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Uveal Melanoma In An Indigenous Black Population: Case series and 5-year Outcome Of Management

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Case Report

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Abstract

Background:

Uveal melanoma is the most common primary malignant intraocular tumor in adults and it is reported to be rare among individuals of African origin. This case series aimed to report the outcome of management in patients with clinico-pathological diagnoses of uveal melanoma managed at a tertiary hospital, Ibadan, Southwest Nigeria. The review of patients diagnosed with uveal melanoma over an18-year period at the University College Hospital Ibadan, Nigeria was conducted. Information on patients' sociodemographic data, clinical and histopathological features, management and outcome are reported.

Case presentation:

Three patients, 2 females and 1 male, aged between 40 and 51 years were referred to the ocular oncology clinic of the University College Hospital, Ibadan with unilateral, gradual loss of vision. Duration of symptoms was between two and seven months prior to presentation and visual acuity of the affected eye ranged between 6/60 and light perception. Radiological, hematological and other pre-operative investigations were done. All patients had primary enucleation with histological diagnoses of choroidal melanoma in two patients and ciliary body melanoma in the third patient. The patients did not receive adjuvant treatment and the two patients with choroidal melanoma fared well with no local recurrence or metastasis five, and five and half years post-operatively respectively. The patient with ciliary body melanoma abandoned out-patient follow up visits, re-presented with metastatic disease, and succumbed while on hospitalization for palliative care.

Conclusions:

Uveal melanoma occurs uncommonly among indigenous African population. Early diagnosis and prompt treatment appears to reduce the high mortality associated with choroidal melanoma.

Background

Uveal melanoma is the most common primary malignant intraocular tumor in adults, with choroidal melanoma being the most common presentation.[1] Uveal melanoma is a potentially life-threatening tumor with a high propensity for metastases and attendant poor prognosis. It is however, relatively uncommon [2] with incidence of about 4.637 per million population over four decades from the Surveillance, Epidemiology, and End Results (SEER) 18 Program database. [3] The incidence is noted to be lower in Blacks, with an incidence rate ratio of 0.076, [3] although, mixed racial ancestry has been suggested as possible risk factor affecting incidence of uveal melanoma in black Americans, [4] making it difficult to extrapolate this ratio to indigenous black African populations. Noteworthy is paucity of reports on uveal melanoma among indigenous black Africans including Nigeria. This study aimed to

describe the clinical profile, management, and outcome of uveal melanoma in an indigenous black African population in Nigeria. A review of patients diagnosed with uveal melanoma over an18-year period at the University College Hospital Ibadan, Nigeria was done. Information on the patients' sociodemographic data, clinical and histopathological features, management instituted and outcome of management are reported.

Case presentation

Three patients, 2 females and 1 male, aged between 40 and 51 years were managed at the ocular oncology clinic of the University College Hospital, Ibadan. The first, a 51-year-old man was referred with complaint of painless visual loss in the left eye of two months duration. The medical, family and social history were not contributory to the complaints. Examination revealed corrected acuity of 6/5 in the right eye and 6/60 in the left, no proptosis, normal ocular motility, and relative afferent pupillary defect in the left eye. Detailed slit-lamp examination of the anterior segment showed no abnormalities and intraocular pressures were 21mmHg and 15mmHg in the right and left eye respectively. Dilated fundus examination revealed a left solitary pigmented mass arising from the choroid superonasally, extending to the optic disc margin and into the vitreous. It measured about 6mm x 6mm with surrounding subretinal fluid and retinal detachment, and B-scan ultrasonography finding of a mixed echoic mass. Detailed systemic examination and hematological investigations were negative for tumor metastases. The clinical diagnosis of choroidal melanoma ($T_1N_0M_{0,}$ Stage I disease) was made and he was counseled for and subsequently had primary enucleation of the eye. Histopathology revealed a malignant neuroepithelial neoplasm composed of cells disposed in sheets and short fascicles. The cells had markedly pleomorphic oval to polygonal vesicular nuclei, prominent cherry red nucleoli, moderate eosinophilic cytoplasm and melanin pigment in their cytoplasm. The sclera demonstrated focal infiltrates, but the optic nerve was free of tumor. Histopathological diagnosis of spindle cell variant of malignant melanoma (Grade G1) was made. He received no adjuvant treatment and was placed on regular follow-up at the Out-patients' Clinic. He remains tumor free five and half years post-operatively.

