A rare case of overlapping Sturge–Weber syndrome and Klippel–Trenaunay syndrome associated with bilateral refractory childhood glaucoma

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A 6-year-old girl presented with blurred vision and was found to have elevated intraocular pressure (IOP) and glaucomatous optic disc damage in both eyes. She also displayed capillary malformations on the face (port-wine stain), upper back and all four limbs, angiomatosis in the brain and had hypertrophy of the left upper and lower limbs typical of overlapping Sturge–Weber syndrome and Klippel–Trenaunay syndromes. She was initially managed with IOP lowering topical medications but required trabeculectomy in the right eye followed by Ahmed valve implantation in both eyes. Despite multiple measures over a 7-year period, her IOP still remained uncontrolled with gradual progression of the glaucomatous damage. This case exhibits a very rare occurrence of overlapping syndromes reported only a handful of times in literature. Most cases with Sturge–Weber syndrome have ipsilateral glaucoma affecting the eye on the same side as the port-wine stain. This case presented with bilateral refractory childhood glaucomas, which is exceedingly rare.

Key words: Bilateral refractory glaucoma, Klippel–Trenaunay syndrome, Sturge–Weber syndrome, trabeculectomy

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Sturge–Weber syndrome is a congenital, sporadic, encephalotrigeminal angiomatosis affecting about 1 in 50,000 and is characterized by facial capillary malformation called port-wine stain involving the eyelids, glaucoma, and vascular lesions seen in the ipsilateral brain and meninges.[1] Klippel–Trenaunay–Weber syndrome is a rare congenital mesodermal phakomatosis, affecting 1 in 100,000, predominantly involving limbs and is characterized by cutaneous hemangiomas, venous varicosities, and asymmetric hypertrophy of soft tissues and bones.[1,2] An overlap of Sturge–Weber syndrome with Klippel–Trenaunay syndrome is extremely unusual and has been reported in only a handful of cases previously.[1-3]

We report a case of a 6-year-old girl who presented to our clinic with overlapping features of both these syndromes and bilateral refractory glaucoma. We also describe the clinical course, surgical management, and long-term outcomes over half a decade of follow-up.

Case Report

A 6-year-old girl complained of diminished vision in both eyes for 3 months. The past medical history was significant for complex partial seizures for which she was on oral carbamazepine for the last 3 years. Her best-corrected visual acuity (BCVA) in both eyes was 20/32. Anterior segment evaluation of both eyes was unremarkable except for a scleral nevus seen in the left eye [Fig. 1a]. Fundus examination revealed a cup to disc ratio of 0.7:1 in the right eye and 0.6:1 in the left eye [Fig. 1b]. On applanation, tonometry intraocular pressure (IOP) was found to be 36 and 38 mmHg in the right and left eye, respectively. A four mirror gonioscopy revealed open angles with dense iris processes and increased trabecular pigmentation in both eyes. Central corneal thickness was 551 μ in both eyes. GDx with variable corneal compensation revealed significant retinal nerve fiber layer thinning in both eyes. The retinal examination was normal and did not reveal any choroidal hemangiomas.

Physical examination revealed erythematous lacy capillary network-like lesions over the face (port-wine stain) [Fig. 2a] and all four limbs. Hyperplasia of the gingiva [Fig. 2b] and reddish

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discoloration of lips, tongue, tips of fingers, and toes [Fig. 2c] were noted. In addition, extensive bluish discoloration of the skin was seen over the upper back. Her left upper and lower limbs showed mild hypertrophy [Fig. 2d].

Magnetic resonance imaging of brain and neck showed enhancement of pial angiomatosis in the parieto-occipital region, greater on the right side [Fig. 3]. Magnetic resonance angiography revealed congenital hypoplasia of the right internal carotid artery (ICA) and vertebral artery with compensatory enlargement of the left ICA and vertebral artery. Prominent medullary collaterals with hypoplasia of right parietal cortical vein were also observed.

Based on the typical clinical features and neuroimaging, the patient was diagnosed to have Sturge–Weber syndrome in combination with Klippel–Trenaunay syndrome.[1,2]

She was started on timolol eye drops 0.5% at baseline and pilocarpine eye drops was added after 5 months in both eyes. Despite this, IOP remained high in the right eye for which she underwent trabeculectomy with Ologen implant in the right eye after 2 months. However, after 2 years, there was bleb fibrosis and failure of trabeculectomy, so the patient underwent an Ahmed Glaucoma Valve (AGV) implant surgery in the right eye. The left eye also showed poor IOP control after 4 years of topical medication with travoprost 0.001%, dorzolamide 2%, and timolol 0.5% eye drops, and underwent AGV implantation.

On follow-up visits, the BCVA was maintained at 20/32 in both eyes. The IOP was 16 and 20 mmHg in the right and left eye, respectively. On subsequent visits, both eyes showed a well-formed conjunctival bleb around the AGV footplate and required only timolol for optimal IOP control. On the last follow-up visit, 2 years post-AGV, the IOP was 26 mmHg in the right eye and 32 mmHg in the left eye with a cup to disc ratio of 0.8:1 in the right eye and 0.7:1 in the left eye despite being on topical travoprost and timolol.

Discussion

We describe a rare case of overlapping Sturge–Weber and Klippel–Trenaunay syndrome with secondary glaucoma. Although the association of Sturge–Weber syndrome and ipsilateral glaucoma is relatively well established,[4] the coexistence of vascular malformations beyond the distribution of the trigeminal nerve and its influence on the IOP control have not been reported frequently. In addition, the glaucoma is ipsilateral to the port-wine stain in most cases, and bilateral affection is exceedingly rare.

