



PAMM and the ischemic cascade associated with radiation retinopathy

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ABSTRACT

Purpose: To report a case of paracentral acute middle maculopathy (PAMM) and evidence of the ischemic cascade documented with spectral domain optical coherence tomography (SD-OCT) following radiation treatment of a choroidal melanoma.

Observations: A healthy young patient was evaluated for an asymptomatic choroidal nevus in the left eye. Fundus examination was remarkable for a choroidal melanocytic lesion that measured 1.8 mm in thickness by initial B-scan ultrasound. Clinical examination 6 months later showed growth of the tumor at several margins with new subretinal fluid, and a B-scan measured thickness of 1.9 mm. The lesion was diagnosed as a small choroidal melanoma and treated with gamma knife radiation with a dose of 3000 cGy. Sixteen months later, examination showed signs of radiation retinopathy including cotton wool spots and PAMM via SD-OCT and OCT angiography and evidence of the ischemic cascade (i.e., alternating zones of middle and combined middle and inner retinal layer infarction).

Conclusions: Radiation retinopathy can include signs of microvascular damage and ischemia including lesions such as cotton wool spots and PAMM. A case is presented in this report of radiation retinopathy with OCT evidence of PAMM and the ischemic cascade.

1. Introduction

The rate of radiation retinopathy after choroidal melanoma treatment varies widely in the literature, ranging from 0 to 87%.¹ There are various factors that increase the risk, including radiation dosage and modality and tumor location and size.¹ Retinal findings are similar to diabetic retinopathy and include microvascular abnormalities such as microaneurysms and signs of retinal ischemia such as cotton wool spots (CWS).¹ Surprisingly, paracentral acute middle maculopathy (PAMM) has, to our knowledge, not been previously reported in association with radiation retinopathy.

PAMM is defined as a hyper-reflective band in the middle retina with optical coherence tomography (OCT) consistent with inner nuclear layer (INL) infarction due to nonperfusion of the deep retinal capillary plexus (DCP).^{2,3} The etiology of PAMM lesions may relate to the recently described ischemic cascade in which the DCP at the venular poles are at greatest risk of oxygen desaturation and INL infarction during global hypoperfusion through the retinal capillary plexus.^{4,5}

In this report, we describe the first documented association of PAMM and radiation retinopathy and also illustrate evidence of the ischemic

cascade with spectral domain OCT (SD-OCT).

1.1. Case report

A healthy young patient was referred for evaluation of an asymptomatic choroidal nevus in the left eye. Past medical and ocular and family history were all unremarkable. Best corrected visual acuity was 20/20 in both eyes. Intraocular pressures, pupillary responses, and anterior segment examination were normal in both eyes.

Ophthalmoscopic retinal examination was unremarkable in the right eye but showed a 6 mm × 4 mm choroidal melanocytic lesion with orange pigment temporal to fixation in the left eye (Fig. 1). B-scan ultrasound was obtained and a choroidal tumor with high internal reflectivity was identified that measured 1.8 mm in thickness. No other signs that were high risk for progression such as subretinal fluid were noted; therefore, the presumed choroidal nevus was monitored for growth.

At the 6-month follow-up, the patient was symptomatic, complaining of new-onset flashing lights. The lesion showed evidence of superior and inferior growth with new subretinal fluid and lesion thickness increased to 1.9 mm with B-scan ultrasound. The diagnosis of small choroidal

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Fig. 1. Zeiss color fundus photograph of the left eye at baseline presentation illustrates a suspicious choroidal melanotic lesion temporal to fixation. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

melanoma was made and treatment with gamma knife radiation at a dose of 3000 cGy was performed in a single session. At the 16-month follow-up visit after therapy, examination illustrated a CWS superior-nasal to the fovea. Two weeks later, the patient developed a new scotoma and visual acuity was reduced to 20/25 in the left eye. Repeat examination showed a PAMM lesion adjacent to the prior CWS (Fig. 2). SD-OCT illustrated multifocal or skip PAMM lesions (i.e., hyper-reflective bands isolated to the middle retina consistent with infarctions of the INL) that alternated with areas of hyper-reflectivity or infarction of both the middle and inner retina (Fig. 3) and evidence of the ischemic cascade and likely the result of global hypoperfusion through the retinal capillary plexus. OCT angiography (OCTA) confirmed corresponding flow deficit of the DCP (Fig. 4).

2. Discussion

Ionizing radiation disrupts molecular bonds and produces free radicals, promoting both immediate and eventual cellular necrosis.¹ Histopathological studies have illustrated evidence of vascular destruction

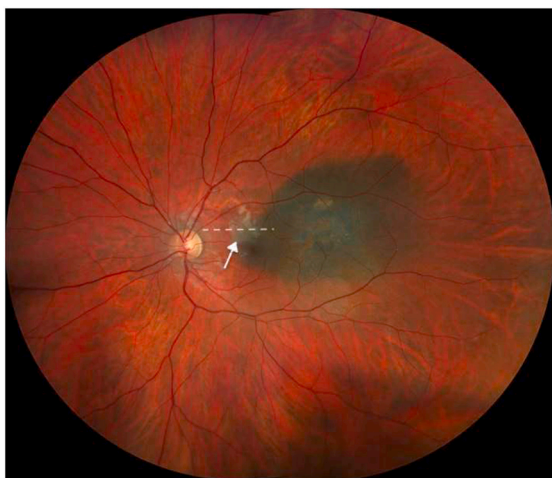


Fig. 2. Zeiss color fundus photograph of the left eye 16 months after radiation treatment illustrates a paracentral acute middle maculopathy (PAMM) lesion (arrow) adjacent to a cotton wool spot. The dotted line corresponds to Fig. 3. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

