Facial segmental haemangioma with PHACE Syndrome successfully treated with oral propranolol

Lim Tzyy Huei, MRCP[1], Evelyn Yap Wen Yee, Adv M Derm[2], Norhatizah Binti Samsudin, MMed(Radiology)[3]

[1]Medical Department Hospital Sultanah Nora Ismail, Batu Pahat, Johor,Malaysia, [2]Dermatology Department Hospital Pakar Sultanah Fatimah, Muar, Johor ,Malaysia, [3]Radiology Department Hospital Pakar Sultanah Fatimah, Muar, Johor, Malaysia

SUMMARY

PHACE syndrome describes the association of large segmental haemangioma with extracutaneous features (posterior fossa anomalies, arterial, cardiac, eye and endocrine anomalies). We report a case of segmental facial infantile haemangioma with PHACE syndrome treated successfully with oral propranolol without neurological sequelae.

INTRODUCTION

Propranolol is the first line treatment of complicated hemangioma.[1] The drug arrests the growth of the infantile hemangioma, reduces potential complications, and reduces psychosocial impacts. Its use is particularly of concern in PHACE syndrome due to the possibility of propranolol-induced hypotension and reduced cerebrovascular perfusion, leading to the increased risk of stroke in affected patients.[3]

CASE REPORT

A 1-month-old Malay boy presented with large segmental infantile hemangioma (more than 5cm in diameter) on the left upper eyelid and left frontotemporal region since day 5 of life (Fig. 1a). MRI/MRA Brain showed left extraconal enhancing lesion abutting the left globe (Fig.2a), vermian and left cerebellar hemisphere hypoplasia with enlarged left posterior fossa retrocerebellar arachnoid space communicating with 4th ventricle which is suggestive of Dandy Walker variant (Fig.2b).There was absence of A1 segment of left anterior cerebral artery with no abnormal territorial brain parenchymal changes which could be an anatomical variant. Right A1 dominance supplying the A2 segment of the left anterior cerebral artery was seen. There was normal flow signal of intracranial internal carotid arteries, anterior, middle and posterior cerebral arteries. ECHO, T4/TSH, eye assessment and other physical examinations were normal. Definite PHACE syndrome was diagnosed based on hemangioma > 5cm in diameter of the head plus structural brain abnormalities.5 He was started on oral propranolol at a dose of 0.5mg/kg/day at the age of 1 month old, slowly increasing over 4 days to 2mg/kg/day in 3 divided doses for the large hemangioma, which he tolerated well up to 1 year old. This resulted in marked involution of his hemangioma seen as early as 1 month post initiation (Fig.1b). He grew up with normal developmental milestones without neurological sequelae.

DISCUSSION

Diagnostic criteria of PHACE syndrome was revised in 2016 by Garzon et al.[5] Definite PHACE syndrome is defined as hemangioma > 5cm in diameter of head plus one major criteria or two minor criterias. Possible PHACE syndrome is defined as hemangioma > 5cm in diameter of head plus one minor criteria (outlined in Table I).

The progression of infantile hemangioma can be divided into 3 phases: proliferation (the first 5 months of life), stabilization and spontaneous involution (lasting for years). When there is a large segmental hemangioma of the face (>5cm in diameter), PHACE syndrome should be suspected as 31% of patients with large segmental hemangioma have PHACE syndrome.[2] The face is divided into segments: frontotemporal, frontonasal, maxillary and mandibular. Infantile hemangioma of frontotemporal/frontonasal segments has higher risk of ocular and CNS involvement. Vascular and structural involvement of the brain increase the risk of cerebrovascular accident. Cardiac malformation such as coarctation of the aorta also increases the risk of stroke. Patient should undergo physical examination, echocardiogram, MRI/MRA brain/neck and ophthalmology exam.

