TMJ
Case Report
Published by OJS
Doi: 10.4314/tmj.v32i4.423.g285
OPEN ACCESS JOURNAL

Metastatic Choroidal melanoma to the Liver, Kidney and Lungs

Cyprian G. Ntomoka[1]*, Jerry Jecha[1], Ahmed Attas[1], Mustafa Yusufal[1], Sonia Vaitha[1]

[1]Eye department, Comprehensive Community Rehabilitation Hospital in Tanzania (CCBRT)

***Corresponding author:**
Dr. Cyprian G. Ntomoka
Comprehensive Community Based Rehabilitation Hospital
P. O. Box 23310
Msasani, Kimweri Avenue
Dar es Salaam, Tanzania
Email: cntomoka@gmail.com

TMJ
Case Report
Published by OJS
Doi: 10.4314/tmj.v32i4.423.g285
OPEN ACCESS JOURNAL

Abstract

Background

Choroidal melanoma presents the most common type of uveal melanoma commonly diagnosed as a local tumor with about 2% already spread to distant organs necessitating early diagnosis and intervention. The case is presented to show the challenge of managing metastatic choroidal melanoma in a Tanzanian setting.

Case report

A 45 years old male presented at The Comprehensive Community Rehabilitation in Tanzania (CCBRT) hospital with four weeks' history of acute painful progressing right eye visual loss associated with headache, nausea and vomiting. On examination the eye had a dome shaped retinochoroidal tumor on the inferior extending to the macula associated with shallow retinal detachment. Ultrasonography showed an acoustically silent zone within the tumor, choroidal excavation with some orbital shadowing whereas orbital CT scan revealed a hyper dense lesion. Systemic evaluation for metastasis gave imaging evidence of spread to the liver, lungs and kidneys. Tissue histology of the enucleated eye confirmed epithelioid melanocytic tumor cells. The patient was counselled on the prognosis, referred for palliative care but absconded and died four months later.

Conclusion

Management of metastatic choroidal melanomas is clinically challenging owing to faster growth with poor prognosis even in good hands. Early diagnosis and treatment is important as the final prognosis depends largely on the size, location and extent of metastasis. Enucleation is the final treatment modality for most of the large tumors though it has limited a value in the metastatic type, which ends up with palliative care or death.

Keywords: *Choroidal melanoma, Metastasis, Enucleation, Prognosis.*

Published by OJS
Doi: 10.4314/tmj.v32i4.423.g285

Background

Choroidal melanoma represents about 85% of the uveal melanoma, the most common primary intraocular malignancy in adults arising from the neuro ectodermal melanocytes within the uveal tract[1]. Risks increases in those with light eye color, white race, older age (peaks at 60 years), certain genetic mutations and inherited skin disorders and exposure to ultraviolet light. It is usually asymptomatic and detected incidentally during fundus examination, occasionally presenting with reduced vision, metamorphosis, flashes of light, floaters or visual fields loss [2]. It is easily confused with pseudo melanomas like choroidal nevus, melanocytoma or hyperplasia of the retina-pigmented epithelium (RPE). Choroidal nevus are flat, <6mm in size and may overly the drusen; melanocytoma are black and often extending to the optic nerve while invading the nerve fiber layer with a feathered appearances. Congenital hyperplasia of RPE is typically a sharply demarcated pigmented lesion with scalloped margins [3].

True choroidal melanoma on the other hand appears clinically as a solid dark brown amelanotic in color with clear borders; biconvex with lenticular cross section shape; overlying clumps of orange lipofuscin pigments with no overlying drusen, secondary sub retinal fluid or exudative retinal detachment may be present and the tumor can penetrate the Bruch's membrane or be like a nodular eruption beneath the retina forming a 'collar button' or 'mushroom' shape. The most useful ancillary test for the clinical diagnosis of choroidal melanoma is ultrasound A and B scan. A scan assesses internal reflectivity, vascularity and elevation and Melanomas typically displays low internal reflectivity and a solid tumor pattern. The B scan can show size, position and thickness of the lesion and the likelihood of extra scleral extension. Most of these melanomas present with exudative retinal detachment that can be shown also by B scan images [4].

