Phakomatosis Pigmentovascularis Coexisting with a Variant of Sturge Weber Syndrome - A Rare Occurrence

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Abstract
The spectrum of phacomatoses is wide and they share common pathophysiological changes. The various entities widely studied and being reported are Sturge Weber Syndrome (SWS), Klippel Trenaunay Syndrome and Phakomatosis Pigmentovascularis (PPV). Here we report a rare case of coexisting Phakomatosis clefoflemmea type of PPV along with a type 1 variant of Sturge Weber Syndrome. Co- existence of PPV with SWS is known but rare. Management of ocular manifestation especially glaucoma, is challenging in such neurocutaneous conditions but this particular case responded well to medical therapy for glaucoma. This case will help us broaden our outlook when dealing with various phakomatosis, keeping in mind overlapping signs of different syndromes and tendency of few syndromes to increase preponderance to malignant transformation which will require close follow up for the same.

Keywords: Phakomatosis Pigmentovascularis, Sturge Weber Syndrome, Choroidal hemangioma, Nevus flemmus

Introduction
The phakomatoses are a group of disorders characterized with variable expressivity, which manifest as multisystem involvement like neural, ocular and cutaneous in variable proportions with possible risks of malignant transformation in few. The first case of Sturge Weber Syndrome (SWS) was reported in 1860 by Schirmer whereas the first case of Phakomatosis Pigmentovascularis (PPV), a neurocutaneous entity was described by Ota et al in 1947. These entities often have a common pathophysiogenetic mechanism accounting for a confusing overlap in their clinical features. The overlap makes it difficult to isolate separate entities in the spectrum of phakomatoses. The choroid can be thickened in all the phakomatoses but PPV in particular needs follow up and careful examination due to higher risks of malignant transformation into melanoma seen in these cases.

Case Report
A 9 year old female child was brought by her parents with complaints of increasing size of both eyes since birth along with a white reflex in the left eye (Figure 1&2). They also complained of reddish discoloration of face and trunk since birth. She was born full term out of non consanguineous marriage, 3rd in order, other siblings were not having any similar complaints. The child underwent some surgery for removal of post auricular skin tag with skin harvesting done from the forehead. There was no history of seizures or neurological deficits. There was no history of ocular trauma or surgery. On general examination, the patient had normal vitals, she had port wine stain on her face along bilateral trigeminal nerve distribution with a scar over the forehead from previous surgery. She had alopecia, gingival hyperplasia with dental malocclusion and a post auricular tag. The nevus flemmus extended below the neck upto the waist in front and infrascapular region behind with a prominent dermal melanocytosis over the abdomen on the left side (Figure 1). There was hypertrophy of left upper limb along with nevus flemmus involving the overlying skin. The x ray showed no bony abnormality with the left upper limb (17 cm) being 2.5 cm more in circumference as compared to the right upper limb (14.5 cm) on physical measurement (Figure 3). Ocular examination revealed that in the right eye,
vision was finger counting 3 meters and in the left eye, she denied perception of light. Both eyes had melanosis oculi with buphthalmos and deep anterior chamber. The right pupil was reacting to light with clear lens whereas the left pupil was fixed and dilated, 6 mm, with sphincter tear at 1’o clock and a mature cataract. The fundus examination OD revealed 0.8 cup-disc ratio with a deep cup. On ultrasound B scan, OD appeared normal whereas OS showed a cataractous lens along with retinal detachment overlying a large choroidal hemangioma (Figure 4). On presentation, the pressures were raised in both eyes (OD 38 mm Hg, OS 36 mm Hg) which was managed by oral acetazolamide 10 mg/kg/day in 3 divided doses, and topical timolol 0.5% twice a day and latanoprost 0.005% at night was started, following which the intraocular pressure was 30 mmHg in the right and 24 mm Hg in the left eye in 2 days. On gonioscopy, the anterior chamber angle was open in both eyes. She was then continued on topical timolol maleate 0.5 % twice a day and latanoprost 0.005% at night, following which the intraocular pressure was under control (OD- 22 mm of Hg OS- 20 mm of Hg) and vision in the right eye improved to finger counting at 5 meters. On pediatric opinion, further tests were done - 2D echo was normal with 60% ejection fraction, Contrast Magnetic Resonance Imaging revealed multiple tortuous venous channel with associated hemiatrophy of the right cerebral hemisphere (Figure 5). Multiple tortuous venous channels are noted in right peri-sylvian subarachnoid space which were seen communicating with petrosal sinus and draining into the right cavernous sinus. The right cavernous sinus appeared asymmetrically enlarged as compared to the left side. The hematologic, biochemical, and urinary laboratory tests were normal. Abdominal ultrasonography revealed no abnormality. Doppler USG of vessels of the upper extremities was normal. The patient responded well to topical anti glaucoma medication and glaucoma surgery was avoided due to increased risk of suprachoroidal hemorrhage during trabeculectomy. Her intraocular pressure was well controlled with topical medication on follow up. The cataract surgery for the left eye was planned along with a posterior sclerotomy, under nil visual prognosis, after sustained control in intraocular pressure of that eye. Medical management of glaucoma was the mainstay of treatment for the right eye. Presence of nevus flemmas along with melanosis oculi, glaucoma and limb asymmetry fell into the Phakomatosis cesioflammea group of PPV and the choroidal hemangioma along with abnormal vascular channels in the brain accompanied with buphthalmos pointed towards a type 1 variant of SWS.

