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Case Report

Amelanotic uveal melanoma in an African patient

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1. Introduction

Uveal melanoma (UM) comprises 5% of all melanomas. This tumor arises from melanocytes in the choroid in 80% of cases, ciliary body in 12% and iris in 8% of cases and it is estimated that half of the primary tumors will develop fatal metastatic disease to the liver and the lung [1]. The 5-year survival rate of uveal melanoma patients is estimated to be 81.6% though this rate declines to 13% and 8% at respectively 1 and 2 years if the patient develops metastasis.

The incidence of UM varies greatly depending on the country in question. In the United States of America, the National Institute of Health estimates that the overall incidence of UM is 4.3 cases/million/year, with a higher prevalence in men (4.9) than in women (3.7) [2].

It most commonly affects people in the sixth decade of life, with an average age at diagnosis of 55 years. Incidence increases with age, peaking at around 70 years [3]. In most epidemiological studies on UM, there is predominance of males over females [4] [5].

Uveal melanoma is 8.5 times more frequent in the white race than in the black race. There is a large difference in predominance between continents, according to the predominant racial group. The region with the lowest prevalence reported is Africa and the one with the highest prevalence is Scandinavia [6].

2. Case report

A 42-year-old black man from Cape Verde was referred to the Ocular Oncology Unit in December 2014 with a clinical diagnosis of "right eye (RE) intraocular tumor". Symptoms had started two months before with painless loss of visual acuity in the RE. He was otherwise healthy and his past medical, ophthalmological and familial history were unremarkable.

Initial examination detected a relative afferent pupillary defect in the right eye with visual acuity reduced to light perception. A retinal detachment could be observed through the pupil (Fig. 1). Ophthalmoscopy revealed a bullous partial retinal detachment and an elevated whitish mass with diffuse limits in the temporal and superior quadrant of the right eye. Anterior segment examination revealed bilateral non-elevated and non-adherent patches of conjunctival pigmented lesions, temporal in the RE and nasal in the LE (Figs. 2 and 3). IOP was normal in both eyes. Visual acuity was 20/20 in the left eye with no evidence of intraocular pathology.

Ultrasonography revealed a heterogeneously echogenic multilobular dome-shaped mass, measuring 6.87 mm in maximum height and 18.51 mm at the base in B-scans. A-scan showed a solid tumor with high initial amplitudes and low internal reflectivity and a shallow elevated high reflective membrane attached to the apex of the lesion (Fig. 4). Magnetic resonance imaging (MRI) was performed and showed a partial retinal detachment with focal thickening at the superior and lateral aspect, involving the ciliary body, T1 hyper-intense and T2 hypo-intense in signal. Mild enhancement was seen on gadolinium–enhanced T1-weighted images. No extraocular tumor spread was detected.

The differential diagnoses included amelanotic uveal melanoma, rare in African patients, and metastasis. A complete systemic survey for metastasis was performed including a full body CT scan, liver and abdominal ultrasonography, and a PET-CT (FDG-F18). No signs of hepatic

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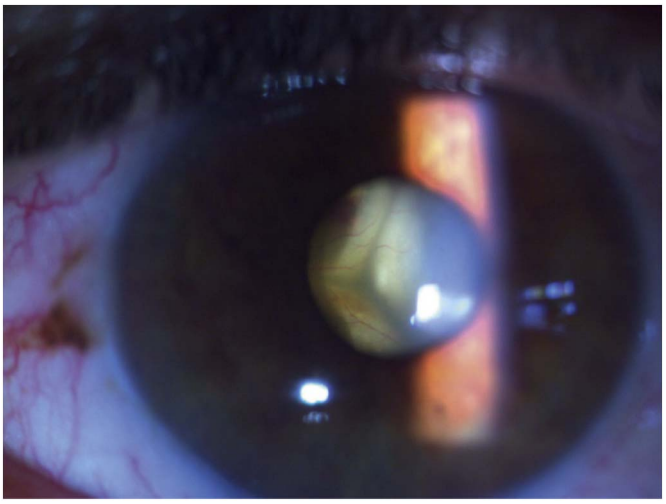

Fig. 1. Right eye: retinal detachment.

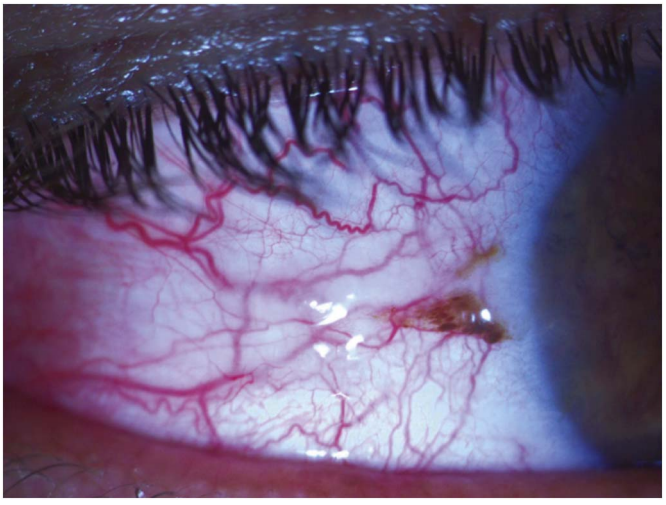

Fig. 2. Right eye: conjunctival melanosis.