The second was a 40-year-old woman referred with a clinical impression of right chorioretinal tumor following complaints of right eye discomfort and incidental finding of right visual loss of two months duration. Her last ophthalmic examination the year prior to presentation reported normal findings. Her medical, family and social history were not contributory to the complaints.Examination revealed acuity of hand movement in the right eye and 6/5 in the left, no proptosis, full ocular motility and right relative afferent pupillary defect. Slit-lamp examination of the anterior segment showed no abnormalities and intraocular pressure measured 15mmHg and 17mmHg in the right and left eye respectively. Dilated fundus examination revealed a solitary pigmented mass at the posterior pole, involving the macula and extending to the optic disc margin and vitreous. The mass had a mushroom-like configuration with areas of hemorrhage on the surface. (Fig. 1) It measured about 7.5mm x 7.5mm with surrounding retinal detachment and subretinal hemorrhage. Detailed systemic examination and screening for tumor metastases were negative. B-scan ultrasonography showed an organized, mixed echoic mass arising from the choroid temporal to the optic disc. There were areas of calcification noted within the mass.

(Fig. 2) Clinical diagnosis of choroidal melanoma ($T_2N_0M_0$, Stage IIA disease) was made, and she was counseled for and had primary enucleation of the eye. Histopathology of the enucleated eyeball revealed a malignant neuroepithelial neoplasm with moderate to marked pleomorphic cells disposed in nests and short fascicles. The component cells had oval to spindle shaped vesicular nuclei, large prominent nucleoli, moderate eosinophilic cytoplasm and some cells had melanin pigment. The sclera showed focal tumor infiltrate, but the optic nerve was free of tumor. (Fig. 3) Histopathological diagnosis of spindle cell variant of malignant melanoma (Grade G1) was made. She fared well postoperatively, with no adjuvant treatment, and no metastatic disease five years post-operatively, and is on regular out-patient follow-up.

The third case was a 45-year-old woman referred with complaints of gradually progressive visual loss in the right eye of seven months duration and complete loss of vision loss in the eye two months prior to presentation. A retrolental hazy glow was noticed in the eye, with associated mild pain and redness. Her family and social history were not contributory. Her acuity was light perception in the right eye and 6/5 in the left with full ocular motility in both eyes and no proptosis. Slit-lamp examination of the right eye revealed injected conjunctiva, microcystic cornea edema with pigment clumps on the endothelium, hairline hyphema, and round, mid-dilated, non-reacting pupil with rubeosis irides. There was cortical lenticular opacity precluding detailed view of the posterior segment. Gonioscopy revealed grade 3 open angles with neovascularization of the anterior chamber angles in the right eye and intraocular pressure of 16mmHg and 14mmHg in the right and left eye respectively. Systemic examination and hematological screening for metastases were negative. B-scan ultrasonography showed a 13-mm globular and vascular mass arising posterior to the lens and filling the anterior two third of the vitreous cavity. (Fig. 4) The clinical diagnosis of ciliary body tumor ($T_{4B}N_0M_0$, Stage IIIB disease) was made, and she subsequently had right enucleation. Histopathology of the enucleated eyeball revealed a gelatinous uveal mass composed of atypical melanocytic cells with spindle to oval shaped nuclei, occasional prominent nucleoli and prominent cytoplasm. The tumor cells were heavily pigmented, and the sclera and optic nerve were free of tumor. Histopathological diagnosis of spindle cell variant of ciliary body malignant melanoma (Grade G1) was made. She fared well in the immediate post-operative period and was on regular out-patient care until she abandoned follow-up visits 20 months post-operatively. She later re-presented to the Emergency Department 30 months post-operatively with breasts masses, chronic cough and abdominal swelling of 4 months duration, and paraparesis of 2 months duration for which she was receiving treatment at a secondary healthcare facility close to her domicile. Diagnosis of metastatic disease was made and she was admitted for palliative care. She eventually succumbed to cardiopulmonary failure on day 2 of admission.