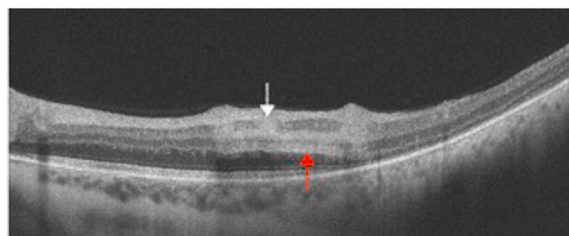


Fig. 3. Spectral domain optical coherence tomography (SD-OCT) of the left eye 16 months after radiation treatment shows multifocal middle retinal hyper-reflective infarctions consistent with PAMM lesions (red arrow) alternating with regions of both middle and inner retinal infarction (white arrow) suggestive of an ischemic cascade and due to global hypoperfusion through the retinal capillary plexus. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

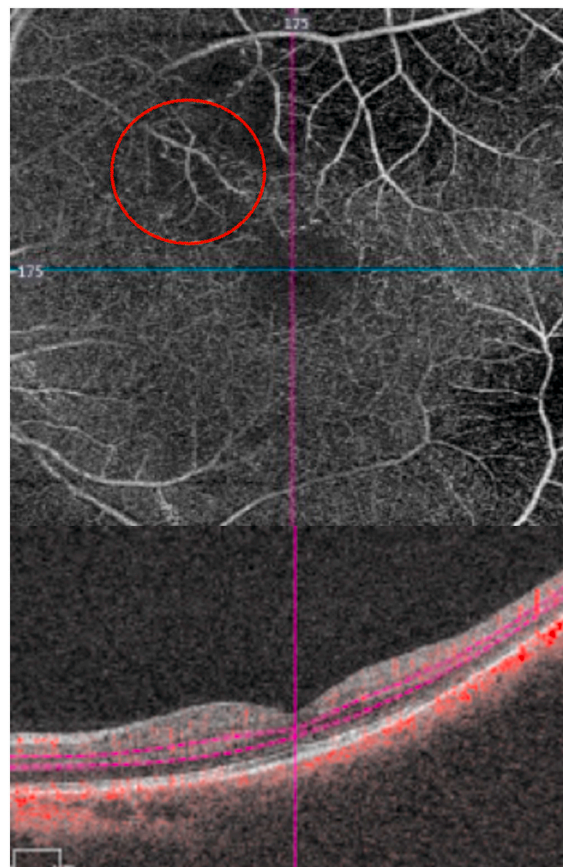


Fig. 4. OCT angiography of the left eye lesion segmented at the level of the deep retinal capillary plexus (DCP) shows hypoperfusion of the DCP (outlined by the circle in red) corresponding to the PAMM lesion. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

with disruption of the endothelial cells and the associated pericytes similar to diabetic retinopathy.¹ Microvascular alterations associated with ischemia and infarction are typical findings of radiation retinopathy, which occurs above a radiation dose range of 2500–3000 cGy and 6 months to 3 years following radiation exposure.^{6,7}

PAMM is a common OCT finding similar to a CWS and can be associated with a wide range of retinal disorders, including diabetic retinopathy, retinal vascular occlusion, sickle cell retinopathy, vasospasm due to migraine disorder, inflammatory retinopathy, and many other conditions.^{8,9} To the best of our knowledge, PAMM has not been

previously reported as a finding of radiation retinopathy, but the association is not surprising given the many other microvascular findings including CWS.

The OCT B-scan in this case is very interesting and shows alternating bands of infarction including skip PAMM lesions alternating with small regions of both middle and inner retinal infarction suggestive of the ischemic cascade and likely the result of global hypoperfusion through the retinal capillary plexus.^{4,5} This indicates that in retinal regions with less severe disruption of retinal capillary flow (and higher oxygen saturation levels), only PAMM lesions develop, whereas in zones with more severe disruption of perfusion (and lower oxygen saturation levels), infarction of both the middle and inner retina occurs. This may be consistent with a predominantly vertical flow of blood in the retinal capillary plexus in which major arterial perfusion occurs at the level of the superficial retinal capillary plexus while major venous outflow occurs at the level of the intermediate and deep retinal capillary plexuses.¹⁰

3. Conclusions

This is the first reported association of PAMM and the ischemic cascade with radiation retinopathy.

Patient consent

Consent to publish the case report was not obtained. This report does not contain any personal information that could lead to the identification of the patient.

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Authorship

All authors attest that they meet the current ICMJE criteria for Authorship.

Declaration of competing interest

Dr. Jay Duker: Carl Zeiss Meditec, Inc. (C, F), Optovue, Inc. (C, F) Dr. David Sarraf: Amgen (consultant), Bayer (consultant), Genentech (consultant, research), Heidelberg (research), Novartis (speaker), Optovue (consultant, research), Regeneron (research), Topcon (research)

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