Pregnancy and Thrombophilic Polymorphisms in Paracentral Acute Middle Maculopathy: A Case Report

Gravidez e Polimorfismos Trombofílicos na Maculopatia Média Aguda Paracentral: Relato de um Caso

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ABSTRACT

We describe a case of a 34-year-old healthy woman in her first trimester of pregnancy presented with painless acute vision loss in the left eye. Fundus examination revealed a paracentral focal area of retinal whitening that appeared on optical coherence tomography (OCT) as an inner who retina hyperreflectivity and on OCT angiography a severe attenuation of the deep capillary plexus, compatible with paracentral acute middle maculopathy (PAMM). Genetic testing found heterozygous *PAI-1 4G/5G* and *MTHFR* (*A1298C*) mutations, therefore she started antiplatelet therapy. This report highlights that PAMM should be one of the possible diagnoses of acute visual disturbances in pregnancy even in otherwise healthy women.

KEYWORDS: Polymorphism, Genetic; Pregnancy; Retinal Diseases; Retinal Vessels; Thrombophilia; Tomography, Optical Coherence.

RESUMO

Descrevemos o caso de uma mulher de 34 anos, saudável, no primeiro trimestre de gravidez, que apresentou uma perda de visão aguda e indolor no olho esquerdo. A fundoscopia revelou uma área, focal, paracentral e esbranquiçada de retina. Esta lesão identificava-se na tomografia de coerência ótica (OCT) como uma zona hiperrefletiva nas camadas mais internas da interna e na angiografia por OCT como uma atenuação grave do plexo capilar profundo. Este conjunto de alterações são compatíveis com maculopatia média aguda paracentral (PAMM). O teste genético revelou mutações heterozigóticas nos genes *PAI-1 4G/5G* e *MTHFR* (*A1298C*), pelo que a doente iniciou terapêutica antiagregante plaquetária. Este caso clínico destaca a PAMM como um dos possíveis diagnósticos clínicos em quadros de alteração visual aguda na gravidez, mesmo em mulheres saudáveis.

PALAVRAS-CHAVE: Doenças da Retina; Gravidez; Polimorfismo Genético; Tomografia de Coerência Óptica; Trombofilia; Vasos Retinianos.

INTRODUCTION

Paracentral acute middle maculopathy (PAMM) was first described in 2013 by Sarraf *et al*[1] as an ocular finding on spectral-domain optical coherence tomography (OCT) characterized by a hyper-reflective band-like lesion involving the inner nuclear layer (INL) usually associated with various retinal vascular disorders.[2,3] OCT angiography (OCTA) is a relatively new non-invasive modality that can identify vascular structures by detecting blood flow without using dye.[4]

In this report, we illustrate a rare case of an apparently healthy pregnant woman who developed a PAMM without other predisposing factors besides minor thrombophilic polymorphisms and emphasize the role of OCT and OCTA in diagnosing these subtle retinal vascular disorders.

CASE REPORT

A 34-year-old white female in her 13th week of an uncomplicated pregnancy presented in our emergency department with a painless acute paracentral scotoma in her left eye. The patient had no relevant medical history besides occasional migraines and denied any previous flu-like illness or hypotensive events. She was a nonsmoker and was not a coffee drinker. Her visual acuity was 20/20 bilaterally, had no relative afferent pupillary defect, and both anterior segments and intraocular pressure were normal. Fundus observation of the left eye revealed an oval focal area of retinal whitening in the macula just inferonasal to the fovea (Fig. 1A). Both optic disk and retinal vessels were normal. The area appeared lighter on red-free imaging (Fig. 1B), was hypoautofluorescent on fundus autofluorescence (Fig. 1C) and on SD-OCT (Spectralis, Heidelberg – Germany) there was a corresponding area

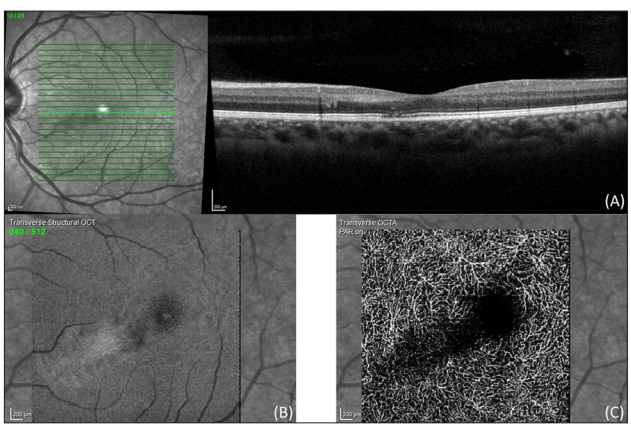

Figure 1. Multimodal imaging of the left eye shows different findings. (A) Color fundus photograph of the left eye showing an ischemic whitening parafoveal area corresponding to paracentral acute middle maculopathy on OCT. (B) Red-free imaging with a lighter appearance. (C) Fundus autofluorescence with an area of hypoautofluorescence.

of hyperreflectivity (Fig. 2A) in the inner layers. On *en-face* OCT (Fig. 2B) and OCTA (Fig. 2C), there was a corresponding area of nonperfusion within the deep capillary plexus (DCP) and irregular vascular network in the intermediate capillary plexus (ICP). The Amsler grid confirmed the paracentral superotemporal scotoma. All these findings were compatible with the diagnosis of PAMM. Due to the absence of precipitating factors, she underwent a systemic workup to rule out ischemic or hypercoagulable disorders, which came positive for the heterozygous mutations of *MTHFR (A1298C)* and *PAI-1 4G/5G*. Although not consensual, she started antiplatelet therapy (150 mg of oral acetylsalicylic acid daily) for the rest of the pregnancy. In the patient's last follow-up, the lesion area was reduced, the OCT showed less hyperreflectivity with initial thinning of the inner layers (Fig. 3A) and on the OCTA, the attenuation area was smaller (Figs. 3B and C).

