Glaucoma in phakomatosis pigmentovascularis in a 4 year old African girl: A case report

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ABSTRACT

The phakomatosis syndromes are a group of neural crest disorders that bear many features in common. They include Sturge-Weber Syndrome, Naevus of Ota, Phakomatosis Pigmentovascularis and Klippel-Trenaunay Syndrome. They have numerous ocular manifestations in common, some of which are described in this case. Glaucoma is one of these manifestations and has peculiar characteristics when seen in association with phakomatosis syndromes.

Key words: Glaucoma, Phakomatosis, Naevus, Congenital, Pigmentovascularis

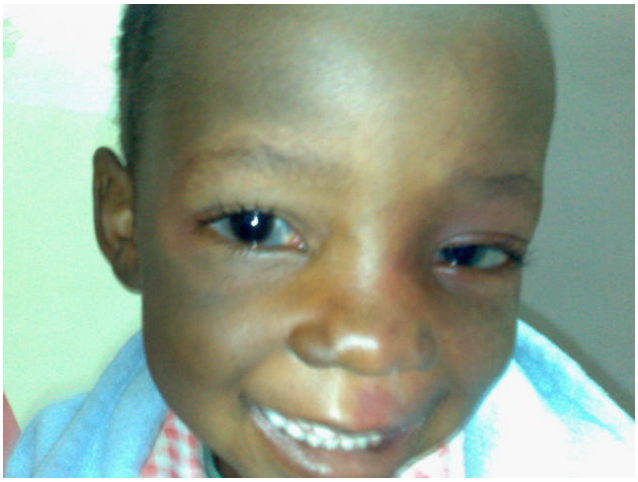
CASE REPORT

A rare case of a patient who was diagnosed with phakomatosis pigmentovascularis was encountered at Kenyatta National Hospital, a teaching and referral hospital in Kenya. It is of particular interest as the condition is very rare among Africans and has a high predisposition to the development of glaucoma. Consent to publish this case report including the photographs was given by the mother.

History of presenting illness: LW was a 4 year old female patient who hailed from Limuru town in Central Kenya. She was first seen on 31st March 2010. Her mother reported that the child had patchy discolouration of both eyes and her skin from birth. The ocular discolouration was described as being greyish in colour and patchy. The skin was described as being hyperpimented on the right side of the face and reddish on the left side of the face. Also reported was dark pigmentation of the abdomen and thighs. There was also reddish discolouration of the palms of the hands. The mother reported that since birth there had only been minor progression of the skin changes. No history of convulsions or other neurological deficits was given. Antenatal and birth history were uneventful. No history of other chronic or major illness was given. No prior admissions for medical or surgical reasons and no history of food or drug allergies were elicited. There was no history of similar manifestations in her siblings.

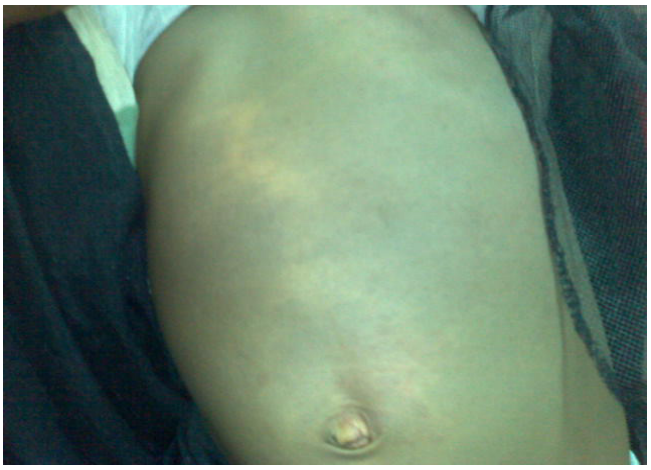
General and skin examination: The child was in good general condition. The right side of her face had hyperpigmentation of the skin in the area over the forehead, upper and lower eyelids, maxillary area and over the cheek and the mandibular area (Trigeminal, V2 dermatome). The left side of her face had thickened skin that was erythematous (Figure 1) and involved the upper and lower lids, nasal bridge, upper lip and cheek (Trigeminal V1 and V2 dermatomes) abnormal discolouration of the buccal mucosa.

