Branch Retinal Artery Occlusion with Paracentral Acute Middle Maculopathy in The Pediatric Age Group: A Case Report and Literature Review

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ABSTRACT

Retinal artery occlusion is usually seen acutely in elderly individuals with systemical disease and results in severe vision loss. It is rare in the pediatric age group. In this case report, we aimed to present a 15-year-old female child diagnosed with left inferior hemiretinal artery occlusion with paracentral acute middle maculopathy (PAMM) secondary to cardiac embolism due to mitral valve disease.

A 15-year-old female child presented with sudden and painless vision loss in the left eye. Visual acuity was 1,0 in the right eye and 0.8 in the left eye from the inferior half of the visual field. Anterior segment examination was normal. The fundus examination of the left eye revealed retinal whitening in the superior temporal and superior nasal of the the optic disc, the superior part of macula, the inferior half of macula and the inferior half of the retina, and segmentation in the blood column in the inferior branches of the retinal artery was observed, while the right eye was normal. On optical coherence tomography (OCT), diffuse thickening and hyperreflectivity in the superficial layers and shadowing in the outer layers of the retina were observed in the inferior macula and retina in the left eye. In the superior part of the macula, OCT revealed a characteristic hyperreflective band-like lesion on the inner nuclear layer consistent with PAMM. The patient was diagnosed with left inferior hemiretinal artery occlusion and her treatment was planned. The systemical examination of the patient revealed mitral valve stenosis and insufficiency.

When retinal artery occlusion is seen in the pediatric age group, a comprehensive etiological investigation is required. PAMM may be associated with BRAO due to mitral valve disease in a pediatric case.

Keywords: branch retinal artery occlusion, mitral valve disease, paracentral acute middle maculopathy, pediatric age group.

INTRODUCTION

Retinal artery occlusion (RAO) is an ophthalmic emergency that causes sudden onset vision loss. It has an incidence of 1 to 2 cases per 100,000 per year and is a major cause of acute vision loss[1]. In RAO cases, the embolism is more often caused by the artery-artery embolism of ipsilateral carotid artery or, less commonly origins from cardiac defects[2,3]. Although there are many different causes, some RAOs are due to other causes such as giant cell arteritis and vasculitis[2]. RAO can be classified clinically as central retinal artery occlusion (CRAO), branch retinal artery occlusion (BRAO), cilioretinal artery occlusion, combined retinal artery and vein occlusion. It can be arteritic or non-arteritic. Additionally, transient RAO, which is mostly caused by a migrating embolus or occurs as a result of a temporary decrease in ocular perfusion pressure or a sudden high rise in intraocular pressure (IOP) has been defined. RAO is extremely rare in the pediatric age group and most of the cases have a systemical pathology[4]. There is a large literature on the visual outcome of RAO, sources of embolism, it's relationship with systemical diseases, hematological abnormalities, and other risk factors. However, there are few studies on the pediatric age group.

Paracentral acute middle maculopathy (PAMM) was first defined by Sarraf et al. in 2013[5]. It is characterized by a hyperreflective band-like lesion around the inner nuclear layer (INL) on optical coherence tomography (OCT) which is caused by ischemia of the intermediate and/or deep retinal capillary plexus[6]. Although the exact etiology is unknown, retinal vascular diseases, systemical

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microvascular diseases or medical drugs/procedures that may affect the retina have been associated with the etiology[7].

In this case report, a 15-year-old female child diagnosed with left inferior hemiretinal artery occlusion with PAMM secondary to cardiac embolism due to mitral valve disease is presented with a literature review. To the best of our knowledge, although PAMM has been associated with BRAO before, a pediatric case of BRAO with PAMM due to mitral valve disease has never been reported.

CASE REPORT

A 15-year-old female child presented with the complaint of blurred vision in the left eye that started 6h ago. There was no pain with the eye movements and she had no relevant medical or family history.

In the examination; visual acuity was 20/20 in the right eye, and 16/20 in the left eye from the inferior half of the visual field with no refractive error. IOP was 16 mmHg in both eyes. Anterior segment examination was unremarkable. The fundus examination of the left eye revealed retinal whitening in the superior temporal and superior nasal of the the optic disc, in the superior part of macula, the inferior half of the macula and the inferior half of the retina, and segmentation in the blood column in the inferior branches of the retinal artery was observed, while the right eye was normal (Figure 1). With these findings, the case was diagnosed with left inferior hemiretinal artery occlusion. In order to lower IOP, local antiglaucomatous drops and acetazolamide tablets were given and ocular massage was applied. She was referred for further examination and treatment.

