Multicentric recurrent uveal melanoma

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Uveal melanoma is a rare malignancy originating from melanocytes within the uveal tract of the eye. True multifocal uveal melanomas (>2melanomas in 1 eye) occurring in the same eye are very rare. We report a clinically and histologically well-documented case of a patient who presented with 3 uveal melanoma lesions in the same eye over a span of 2.5 years. The eye had to be enucleated finally and diagnosis confirmed histologically. This case report highlights the need for a close follow-up, even after successful treatment of the presenting lesion in uveal melanomas.

Key words: Brachytherapy, choroidal melanoma, ciliarybody melanoma, enucleation

Uveal melanoma is a rare malignancy originating from melanocytes within the uveal tract of the eye.[1] Choroidal melanoma is the most common subtype of uveal melanoma. Ciliary body melanoma is found rarely, reported in 1 of 10 cases of all intraocular melanomas.[2] Unilateral double melanomas have been reported in association with ocular melanocytosis and as a syndrome with other systemic malignant neoplasms.[3,4] True multifocal uveal melanomas (>2 melanomas in 1 eye as opposed to double) are very rare, with only two cases reported to date.[5,6] We report a patient with three uveal melanoma lesions in the same eye.

Case Report

A 59-year-old man presented to us 4 years ago with flashes in left eye (LE). The best corrected visual acuity (BCVA) was 6/6 in both eyes. Anterior segment examination and intraocular pressure (IOP) were within normal limits. Fundus examination of LE revealed a dome shaped pigmented mass with surface exudates and hemorrhage in the supero-nasal quadrant [Fig. 1a]. B-scan ultrasonography, fluorescein angiography, and magnetic resonance imaging (MRI) orbit findings were consistent with choroidal melanoma. B-scan ultrasonography showed a choroidal mass of 11 × 6.1 mm with acoustic hollowing. He had history of hypertension for last 5 years for which he was under treatment. Family history was negative for malignancy. He underwent plaque brachy therapy (Ruthenium-106), 10,000 cGy to the tumor apex at 6mm, following which the lesion regressed [Fig. 1b]. He developed mild radiation retinopathy in the treated eye and was on regular 3-monthly follow-up.

Patient was doing well for 2.5 years, asymptomatic without any evidence of local or systemic recurrence. BCVA was 6/6 in right eye (RE) and 6/12 in LE. During a routine follow-up, fundus examination of LE showed new dome shaped pigmented masses in the periphery of temporal and nasal quadrants. The supero-nasal primary tumor appeared all scarred and regressed [Fig. 1c and 1d]. A suspicion of recurrent uveal melanoma was made. Ultrasound biomicroscopy revealed solid masses in nasal (8 × 8 × 5.37 mm) and temporal (11 × 8 × 3.8 mm) ciliary body areas with low internal reflectivity [Fig. 2a and 2b]. MRI orbits showed the presence of mass lesions along the temporal and nasal aspects of the left globe, hyper-intense on T1 and hypo-intense on T2 weighted images. Positron emission tomography scan, ultrasound abdomen, chest x-ray, and liver function tests were done. Systemic screening was negative for metastases elsewhere in the body. A diagnosis of recurrent multi-centric uveal melanoma was made. Enucleation of LE with orbital implant was done. Histopathological and immunohistochemical analysis confirmed multi-centric malignant melanoma, epithelioid type [Fig. 2c and 2d] involving ciliary body and choroid, positive for HMB-45. The intervening areas of choroid were normal on serial sections which ruled out underlying diffuse melanoma. Genetic analysis showed chromosome 6q deletion. The patient is on 3-monthly follow-up without any metastasis at the end of 18 months.

Discussion

A case in which a patient's eye is harboring more than two uveal melanomas is indeed a rare occurrence. To our knowledge, true multifocal cases are reported only twice with one lacking histological evidence and the other lacking a cytogenetic proof.[5,6]

Rosen and Moulton (1953) reported a case of one large and four small flat discrete tumor nodules seen in the vicinity of the optic nerve head. They concluded that at least two of the lesions are completely independent and the exact number of lesions cannot be stated in the absence of serial sections through the whole eye.[5]

