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Paracentral acute middle maculopathy in systemic sclerosis and subsequent branch retinal artery occlusion

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ABSTRACT

Purpose: We report a case of systemic sclerosis-associated paracentral acute middle maculopathy (PAMM) in a young woman who subsequently developed branch retinal artery occlusion.
Observations: A 22-year-old woman presented with a paracentral scotoma. Optical coherence tomography (OCT) revealed bilateral paracentral acute middle maculopathy. Upon systemic examination, she was diagnosed with systemic sclerosis (SSc). She subsequently developed branch retinal artery occlusion despite vasodilator medications. After the prescription of aspirin, she did not experience a new event for one year.
Conclusion and importance: This case illustrates that SSc may affect the retinal vascular system and vision and cause PAMM. The optimal prophylaxis for patients with recurrent retinal events should be investigated in future studies.

1. Introduction

Systemic sclerosis (SSc), also known as scleroderma, is an autoimmune disease that causes chronic inflammation and fibrosis in the connective tissue. The disease primarily affects the skin but may also involve other organs and small blood vessels, sometimes the eyes. Raynaud's phenomenon, color changes of the fingers and toes, is a common symptom of SSc. Raynaud's phenomenon is a reversible vasospasm; patients with SSc are more hypersensitive to cold stimuli due to progressive structural changes in the vessels, including arterial intimal proliferation, adventitial fibrosis, and collagen deposition, resulting in more intense and frequent vasospasm.[1] Ophthalmic complications of SSc include eyelid, corneal, and iris changes; retinal exudates; and fibrinoid changes in the retina. More severe complications, such as central retinal vein and artery occlusion, have occasionally been reported.[2,3]

Paracentral acute middle maculopathy (PAMM) is a recently reported optical coherence tomography (OCT) finding characterized by hyper-reflective band-like lesions in the inner nuclear layer (INL). Impairment of the retinal intermediate and deep capillary plexuses (ICP and DCP) causes focal ischemia of the INL and presents as a PAMM.[4] PAMM generally leads to INL thinning and sometimes causes persistent scotomas. PAMM is generally associated with retinal and systemic vascular diseases, such as central retinal vein occlusion[5,6] and central or branch retinal artery occlusion.[7] Other causes include hypertensive retinopathy, diabetic retinopathy, eye surgery, endovascular treatment, hypertension, hyperlipidemia, caffeine, vasopressors, and migraine headaches.[4] However, the etiology remains unknown in some cases. Herein, we present the case of a young woman with PAMM diagnosed with SSc and subsequently developed branch retinal artery occlusion (BRAO).

2. Case report

A 22-year-old woman presented with a paracentral scotoma in the right eye that had developed 1 week previously. The best-corrected visual acuity was 1.2 (20/16) in both eyes, and the relative afferent pupillary defect was negative. No signs of intraocular inflammation were observed. Fundus examination revealed multiple retinal nerve fiber bundle defects and optic disc hypoplasia (Fig. 1 A, B). Goldman perimetry (GP, HAAG STREIT, Bern, Switzerland) showed nasal scotoma corresponding to optic disc hypoplasia and paracentral scotoma (Fig. 1 C, D). Spectral domain OCT (Spectralis, Heidelberg Engineering, Heidelberg, Germany) showed a hyper-reflective band-like lesion at the

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level of the INL corresponding to the area of paracentral scotoma (Fig. 1 E, G). In addition, multiple scattered lesions of focal thinning of the inner retina were observed (Fig. 1 E, F). Decreased perfusion in the ICP and DCP in the area of PAMM was detected on OCT angiography (Optovue, Visionix, IL) (Fig. 1 H). The patient was diagnosed with PAMM based on the OCT findings.

The patient's medical history included childhood migraine and atopic dermatitis. She had no regular medications except for acetaminophen when she had a headache.

She frequently had Raynaud's syndrome for a long time, which prompted us to suspect the presence of a connective tissue disease such as SSc. Raynaud's phenomenon was observed on bilateral fingertips, and skin stiffness was observed on the fingers and forearms. A biopsy of the sclerotic skin was performed, and the findings of edematous changes in the dermis layer and collagen fibrosis from the dermis layer to the subcutaneous tissue were consistent with SSc. A thorough examination of various antibodies revealed positive results for anti-nuclear and anti-centromere antibodies specific to SSc. We also screened for coagulopathy but antiphospholipid antibodies, protein C, and protein S levels were within normal range. Head magnetic resonance imaging and truck computerized tomography were conducted, but there were no abnormal findings in the other organs. Therefore, we made a diagnosis of limited cutaneous type systemic sclerosis associated with PAMM. The scattered areas of INL thinning indicated subclinical past events. Frequent episodes of Raynaud's phenomenon suggested that peripheral circulation was still unstable, and she was at risk of further events. Thus, we started diltiazem 30 mg and 40 μg of beraprost sodium to suppress vasospasm and alleviate symptoms, but the intensity and frequency of Raynaud's phenomenon were unchanged. Diltiazem was increased to 60 mg but was not effective. Eight months after the initial presentation, she subsequently developed BRAO in the left eye despite vasodilator medications (Fig. 2). There was no sign of active inflammation. To prevent further events, we added aspirin. After the prescription of aspirin, she was free from new events for one year. Her visual acuity was maintained throughout the disease course.

