Two Melanomas, One Eye

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Uveal melanoma (UM) affects approximately six individuals per million per year in the United States, with similar rates in Mediterranean countries. Although it appears to have a low prevalence, it is the most common primary intraocular malignancy in adults. Clinically, it presents in most patients as a painless loss or distortion of vision, although it may also be accidentally discovered at routine ophthalmic examination. Associated risk factors include fair skin tone, light eye color, presence of a choroidal nevus, oculodermal melanocytosis (nevus of ota), dysplastic nevus syndrome, and germline BRCA-associated protein 1 mutations (BAP1 mutations) [1].

Having more than one discrete UM in one eye is a rare phenomenon. Since the first reported case in 1882 by Ernst Fuchs, only 30 others have been published. A summary of cases described until 2002 indicates a median age of 60 years and a male predominance. Eighteen patients had two lesions unilaterally with various combinations of iris, ciliary body, and mostly choroidal melanomas [2]. Published cases include seven men and six women with a median age of 55 years at diagnosis. Five cases were presented with two unilateral lesions simultaneously, while eight developed two tumors consecutively. Among the simultaneous presentation cases, two were treated with primary enucleation, one received proton beam therapy, one received a large custom-designed Iodine 125 plaque, and one received sequential plaque placement.

We report an unequivocal case of two discrete uveal melanomas that occurred unilaterally, presented simultaneously, and were treated by an unusual sequential plaque placement [3].

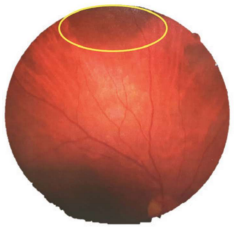
PATIENT DESCRIPTION

A 72-year-old man of Hungarian-Jewish origin with hypertension, diabetes, and unspecified steroid treated lung disease without co-morbidities first contacted a community ophthalmologist due to decreased visual acuity in the right eye (RE) over 2 months. A suspicious macular lesion necessitated urgent ultrasound and spectral domain optical coherence tomography (SD-OCT) (Heidelberg Engineering Spectralis, USA) scans. He was promptly referred to the ocular oncology service at our institute. Excluding bilateral cataract extraction, he had no prior history of ocular disease or surgeries.

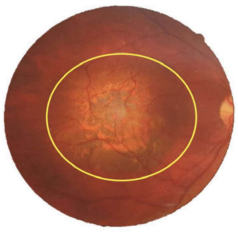
On presentation, there was no history of any personal or family malignancies, including cutaneous melanoma, nor any known risk factors such as nevus of ota, dysplastic nevus syndrome, or BAP1 mutations. On ophthalmologic examination, visual acuity on the Snellen chart was 20/50 in the RE and 20/40 in the left eye (LE). Both eyes had normal anterior segment intraocular pressure, and pupil function tests. A dilated exam demonstrated two lesions. One central macular elevated lesion in the RE that was bounded by the superior and inferior vascular arcades with reticular orange pigment and subretinal fluid. Another discrete, elevated pigmentary dome shaped superior lesion was seen [Figure 1]. SD-OCT scan revealed subfoveal choroidal elevation with RPE changes above it and subretinal fluid with hyperreflective foci in the fluid and in the outer retina. The central macular thickness was 342 microns. Ultrasound B-mode scan revealed a macular dome shaped, slightly hypoechogenic lesion lesion. The thickness was 1.7 mm and the width was 6.19 mm. A-mode showed medium frequencies. A second dome shaped hyperechogenic solid lesion was seen at the 12 o'clock position. The thickness was 3.24 mm and the width was 8.51 mm, with high frequencies in A-mode. Both modalities

Figure 1. A color photography of the right eye at first presentation (Moore Institute)

[A] A melanotic lesion is seen on the upper part of the retina



[B] A macular lesion with orange pigment



indicated a normally appearing optic disc with intact attached retina, and most importantly, no association or sign of continuity were demonstrated between the two lesions.