Discussion and Conclusions

Uveal melanoma is the most common primary intraocular malignant tumor in adults, arising mostly from the choroidal melanocytes. [5] It remains exceedingly uncommon among individuals of African origin, hence limited representation in the literature. Previous studies [6–11] in Nigeria, which were mostly

retrospective histopathological reviews, equally documented very few or no cases of uveal melanoma. Out of about 1,024 patients with ocular tumors managed at our facility over the 18-year period, only three patients had uveal melanoma, depicting the rarity of the tumor in our region. There are proposed theories on the relative rarity of the tumor in blacks and the varied prevalence among different races. It is postulated that the lesser degree of choroidal pigmentation in Caucasians is responsible for the lack of protective effect of melanocytes from toxins of solar radiation. [12] In addition, the higher prevalence of choroidal nevi among Caucasians predispose them to a higher risk of transformation into melanoma. [12]

Uveal melanoma is commoner in older individuals, [13] however, the age range of the patients in this series was between 40 years and 51 years. A lower mean age at presentation had been noted in blacks in comparison with Caucasians [4, 13, 14] with a mean age of 62 years among Caucasians, compared to an average of 53.9 years in blacks reported by Phillpotts et al. [4] Quite rarely, reports in young children had been documented with the youngest case in a five-year old [15, 16] It also was noted that two of the three cases in this series were females and no significant gender predilection had been reported in literature for uveal melanoma. [1, 14]

All three patients in this series were indigenous black Africans who had no known predisposing risk factors to uveal melanoma. There are few cases of uveal melanoma in non-Caucasians reported in literature. [16–19] Al-Sadhan et al [17] reported a black Kuwaiti female in Saudi Arabia with choroidal melanoma and oculodermal melanosis, Gambrelle et al [18] reported an 18-year old black African teenager from Cameroon with choroidal melanoma in France, while Li et al [16] reported a 15-year old black female in the United States with uveal melanoma arising from a melanocytoma. Although some authors [3, 13, 14, 20, 21] reported that the incidence of uveal melanoma is affected by race, being more common in Caucasians, Salvi and co-worker [22] suggested that this finding should be interpreted with caution due to increasing mixed-race populations. In addition, ethnicity serves as a marker for socioeconomic status, and it has been postulated that there could be protective factors to uveal melanoma related to the home or work environment. [21]

All patients in this series presented with blurred vision and this is the most common presenting symptom in uveal melanoma. [1] In addition, the patient with ciliary body melanoma presented with complicated cataract that precluded detailed view of the fundus. Ciliary body tumors are particularly challenging to diagnose early, despite advances in medical imaging, because of their varied presentation and high possibility of being missed at indirect ophthalmoscopy until the tumor attains a large size with iris or choroidal extension. [1.22] This might partly explain the delayed presentation in the case of ciliary body melanoma in this series. A case of uveal melanoma in a blind eye with staphyloma and cataract was also reported by Khetan et al, [23] thus highlighting the need for B scan ultrasonography in patients with suspected uveal melanoma and media opacity so as to avoid delayed diagnosis and consequent poor outcome.

Uveal melanomas can be classified as small, medium, or large according to the size of the tumor. [24] This classification has however, been modified with changes reflecting ciliary body involvement, extra-scleral extension and size criteria for T_1– T_4, in the American Joint Committee on Cancer (AJCC) staging system, and this modification has been shown to correlate with the risk of metastasis and death. [25, 26] The rate of metastasis and death in uveal melanoma AJCC stage II disease is three times greater than AJCC stage I, while stage III disease has a 10 times greater risk. [27] Cases 1 and 2 in this series were classified as Stages I and IIA disease respectively, and this could partly explain the good outcome noted in them. The third patient with Stage IIIB disease, also abandoned out-patient follow-up visits and died from complications of tumor metastases.

Tumor histopathology has been noted to be a race-specific prognostic indicator for uveal melanoma. [4] and of the three histopathology types defined by AJCC (spindle cell melanomas, epithelioid cell melanomas, and mixed cell melanomas), the spindle cell variant (grade G1) has the most favorable prognosis for patient survival. [29]. All three patients in this series had histologic grade G1, which could partly explain the good prognosis recorded in the two cases.

People of African descent are also noted to have higher rate of ocular morbidity associated with uveal melanoma when compared with Caucasians. [4.28] Phillpotts et al [4] reported that one out of the ten black patients had intraocular inflammation with secondary glaucoma, significant delay in presentation, presenting acuity of nil perception of light, and average tumor size of 12mm. Margo and Mclean [28] also noted that ocular inflammation and secondary glaucoma leading to enucleation were more common in black patients. These were attributed to the higher rate of tumor necrosis in blacks with clinically significant delay in diagnosis, as was noted in our patient with ciliary body melanoma. A higher rate of mortality has also been noted in black patients with epithelioid cell-type histopathology. [28] However, Shields et al [14] analyzed a large cohort of 8100 patients over 40 years and concluded that the prognosis for uveal melanoma does not vary with race, and that the reported estimates for melanoma-related metastasis and deaths in African-Americans, were not statistically significantly different when compared with Caucasians or other races. [14] Hence, they postulated that an interplay of background choroidal pigmentation, genetic alterations, and immunologic mechanisms give protective influence and similar outcomes in non-Caucasians despite presenting with larger tumors.