Majority of the patients with the melanoma (98%) have no detectable metastatic diseases though should undergo complete metastatic work up including complete physical exam, FBP, LFTs, Chest x-ray, abdominal ultrasonography. Hematogenous metastasis is the usual route to commonly the liver, occasionally the lungs, bone, skin and brain [5].

Management of the melanomas is usually dependent on the size, location and visual status. Conservative globe saving therapy is by observation in small nevi like tumors; brachytherapy in those whose base diameter is <20mm; proton beam radiation for tumor close to the optic nerve and trans pupillary thermotherapy as a primary therapy for small tumors. Enucleation, an excision of the eye is the last resort for the large tumors, painful blind eyes, and occasionally chosen by patients themselves even in small tumors over conservative

management [6]. In Tanzania like other countries most tumors are large and with poor vision and enucleation has always been the best treatment modality followed by radio chemotherapy for some selected case and for palliative care in those with distant metastasis [7]. Despite advert of new technology detection, treatment and prognosis has remained stable. Five years all cause survival from diagnosis is 90% for small melanomas, 70% for medium, and 50% for large. Disseminated melanoma at the time of diagnosis is usually fatal within one year [8].

Case Presentation

A 45 years old male presented with four weeks' history of acute painful progressive visual deterioration in the right eye associated with nausea and vomiting, severe headache without loss of consciousness or other features of raised intracranial pressure. No prior visual problem or ocular trauma, had no loss of consciousness. No any other systemic symptom apart from previous diagnosis of hypertension, which was well controlled with medication. Physical examination could not detect any chest or abdominal abnormality except for the index eye which dilated fundus slit lamp examination findings using 90D retina lenses are as shown in Table 1, the other eye was normal.

Table 1. Slit lamp bio microcopy dilated fundus examination findings

Section	Findings
Presenting Visual acuity	Counting fingers near
Best Corrected Visual acuity	Counting fingers near
Intra Ocular pressure (IOP)	16mmHg
Eye lid	Blepharospasm
Conjunctiva	Hyperemia
Cornea	Normal
Anterior chamber	Deep with cells + and flare+
Iris/pupil/Lens	Normal
Vitreous body	Cells in the mid and posterior
Retina	Pigmented dome shaped mass about 10mm from the base of the inferior retina extending to the macular with shallow retinal detachment

Published by OJS
Doi: 10.4314/tmj.v32i4.423.g285

Ancillary tests

Examination B scan ultrasonography using Ultrasonic A/B Scanner and Pachymeter UD-800 machine with 10 MHz frequency, showed dome shaped tumor with high internal reflective on the inferior of the retina extending close to the optic nerve with shallow retinal detachment as shown in figure 1.

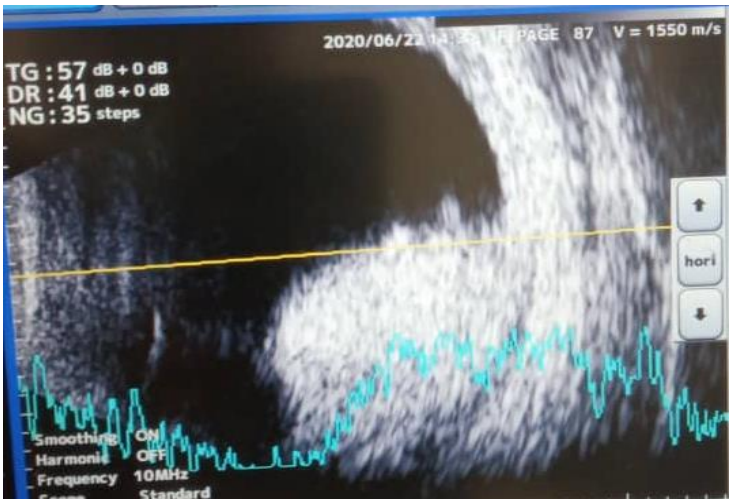

Figure 1. Dome shaped highly internal reflective retinochoroidal tumor on ultrasound B scan

MVCT Emotion 6 Siemens CT scan machine with and without contrast revealed a high attenuating enhancing right retinochoroidal mass measuring 2.17x0.91 cm as it is in figure 2.

