• Letter to the Editor •

Retinal vein occlusion coinciding with paracentral acute middle maculopathy in patient with menorrhagia causing life-threatening anemia

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Dear Editor,

We present two cases of retinal vein occlusion, one central retinal vein occlusion (CRVO) and one branch retinal vein occlusion (BRVO) respectively, coinciding with paracentral acute middle maculopathy (PAMM) on optical coherence tomography (OCT) in patients with menorrhagia causing life-threatening anemia. PAMM is considered a manifestation of acute ischemia affecting the deep macular capillary plexus, as observed on spectral domain OCT. It has been reported to be associated with retinal ocular diseases such as retinal vein or artery occlusion, as well as medical interventions or following an ocular surgery[1-3]. Severe anemia could result in retinopathy, particularly when the hemoglobin level falls below 8.95 g/dL, exhibiting a sensitivity of 85.8% and a specificity of 68.9% in predicting the presence of anemic retinopathy in patients[4]. Retinal hypoxia induced by severe anemia may lead to endothelial cell damage, disrupting the blood-retinal barrier, and eventually causing retinal edema, which is the potential mechanism of retinal vein occlusion[5]. Menorrhagia is one of the most common causes of anemia in premenopausal women, affecting women's quality of life, productivity, and healthcare cost. Heavy menstrual bleeding might lead to severe anemia, and even become life threatening if left untreated. Therefore, we herein describe two patients with life-threatening anemia, who were diagnosed with retinal vein occlusions, coinciding with PAMM on OCT, showing improvement in visual acuity and resolution of PAMM after receiving a total hysterectomy.

This study was approved by the Institutional Review Board (IRB) of Chang Gung Memorial Hospital (IRB number 202000890B0). Informed consent from all subjects for publication of identifying information/images in an online open-access publication was obtained.

In case 1, a 45-year-old female with a past medical history of chronic menorrhagia due to adenomyoma experienced sudden painless blurred vision in the right eye for four days. She had profound microcytic anemia with hemoglobin of 5.3 g/dL. Her initial visual acuity was 20/800 and 20/20 in the right and left eye, respectively. The fundoscopic examination of the left eye proved unremarkable, while the examination of the right eye revealed a tessellated fundus with four quadrants of dilated and tortuous vessels, optic disc edema, and cotton wool spots (Figure 1A). She was diagnosed with CRVO in her right eye. OCT showed several hyper-reflective band-like lesions involving the junction between the retinal outer plexifom layer and the inner nuclear layer, suggesting a diagnosis of PAMM (Figure 1C). Under the impression of CRVO related to anemia disorder, an extensive work-up was undertaken. All other laboratory parameters were normal including: white cell count, electrolytes, liver function, coagulation profiles, thrombophilia screen, anti-nuclear antibodies, anti-cardiolipin antibodies, anti-beta 2 glycoprotein, protein C, protein S, D-dimer, vitamin B12, and folate. The neuro-imaging in the form of brain computed tomography revealed no definite abnormal enhancing intracranial lesion. The patient was subsequently referred to a gynecologist and underwent a total hysterectomy to address the underlying condition of chronic menorrhagia.

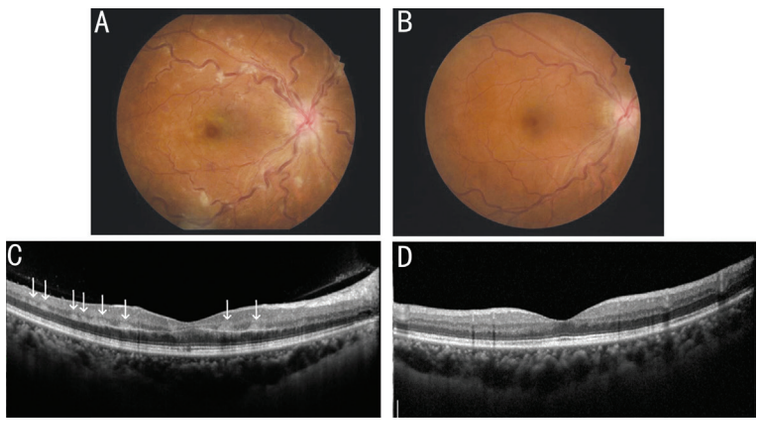

Figure 1 Pre- and post-treatment (after receiving a total hysterectomy) of the slit-lamp photography and OCT of the right eye of case 1 A: A tessellated fundus with four quadrants of dilated and tortuous vessels, optic disc edema, and cotton wool spots; B: A nearly complete resolution of cotton wool spots, dilatation and tortuosity of vessels, and a residual optic disc swelling as previously noted; C: Several hyper-reflective band-like lesions involving the junction between the retinal outer plexiform layer and the inner nuclear layer, suggesting a diagnosis of PAMM (arrow); D: A resolution of hyper-reflective band-like lesions and thinning of the inner nuclear layer. OCT: Optical coherence tomography; PAMM: Paracentral acute middle maculopathy.