3. Discussion

The present case showed PAMM and multiple lesions of inner retinal thinning at the first presentation. The findings indicated that the patient experienced multiple episodes of PAMM and/or more severe ischemic events despite she was young and prompted us to screen her for systemic diseases which led to the diagnosis of SSc. We conducted a literature review on PubMed (https://pubmed.ncbi.nlm.nih.gov/accessed on 1st Oct 2023) using the key words paracentral acute middle maculopathy, systemic sclerosis, and scleroderma but we did not find any prior report.

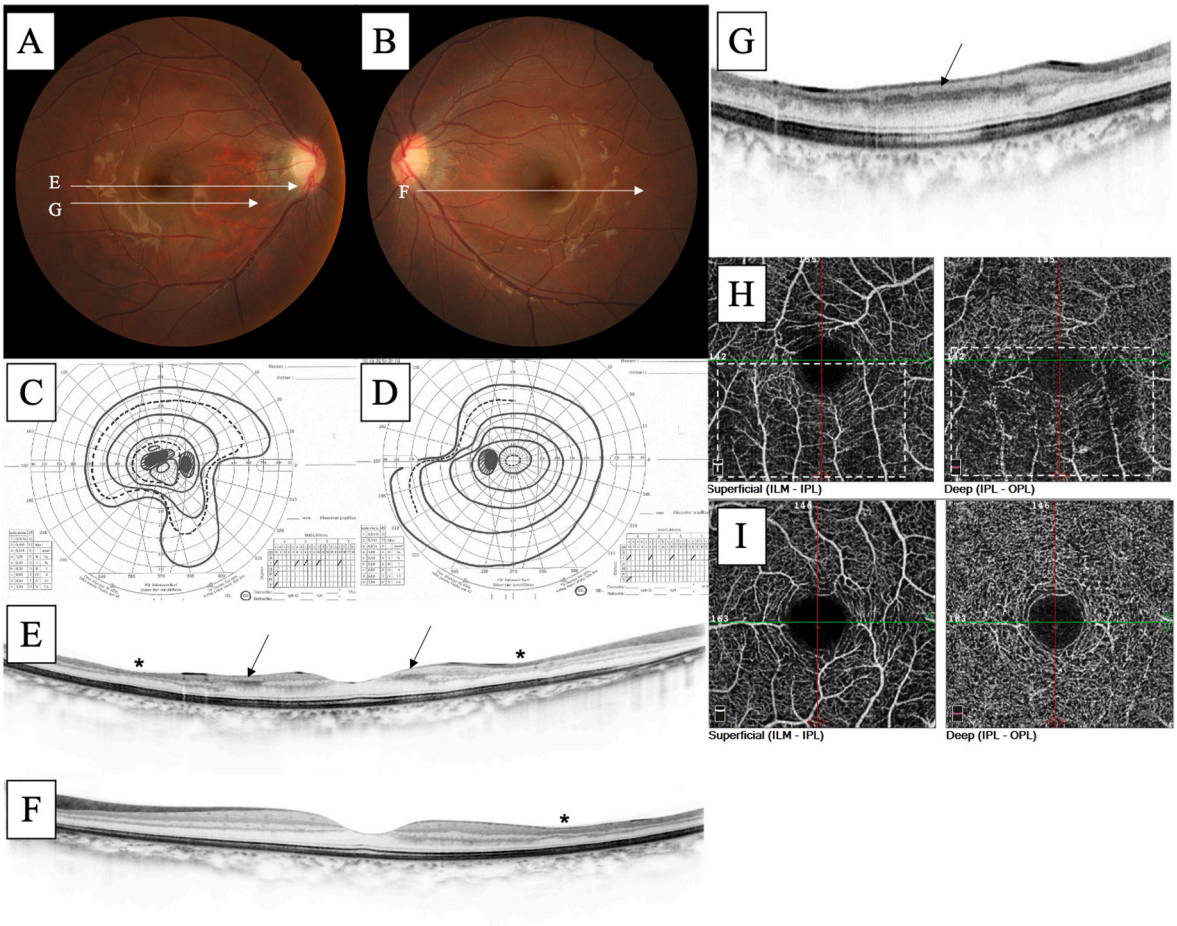

Fig. 1. Multimodal imaging, including color fundus photography and cross-sectional spectral-domain OCT at the first visit. A, B. Color fundus photography illustrates optic nerve hypoplasia and multiple retinal nerve fiber bundle defects in both eyes. C, D. The Goldmann perimeter reveals a paracentral, temporal, and nasal lower scotoma in the right eye. (C) Temporal upper visual field defects in the left eye (D). OCT of the right eye (E, G) reveals a hyper-reflective zone in the INL (arrows), corresponding to the area of paracentral scotoma and scattered areas of inner retinal thinning (asterisks). (F) The left eye shows INL thinning (asterisk). 3×3 mm^2 en face OCTA image of the right eye (H) shows decreased perfusion in the ICP and DCP in the area of the PAMM (white box). No abnormalities are observed in the left eye (I). OCT, optical coherence tomography; INL, inner nuclear layer; OCTA, optical coherence tomography angiography; ICP, retinal intermediate plexus; DCP, deep capillary plexus; PAMM, paracentral acute middle maculopathy. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