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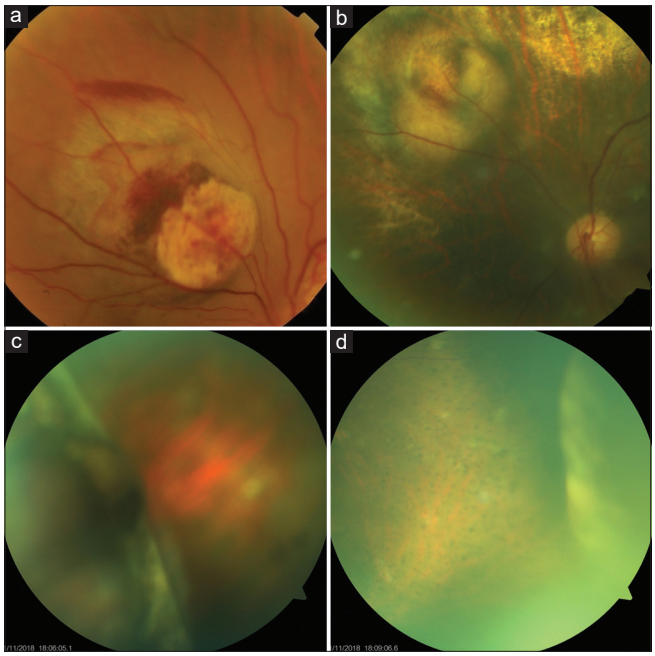

Figure 1: (a): Choroidal melanoma: a pigmented dome shaped choroidal mass with surface exudates and hemorrhage in the supero-nasal quadrant of left eye. (b): Regressed melanoma following plaque brachy therapy. (c): Ciliary body melanoma in the periphery of nasal quadrant of left eye. (d): Ciliary body melanoma in the periphery of temporal quadrant of left eye

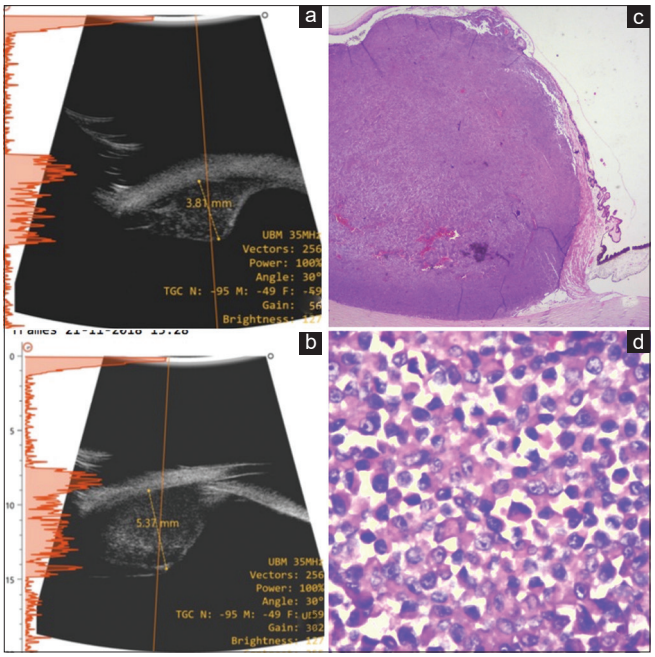

Figure 2: (a): Nasal ciliary body melanoma (8 × 8 × 5.37mm) with low internal reflectivity on ultrasound biomicroscopy.(b): Temporal ciliary body melanoma (11 × 8 × 3.8 mm) with low internal reflectivity on ultrasound biomicroscopy.(c): Haematoxylin and eosin (H and E) stained section of a mushroom shaped, endophytic ciliary body melanoma, under low magnification (4×).(d): H and E stained section of melanoma showing epithelioid cells with abundant eosinophilic cytoplasm, large eccentrically placed vesicular nucleus and prominent nucleolus, under high magnification (×400)

Bluementhal and Pe'er (1999) published a case of three separate uveal melanomas in a single eye but were unaware of a genetic or other marker that could unequivocally ascertain whether the distinct tumors originated from a single cell line.[6]

We report on a histologically verified case of a single eye harboring three non-contiguous uveal melanomas of epithelioid type positive for HMB-45 with genetic analysis showing chromosome 6q deletion. The presence of several uveal neoplasms may be secondary to metastatic dissemination from a single primary tumor, but its possibility would be less likely in the case described, as there was no other positive systemic focus of metastasis at the end of 18 months follow-up.

Recent studies have shown that Chromosome 3 deletion, BAP1 loss, chromosome 8q gain, chromosome 1p loss, and chromosome 6q loss are associated with poor prognosis. Disomy 3 and chromosome 6p gain are associated with a better prognosis.[7] In fact, it is now recognized that genetic changes play a very significant role in the growth, as well as metastatic potential of these tumors.[8,9]

The prognosis of uveal melanoma can be predicted by clinical, histopathological, and cytogenetic markers.[10] This case of multi-centric recurrent uveal melanoma of epithelioid type involving ciliary body and choroid with chromosome 6q loss indicates poor prognosis. The most effective way to improve the prognosis is early detection of melanoma and close follow-up with systemic monitoring.

Conclusion

Development of 3 uveal melanomas in a single eye is very rare. To the best of our knowledge, this is the first reported case of true multifocal uveal melanomas with histopathological and cytogenetic evidence. Such patients with unfavorable genetic mutations have high risk of metastasis and hence closer follow-up is suggested.

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Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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