

## Unilateral sequential papillophlebitis and central retinal artery occlusion in a young healthy patient

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A 23-year-old girl presented to the clinic with metamorphopsia and photopsia in her left eye. After detailed ophthalmic examination, central retinal vein occlusion with optic disc edema was detected in that eye. Three days after diagnosis, the patient returned to our clinic with visual acuity decrease. Central retinal artery occlusion sparing cilioretinal artery was detected. All the laboratory tests were normal except for heterozygous methylenetetrahydrofolate reductase mutation (A1298C

genotypes) and an indefinite Lyme disease seropositivity. Symptoms and visual disturbance recovered without any further treatment other than acetylsalicylic acid for prophylaxis.

**Key words:** A1298C mutation, central retinal artery occlusion, central retinal vein occlusion, methylenetetrahydrofolate reductase gene mutation, papillophlebitis

Retinal vascular occlusions, including arterial and venous obstructions, are serious pathologies that can cause blindness. The clinical characteristics and prognosis are influenced by the location of the occlusion. The presence of cilioretinal artery is vitally important for visual prognosis in central retinal artery occlusions (CRAO).<sup>[1]</sup>

Central retinal vein occlusion (CRVO) in the young is also known as papillophlebitis and is caused by compression of the central retinal vein due to inflammation of the optic nerve head. CRVO is mostly seen as an isolated event in young adults; however, a previous report showed that there might be some underlying systemic associations in up to 50% of affected individuals.<sup>[2]</sup>

CRAO in young patients may be caused by hyperhomocysteinemia, systemic lupus erythematosus,

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trauma, sickle cell disease, platelet abnormalities, in addition to embolic disease.<sup>[3,4]</sup>

Combined papillophlebitis and CRAO in the same eye are a devastating and rare entity, especially in an otherwise healthy young patient. Herein, we are trying to report this unusual entity with an extensive laboratory workup to determine the etiological factor. The present case provides, to our knowledge, the first description of this combined entity with sparing cilioretinal artery and excellent visual prognosis in the affected eye.

## Case Report

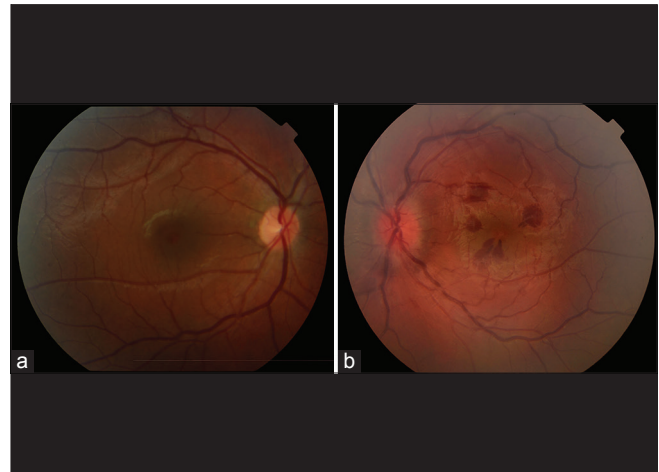
A 23-year-old healthy female patient presented with metamorphopsia and photopsia in her left eye. At presentation, the best-corrected visual acuity (BCVA) was 20/20 in both eyes. Her medical history was unremarkable except her smoking habit (20/day) and coke drinking habit (2l/day). Anterior segment examination and intraocular pressures were within normal limits (17 mmHg) in both eyes. Dilated fundus examination of the left eye showed blurred optic disc margins with hyperemic disc swelling, venous engorgement, and preretinal hemorrhages in the macula. No abnormalities were found in the right eye [Fig. 1a and b]. The optical coherence tomography revealed retinal thickening in the left eye.

Extensive laboratory workup including the complete blood count, serum C-reactive protein, erythrocyte sedimentation rate (ESR), C-protein, S-protein, D-dimer, lupus test, antinuclear antibody, prothrombin time/partial thromboplastin time, antithrombin III activity, factor V Leiden and prothrombin gene mutation, anticardiolipin antibody, antineutrophil cytoplasmic antibodies, angiotensin converting enzyme, and homocysteine levels were ordered to rule out underlying conditions that might cause papillophlebitis.

At the 3<sup>rd</sup> day of follow-up, she noted a sudden visual loss in the left eye. BCVA was 20/20 in her right eye and 20/200 in the left eye. Dilated fundus examination revealed CRAO [Fig. 2] and intact cilioretinal artery circulation was determined by fundus fluorescein angiography [Fig. 3]. Since the macular perfusion was good, there is no proof to accompany of an embolism; the emergency treatment of CRAO, including hyperbaric oxygen or anterior chamber lavage, were not done; only acetylsalicylic acid (ASA) drug 100 mg/day treatment was started.

Routine laboratory findings only showed a mild elevation of white blood cells, ESR, and C-reactive protein. The chest X-ray and magnetic resonance imaging of brain and orbits were normal. All of the tests which were studied to determine the cause of the papillophlebitis were negative except heterozygous (A1298C) methylenetetrahydrofolate reductase (MTHFR) mutation. Despite the fact that the heterozygous mutation of this gene is very common and harmless, the patient was consulted to a hematologist because of the clinical signs. It was reported that this kind of mutation could not cause this condition alone. She was consulted by a cardiologist and a dermatologist who did not reveal any etiological factor.