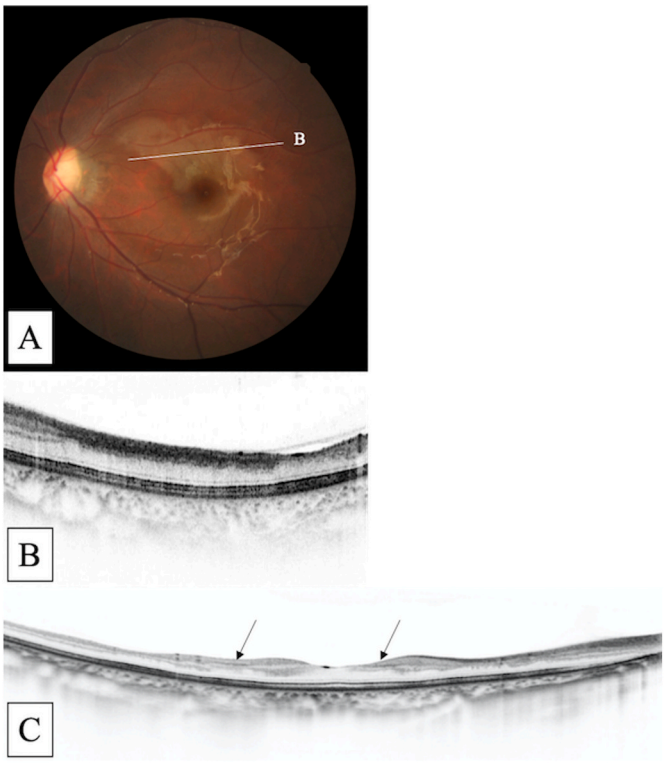

Fig. 2. Fundus photograph and OCT of the patient in Figs. 1 and 8 months later the patient developed branch retinal artery occlusion in the left eye despite vasodilator medications. Localized retinal edema is noted in color fundus photography. (A) OCT reveals a hyper-reflective appearance (B). The PAMM lesions observed during the first examination of the right eye turned into INL thinning (arrows) (C). OCT, optical coherence tomography; INL, inner nuclear layer; PAMM, paracentral acute middle maculopathy. (For interpretation of the references to color in this figure legend, the reader is referred to the Web version of this article.)

In patients with SSc, various cytokines released by endothelial activation lead to fibrosis and microvascular dysfunction.[1] Studies using fundus and OCT angiography have suggested that patients with SSc experience microcirculatory disturbances in the retina and choroid.[8,9] Pathological examination revealed fibrous thickening and luminal narrowing of the retinal and choroidal arterioles in the eyes of patients with SSc.[3] In the present case, we considered that vascular changes due to SSc caused PAMM and BRAO.

In addition, the present case had a migraine. Migraines are associated with systemic autoimmune diseases, including SSc.[10] Migraine can cause PAMM[6,11] and is associated with a higher risk of retinal artery occlusion.[12] However, the previously reported cases of PAMM and migraine are unilateral and do not show multiple lesions, as observed in the present case. In addition, frequent retinal vascular events in patients in their 20s, even those with migraine, is rare. There was no other history of any particular cause or medication in the present case. We believe that the combination of vasoconstriction due to migraines and vascular impairment due to SSc may have caused multiple lesions and resulted in a refractory course in the present case.

PAMM is an OCT-based clinical finding and can be caused by a variety of retinal and systemic vascular diseases,[4] BRAO being one of them[7,13] and the patient presented with BRAO at the final episode. The BRAO developed despite that we prescribed vasodilators to improve the microvascular circulation because of the recurrent episodes and severe Raynaud's phenomenon. Several studies have reported prophylactic administration of calcium channel blocker for transient monocular visual loss associated with vasospasm was successful,[14–16] but it was ineffective in this case. Only after we prescribed aspirin was she free from new events. However, it should be noted that although the efficacy of aspirin for RAO in preventing secondary cerebrovascular events has been verified,[17–19] its efficacy in preventing retinal vascular disease after RAO is not proven. Nevertheless, there are some reports of aspirin prescribed for PAMM.[20] In addition, another antiplatelet drug Cilostazol is sometimes used in scleroderma patients[21] Although we cannot draw conclusions from a single case, antiplatelets may be required to prevent recurrent retinal events in some high-risk cases.

4. Conclusions

We report a case in which PAMM led to the diagnosis of SSc. The optimal prophylaxis for patients with recurrent retinal events should be investigated in future studies.

Patient consent and ethics statements

The patient gave written informed consent for publishing her data.

Ethical approval was not required for this study in accordance with national guidelines.

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Authorship

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

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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