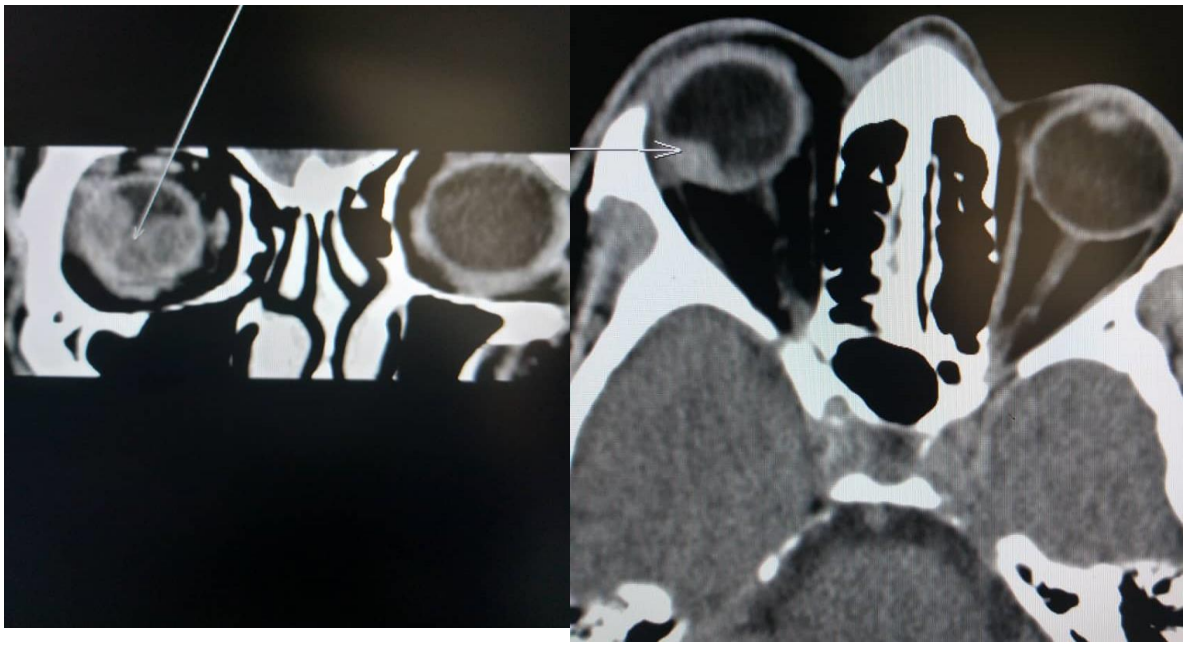

Figure 2. Hyper reflective tumor mass at the back of the right eye

Published by OJS
Doi: 10.4314/tmj.v32i4.423.g285

Chest X ray showed Secondary right suprahilar lymphadenopathy with suspicious lungs micro nodular deposits as it is in figure 3.