The strength of this study is that it is first report on long term outcome of management of uveal melanoma, an uncommon tumor, in an indigenous African population. There are however, some limitations to the study. The number of cases studied is a reflection of the rarity of this tumor in Africans. Genetic analysis and molecular biology study of the ocular specimens to better characterize the tumors could not be carried out as these were not available at our Center at the time.

In conclusion, uveal melanoma is uncommon in our region and a high index of suspicion by practicing ophthalmologists may likely lead to earlier diagnosis, referral, prompt management and better prognosis in our patients.

Declarations

Ethics approval and consent to participate:

Ethical approval was received for the study and the study adhered to the tenets of Helsinki declaration

Consent for publication:

Patients' written informed consent for their personal or clinical details along with identifying images to be published in this study was received.

Funding:

Nil

Author Contribution

OF was involved in the management of the patients, collection of patients' data and was a major contributor in writing the manuscript. MA performed the histological examination on the enucleated eyeballs, and contributed to writing the manuscript. EO was involved in collection of patients' data, and was a contributor in writing the manuscript. All authors read and approved the final manuscript

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Not applicable

Data Availability

All data generated or analysed during this study are included in this published article

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Figures

Figures

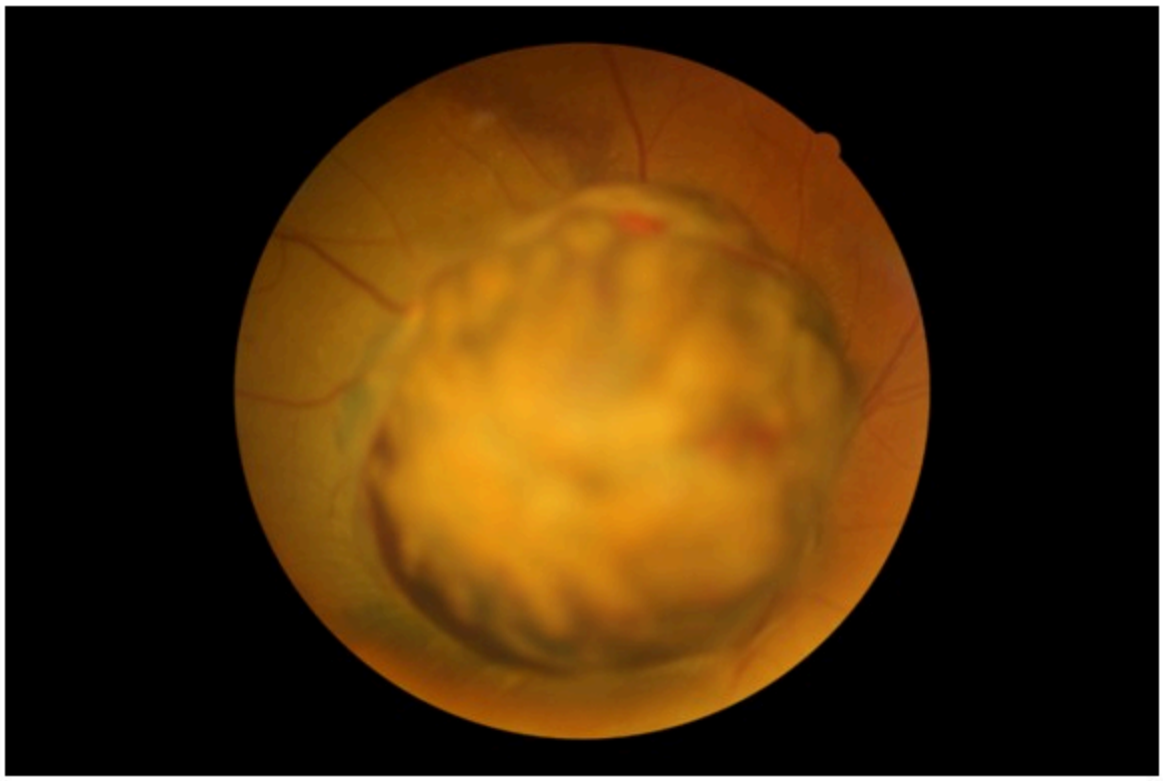


Figure 1

Figure 1

Fundus photograph of patient 2 showing a large, solitary, brown mass with mushroom-like contour measuring about 7.5mm x 7.5mm. Tumor was pigmented with areas of hemorrhage and involved the macula and the optic disc