Figure 1: Facial appearance



Her abdomen had a diffuse hyperpigmentation without sparing of the midline. Her thighs had a similar patchy, slate gray hyperpigmentation (Figure 2).

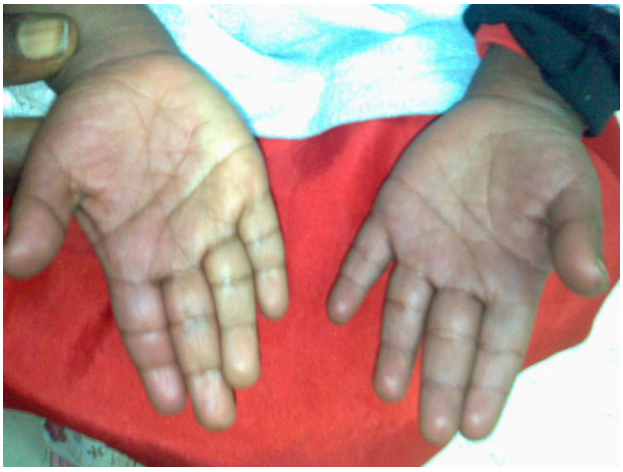
Figure 2: Appearance of skin over abdomen



Her right hand had erythematous lesions on the palms in the distribution of the radial (C6 dermatome) and median (C7 dermatome) nerves involving the thenar

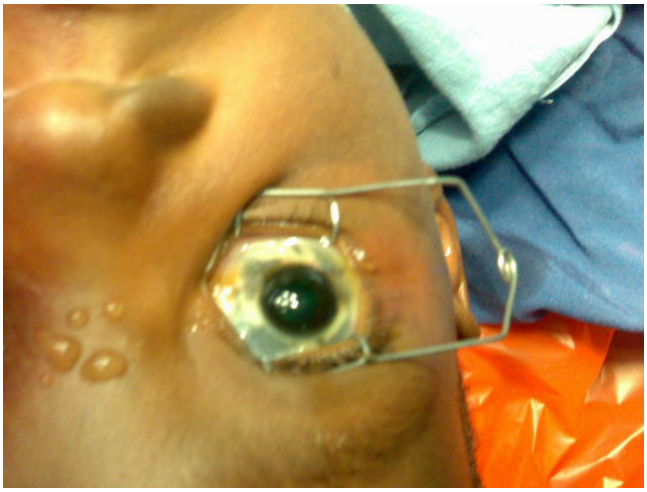
eminence, thumb, index and middle fingers. Her left hand had the same erythematous appearance but involving the entire palm and all the fingers thus involving C6, C7 and C8 dermatomes (Figure 3).

Figure 3: Appearance of palms



Ocular examination: Visual acuity by Lea's was 3/3 in the right eye (OD) and 3/30 in the left eye (OS). She had free extraocular motility in both eyes. Intraocular pressure (IOP) by tonopen was 12mmHg OD and 24mHg OS. Her OD had patchy, slate grey hyperpigmentation of the sclera. The cornea was clear and the anterior chamber was deep and quiet (Figure 4). The iris was brown in colour and the pupillary reaction was normal. She had a cup-to-disc ratio (CDR) of 0.7, the cup was not deep, and the macula was normal.

Figure 4: Appearance of right eye with wire speculum in place



The OS also had patchy slate-grey hyperpigmentation of the sclera. It also appeared buphthalmic. The cornea was clear, the anterior chamber was deep and quiet, the iris normal, the pupil had a sluggish reaction to light and the lens was clear (Figure 5). Fundus examination revealed a CDR of 0.9 with a deep cup and the ISNT (inferior-superior-nasal-temporal) rule was broken. The macula was normal (Figure 6).