On OCT, diffuse thickening and hyperreflectivity in the superficial layers of the retina and consequently shadowing in the outer layers of the retina except the foveal depression were observed in the sections passing through the inferior macula and retina in the left eye. In the superior part of the macula, OCT revealed a characteristic hyperreflective band-like lesion on the inner nuclear layer consistent with PAMM (Figure 2). Fundus fluorescein angiography (FFA) showed normal arterial filling and arteriovenous transit time in both eyes, and no clinical finding related to PAMM was observed in FFA (Figure 3). No finding was detected in the left eye, except for optic disc staining in the late period. Systemical examination by pediatrics department showed no pathological findings. Carotid and vertebral artery doppler ultrasonography was normal. A transthoracic echocardiography performed by the pediatric cardiology unit demonstrated moderate mitral stenosis and insufficiency. It was reported that BRAO might have developed as a result of thromboembolism due to mitral valve pathology. Furosemide 40 mg 1x1 tablet, enalapril 1x5 mg tablet, acetylsalicylate 1 x 100 mg tablet and depo-penicillin 1.2 million iu 1x1 intramuscular injection (once in 21 days) treatment was initiated for bacterial endocarditis prophylaxis. Cranial magnetic resonance imaging was normal. Normal test results were found in the

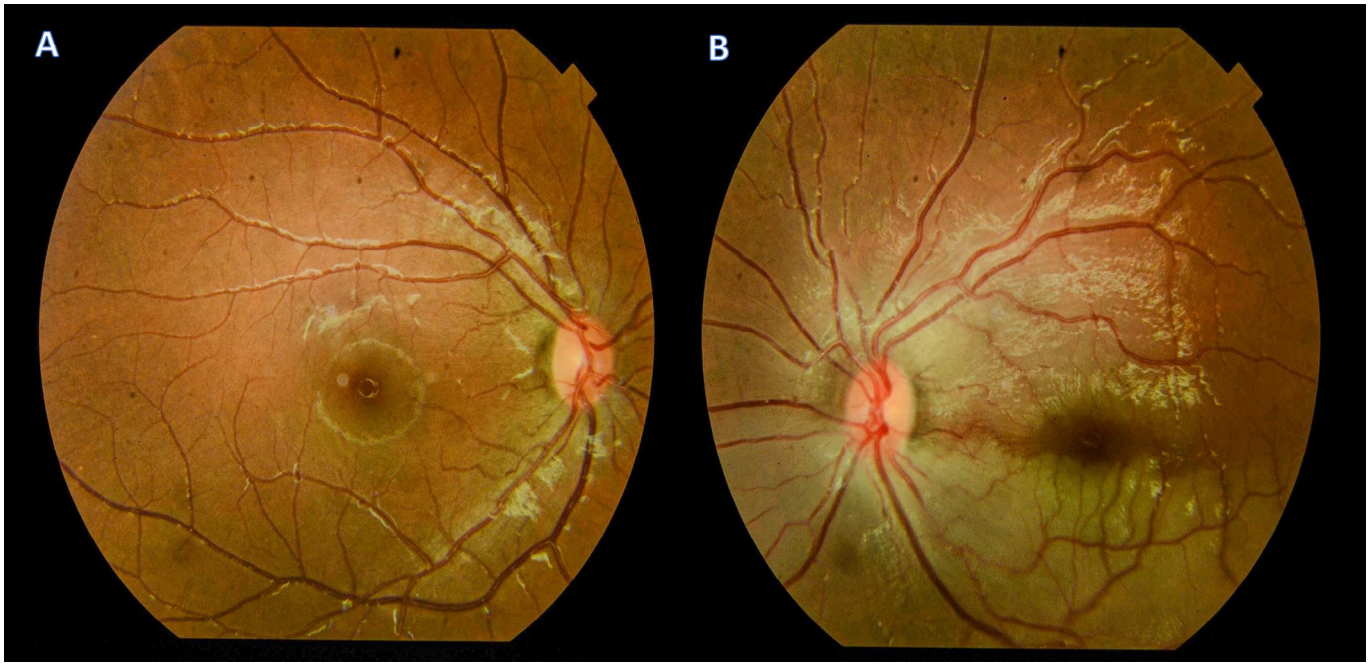

Figure 1: *Color fundus photograph of both eyes showing retinal whitening in the superior temporal and superior nasal of the the optic disc, superior part of macula, the inferior half of macula and the inferior half of the retina in the left eye* (B)*; and no finding in the right eye* **(A)**.