**Discussion**

Phakomatosis Pigmentovascularis is a rare congenital condition characterized by capillary malformations and dermal melanosis with or without ocular and systemic involvement. It was first reported by Ota et al in 1947. Only fewer than 250 cases have been reported till date, with preference to oriental population. The first case of PPV in India was reported in 2010. It was further classified by Hasegawa and Yasuhara into four types (I-IV) based on various pigmented lesions found with further subdivisions ‘a’ and ‘b’ based on whether they had only cutaneous or extracutaneous lesions respectively. Later in 2003, another type five (V) was added which comprised of cutis marmorata
and dermal melanocytosis. The working classification introduced by Happle in 2005⁹, classified PPV into 3 types. The first and most frequent type is Phakomatosis cesioflammea which features nevus flammeus and dermal melanocytosis with occasionally having nevus anemicus, focal alopecia, glaucoma and limb asymmetry, as was seen in the present case we reported. The second variety is Phakomatosis spilorosea which features nevus spilus and telangiectatic nevus occasionally associated with hemiparesis, seizures, lymphedema and limb asymmetry. Thirdly, Phakomatosis cesiomarmorata features nevus caesius which is Mongolian spots and cutis marmorata telangiectatica congenital, which may be associated with blue sclera, leg hyperplasia and asymmetry of cerebral hemispheres. The present case had nevus flemmus along with melanosis oculi, glaucoma and limb asymmetry and thus fell into the Phakomatosis cesioflammea. The ocular melanosis of PPV needs careful fundus evaluation and follow up to monitor for development of uveal melanoma.

The incidence of Sturge Weber Syndrome (SWS) is 1:50,000 infants with no predilection for sex. Shirley et al identified GNAO gene which effects the RAS pathway hence stimulates proliferation and inhibits apoptosis.⁹ Its characteristic findings are leptomeningeal angiomatosis, unilateral port wine stain and glaucoma. Based on symptoms, its has been classified into 4 types (1) classic SWS: leptomeningeal and facial angiomas, with/without glaucoma (2) port wine stain without cerebral involvement, with/without glaucoma (3) isolated leptomeningeal angiomia (4) classic form with systemic abnormalities e.g. tuberous sclerosis. The present case was a type 1 SWS with Port wine stain, cerebral hemiatrophy and glaucoma along with choroidal hemangioma. The mechanism of glaucoma in phakomatosis has multiple explanations like mechanical obstruction due to congenital malformations of angle, increased episcleral venous pressure, fluid hypersecretion by choroidal hemangiomas or premature aging and dysfunction of trabecular meshwork. This case had open angles on gonioscopy hence the pathophysiology of glaucoma was most likely due to raised episcleral venous pressure and choroidal hemangioma. She responded well to topical medications and was continued on latanoprost 0.005% at night in both eyes, offering a sustained control in the intraocular pressure.¹⁰ Prognosis of left eye remained poor due to underlying choroidal hemangioma and retinal detachment.

**Conclusion**

The occurrence of overlapping syndromes should always be kept in mind in cases of phakomatosis. Management of glaucoma is challenging due to varied underlying mechanisms, which in this case was managed conservatively. Prompt diagnosis, follow up and treatment of such cases can improve prognosis and quality of life of the patient.

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