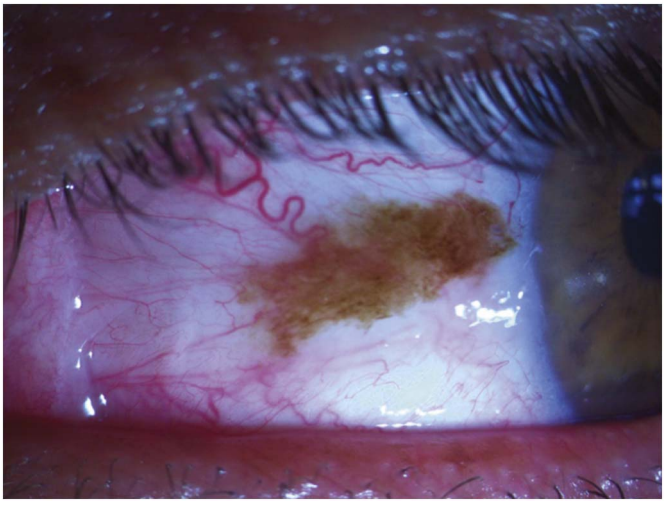

Fig. 3. Left eye: conjunctival melanosis.

metastatic disease were found. PET-CT images did not reveal any signs of increased metabolic activity other than in the RE. In one month patient developed ocular hypertension and rubeosis iridis in the RE and after a thorough discussion of the treatments option it was decided to proceed with enucleation. Conjunctival melanosis in the LE was also excised.

Macroscopic pathologic examination revealed a 22 × 22 × 23 mm right eye globe with a 1 cm optic nerve. After transillumination, the globe was cut through the 10–4 o'clock plan including the optic nerve. A multilobular whitish mass was observed extending from the iris to the optic nerve, measuring 7 mm in thickness, with a total retinal detachment (Fig. 5).

Light microscopy disclosed a ciliochoroidal malignant melanoma comprised predominantly of epithelioid cells, with 1 mitotic figure per 10 HPF (Fig. 6). The tumor cells infiltrate Bruch's membrane and inner scleral layers and extended to the ciliary body with anterior chamber angle closure and iris neovascularization (Fig. 7). The tumor showed abundant vascularization and low pigmentation, in contrast with the heavy pigmentation of the uveal tract further away from the melanoma (Fig. 8). No extrascleral extension was found. Immunohistochemical studies showed positive tumor cells for S-100 and HMB 45 (Fig. 9). This was consistent with the diagnosis of epithelioid melanoma of the choroid and ciliary body T4b (pT4N0M0, AJCC classification 8th edition).

Conjunctival lesion pathology in both eyes disclosed melanocytes showing no cellular atypia and confined to the basal layer of the epithelium, compatible with a conjunctival melanocytic intraepithelial neoplasm without atypia (Fig. 10).

3. Discussion

Racial differences in the incidence of uveal melanoma are well known, with Africans and other ethnic groups having significantly less uveal melanoma than Caucasians.

Data from one of the first studies in melanoma epidemiology, the Third National Cancer Survey (1969–1971), discovered that uveal melanoma is 8 times more frequent in Caucasians than in African Americans [7] A review from the National Cancer Institute Surveillance, Epidemiology, and End Results (SEER) database between 1973 and 2012 analyzed 7516 recorded cases of uveal melanoma and showed that the majority of cases occurred in Caucasians (94.7%), followed by Hispanic patients (3.9%) and finally African Americans (0.5%). < 1% corresponded to other ethnicities [8] Another study performed at the Wills Eye Hospital studied 8033 consecutive uveal melanoma patients and found only that only 33 patients were African American (< 1%) and 105 (1%) were Hispanic [9] Margo et al. in a retrospective study of malignant melanoma of the choroid and ciliary body in black patients identified only 39 of 3876 (1%) patients of African American descent [10] Phillpotts et al. also agreed with other studies that revealed racial differences in the black to white ratio in the United States (8–15:1), which is higher than that of reported by Miller et al. in South Africans (80:1) [11,12] The authors suggested that a possible reason for this discrepancy might be the mixed ancestry among African Americans [12]

Although data clearly shows the variance in the incidence of uveal melanoma in different ethnicities, the reasons for this disparity are not conclusive. Granting a lot of studies have been published, the etiology of uveal melanoma is still not fully understood and, contrary to cutaneous melanoma, the link between ultraviolet radiation pigmentation and uveal melanoma has not been definitively proven [4,7,12,13–15], Its etiology is probably multifactorial with both genetic, host factors and environmental factors playing a part in its development. A recent meta-analysis of uveal melanoma risk factors identified nine risk factors, atypical cutaneous nevi, welding, occupational cooking, fair skin color, light eye color, common cutaneous nevi, propensity to sunburn, iris nevi and cutaneous freckles. However, outdoor leisure activity, occupational sunlight exposure, latitude of birth, and hair color were not statistically significant risk factors [16].

Margo and McLean's study also analyzed the histopathology and survival outcomes in both Caucasian and African American patients