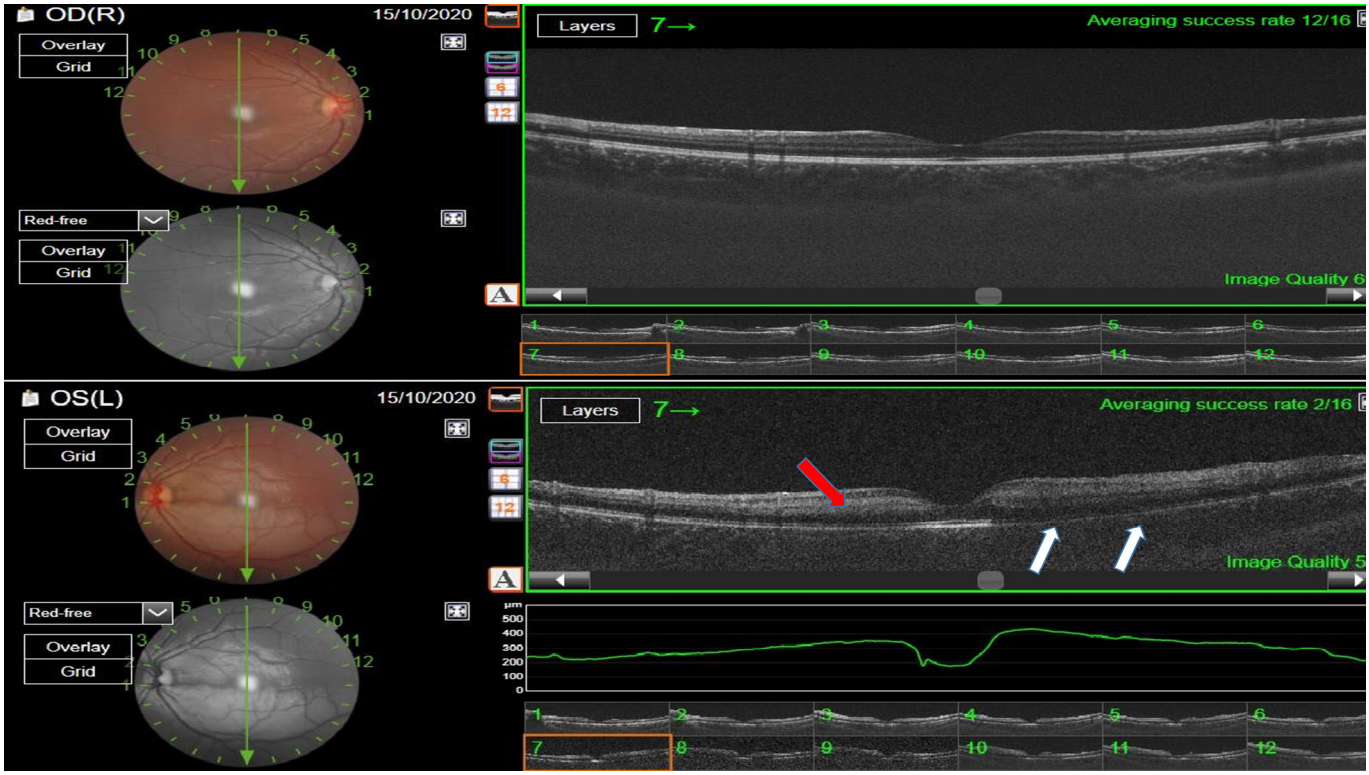

Figure 2: *OCT vertical sections display thickening and hyperreflectivity in the superficial layers of the retina and shadowing in the outer layers in the inferior macula (white arrows); hyperreflective band-like lesion on the inner nuclear layer consistent with PAMM in the superior part of the macula (red arrow). The right eye was normal.*

OCT: optical coherence tomography, PAMM: paracentral acute middle maculopathy.