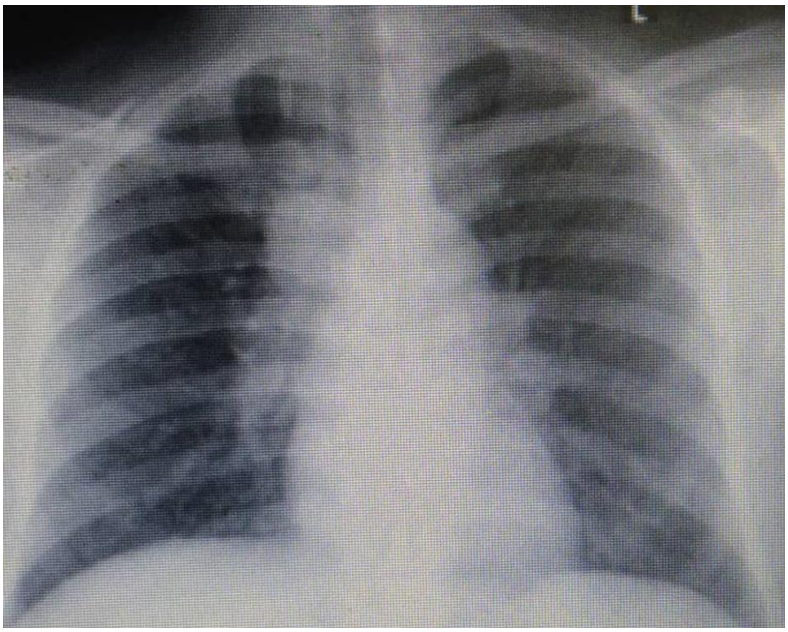

Figure 3. Secondary right hilar lymphadenopathy

Abdominal ultrasonography done using SIEMENS ACUSON X-500, Convex transducer Multi frequency 2.5 - 5.0 MHz to rule out metastasis showed multiple round shaped nodular liver lesions disseminated throughout its parenchyma, largest located sub-capsular on left lobe measuring 3.10 x 2.04 cm. as in figure 4, whereas the kidney scans showed distorted left kidney structures indicating infiltrative lesion as in figure 5.