Oral propranolol is now considered to be first-line therapy for most infantile hemangioma that require treatment. It is a theoretical concern that propranolol induced hypotension and reduced cerebrovascular perfusion could increase the risk of stroke in such patients. Thus, these infants should be evaluated with MRI/MRA of head and neck and cardiac imaging to include aortic arch prior to starting propranolol.[3] MRA findings that confer the highest risk of stroke include severe long segment narrowing or non-visualization of the major head or neck arteries without adequate collateral circulation,[3] which was not seen in our patient. In a study by Metry D et al., in 2013 on the use of propranolol in 32 patients with PHACE syndrome, 7 patients were categorised as high-risk for stroke according to MRI features.[3] Only one patient developed mild hemiparesis that remained static and improved while propranolol was continued. In this case, oral propranolol was indicated as patient had large segmental hemangioma involving the left periorbital and left frontotemporal regions which may compromise normal visual development and cause disfigurement. Oral propranolol was started despite the absence of A1 segment of the left anterior cerebral artery as it has adequate collateral

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Corresponding Author: Dr. Lim Tzyy Huei
Email: savy117@gmail.com

Table I: Diagnostic criteria of PHACE Syndrome based on consensus-derived diagnosis and care recommendations 2016 by Garzon et al[5]

Definite PHACE	**Possible PHACE**
1. Hemangioma >5 cm in diameter of the head, including scalp PLUS one major criteria or two minor criteria 2.Hemangioma of the neck, upper trunk or trunk, and proximal upper extremity PLUS two major criteria	1.Hemangioma >5 cm in diameter of the head, including scalp PLUS one minor criteria 2.Hemangioma of the neck, upper trunk or trunk, and proximal upper extremity PLUS one major criteria or two minor criteria 3.No hemangioma PLUS two major criteria

Organ systems	**Major criteria**	**Minor criteria**
Arterial anomalies	Anomaly of major cerebral or cervical arteries,Dysplasia ,Arterial stenosis or occlusion with or without collaterals, Absence or moderate-severe hypoplasia of the large cerebral and cervical arteries,Aberrant origin or course of the large cerebral or cervical arteries 6.Persistent carotid-vertebrobasilar anastomosis	Aneurysm of any of the cerebral arteries
Structural brain	Posterior fossa brain anomalies, Dandy-Walker complex	Midline brain anomalies, Malformation of cortical development
Cardiovascular	Aortic arch anomalies,Coarctation of the aorta,Dysplasia,Aneurysm,Aberrant origin of the subclavian artery with or without a vascular ring	Ventricular septal defect,Right aortic arch/double aortic arch, Systemic venous anomalies
Ocular	Posterior segment abnormalities Persistent hyperplastic primary vitreous,Persistent fetal vasculature, Retinal vascular anomalies, Optic nerve hypoplasia, Peripapillary staphyloma	Anterior segment abnormalities,Micropht halmia,Sclerocornea,Coloboma,Cataracts
Ventral/midline	Anomaly of the midline chest and abdomen, Sternal defect,Sternal pit, Sternal cleft, Supraumbilical raphe	Ectopic thyroid hypopituitarism,Midline sternal papule/hamartoma