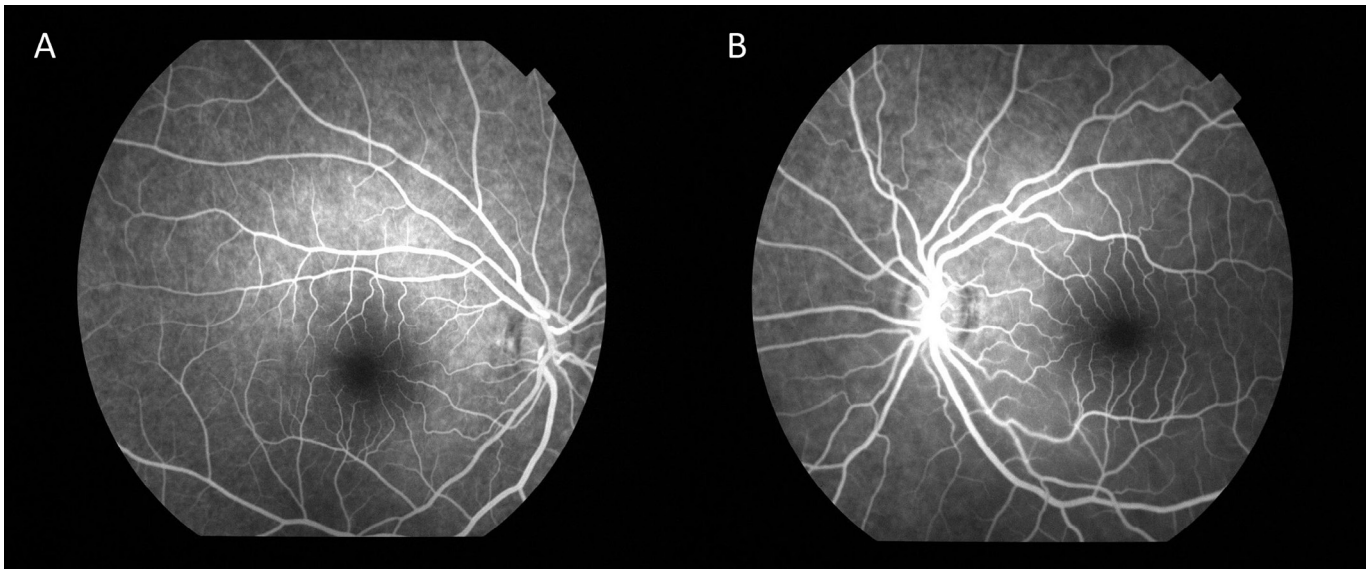

Figure 3: *Venous phase FFA images of both eyes. The right eye was normal (A), no perfusion defect related to PAMM in the left eye (B) was observed.*

FFA: fundus fluorescein angiography, PAMM: paracentral acute middle maculopathy.

laboratory analysis. Hyperbaric oxygen therapy (HBOT) was performed to the patient for 20 sessions. In the fundus examination performed 5 weeks later, the pathological whitening appearance of the retina had regressed, and a superior altitudinal visual field defect was observed in the visual field test (Figure 4). Retinal thinning in the area of RAO, disappearance of PAMM lesion and thinning of INL at the superior side of the macula was noted on OCT (Figure 5). Monthly follow-up was recommended with prescribing enalapril 1x5 mg tablet, acetylsalicylate