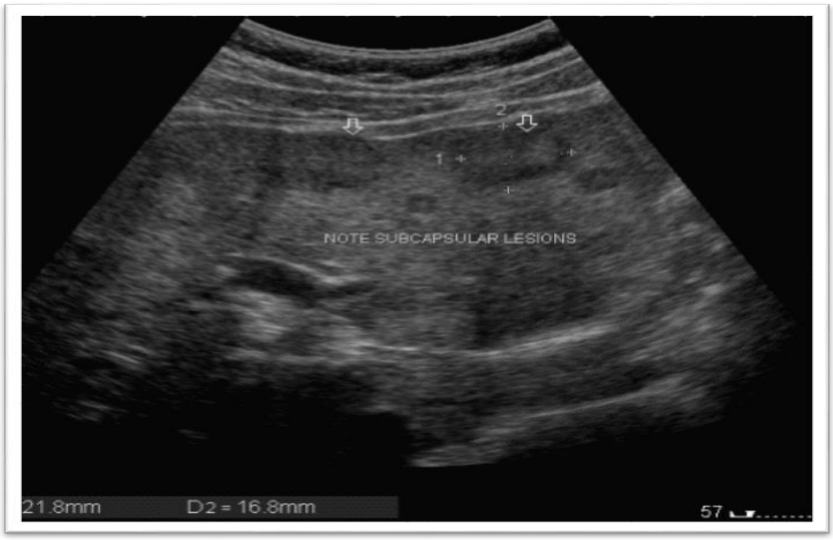

Figure 4. Sub capsular left lobe lesions on the Liver

Published by OJS
Doi: 10.4314/tmj.v32i4.423.g285

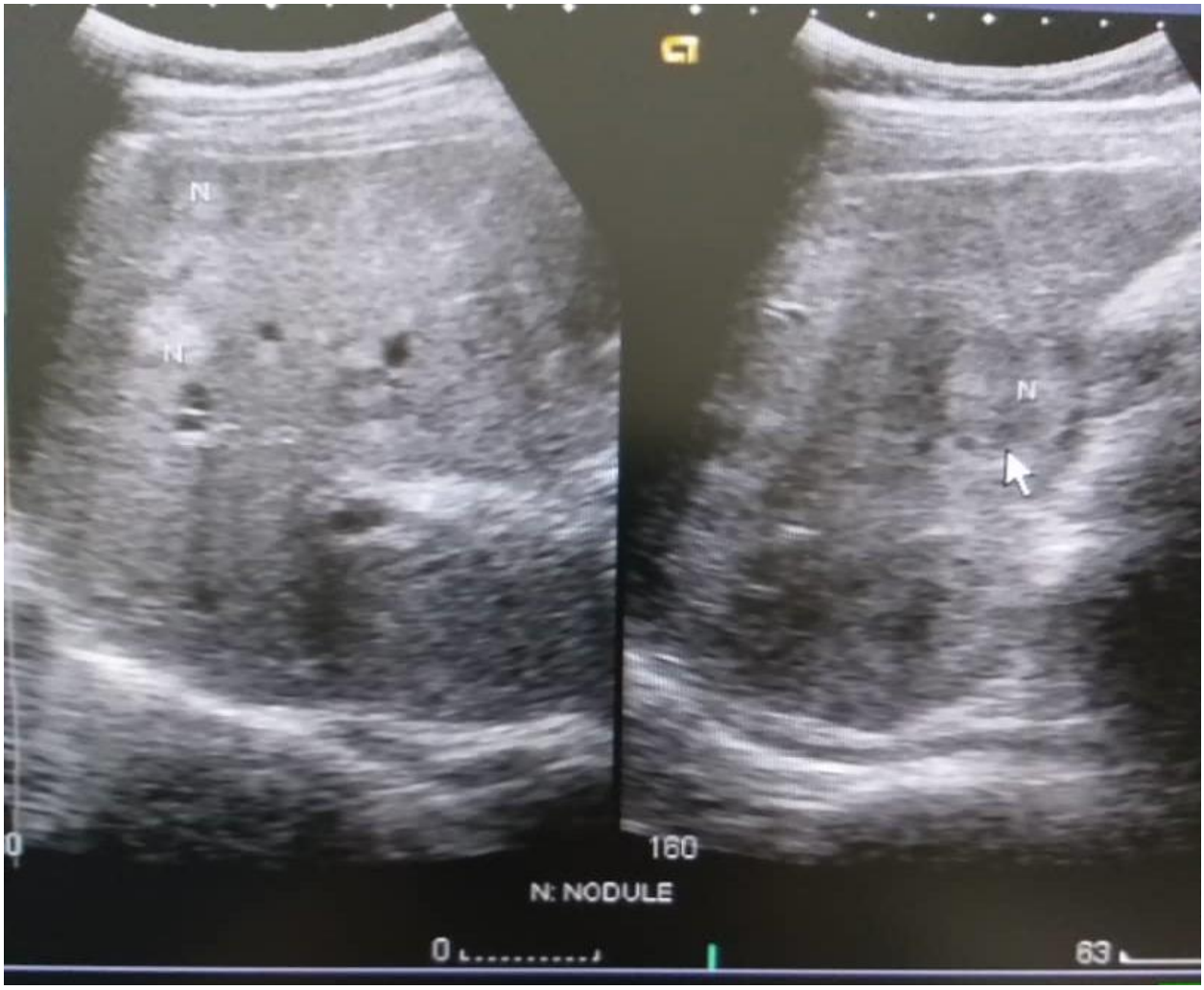

Figure 5. Distorted left kidney structures indicating infiltrative lesion

In addition to the work ups various laboratory tests were done whose findings are summarized in table 2 below.

Table 2: Laboratory tests

Description	Value	Comment
Hemoglobin	10.7	low
ASAT	30	normal
ALAT	31	normal
Total Bilirubin	0.5	reduced
Serum creatinine	1.20	Slightly above normal
Serum alkaline phosphatase	102	Normal

Published by OJS
Doi: 10.4314/tmj.v32i4.423.g285

Diagnosis and management

Basing on the subjective, objective and diagnostic findings provisional diagnosis of malignant Choroidal melanoma with metastasis to the liver, lungs and kidney was reached. Discussion with the patient and relatives on the possible management modalities was done and all parties agreed for enucleation and for tissue histology.

Regarding surgery, under general anesthesia the conjunctival peritomy, isolation of the four recti muscles and displacement of the oblique muscles followed by blunt approach to optic nerve was carried out with a curved blunt end scissors in order to cut as far as possible from the sclera, the tissue was fixed in 10% formalin and sent to histopathology department of Lancet Laboratory.

Histopathological results revealed cytological atypical melanocytes involving the posterior inferior choroid expanding upwardly causing retinal detachment. The melanocytes proliferated in nests and solid cystic pattern with marked pleomorphism, prominent eosinophilic nucleoli and moderate amount of vacuolated cytoplasm: epithelioid type of choroidal melanoma was confirmed.

Because of possible metastatic level of the disease reported earlier the patient was advised for the possible treatment prognosis and was referred for oncological care at Ocean Road Cancer Institute (ORCI). During follow up of the patient it was established that he absconded attending ORCI, went for local herbal treatment and eventually he died four months after the diagnosis.