Figure 5: Appearance of left eye with wire speculum in place

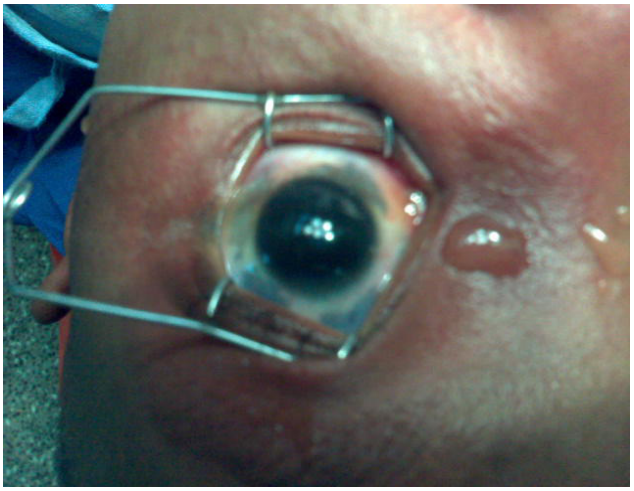
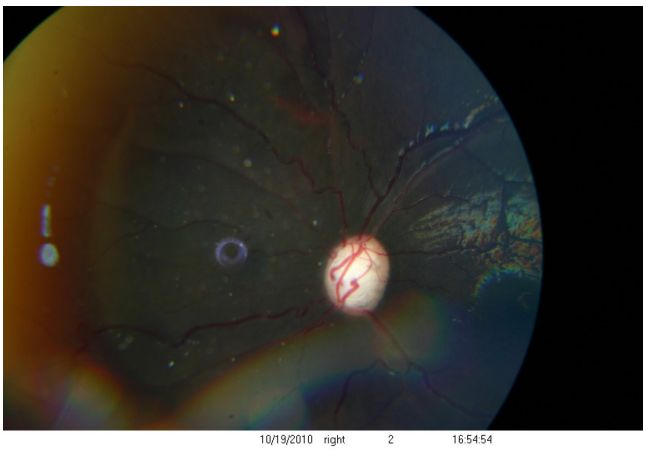


Figure 6: Appearance of left disc



Central Nervous System (CNS) examination: Her CNS examination revealed a GCS 15/15, normal power in all limbs, no cranial nerve palsies and no cerebella ataxia. A Computerised Tomography (CT) scan done showed hemiatrophy of the left side of the brain with frontal lobe atrophy.

Management: The child was started on Timolol 0.5% 12 hourly OS and booked for examination under anaesthesia (EUA) and OS trabeculectomy + 5 fluorouracil (5FU, 50mg/ml) which was done on the 2nd August 2010 (Table 1).

Table 1: Examination under anaesthesia findings

	OD	OS
IOP (mmHg) (On Timolol)	Perkins 12 Schiotz 14.6	Perkins 15 Schiotz 17.3
Horizontal corneal diameter (mm)	11.5	14
Axial length (AL)	21.6	25.02
Central Corneal Thickness (CCT) (μm)	483	475
Retinoscopy	+1.50DS/-0.5DC*90	-8.00DS
Fundoscopy	CDR 0.7. ISNT rule obeyed	CDR 0.9; deep cup; ISNT rule disobeyed; normal macula

Post-operative assessment: The patient was discharged on the 5th post-op day. The visual acuity was 3/3 OD by Lea's chart and counting fingers at 2m OS. The IOPs were 17mmHg OD and 9mmHg OS. The anterior chamber OS was deep. The patient was discharged home on ofloxacin antibiotic and dexamethasone steroid eye drops. She was reviewed one week later and visual acuity OS was still counting fingers at 2m and the IOP was 18mmHg. There was a diffuse bleb, the anterior chamber was deep and there was a normal retinal appearance with a CDR of 0.9. She was started on timolol 0.5% drops twice daily both eyes (OU) and dexamethasone was tapered off and she continued on ofloxacin OS. On subsequent follow-up ofloxacin was stopped. Vision remained at CF2m OS. IOP check revealed an IOP of 16mmHg OU and the patient was switched to betagan eye drops.