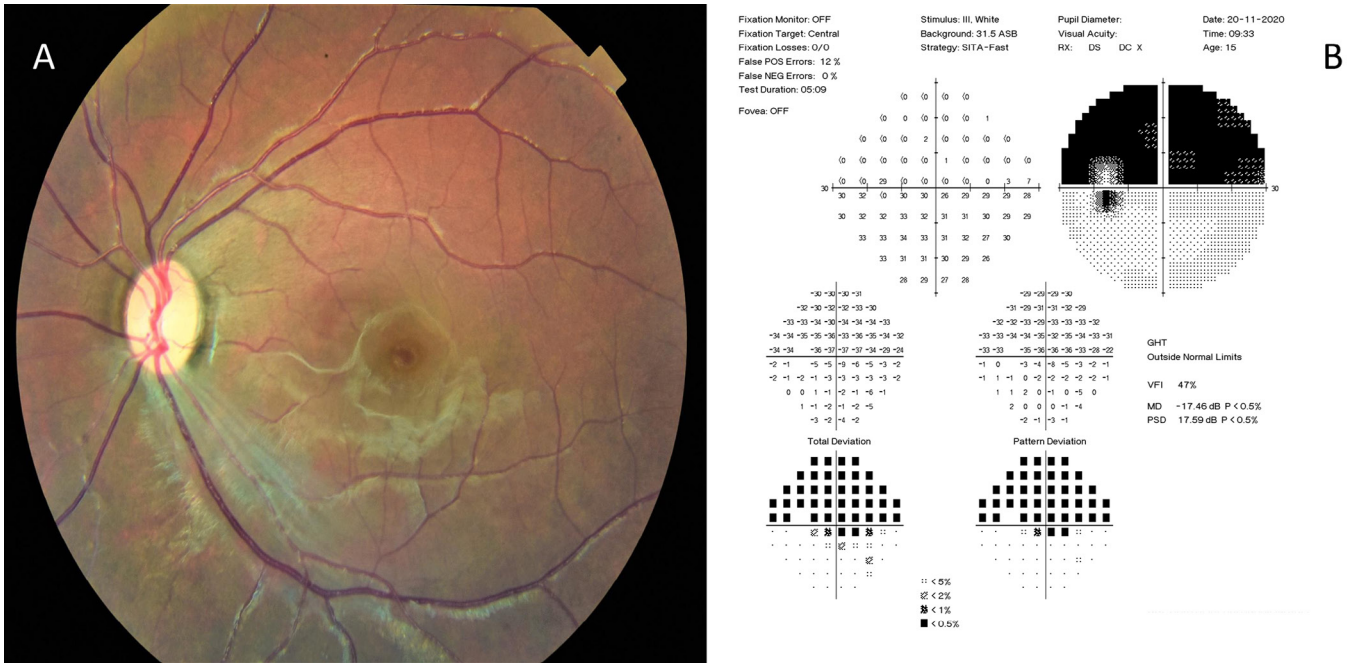

Figure 4: *Color fundus photograph and visual field test of the left eye at the end of 5th week. The pathological retinal whitening had disappeared* **(A)**, *and a superior altitudinal visual field defect was detected* **(B)**.

Figure 5: *OCT vertical section of the left eye at the end of 5th week. Retinal thinning in the area of RAO (white arrows), disappearance of PAMM lesion and thinning of inner nuclear layer at the superior side of the macula (red arrow) was remarkable.*

OCT: optical coherence tomography, RAO: retinal artery occlusion, PAMM: paracentral acute middle maculopathy

1 x 100 mg tablet and once in 3 weeks depo-penicillin 1.2 million iu 1x1 intramuscular injection therapy.

Written consent was obtained from the family of the case, indicating the permission to share.

DISCUSSION

RAO was first described in 1859 by von Graefe in a case of endocarditis with systemic multiple embolism[8]. Schweigger reported this pathology by ophthalmoscopy in 1864[9]. RAO is a well-known pathology with acute onset, resulting in severe visual loss due to superficial retinal ischemia[2]. It is frequently seen in elderly individuals[1]. RAO in children is extremely rare and it's incidence is less than 1/50.000 outpatients presenting to an ophthalmologist younger than 30 years old[4]. Although there are various etiological reasons, the most common cause of RAO in

elderly people is an embolism caused by carotid artery atherosclerosis. The most common cause in children and young adults is cardiogenic embolism[4,10]. In the literature, some of the RAO cases reported in children have been considered idiopathic because the etiology could not be determined[4,11].

Differential diagnosis of RAO in the childhood age typically includes hypercoagulation syndromes, heart diseases, endocarditis secondary to intravenous drug abuse, infectious endocarditis and orbital trauma. Less commonly reported causes are Susac syndrome, some infectious diseases, neoplastic diseases, lymphoma, myeloproliferative diseases, vasculitis, iatrogenic causes, fibromuscular dysplasia and even prolonged carotid compression of the mobile phone[4,10,12-16]. The most common etiological cause was valvular heart disease (19 %) in the study conducted by Greven et al. in 21 patients between the ages of 22-38 years with nontraumatic RAO[10]. In the study of Brown et al. in 27 patients between the ages of 9-29 years who were diagnosed with RAO before the age of 30, migraine and coagulation disorders were stated as the two most common causes[4]. No atheromatous lesions were detected in these cases, and it was emphasized that the etiology of RAO in young adults could be multifactorial. In the study of Ratra and Dhupper evaluating 35 eyes of 32 patients under the age of 40 with nontraumatic RAO, the most common cause was hyperhomocysteinemia (21.9 %)[13].

