CASE REPORT

A Case of PHACES Syndrome with Successful Treatment of Facial Haemangioma With Propranolol

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We report a case of a 29 day old infant who was referred for evaluation of a vision threatening extensive segmental facial haemangioma. She developed a small reddish patch over her left cheek since birth which was progressively increasing in size and thickness to involve almost the whole of the left side of her face, associated with ulceration and abrasion of her left eyelid. She was born full term with birth weight of 3.2kg and was the second child of parents of non-consanguineous marriage. She was started on Prednisolone 2mg/kg/day and given intralesional triamcinolone and dexamethasone by the ophthalmologist. Ophthalmological assessment showed mechanical ptosis of the left eye and mild left retinal vessel tortuosity. A magnetic resonance imaging (MRI), magnetic resonance angiography (MRA) and magnetic resonance venography (MRV) of the brain revealed Dandy Walker malformation and right posterior parietal pial angiomatosis. In view of the presence of a facial segmental haemangioma and posterior fossa malformation, a diagnosis of PHACES syndrome was made. PHACES is an acronym for posterior fossa malformations, haemangiomas, arterial anomalies, cardiac abnormalities, eye abnormalities and sternal defects or supraumbilical raphe[1].

At 2 months of age she developed symptoms of cardiac failure with weak distal pulses and was started on anti-failure medications. An echocardiogram showed severe long segment coarctation of aorta and severe hypertrophic obstructive cardiomyopathy. Prednisolone was tapered and slowly stopped as it could cause worsening of the obstructive cardiomyopathy. Propranolol was initiated at a dose of 0.5mg/kg/day in 3 divided doses increased daily within 4 days to 2mg/kg/day in 3 divided doses as the facial haemangioma worsened with steroid tapering. Blood pressure, heart rate and blood sugar was monitored closely. Within a week of starting propranolol the facial haemangioma improved (Figure 1 and 2). When the oral corticosteroids was stopped at 3.5 months of age, there was no regrowth of the haemangioma. A month later the improvement of the facial haemangioma was more remarkable and 3 months later it was stable (Figure 3). A multi-slice CT Scan was also done which showed that there was aberrant origin of right subclavian artery and narrowed aortic arch. Ventriculoperitoneal shunt was inserted at 5 months of age due to progressive hydrocephalus secondary to the Dandy Walker malformation.

PHACES (OMIM 606519) is an acronym for posterior fossa malformations, haemangiomas, arterial anomalies, cardiac abnormalities, eye abnormalities and sternal defects or supraumbilical raphe [1]. Diagnosis of PHACES syndrome, proposed by Frieden in 1996 requires the presence of facial haemangioma >5 cm in size and one major or 2 minor criteria [2]. Major criteria include anomaly of major cerebral arteries, posterior fossa anomaly like dandy-walker complex, aortic arch anomaly, posterior segment ocular anomalies and sternal defect. The minor anomalies are persistent embryonic artery other than trigeminal artery, intracranial hemangioma or midline anomaly or neuronal migration disorder, ventral septal defect, anterior segment ocular anomalies and hypopituitarism [2].

Large cervicofacial haemangiomas are the hallmark of PHACES syndrome. Twenty percent of infants with large cervicofacial haemangiomas have PHACES syndrome. Most of the hemangiomas associated with PHACES have a unique appearance, described as "segmental". It is 8 times more likely to require treatment and 11 times more likely to cause complications [1]. Haemangiomas in PHACES syndrome are not always located on the face and can be found on the chest or arm. PHACES syndrome are much more common in females in 9:1 ratio [2].

Published reports of 317 cases up to 2009 showed that the most common extracutaneous anomaly associated with PHACES is posterior fossa anomaly occurring in one third of cases followed by sternal defects in one fifth and coarctation of aorta in 14.5 percent. Abnormalities of cerebrovascular system was also common involving dysplasia, stenosis, occlusion, agenesis or hypoplasia of arteries or aberrant origin or course of arteries [2].

67% of patients have only one extracutaneous manifestation of the syndrome [2]. Our case is unique as our patient has at least one extracutaneous manifestation from 3 organ systems. Infants with large, segmental, facial haemangioma should have a full workup for PHACES syndrome [1]. This includes physical examination and investigations to elucidate associated features of PHACES including an MRI and MRA of head and neck region, echocardiogram and ophthalmologic assessment.

Treatment is multidisciplinary and directed towards the associated anomalies. For complicated haemangiomas oral corticosteroids used to be the treatment of choice. Currently propranolol is used as first-line treatment for head and neck haemangiomas. The response of infantile haemangiomas to

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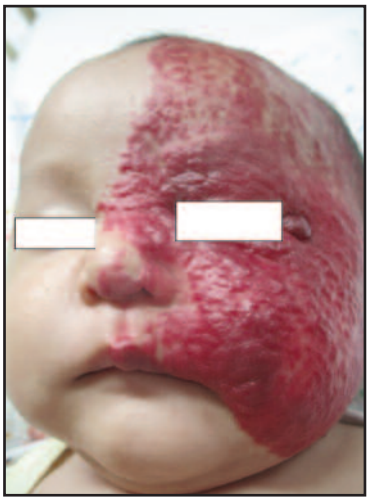

Fig. 1 : Before starting propranolol.

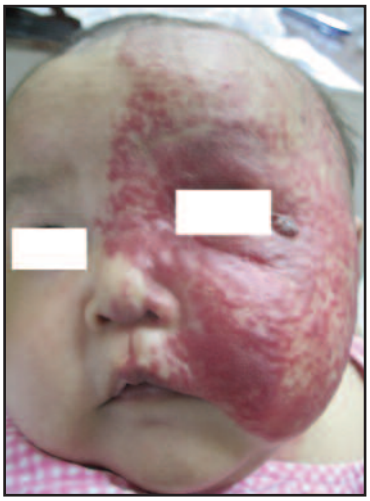

Fig. 2A: One week after starting propranolol.

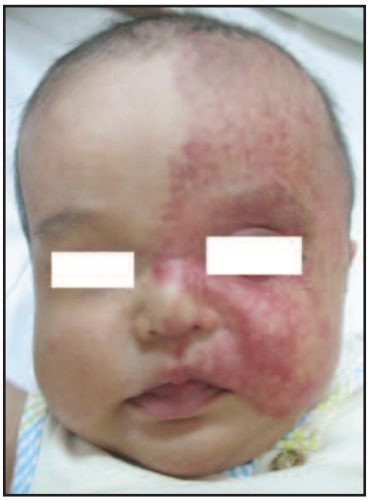

Fig. 2B: Three months after starting propranolol.

propranolol was first reported by Léauté-Labrèze C *et al.* In their series of 11 patients all responded to propranolol within 24 hours. Propranolol acts by causing vasoconstriction, decreased expression of vascular endothelial growth factor *(VEGF)* and basic fibroblast growth factor *(bFGF)* genes and triggering of apoptosis of capillary endothelial cells [3]. In patients with PHACES syndrome, caution must be exercised when initiating propranolol due to increased risk of acute ischaemic stroke if there is aplasia, hypoplasia, or occlusion of a major cerebral artery especially when >1 vessel is involved or if there is coarctation of the aorta [4]. The largest report of patients with PHACES syndrome treated with propranolol found that in a group of 32 infants only one patient developed a change in neurologic status during propranolol treatment: mild right hemiparesis that remained static and improved while propranolol was continued [5].

PHACES syndrome although uncommon maybe under diagnosed. It is important for physicians caring for patients with facial haemangiomas to be aware of this syndrome so that appropriate investigations are arranged to detect associated anomalies before complications arise.

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