (Fielding JA, 2001).

Management options for Choroidal melanoma includes transpupillary thermotherapy, plaque brachytherapy, charged particle irradiation, photocoagulation, local resection, enucleation or, rarely, observation and various combinations of these methods. The two most frequently employed treatment methods are enucleation and plaque brachytherapy. Choice of treatment depends on multiple factors including tumour size, visual acuity of the affected eye and contralateral eye, age and general health of the patient, and presence of metastases (Shields CL et al, 2004). Among eight patients seven underwent enucleation with implant and one patient underwent plaque brachytherapy.

Plaque brachytherapy is the most common conservative treatment used in the management of choroidal melanoma followed by charged-particle radiotherapy. Currently, Iodine 125 & Ruthenium 106 sources are widely used. It is also associated with radiation related complications as visually significant maculopathy developed at 5 years in 40% of the patients, cataract in 32%, papillopathy in 13%, and tumor recurrence in 9%. In a study 69 eyes (11%) were enucleated because of radiation

complications and recurrence during treatment (Gunduz K et al, 1999). Plaque brachytherapy is the most frequently used eye sparing treatment for choroidal melanoma. But, radiation therapy is about twice as expensive as enucleation and there appears to be no significant quality of life difference between patients treated with radiation or enucleation (VIMS, 2015). As one of our patient with Ciliochoroidal melanoma of 10mm size underwent plaque RE Ruthonium 106 Radioactive plaque brachytherapy 10,000 c Gy at 6mm thickness for 5 days and recovered well. Where as other patients those who were fit for plaque brachytherapy refused due to high cost of treatment and travel, as it is not available in Nepal.

Histologic evaluation of the tumor after enucleation can confirm the diagnosis & determine the prognosis (COMS report no.6, 1998). In our series all the enucleated eyes were sent for HPE, reports revealed epitheloid cell melanoma grade three in four cases and spindle cell melanoma in three cases. Scleral involvement was seen in one each case of epitheloid cell melanoma & spindle cell melanoma. The patients with scleral involvement obtained EBRT.

The four important factors affecting the prognosis of choroidal malignant melanoma are size, cell type, scleral extension, and mitotic activity. The modified Callender's classification of uveal melanomas has four categories: Spindle cell type 45%, Pure epitheloid cell Melanomas 5% (rare occurrence), mixed cell melanoma 45% (spindle cell & epitheloid cell types) and Necrotic melanoma 5% (McLean IW et al, 1978). In our series four patients had Epithelial cell melanoma. Clinical features associated with poor prognosis are, size of >15 mm in maximal linear dimension of tumor growth, Ciliary body involvement, sclera involvement, anterior location, juxtapapillary location, extrascleral tumor extension, older age at diagnosis, regrowth after globe conserving therapy (Kath R et al, 1993). The cell type of uveal melanomas is also an important prognostic parameter. Epithelioid cell melanomas are associated with monosomy 3 and class 2 molecular profile, a higher metastatic and mortality rate and thus displays the worst prognosis. The prognosis worsens with increasing number of epithelioid cells per high power field (HPF) (Seddon JM et al, 1987). In a study of 232 enucleated eyes from patients with uveal melanoma, the 10-year survival was 82% in patients with <0.5 epithelioid cells/HPF, 55% for 0.5 to 4.9 epithelioid cells/HPF, and 33% in patients with >5 epithelioid cells/HPF (Seddon JM et al, 1987). There was one case of ciliochoroidal melanoma. In one case melanoma was juxtapapillary in location. Three cases were histologically diagnosed as Epitheloid cell melanoma and one was Epitheloid cell melanoma with scleral involvement. One case was histopathologically diagnosed as spindle cell melanoma with scleral involvement. These were the poor prognostic factor in this series.

Physical examination, chest X-ray, LFT, alkaline phosphatase, alanine transaminase, aspartate transaminase, gamma-glutamyl transpeptidase, LDH & bilirubin levels was all normal in our series. An abdominal CT, MRI, or liver ultrasound may also be performed to rule out metastasis if the LFT is abnormal. Furthermore, needle aspiration biopsy is required if low attenuation of nodules are found on CT exam to confirm metastasis.

Uveal melanoma can lead to visual loss and death. Studies of patients treated for uveal melanoma have shown tumor related mortality rates of the order of 50% within 10-15 years after enucleation. Survival from the time of the development of systemic metastasis ranges between one and thirty-one months (median 7 months), with one-year survival rate of 29% (Bedikian AY et al, 1981).

COMS showed a 5-year tumor related mortality rate of 26–28% in large tumors (greater than 8.0 mm in apical height or greater than 16.0mm in largest basal dimension), 9–11% in medium size tumors (3.1to 8.0mm in apical height and 16.0 mm or less in largest basal dimension) and 1% in small size tumors (1.0 to 3.0mm in apical height and 5.0 to 16.0 mm in largest basal dimension) (COMS 5, 1997; COMS 10, 1998; COMS 11, 1998; Willson JKV et al, 2001). Common sites of metastases include liver (90%), lung (24%), and bone (16%) (Diener-West M et al, 2004). None of our study patients developed metastasis. All the study patients are still under regular follow up.

## Conclusion

The patients with Choroidal melanoma usually present only when there is decrease in the vision and examination and investigation reveal the presence of tumor. Being rare among Asians, it is sight & life threatening. Going for annual eye examination with routine dilated fundus exams can help in prevention & early diagnosis of this condition. Early diagnosis and treatment reduces the mortality rate.

Malignant melanoma of the uvea has an intermediate prognosis so, annual physical exam, annual chest X-ray & semi-annual LFT, an abdominal CT, MRI, or liver ultrasound may also be performed to rule out metastasis if the LFT is abnormal. Rare Epitheloid cell melanoma with poor prognosis occupied more than half the cases in our series. Awareness of Choroidal melanoma and a good infrastructure like plaque brachytherapy for its management is mandatory in Nepal.

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