Discussion

The choroid is a layer of the eye ball between the retina and sclera and is considered part of the uveal tissue which is composed of the iris and ciliary body anteriorly and choroid posteriorly. The choroid has the highest blood flow in the body. Choroidal melanoma is the most common primary intraocular malignant tumor and second most common site of ten malignant melanoma sites in the body [14]. Current diagnosis of choroidal melanoma is based on both the clinical experience of the specialist and modern diagnostic techniques such as indirect ophthalmoscopy (IO), A- and B- ultrasonography scans, fundus fluorescein angiography (FFA), and trans illumination. Invasive studies such as FNAC can have a significant morbidity and should only be considered if therapeutic intervention is indicated and diagnosis cannot be established by any other means. The rate of misdiagnosis of eyes enucleated for choroidal melanoma was approximately 20% during the years up to 1970, but

Published by OJS
Doi: 10.4314/tmj.v32i4.423.g285

diagnosis of choroidal melanoma has improved tremendously in the past three decades, and incorrect diagnosis since that time has progressively decreased to approximately 10%[15-19].
The estimated incidence of primary choroidal melanomas in USA is 6-7.5 cases per 1 million populations with Caucasians. There are no data regarding the magnitude of this condition in Tanzanian but it is reported to be rare in blacks[10]. Usually it affects people aged 40-60 years with the peak at 55 years. The index patient in this study was 45 years old[7, 10]. It is the most common adult primary intra ocular malignant tumor arising from the choroid, ciliary body or iris. The common site involved is the choroid posterior to the equator, with approximately 85% of cases localized to this area [11]. About 2% of the choroidal melanoma are diagnosed at a metastasis stage and caries the worst prognosis in the ocular melanomas [5, 10].

Generally, many melanoma patients have asymptomatic tumors discovered on routine eye examination. Other patients will be asymptomatic complaining of visual loss, photopia, visual field defects and visible tumor. Usually decreased vision is due to tumor encroaching the fovea, exudative retinal detachment that involve the macula or tumor contacting the lens. Symptoms like severe pain are unusual for melanoma except in cases of inflammation, massive extraocular extension or neovascular glaucoma. The past medical history may show a non-ocular malignancy which usually give a clue of a metastatic lesion though one should carefully take this information because 6% to 10% of uveal melanoma patients have primary neoplasms somewhere [9, 15,20]. Our patient's history was in line with the current evidence from other studies as he presented with visual loss with mild pain and headache, he had no systemic disorder except for a controlled essential hypertension.
Clinical examination and IO or using direct examination using magnifying diagnostic retina lenses like 78D or 90 D through a well dilated pupil is the most important examination modality in the diagnosis of choroidal melanoma. It has been reported that IO and using retina lenses correctly diagnose melanoma in more than 95% cases [21]. The classic appearance of choroidal melanoma on IO and using retina lenses is a pigmented dome-shaped or collar button-shaped tumor a presentation which matches what was in our case. In this case we used the direct examination approach with 90D retina lenses to diagnose a dome shaped retinochoroidal tumor on the inferior retina extending to the macula associated with shallow retinal detachment. Histological examination of the enucleated tissues was based on H&E morphology. Ancillary studies like eh HNB45 was not done posing some limitation to the final diagnosis because choroidal melanoma may morphologically mimic choroidal nevus, choroidal metastasis, choroidal hemangioma, choroidal osteoma,

Published by OJS
Doi: 10.4314/tmj.v32i4.423.g285

melanocytoma, benign lymphoid tumor, choroidal hemangio-pericytoma, choroidal leiomyoma, extra-macular disciform lesion, ruptured arteriolar macro aneurysm, localized choroidal detachment, retinal pigment epithelial hypertrophy, posterior scleritis, hemorrhagic retinal detachment, massive retinal gliosis, and retinal glioma.

Ocular ultrasound mode is the most common ancillary test done where the A scan choroidal melanoma shows medium to low internal echoes with smooth attenuation [22]. By B scan mode three classic features are commonly seen namely acoustically silent zone within the melanoma, choroidal excavation and shadowing of the orbit. Our case study used a distinctive ancillary test where the ultrasound showed the typical features of the choroidal melanoma as presented before.

In most of the studies, the most important factor for metastasis remains tumor size where by the larger the size the more the risk of metastasis. Other predictive factors of largest basal tumor diameter, closed loops, epithelioid cells, mitotic rate and extraocular spread. Further analysis estimates that metastases occur an approximate tumor volume of 7 mm^3, when the tumor is clinically visible at roughly 3 mm diameter and 1.5 thickness[22]. Screening for choroidal melanoma includes doing liver function tests, physical examination, and lung and liver imaging. In our case the liver, lungs and kidney imaging were all suggestive of metastasis nevertheless the fact that metastasis was only seen on imaging and not confirmed by histology could be real or presenting other co-existing pathology which could not be established.