On review 6 months later the IOP was noted to have dropped significantly to 3 mmHg OS. She had a grade 2 Relative Afferent Papillary Defect (RAPD) and fundus examination revealed tortuous vessels, CDR of 0.9 and a normal macula. The hypotony was secondary to uveitis. Betagan was stopped in this eye and she was started on a tapering dose of Predforte (prednisolone acetate) for the uveitis. IOP rose to 5mmHg after 1 month and to 8mmHg after another month with a low diffuse bleb present. A choroidal effusion was however not ruled out. On her last review IOP was 8mmHg OD on betagan and 9mmHg in the OS on no ocular hypotensive drugs.

DISCUSSION

Phakomatosis Pigmentovascularis (PPV) is a condition that presents with extensive cutaneous vascular malformations and pigmentary nevi[1]. It was first described by Ota in 1947 and is characterized by defects of various organs, especially the eyes and nervous system. Four types have been described[2]. They are subdivided further into cutaneous or systemic disease (Tables 2 and 3)[3, 4]. It is found almost exclusively in Asians[1].

Table 2: Classification of phakomatosis pigmentovascularis (PPV) [3]

Type	Features
Ia, b*	Nevus flammeus + Nevus pigmentosus et verrucosus
IIa, b	Nevus flammeus + Dermal Melanocytosis± Naevus anemicus
IIIa, b	Nevus flammeus + Nevus spilus ± Nevus anemicus
IVa, b	Nevus flammeus +Dermal Melanocytosis +Nevus spilus ± Nevus anemicus
Va, b	cutis marmorata telangiectatica congenital + dermal melanocytosis

*a, Cutaneous disease; b, Systemic disease.
A simpler classification was suggested by Joshi *et al*[4].

Table 3: Simplified classification for PPV[4]

Type	Features
I	Capillary malformation and dermal melanocytosis
II	Capillary malformation and epidermal melanocytosis
III	Capillary malformation, and, dermal and epidermal melanocytosis

The cutaneous vascular malformation found in PPV is always naevus flammeus and this component is present in all except type V. The pigmentary abnormalities may consist of naevus pigmentosis verrucosus, naevus spilus, naevus anaemicus, or slate-grey pigmentation, which could be mongolian spots, naevus of Ito, or naevus of Ota. Naevus of Ota and aberrant Mongolian spots are the most common[5]. Ocular findings in PPV include bluish mottling or a more diffuse slate-grey colouration of the sclera.

PPV is a disorder of neural crest cell migration and differentiation. Dermal melanocytes are of neural crest origin[1]. The nevus of Ota seen as part of this syndrome shows dendritic melanocytes that are surrounded by fibrous sheaths and there is an increase in number, size and pigmentation of melanocytes.

Ultrastructural and immunohistochemical examination results of a nevus flammeus both showed absent perivascular nerves. This developmental anomaly of neural crest-derived vasomotor nerves was postulated to account for altered sympathetic modulation of vascular tone, leading to progressive vascular ectasia found in this disorder[1]. The ratio of female to male patients is approximately 1.34:1[4,6]. However the series by Montse *et al*[5] showed a large female predominance of 11:4 which may be a result of the female concern about cosmetic image[5]. PPV without systematic complications is benign and requires no treatment.

In a study by Teekhasaenee and Ritch[1] they observed that the most frequent central nervous system finding on Computed Tomographic (CT) scanning was frontal or temporal lobe cortical atrophy. A CT scan done on our patient showed hemiatrophy of the left side of the brain with frontal lobe atrophy. The characteristic CNS manifestation of Sturge-Weber Syndrome (SWS) is ipsilateral leptomeningeal haemangiomatosis, which causes atrophy of the cortical parenchyma of the brain, seizures, and frequently mental retardation[7]. It must therefore be entertained as a valid differential in this case due to the presence of the nevus flammeus and CNS findings. However the more extensive cutaneous vascular malformations and cutaneous pigmentation make it less likely.