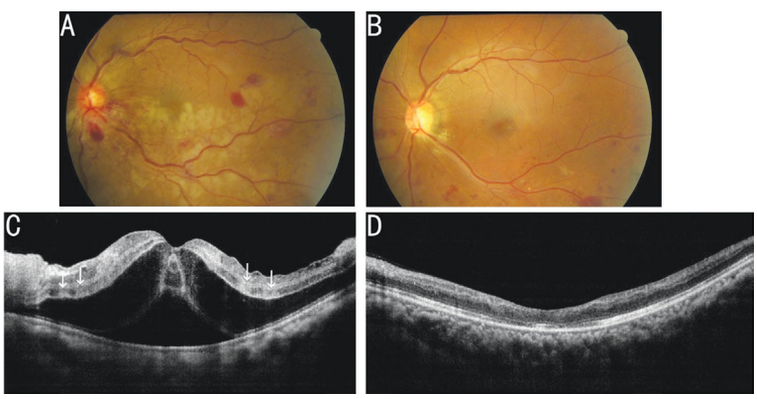

Figure 2 Pre- and post-treatment (after receiving a total hysterectomy) of the slit-lamp photography and OCT of the left eye of case 2 A: A swollen optic disc, flame-shaped hemorrhages, dot and blot hemorrhages, and dilated and tortuous vessels in the inferior arcade; B: A resolution of flame-shaped hemorrhages, dot and blot hemorrhages, dilatation and tortuosity of vessels, and optic disc swelling; C: Macular edema with a central retinal thickness of 472 μm, and hyper-reflective band-like lesions (arrow) in the middle retinal layers; D: An absence of macular edema with a central retinal thickness decreased to 198 μm, and a resolution of hyper-reflective band-like lesions and thinning of the retinal inner nuclear layer. OCT: Optical coherence tomography.

Following the total hysterectomy, her severe anemia was resolved, with a hemoglobin level of 11.4 g/dL noted in the one-month follow-up. Additionally, her visual acuity in the affected (right) eye improved to 20/66. The fundoscopic examination revealed a nearly complete resolution of cotton wool spots, dilatation and tortuosity of vessels, and a residual optic disc swelling as previously noted (Figure 1B). OCT images in the right eye revealed that a resolution of hyper-reflective band-like lesions and thinning of the inner nuclear layer were noticed (Figure 1D). Four months later, her visual acuity in the affected (right) eye returned to 20/20.

In case 2, a 44-year-old female, with a past medical history of iron deficiency anemia and chronic menorrhagia due to adenomyoma, visited our ophthalmology outpatient department due to intermittent dizziness and progressive blurred vision in the left eye for 2wk. Her hemoglobin level was 7.7 g/dL. Her visual acuity was 20/20 and 20/400 in the right and left eye, respectively. The fundoscopic examination of the left eye revealed a swollen optic disc, flame-shaped hemorrhages, dot and blot hemorrhages, and dilated and tortuous vessels in the inferior arcade (Figure 2A). Inferior non-perfusion areas and leakage at a late stage were noticed over fluorescein angiography in the left eye, consistent with a diagnosis of BRVO. The OCT scan of the left eye showed macular edema with a central retinal thickness of 472 μm and several hyper-reflective band-like lesions in the middle retinal layers, corresponding to the feature of PAMM (Figure 2C). The patient also underwent a total hysterectomy following consultation with a gynecologist to address the underlying condition of chronic menorrhagia. One month post-surgery,

her hemoglobin level was measured at 12 g/dL. During the follow-up two months later, her visual acuity declined to 20/200 in the affected (left) eye. Fundoscopic examination revealed a resolution of flame-shaped hemorrhages, dot and blot hemorrhages, dilatation and tortuosity of vessels, as well as optic disc swelling in the affected (left) eye (Figure 2B). The OCT images in the left eye revealed an absence of macular edema with a central retinal thickness decreased to 198 μm, and a resolution of hyper-reflective band-like lesions as well as thinning of the retinal inner nuclear layer were noticed (Figure 2D). Seven months later, her visual acuity in the affected (left) eye improved to 20/32.

In the previously reported cases of patients with CRVO manifesting PAMM on OCT by Casalino *et al*[6-7], retinal inner nuclear layer thinning was noticed after the resolution of PAMM. This natural course of PAMM provides additional supportive evidence of its causative mechanism, which involves focal ischemia of the intermediate and deep capillary plexus. Similarly, both of our cases revealed the resolution of PAMM and thinning of the retinal inner nuclear layer one month and two months after undergoing total hysterectomy to address the underlying condition of chronic menorrhagia, respectively. Severe anemia-induced CRVO[8] and subsequent findings of PAMM on OCT[6-7] have been presented in some cases; however, anemia-induced BRVO, to the best of our knowledge, has not been reported in the literature. In our presenting case 2, BRVO coincided with PAMM on OCT was noted, showing the resolution of PAMM as well as retinal inner nuclear layer thinning on the follow-up examination as demonstrated in the previously reported cases by Casalino *et al*[6-7]. Interestingly, aside from the resolution of dilated and tortuous vessels, optic disc edema, and retinal hemorrhages on the fundoscopic examination and the resolution of PAMM on OCT, the result of undergoing a total hysterectomy yielded different outcomes on the improvement of visual acuity in both of our cases. In cases 1 and 2, the visual acuity of the affected eye returned to 20/20 in four months and 20/32 in seven months, respectively. The variation in visual acuity outcomes among patients with PAMM secondary to retinal vein occlusion may be attributed to factors such as the extent of the deep capillary plexus involvement and the timing of reperfusion following an acute retinal ischemic event[6-7].

To date, no treatment for PAMM is available. The management is recommended to target the identification and treatment of the underlying vasculopathy and systemic diseases[9]. As demonstrated in both of our cases, the resolution of PAMM on OCT and the improvement in visual acuity were observed following a total hysterectomy, which address the underlying cause of life-threatening anemia resulting from chronic menorrhagia. With thorough ophthalmologic examination and proper referral and treatment, the outcome of retinal vein occlusion coinciding with PAMM in patients with life-threatening anemia is favorable. Therefore, we as ophthalmologists recommend that clinicians should acquire the detailed information about the menstrual cycle and gynecology history in female patients with life-threatening anemia and blurred vision. When the patients have been suffering from chronic menorrhagia, a referral to a gynecologist for proper treatment might improve their visual impairment without further ophthalmologic interventions.

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Conflicts of Interest: Lin WY, None; **Wang JJ,** None; **Lai CH,** None.

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