Although the provisional diagnosis was primary ocular melanoma, ruling out a secondary finding of unknown primary tumor was imperative. Additional workup included normal laboratory tests except for mild leukocytosis with a left shift attributed to chronic steroid use and normal cancer markers. Chest-abdomen-pelvis computed tomography (CT), scout CT chest abdomen pelvis, ^{18}F-fluorodeoxyglucose positron-emission tomography/computed tomography (FDG PET/CT), and PET/CT body scan ^{18}F-FDG diagnostic CT (iDose, Philips Healthcare, Cleveland, OH, USA) did not demonstrate any hypermetabolic process indicating other primary disease. Magnetic resonance imaging (MRI), (MRI ORBITS, T1, T2, FLAIR, DWI, SWI, TSE) scans of the brain and orbits validated two distinct choroidal processes in the RE, with presumably melanin content as a manifestation of nevus or melanoma. A biopsy was offered to the patient but was declined. A clinical diagnosis of two unilateral primary ocular melanomas was made.

Due to the distance between the two lesions, it was impossible to use the 22 mm diameter plaque to treat both lesions simultaneously. A shared decision by the patient, the family, and physicians included consecutive 80 gray ruthenium plaque radiotherapy. In the first surgery, a plaque covering the macular lesion was inserted, requiring temporal displacement of the inferior oblique and lateral rectus muscles. The following day, it was removed, the muscles were reconnected, and a second plaque covering the superior lesion was placed. On the third day, the second plaque had been removed, followed by an intravitreal bevacizumab injection. It is important to note that at the time of surgery, the transillumination test also failed to demonstrate anatomical continuity between the lesions.

The patient received five more intravitreal bevacizumab injections (1.25 mg /0.05 ml) with a 2-month interval between injections. During 3-years of follow-up, visual acuity was 20/40 in the RE and 20/25 in the LE and lesions remained well controlled. No signs of subretinal fluid were detected by SD-OCT scans. Genetic testing for BAP-1 predisposition syndrome and BRCA2 was negative.

COMMENT

UM is the most common primary intraocular malignancy in adults, yet it is rare. The presentation of two unilateral discrete melanomas is exceptional.

Although the fair skin tone and blue eye color make our patient a more susceptible host, he had only a few commonly described risk factors previously associated with UM [3].

It is challenging to define, and perhaps even harder to show, the distinction between the two lesions. Several conditions may simulate multifocal unilateral primary choroidal melanoma, and since a small proportion of cases were treated by enucleation, it is clinically and histopathologically impossible to confirm the discreteness of all the former ostensibly distinct lesions. Our case represents a clinical diagnosis assisted by all appropriate means to validate, without enucleating, the distinction between the two simultaneously discovered unilateral lesions.

Two unilateral discrete melanomas rarely arise simultaneously. Over the last 15 years, only 5 cases were described. While two of them required enucleation at first, globe salvage was made possible by either proton beam irradiation of the entire tumor field [4] or plaque radiotherapy.

When the distance between the lesions was close enough and anatomically feasible, a large enough custom-designed Iodine 125 brachytherapy device was placed [5]. The sequential plaque placing technique was applied only once in the past, to the best of our knowledge [5]. Early detection of the lesions and smaller mass sizes probably enabled eye preservation therapy rather than enucleation in our case.

The typical clinical presentation of UM with painless loss or distortion of vision may be misleading since some patients present with a subtle difference in visual acuity between the two eyes, and some patients are totally asymptomatic. These findings herald a much more ominous problem. Due to the dire consequences of UM metastasis and subsequent death, they must be treated promptly and efficiently. Nevertheless, maintenance of vision, eye preservation, and quality of life must also be considered in management planning.

CONCLUSIONS

We reported a case of two discrete unilateral choroidal melanomas discovered simultaneously in a symptomatic patient that were effectively treated by sequential plaque brachytherapy. At 3 years of follow-up, the patient had good tumor control without any evidence of relapse or metastasis. Sequential plaque brachytherapy is an effective and safe method of treating patients with two discrete unilateral choroidal melanomas.

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