At the 5<sup>th</sup> day of follow-up, BCVA increased but there were cells (2+) bilaterally in the anterior chamber and serologic study was conducted for iridocyclitis. Only the Western blot test for *Borrelia burgdorferi* was positive. Since Turkey was



**Figure 1:** (a) Fundus photography of the normal right eye at the initial presentation (b) fundus photography of the left eye at the initial presentation. Note mildly edematous optic disc, dilated and tortuous retinal veins, and preretinal hemorrhages in the macula



**Figure 2:** Fundus photography of the left eye on the 3<sup>rd</sup> day of the presentation with central retinal artery occlusion. Note retinal edema except foveal region



**Figure 3:** Fundus fluorescein angiography of the left eye on the 3<sup>rd</sup> day of the presentation. Note intact cilioretinal artery circulation

an endemic region for this infection, the infectious disease specialist suggested starting antibiotherapy although there was no history of any tick bite.

At the 20<sup>th</sup> day of the examination, left optic disc was pale; the hemorrhages and retinal edema were decreased, and arteries were attenuated [Fig. 4]. On the other hand, BCVA was 20/20 in both eyes. Since the cardiology department suggested the patient to be on ASA, we decided to continue her medication.

## Discussion

Papillophlebitis is believed to be a type of CRVO in young people; the exact cause is still not known. It can be isolated or can be seen with retinal artery occlusion, most commonly cilioretinal artery.<sup>[5]</sup> In the current case, the occluded artery after papillophlebitis was central retinal artery. The increased venous pressure after CRVO may have impaired the retinal blood flow, so these two vascular entities may be related. The second possible pathomechanism that is caused to suggest the linkage between them is inflammation of optic disc that caused to disruption of retinal blood flow. The inflammation may be related to smoking, nutritional deficiency, and unhealthy lifestyle of the patient. Because of the papillophlebitis has a better natural course compared retinal vein occlusion in older adults and the presence of an intact cilioretinal circulation, our patient gained her visual acuity without any further treatment.

The enzyme MTHFR has an important role in homocysteine metabolism; therefore, decreased enzyme activity leads to buildup of homocysteine and can cause thromboembolic events.<sup>[6]</sup> Turaka *et al.* reported a case of young female with unilateral papillophlebitis who was found to have positive homozygous mutations for MTHFR C677T and A1298C genes. Although there was no information about the blood level of homocysteine in that case report, presumed hyperhomocysteinemia was thought as the main cause for that hypercoagulable state.<sup>[7]</sup> Conversely, in our patient, there was a heterozygous mutation of A1298C MTHFR and homocysteine level was normal ( $=6,9 \mu\text{mol/L}$ ). A previous study showed mutation of A1298C MTHFR was a risk for early coronary disease without hyperhomocysteinemia.<sup>[8]</sup> Thus, heterozygous A1298C mutations may also present an independent risk factor for thrombosis, especially if combined

with unhealthy lifestyle and some risk factors such as smoking, high stress, and toxic exposures.

Lyme is a spirochetal disease responsible for a multitude of ocular and systemic manifestations. While it is an uncommon cause of papillitis, it can be presented with severe acute anterior uveitis, howbeit previous cases reported unilateral papillitis as the sole significant ocular sign of Lyme disease.<sup>[9]</sup> Therefore, due to accompanying bilateral anterior chamber reaction, Lyme seropositivity, and being in an endemic area for Lyme, she was treated with intravenous ceftriaxone with the recommendation of infectious diseases department, despite the lack of any bite story.

Performing extensive laboratory workup is very important in such patients to rule out some etiologic factors. Furthermore, it should be known that heterozygous mutation of A1298C MTHFR gene may cause thromboembolic events even if with the presence of normal homocysteine levels.<sup>[8]</sup> Based on this knowledge, we decided to recommend systemic anticoagulant therapy, other than ASA to our patient for prophylaxis. The limitation of our paper is that the exact cause of anterior chamber reaction was not clearly determined, and it might have been a simultaneous self-healing iridocyclitis with false positive Lyme serology.

Although combined CRVO (or papillophlebitis) and CRAO entity tend to develop devastating complications such as rubeosis iridis, macular ischemia, and neovascular glaucoma,<sup>[10]</sup> in the present case, even in the 3<sup>rd</sup> month of vascular occlusion, neovascularization or macular ischemia was not seen and the visual prognosis was excellent, due to good perfusion of cilioretinal artery in the affected eye. In this regard, this patient is one of the rare cases which vision is preserved despite the combined CRVO and CRAO. The most important challenge for this case is to determine the exact etiology.

Last, heterozygous mutation of A1298C MTHFR with an unhealthy lifestyle or Lyme disease with an atypical presentation may be the reason for this condition in such a young healthy person.

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## Conflicts of interest

There are no conflicts of interest.

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**Figure 4:** The left eye with the pale optic disc and attenuated arteries on the 20<sup>th</sup> day of the presentation

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