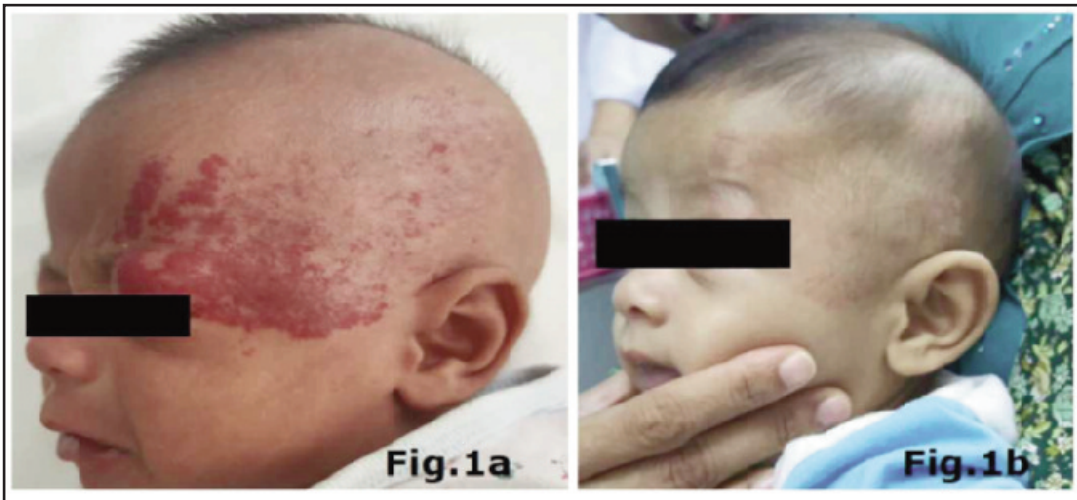

Fig.1a Segmental infantile hemangioma on the left upper eye lid and left frontotemporal region.
Fig.1b Marked involution of hemangioma after being treated with oral propranolol.

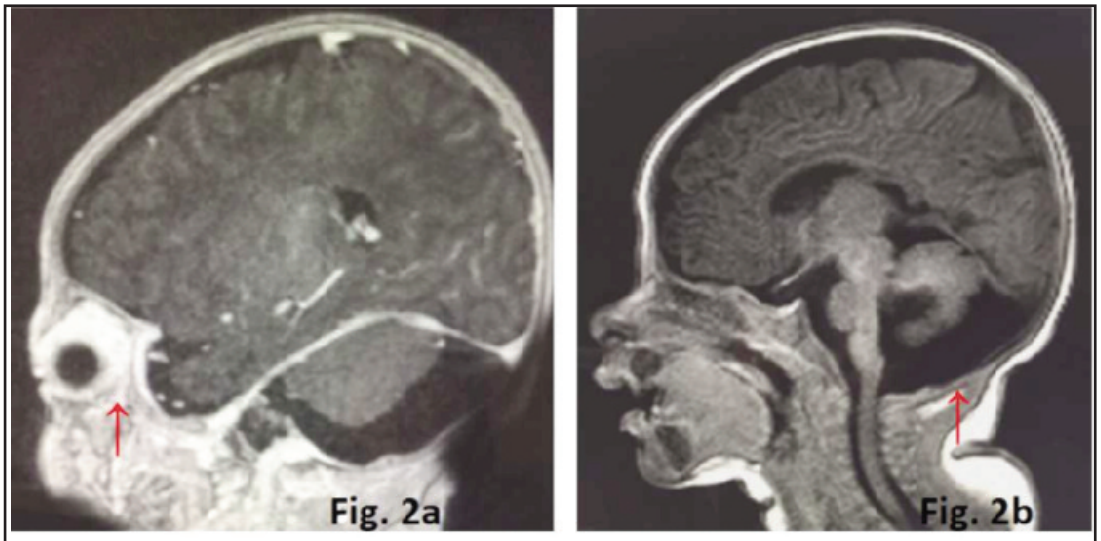

Fig. 2a MRI orbit T1W post contrast sagittal image showed left extraconal enhancing lesion (red arrow) abutting the left globe.
Fig. 2b MRI brain T1W sagittal image showed posterior fossa anomaly (red arrow) suggestive of Dandy Walker variant.

circulation and it is not high risk for developing stroke. In this case, the absence of A1 segment of left anterior cerebral artery can be a feature of PHACE syndrome but it could also be an anatomical variant.[4] In an article of normal variants of the cerebral circulation by Dimmick SJ in 2009, hypoplasia of anterior cerebral artery A1 segment is present in 10% of autopsies, and absence of A1 segment is seen in 1 to 2%.

CONCLUSION

In patients with high risk MRA features for stroke, the risks and benefits of propranolol should be discussed with paediatric neurologists. If the decision to administer propranolol is made, it should initially be given at the lowest possible dose, with slow upward dose titration and three times daily dosing to minimise abrupt blood pressure fluctuation that may increase the risk of stroke.[1]

CONFLICT OF INTEREST DECLARATION

The authors have no conflict of interest to declare.

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