Reduction of Orange Pigment Overlying Choroidal Melanoma Following Plaque Radiotherapy

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Orange pigment is a feature often associated with active small choroidal melanoma. This finding appears as fine or granular orange-colored deposits that accumulate on the surface of several types of tumors, but in particular choroidal melanoma.[1] Orange pigment, if extensive, can rarely form an orange pigment pseudohypopyon-like sediment overlying melanoma.[2] The detection of overlying orange pigment is most efficient with fundus autofluorescence (FAF), appearing as focal accumulations of bright hyperautofluorescence. On histopathology, orange pigment represents aggregates of macrophages with phagocytized lipofuscin and melanin pigment released by retinal pigment epithelial cells (RPE) that have been disrupted by an actively growing tumor.[1] The importance of orange pigment as a sign of active small melanoma is understood, but its fate following therapy is not well described. Herein, we explore the outcome of orange pigment following plaque radiotherapy of choroidal melanoma.

CASE DESCRIPTION

A 55-year-old white woman presented with a history of light flashes in the right eye (OD) for 2 weeks. Visual acuity was 20/20 in both eyes (OU). Anterior segment examination was normal OU. Fundus examination of the left eye was unremarkable. Fundus examination OD revealed a 7x6x3-mm pigmented choroidal lesion temporal to the fovea with prominent overlying orange pigment near the margin of the tumor (Figure 1A), confirmed with hyperautofluorescence on FAF (Figure 1B). Optical coherence tomography demonstrated shallow subretinal fluid. B-scan ultrasonography revealed an acoustically hollow choroidal mass of 3-mm thickness. Based on the clinical and imaging findings, the lesion was diagnosed as choroidal melanoma OD.

The choroidal melanoma was treated with iodine-125 plaque radiotherapy. At 4 months follow-up, tumor thickness decreased to 2.7 mm, and the overlying orange pigment appeared to show slow resolution (Figure 1C and D). Further tumor regression and reduction of orange pigment was evident at 12 and 17 months follow-up (Figure 1E-1H).

DISCUSSION

Clumped orange pigment overlying an intraocular tumor represents lipofuscin-laden macrophage accumulation on the surface of Bruch membrane, posterior surface of the retina, or free floating within the subretinal space. This finding results from degenerated photoreceptors within retinal pigment epithelial cells that have transformed into macrophages. This material appears orange in color against a darkly pigmented tumor, like a pigmented choroidal melanoma, and it appears more yellowish or brown in color against a nonpigmented tumor, like a choroidal metastasis. Orange pigment is generally regarded as a sign of tumor activity.

Orange pigment can occur with both benign and malignant tumors, but its presence over a melanocytic lesion is particularly important, as it can be a sign of activity or growth. Clumped orange pigment over a melanocytic

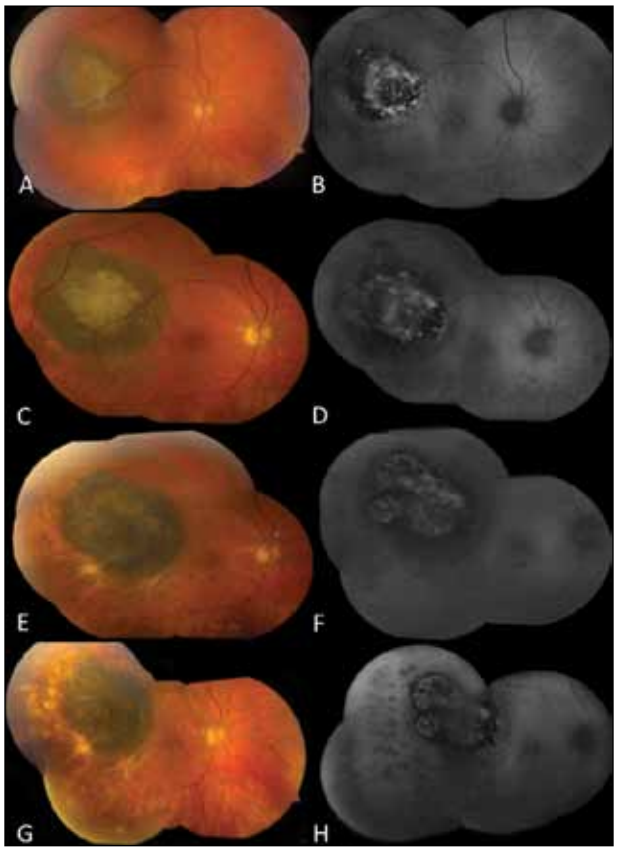

Figure 1. Reduction of orange pigment overlying choroidal melanoma following plaque radiotherapy in a 55-year-old female. (A) Fundus examination of the right eye showing perifoveal choroidal melanoma with overlying orange pigment (B) confirmed as bright hyperautoflourescence on fundus autofluorescence. Reduction of orange pigment following plaque radiotherapy at 4 months (C, D), 12 months (E, F), and 17 months (G, H).

choroidal tumor is a strong indicator of choroidal melanoma. Other choroidal tumors, such as choroidal nevus, hemangioma, metastasis, and lymphoma, can also manifest orange pigment.

Orange pigment can be visualized ophthalmoscopically as a granular, often geographic, dusting of orange debris overlying a choroidal mass. It is best detected, however, on FAF as bright geographic focal hyperautofluorescence.[3,4] Gunduz et al[4] studied 13 consecutive patients with choroidal nevus and melanoma and showed FAF correlation of hyperautofluorescence with orange pigment in 8 tumors (62%). The concentration and the amount of intracellular lipofuscin determine the intensity of the hyperautofluorescence. Shields et al[3] studied 51 consecutive patients with choroidal melanoma, and 39 displayed visible overlying orange pigment, described with hyperautofluorescence as mild in 11 (28%) tumors, moderate in 19 (49%), and intense in 9 (23%) tumors[3] Identification of orange pigment by FAF is critical for the judgment of tumor activity with small choroidal melanoma.

Few studies have examined the course of orange pigment following therapy. Anselm et al[5] reviewed 8 cases of choroidal melanoma and noted increase in orange (lipofuscin) pigment in 90% following plaque radiotherapy, presumed due to oxidative stress suffered by the RPE cells following treatment. In contrast to these findings, Hashmi et al[1] noted fading of orange pigment as a result of cell death. In our case, the orange pigment slowly faded following plaque radiotherapy. We speculate that the reduction in orange pigment could be attributed to the attrition of lipofuscin-containing macrophages following plaque radiotherapy.

In summary, we describe a small choroidal melanoma with prominent overlying orange pigment. Following plaque radiotherapy, tumor regression was documented, and slow resolution of the overlying orange (lipofuscin) pigment was clinically noted and confirmed on FAF. ■

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