In this case, the cause of the left inferior hemiretinal artery occlusion was determined as mitral valve disease. Although the diagnosis of rheumatic heart disease can't be confirmed by the pediatric cardiology unit, it seems to be the most probable cause. No embolism was observed in the fundus examination and FFA of the case. However, in the studies of Hayreh et al., it was stated that the most of RAO cases were caused by microembolisms, and that the embolism could not be detected because it progressed to more end branches in the retinal vascular bed or disappeared[3]. In addition, hemodynamic related retinal ischemia may occur due to the sudden decrease in ocular blood flow caused by internal carotid artery stenosis or narrowed retinal arterioles. Animal studies have shown that platelet aggregation in atherosclerotic plaques in the carotid system may release serotonin, which may contribute to the reduction of retinal blood flow and play a role in RAO[3]. This case was diagnosed as left inferior hemiretinal artery occlusion. But, there was retinal whitening not only in the all inferior half, also in the superior part of the macula, in the superior nasal and superior temporal of the optic disc. Retinal whitening in the superior side may be explained with short-term occlusion of central retinal artery, and then the embolism may have migrated to inferior branch resulting in inferior hemiretinal artery occlusion. The time interval between the onset of blurred vision and reaching the ophthalmology clinic in this case is 6h, and the embolism that caused the occlusion may have disappeared by migrating to the end branches.

On OCT, the characteristic hyperreflective band-like lesion of PAMM on INL in the superior side of the macula has been noted. Rather than being a specific retinal disease, it is a new clinical finding caused by ischemia of the intermediate and/or deep retinal capillary plexus[5]. In some patients, no clinical finding in fundus examination or FFA can be seen[17,18]. Because of that OCT is the most important tool for diagnosis and follow-up. Although PAMM may occur as an isolated finding, it can usually be associated with retinal vascular diseases such as retinal artery and vein occlusions, diabetic retinopathy, sickle cell retinopathy and hypertensive retinopathy[7]. When PAMM occurs as an isolated finding, the patient usually presents with visual field defects and nonspecific visual loss. In such patients, a systemic microvascular disease/factor causing ischemia must be investigated[19]. There is no specific treatment for PAMM. Visual defect caused by PAMM may resolve spontaneously, but in cases with thinning of INL in the chronic period, paracentral scotoma may be permanent[20]. In this case, PAMM was associated with BRAO secondary to embolism caused by mitral valve disease. PAMM lesion disappeared and no permanent inferior visual field defect was observed related to PAMM lesion occured in the superior part of the macula, except the superior altitudinal visual field defect due to inferior BRAO.

There are many factors affecting the visual prognosis in patients with RAO. The duration of acute retinal ischemia is the most important visual prognostic factor. According to the study conducted by Hayreh et al. in monkeys, if retinal blood circulation is restored within 97 min, there is no damage to the retina, but the longer the ischemia lasts after this period, the greater the permanent damage occurs. CRAO lasting about 240 min results in massive, irreversible retinal damage. Therefore, the recovery rate and speed in terms of visual field and visual acuity are higher in transient RAO cases. Hayreh showed the possibility of spontaneous recovery of RAO, contrary to what is known correctly[2]. Hattenbach et al. showed that patients treated within 6.5h after vision loss had a better visual outcome than those treated between 6.5 and 12h after the onset of vision loss[21]. Except for the duration of retinal ischemia, the presence of a cilioretinal artery and nonarteritic occlusion are good prognostic factors for visual outcome[2].

In RAO cases, advocated treatments are as follows; ocular massage to dislodge the embolism to the periphery; anterior chamber paracentesis, oral acetazolamide, intravenous mannitol and topical antiglaucomatous drops to reduce

IOP; 95 % oxygen-5 % carbon dioxide inhalation and inhalation in a bag to increase ocular blood flow. Except from ocular massage, there is no evidence that the rest of the treatments provide any benefit[2]. Although it's effectiveness in the treatment of RAO has not been completely proven, we preferred to perform HBOT because of publications in the literature reporting beneficial effects in improving visual acuity[22]. Also pediatric age and early appeal of the case were other reasons for performing HBOT.

RAO is an indicator that there is a risk of vascular occlusion in other organs of the cases. In these cases, the risk of cardiovascular and cerebrovascular disease increases and life expectancy may decrease[23]. For this reason, it is necessary to conduct a rapid investigation after the diagnosis, especially in young cases. Ophthalmologists can evaluate the vascular structure of the patient by directly monitoring the retinal vessels compared to other medical specialists.

There were some limitations in this case report. Firstly, FFA could have been performed better. Because the arterial phase imaging of the left eye have not been captured well and the FFA device had no time counter. Secondly, ischemic changes of the intermediate and/or deep retinal capillary plexus couldn't be demonstrated due to the lack of an OCT-angiography device.

In conclusion, RAO cases in the pediatric age group require a more comprehensive etiological investigation. The recognition, treatment and clarification of the etiological cause of this emergency, which is more common in the elderly but rarely seen in the young age group, are important in terms of prognosis. PAMM may be associated with BRAO due to mitral valve disease in a pediatric case.

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