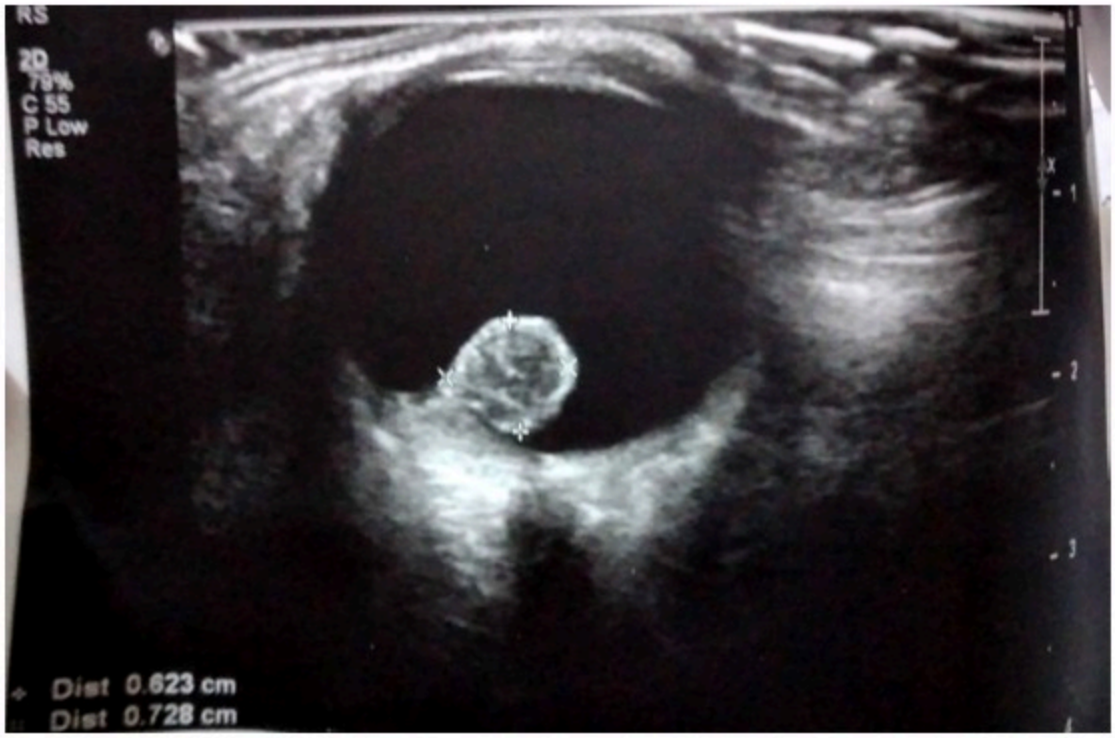


Figure 2

Figure 2

Ultrasound B-Scan of patient 2 showing a mixed echoic mass arising from the choroid with a calcific rim and areas of calcification noted within the mass which demonstrated high vascularity