Clinically it may present as ocular, dermal or oculodermal (naevus of Ota). Ocular features include multifocal, slate grey pigmentation of the episclera. With cutaneous involvement there is deep bluish or black hyperpigmentation of facial skin most frequently in the distribution of the 1st and 2nd divisions of the trigeminal nerve[8]. Associated findings include iris hyperchromia, iris mamillations, fundus and trabecular hyperpigmentation. Glaucoma is found in 10% of patients[8] and uveal melanoma especially in white people has also been documented[9]. The aetiology of glaucoma could be due to the direct infiltration of the trabecular meshwork by the accumulated melanocytes and may present as a gradual increase in IOP, an acute glaucoma with uveitis, as An Angle Closure Glaucoma (ACG) or as a congenital glaucoma[8]. Glaucoma has also been thought to be due to a faulty development of the angle (isolated trabeculodysgenesis) especially considering that the trabecular meshwork cells are of neural crest origin. It has also been thought to be due to increased episcleral venous pressure associated with an arteriovenous communication in an episcleral haemangioma[7]. In a study by Teekhasaenee and Ritch[1] they found that 100% of patients with both Episcleral Venous Malformation (EVM) and ocular melanocytosis developed glaucoma and that EVM was associated with a higher incidence of glaucoma than ocular melanocytosis. Those patients with more extensive pigmentation of the anterior chamber angle were also noted to have a higher incidence of glaucoma. In patients with oculodermal melanosis or phakomatosis pigmentovascularis the target IOP is set at the mid teens or close to the IOP of the fellow uninvolved eye if the condition is unilateral[8].

Treatment usually begins with either a prostaglandin analogue, alpha 2-agonist or a beta blocker. If the initial IOP is very high or one drug is not sufficient then combining drugs from different classes should be attempted. A carbonic anhydrase inhibitor could also be tried in combination with the above. Most authors do not advocate use of more than three drugs simultaneously[8]. As far as laser is concerned, there are no studies showing effectiveness in this condition specifically and there are no clear guidelines on how and where to apply the laser. The next step for children would be surgery. This would be trabeculectomy or trabeculotomy-trabeculectomy with mitomycin (0.2mg/ml for 2 min; 0.4mg/ml for 3-5min) or 5-fluorouracil 50mg/ml. Failure of trabeculectomy would necessitate the use of a glaucoma drainage device such as the Baerveldt implant or Ahmed valve[8]. In patients with naevus flammeus where trabeculodysgenesis is present, surgical treatment is preferred[10]. EUA with experience in paediatric gonioscopy and a flexible surgical plan is needed as surgery is dependent on what is found intraoperatively.

Trabeculectomy has been proposed as a primary treatment for glaucoma in children but can be technically challenging due to difficulty in raising a partial thickness flap in buphthalmos and adjusting tension in the perioperative period. Other common post-operative complications include hypotony, hyphema, flat anterior chamber and their risk for causing amblyopia. In cases in which conventional glaucoma surgery has failed to control IOP, cycloablative procedures such as cyclocryotherapy or laser cyclophotocoagulation done under general anaesthesia may lower the IOP. For our patient who had glaucoma in the setting of PPV then it would seem that starting anti-glaucoma medication pending surgery was a good decision and that surgery (trabeculectomy with 5-fluorouracil) which was performed at the nearest opportune moment was in keeping with current practice in management of glaucoma in patients with this condition. Combined trabeculotomy-trabeculectomy has been shown to have an overall success rate of 79% in children of African descent with primary congenital glaucoma[11]. 5-FU with combined trabeculotomy-trabeculectomy surgery appears to be a more effective procedure for congenital glaucoma refractory to goniotomy[12].

Looking at the effects of antimetabolites, combined surgery augmented with MMC has been noted to be associated with a more long-term effect on IOP control[13]. Trabeculectomy with adjunctive 5-FU and MMC may also be an option for the control of paediatric glaucoma with a poor surgical prognosis[14]. However, some studies have shown that it may also

serve as the primary procedure in a selected group of paediatric patients with glaucoma where it was shown that 86% of IOPs remained stable after surgery for up to 3 years after surgery[15]. Refraction will also be necessary to manage the high refractive error in the left eye due to the buphthalmos. Any attempt at correcting this refractive error will however have to take into consideration any amblyopia that may have set it, the high degree anisometropia and the aniseikonia that may result from its correction. Close follow-up to monitor further disc damage will also be necessary.

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