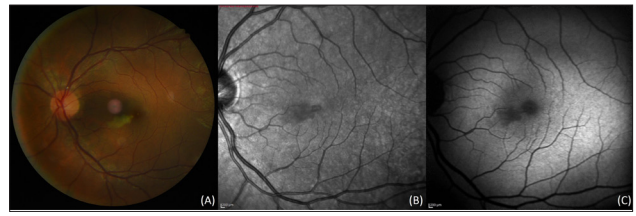

Figure 2. OCT imaging of the left eye. (A) OCT shows the corresponding hyperreflective area in the inner nuclear layer consistent with paracentral acute middle maculopathy. (B) En-face OCT delimitates the affected area of ischemia. (C) OCT angiography view of the deep capillary plexus with severe attenuation of the blood flow.

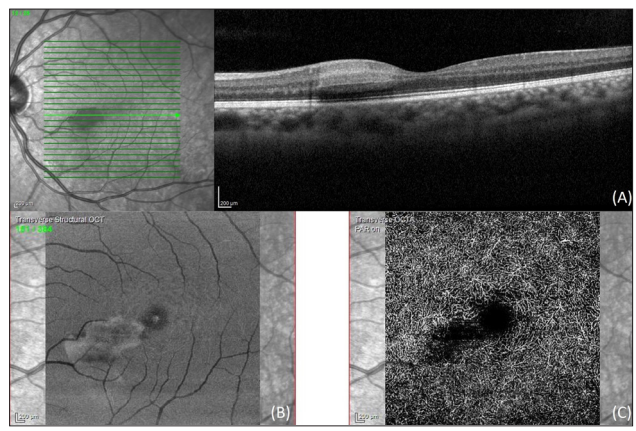

Figure 3. Two-month follow-up of the left eye with partial anatomic recovery. (A) OCT shows less hyperreflectivity and an evident thinning and atrophy of the inner nuclear layer. (B) OCT angiography with incomplete revascularization of the affected area.

DISCUSSION

This case describes a young pregnant woman who presented a paracentral scotoma compatible with PAMM in the left eye which was confirmed on OCT by a corresponding hyperreflective band-like lesion. The pathophysiology of this condition is related to ischemia in the deep vascular complex (ICP and DCP) due to hypoperfusion, and results in an infarction of the INL.[5] These lesions usually tend to progress

to atrophy of the INL, leading to persistent visual scotoma.[3]

There are many possible conditions to cause PAMM, from local retinal vascular conditions such as retinal vein/artery occlusions and diabetic/hypertensive retinopathy to other conditions such as vascular surgeries or even medications (PDE-5 inhibitors for example). On the other hand, there are rare reports of apparently healthy patients with PAMM,[2,3] even in young pregnant women.[6]

In pregnancy, there is a physiologic hypercoagulability and thrombophilia that can play a role in the risk of retinal vascular disorders.[7] Adding other preexisting conditions to further imbalance the vascular homeostasis, such as some thrombophilic mutations, might increase the risk of PAMM.[7] A very recent report described a similar case of a pregnant female in her second trimester with PAMM and a possible hypercoagulable state due to elevated factor VIII activity.[8] Although our case had a positive heterozygous mutation for *MTHFR (A1298C)* and *PAI-1 4G5G*, there is still no connection to retinal vascular conditions in the literature.[9,10]

In situations like this case where there is an impossibility of using invasive fluorescein angiography to evaluate the underlying vascular network, OCTA gains importance as it can visualize the ischemia of deep vascular complex both in the acute and chronic phases. Also, *en-face* OCT can identify patterns of distribution which can clarify the real predisposing condition.[2]

All these newer imaging modalities can help differentiate from other similar entities, such as acute macular neuroretinopathy (previously thought to be the same entity) that share risk factors and clinical manifestations but have discrete differences on OCT.[2,3]

This report highlights that pregnancy can also be a risk factor for PAMM, but it does not exempt a systemic workup using a multidisciplinary approach to exclude other potential disorders such as hypercoagulable conditions. Using the myriad of imaging alternatives that the non-invasive imaging OCT offers, especially OCT angiography, we can provide an accurate diagnosis and guarantee a detailed follow-up of multiple retinal vascular pathologies in pregnancy.

CONTRIBUTORSHIP STATEMENT / DECLARAÇÃO DE CONTRIBUIÇÃO

JCA: Conception and design of the work, draft of the paper, critical review, and approval of the final version.

TC, MV and CM: Draft of the paper, critical review.

ASL and DS: Conception and design of the work, critical review, and approval of the final version.

FTV and IP: Critical review and approval of the final version.

JCA: Conceção e desenho do trabalho, rascunho do artigo, revisão crítica e aprovação da versão final.

TC, MV e CM: Rascunnho do artigo e revisão crítica.

ASL e DS: Conceção e desenho do trabalho, revisão crítica e aprovação da versão final.

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