Bilateral combined central retinal artery and vein occlusion in a 3-year-old child with nephrotic syndrome

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Nephrotic syndrome (NS) is a common disease of childhood but ophthalmic manifestations are seldom reported. We report a rare occurrence of bilateral combined central retinal artery and vein occlusion in a 3-year-old with NS. The child presented with bilateral painless loss of vision, central pallid retinae with cherry red spots, vascular tortuosity, and retinal hemorrhages. There was delayed filling of the arteriolar circulation and a delay in arteriovenous transit time on angiography and increased central retinal thickening on optical coherence tomography. She was treated with oral steroids, subcutaneous low molecular weight heparin, and oral acetylsalicylic acid. The central retinae showed resolution of the hemorrhages, tortuosity, edema, and pallor within 3 weeks. Visual acuity recovered bilaterally to 20/360, 20/190, and 20/40 at 1, 3, and 6 weeks, respectively. We discuss the possible reasons for good recovery in our patient. Though bilateral combined central retinal artery and vein occlusion is rare in pediatric NS, the treating physician should be aware of this entity as it can be successfully managed.

Key words: Bilateral central retinal artery occlusion, combined central retinal artery and vein occlusion, low molecular weight heparin, nephrotic syndrome

Nephrotic syndrome (NS), with a worldwide incidence between 1.52-16.9/100,000/year, is characterized by a deranged renal filtering system with proteinuria, hypoalbuminemia, and hypercholesterolemia. It is associated with a hyperviscosity state, which can cause spontaneous peripheral arterial or venous thrombosis, renal vein thrombosis, and pulmonary emboli. Combined central artery and vein occlusion is very rare in the pediatric

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population.[2] In adults, bilateral combined retinal vascular occlusions have been reported in acquired immunodeficiency syndrome, systemic lupus erythematosus, hepatitis C, thrombotic thrombocytopenic purpura, protein C deficiency, and in pregnancy.[3,4] To the best of our knowledge, this is the first report of a bilateral combined occlusion with a good visual outcome in a 3-year-old female child with acute exacerbation of chronic nephrotic syndrome.

Case Report

A 3-year-old female child on treatment for NS since the age of 18 months, presented with sudden, acute, bilateral painless loss of vision in both eyes while she was admitted for the management of an acute exacerbation of NS elsewhere. A diagnosis of bilateral central retinal artery occlusion (CRAO) was made by the primary physician and emergency measures like anterior chamber paracentesis and ocular digital massage had been performed with no improvement. Four days later, the child presented to us with a visual acuity of perception of light in both eyes. On presentation, fundus examination revealed bilateral central pallid retina with a cherry red spot, increased vascular tortuosity, and few retinal hemorrhages, which was imaged on the RetCam (Clarity MSI, CA, USA) [Fig. 1]. The retina corresponding to the distribution of the cilioretinal distribution appeared better perfused than the surrounding macula.

Fundus fluorescein angiography (FFA) and spectral domain optical coherence tomography (SDOCT) were performed using the Spectralis (Heidelberg Engineering, Germany). The FFA revealed delayed filling of the arteriolar vascular tree and a delay in the arteriovenous transit time [Fig. 2]. There was an indistinct preservation of perfusion in the distribution of the cilioretinal artery suggesting its possible sparing. The SDOCT scan showed an increased retinal thickness of 816 and 788 microns in the right and left eyes, respectively [Fig. 3].

The child was treated for acute nephrotic disease by the pediatrician with oral steroids (prednisolone) 60 mg/m²/day for 4 weeks and tapered to 40 mg/kg/day for 12 weeks. Oral levamisole, an immunomodulator, was concurrently given during the tapering period (25 mg/day). For the hypertension, she was given nifedipine at the dose of 1 mg/kg/day, 8 hourly initially. Five days later the blood pressure (BP) stabilized at the 50th percentile for age. This increased on day 7 owing to the steroids to the 75th-90th percentile and long-acting amlodipine (0.5 mg/kg/day) was initiated. The BP was normal for age at the time of discharge. The child was empirically started on subcutaneous low molecular weight heparin (LMWH) which was given for 6 weeks (loading dose 1 mg/kg/12 hourly) followed by a maintenance dosage of 0.5 mg/kg/12 hourly which was titrated based on the Activated Factor X levels. After tapering of LMWH, the child was treated with oral acetylsalicylic acid (37.5 mg/day) for 6 months. The systemic parameters of NS including the proteinuria, hypertension, and urine output recovered over this period. The fundi showed resolution of pallor, hemorrhages, and tortuosity and disappearance of the cherry red spot [Fig. 4].

A repeat optical coherence tomography at 12 weeks showed resolution of macular edema with thinning of inner retinal layers in both eyes [Fig. 5]. Visual acuity measured using Teller Acuity Cards showed an improvement from light perception to 20/360, 20/190, and 20/40 in both eyes at 1, 3, and 6 weeks, respectively. This vision remained stable at 20/40 in both eyes at the end of 6 months with mild disc pallor at last visit.

Discussion

Systemic findings associated with combined retinal vascular occlusion includes disorders that are inflammatory, coagulopathic, and tumorous in nature.[2,4,5] The first reported case of a combined central retinal artery and vein occlusion in the pediatric age group was by Saatci et al. in a child with systemic non-Hodgkin lymphoma.[2] While there are a couple of other reports of combined retinal vascular occlusion in the young, there are none in NS.[6,7]

Hypercoagulable states, a known predisposing factor for vascular occlusions, is a recognized complication of NS. The pathomechanism of thromboembolism is attributed to a primary glomerular defect leading to loss of hemostatic proteins like antithrombin, protein C, and protein S. As a result, during active nephrotic-range proteinuria, there is a net shift in the hemostatic balance toward a prothrombotic state resulting in an increased risk of thromboembolism in these patients.[4] The combined arterial and venous occlusion in our case can be explained by two mechanisms. The central vein occlusion could have been secondary to the arterial occlusion. Disruption of arterial blood flow by emboli leads to stagnation of capillary blood flow followed by venous stasis and thrombi.[7] The second mechanism is progressive venous stasis due to an expanding thrombus in the central retinal vein (CRV).[8] As the thrombus completely blocks the CRV, the retinal venous pressure equals the arterial level leading to a CRAO.

To our best knowledge, bilateral combined retinal vascular occlusion in NS has not been reported. Our patient had a good clinical outcome in both eyes on follow-up. The visual acuity started improving within 1 week after presentation and continued until 6 months. It is currently unsure which factors could have influenced the visual recovery. We hypothesize some of these. First, the cilioretinal artery sparing seen in our patient could have contributed to the improvement in visual acuity as reported by Hayreh in two-thirds of patients with nonarteritic CRAO.[9,10] Second, the LMWH and acetylsalicylic acid may have played a role by balancing the prothrombotic state.[10] Third, the increased vascular tortuosity and retinal edema in our case could suggest that venous blood flow stasis secondary to hyperviscosity could be a contributory factor. Finally, the natural history of combined retinal artery and venous occlusions in very young patients is unknown and may have also influenced the final outcome.

Conclusion

Our case highlights a rare ocular complication in a relatively common systemic condition affecting children. Pediatricians must be aware of this sequela and institute a prompt ophthalmology referral for early management and follow-up.
Declaration of patient consent
The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest
There are no conflicts of interest.

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