Numerous pathophysiogenetic mechanisms have been suggested for these vascular malformations in Sturge–Weber syndrome such as venous dysplasia of the emissary veins in the intracranial circulation, neural crest alterations leading to alteration of autonomic perivascular nerves, and mutation of the GNAQ gene in the Sturge–Weber syndrome.[5] In addition, PIK3CA mutations have been implicated in the pathogenesis of malformative/overgrowth syndromes such as the Klippel–Trenaunay syndrome.[6,7]

Glaucoma in these syndromes is attributable to malformations of the anterior chamber angle or high episcleral venous pressure. We believe that a combination of underlying genetic factors in overlapping syndromes may alter the composition or ultrastructure of the trabecular meshwork in, as yet, unexplained ways. These variations may, in turn,

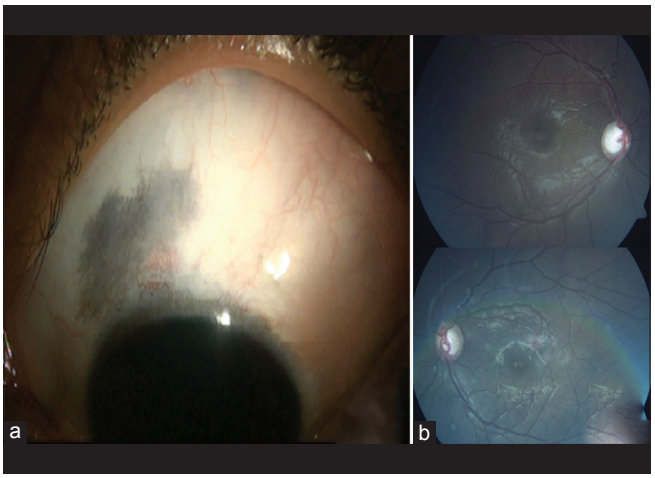

Figure 1: The ocular features including scleral discoloration (a) and bilateral glaucomatous disc damage (b)

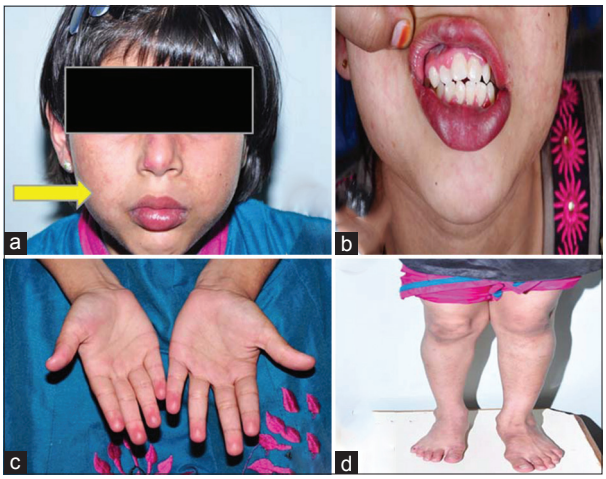

Figure 2: Systemic features including facial port-wine stain (arrow, a), gingival angiomatosis (b), reddish discoloration of the fingertips (c) and hypertrophy of the left lower limb along with cutaneous capillary malformations (d)

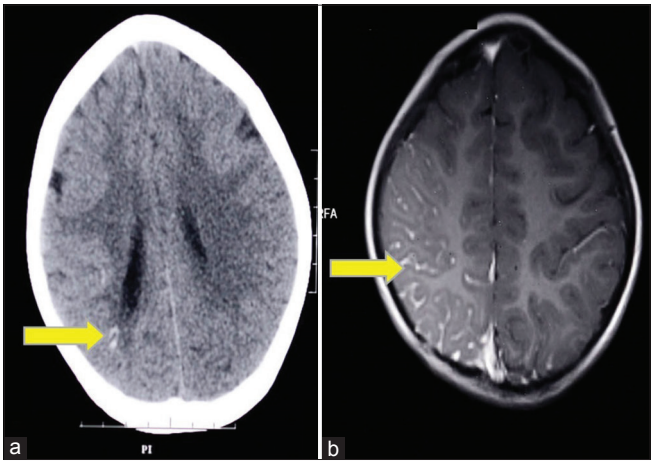

Figure 3: Computed tomography brain shows tram-track calcification in the right parieto-occipital region (arrow, a) and T1-weighted postcontrast magnetic resonance imaging image showing pial angiomatosis (arrows, b) in parieto-occipital region, predominantly involving the right hemisphere

make the glaucoma more refractory to medical and surgical management, as evidenced by our case where, over a period of 7 years, the child initially responded favorably, in terms of IOP control, to both trabeculectomy and AGV but gradually tended to become refractory again.

The child had convulsions for 3 years before presenting to us with trivial symptoms. Even though the child displayed copy– book systemic features, the diagnosis of the coexistent syndromes and glaucoma was only identified after the ophthalmic examination. Ophthalmologists should keep a high degree of suspicion to identify syndromic associations of childhood glaucoma and alert their pediatrician colleagues of this possibility.

Conclusion

We present a very rare case of overlapping Sturge–Weber syndrome and Klippel–Trenaunay syndrome with bilateral refractory glaucoma that was managed both medically and surgically over a 7-year period, but despite our best efforts, the IOP remained refractory, heralding a guarded prognosis.

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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