Treatment of the melanoma on several modalities varying depending on multiple factors like visual acuity of the affected eye, visual acuity of the contralateral eye, tumor size, location, ocular structures involved and presence of metastasis usually depends on the size at diagnosis, visual acuity of the affected and the contralateral eye, and location of the tumor. Enucleation tends to be the method usually preferred for medium and large ocular melanomas, considered primarily in case of diffuse melanomas and in the presence of extraocular extension [10, 11.]

Basing on the tumor size, location and possible metastasis our patient had to undergo enucleation. This is in line with other literatures regarding tumors at this stage, nevertheless in the trial collaborative ocular melanoma study (COMS) enucleation was seen as a precipitant for tumor metastasis and shortened survival though radiation complications or tumor recurrence may eventually make enucleation necessary in some cases [22]

Like what is reported in our study, uveal melanoma in its entirety have a high tendency to metastasize resulting in high mortality. Approximately 50% of patients with this kind of melanoma is reported to succumb to metastasis within 10 years of diagnosis, irrespective of types of treatment offered. Median survival after metastasis is 6 to 12 months. This conforms to the findings in our study in which the patient died four months after diagnosis. Despite the fact that survival rate of patients with metastatic uveal melanoma is poor, median survival of patients receiving treatment for metastasis is better than those receiving no treatment justifying our patient referral to the oncology consultants for further management in our first decision[12, 13]

Conclusion

Choroidal melanoma is one of the common uveal melanoma affecting people between 40 to 60 years presenting with visual loss, pain and sometimes symptomless. It is clinically diagnosed with direct or indirect ophthalmoscopy assisted by ancillary testing like ultrasound A and B scan, OCT, CT scans and occasional fundus fluorescing angiography. Early diagnosis of the tumors saves for better outcome of treatment which may be enucleation of the affected eye, radiation or brachytherapy. Metastatic cases to distant organs like liver and lungs pose challenges in management because for most of them their prognosis is reduced to as minimal as 6 months. There is a necessity of doing proper fundus examination in all adults aged 40 and above attending eye examination for even reading spectacles prescription.

Declarations

Ethical approval

Written informed consent was obtained from the patient via the escorting close relative (uncle) for publication of the case and accompanied images.

Consent for publication

The patient consented to the publication of this case, knowing that the manuscript may include potentially identifying information.

Funding

No funding to report.

Published by OJS
Doi: 10.4314/tmj.v32i4.423.g285

Availability of data and materials

No data sets or materials were generated in this study.

Competing Interests

All authors declare that they have no competing interests.

Authors' Contribution

CGN consulted the patient and planned the management, researched the literatures and wrote the manuscript. SV, MY; Panel discussion members for the eye enucleation procedures. AA; Oculoplastic consultant on the surgical approach and future socket reconstruction. JJ; operating surgeon.

Acknowledgements

Special thanks to CCBRT Hospital executive committee for allowing publication of the case, hospital administration for supporting and encouraging hospital staff in doing research and publication.

Abbreviations

IOP	Intra Ocular Pressure
FNAC	Fine Needle Aspiration Cytology
OCT	Ocular Coherence Tomography
RPE	Retina Pigmented Epithelium
IO	Indirect Ophthalmoscopy