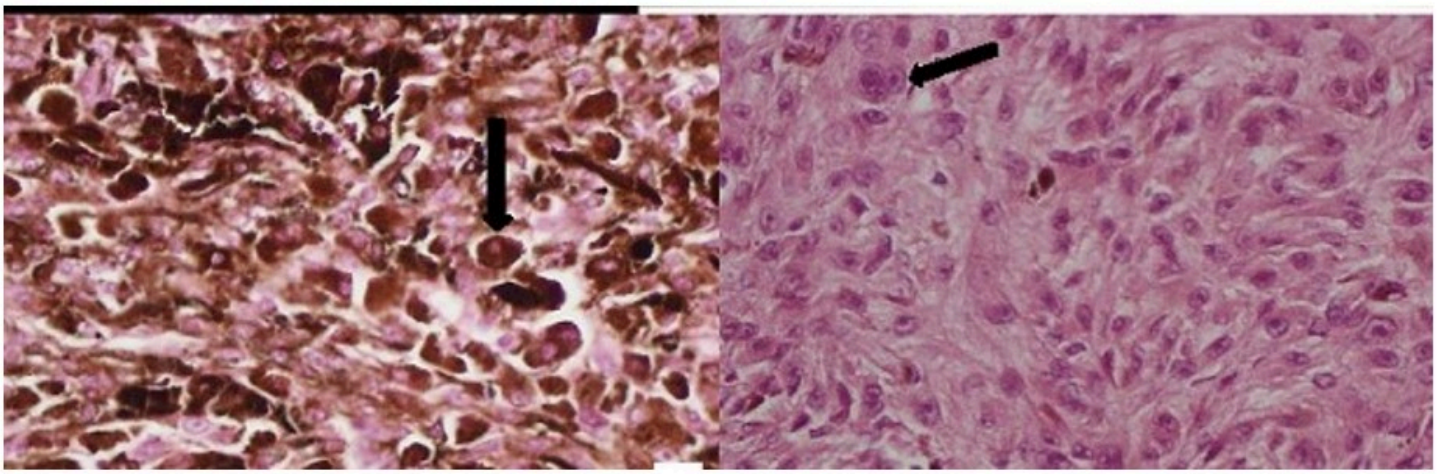


Figure 3

Figure 3

(Left) Photomicrograph (Haematoxylin and eosin stains, X400) of Patient 2 showing malignant melanoma

with extensive area of melanin pigment (arrow).

(Right) Photomicrograph (Haematoxylin and eosin stains, X400) of Patient 2 showing malignant melanoma having large vesicular nuclei with prominent eosinophilic nucleoli (arrow).

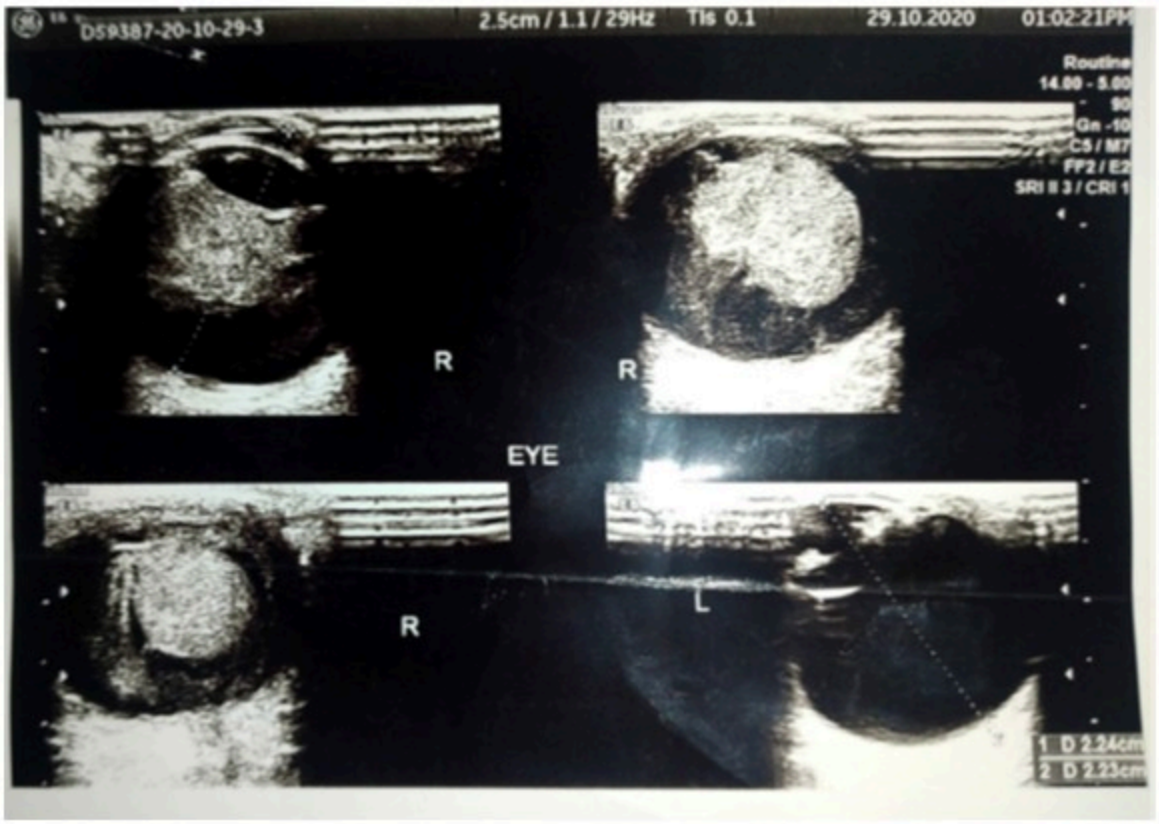


Figure 4

Figure 4

B-Scan Ultrasound of Patient 3 showing 13mm globular mass posterior to the lens filling anterior two-third of the vitreous