Published by OJS
Doi: 10.4314/tmj.v32i4.423.g285

References

1. Margo CE. **The collaborative ocular melanoma study: an overview.** Cancer Control. 2004; 11(5):304–309
2. Kanski J. **Signs in Ophthalmology: Causes and Differential Diagnosis.** St Louis: Mosby/Elsevier. 2010; pp 310-318
3. Shields CL, Furuta M, Berman E, Zahler J, Hoberman D, Mashayekhi, Shields J. Arch Ophthalmol. 2009;127(8):981-987
4. **Section 8.2 Uveal Melanoma.** In: Yanoff M., Duker J. Ophthalmology, 4th ed.St. Louis: Mosby/Elsevier. 2014; pp 801-809
5. Rankin SJA, Johnston .B. **Metastatic disease from untreated choroidal and ciliary body melanomas.** Int Ophthalmol. 1991;1 5:75-78
6. Kanski J., Bowling B. **Clinical Ophthalmology: A Systematic Approach, 7th ed.** New York: Elsevier/Saunders. 2011; pp 501-504
7. Singh P, Singh A. **Choroidal melanoma**. Oman J Ophthalmol. 2012 Jan;5(1):3-9. doi: 10.4103/0974-620X.94718. PMID: 22557869; PMCID: PMC3339671.
8. **Basic and Clinical Science Course: Section 12.** Retina and vitreous. San Francisco: American Academy of Ophthalmology. 2006-2007
9. Krantz BA, Dave N, Komatsubara KM, Marr BP, Carvajal RD. **Uveal melanoma: epidemiology, etiology, and treatment of primary disease.** Clin Ophthalmol. 2017; 11:279-289. Published 2017 Jan 31. doi:10.2147/OPTH.S89591.
10. Terzidou C, Trivli A, Dalianis G, Apessou D, Spandidos DA, Goulielmos GN. **Advanced choroidal melanoma with a desirable aesthetic outcome after enucleation: A case report.** Oncol Lett. 2018;16(1):511-514. doi:10.3892/ol.2018.8661
11. Shields CL, Kaliki S, Furuta M, Mashayekhi A and Shields JA: **Clinical spectrum and prognosis of uveal melanoma based on age at presentation in 8,033 cases.** Retina 32: 1363-1372, 2012.
12. Kaliki S, Shields CL, Shields JA. **Uveal melanoma: Estimating prognosis.** Indian J Ophthalmol 2015;63:93-102
13. Diener-West M, Reynolds SM, Agugliaro DJ, et al. **Development of metastatic disease after enrollment in the COMS trials for treatment of choroidal melanoma: Collaborative Ocular Melanoma Study Group Report No. 26.** Arch Ophthalmol. 2005; 123(12):1639-1643. doi:10.1001/archopht.123.12.1639
14. Albert DM. **Principles and Practice of Ophthalmology.** In: Albert, Jakobiec, editors. Philadelphia, PA: W.B. Saunders Co; 1994. pp. 3197–8. Ch. 258

15. Singh P, Singh A. **Choroidal melanoma.** Oman J Ophthalmol. 2012;5(1):3-9. doi:10.4103/0974-620X.94718
16. Ferry AP. **Lesions mistaken for malignant melanoma of the posterior uvea: A clinic pathological analysis of 100 cases with ophthalmoscopically visible lesions.** Arch Ophthalmol. 1964; 72:463–9.
17. Shields JA. **Lesions simulating malignant melanoma of the posterior uvea.** Arch Ophthalmol. 1973; 89:466–71.
18. Zimmerman LE. **Bedell Lecture: Problems in the diagnosis of malignant melanoma of the choroid and ciliary body.** Am J Ophthalmol. 1973; 75:917–9.
19. Chang M, Zimmerman LE, McLean IW. **The persisting pseudo melanoma problem.** Arch Ophthalmol. 1984; 102:726–7.
20. Jensen oa. **Malignant melanomas of the uvea in Denmark 1943-1952. a clinical, histopathological, and prognostic study.** Acta Ophthalmol (Copenh). 1963;43: SUPPL 75:1-220. PMID: 14050563.
21. Char DH, Stone RD, Irvine AR, Crawford JB, Hilton GF, Lonn LI, et al. **Diagnostic modalities in choroidal melanoma.** Am J Ophthalmol. 1980; 89:223–30.
22. Shields CL, Furuta M, Thangappan A, et al. **Metastasis of Uveal Melanoma Millimeter-by-Millimeter in 8033 Consecutive Eyes.** Arch Ophthalmol. 2009;127(8):989–998. doi:10.1001/archophthalmol.2009.208
23. Hawkins BS Collaborative Ocular Melanoma Study Group. **The Collaborative Ocular Melanoma Study (COMS) randomized trial of pre-enucleation radiation of large choroidal melanoma: IV. Ten-year mortality findings and prognostic factors.** COMS report number 24. Am J Ophthalmol. 2004; 138:936–51.