CASE REPORT

PHACE syndrome misdiagnosed as a port-wine stain

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Accepted 26 May 2015

SUMMARY

We present the case of a boy born with a large macular, segmental vascular anomaly over the left face, initially diagnosed as a capillary malformation (port-wine stain) by the postnatal paediatric team. The vascular anomaly in the face then grew rapidly during the first few weeks of life and started to occlude the left eye, causing parental concerns about the infant's vision. A dermatological opinion established that the lesion was a segmental infantile haemangioma (IH). This, in combination with the posterior fossa malformation previously detected on antenatal scanning and confirmed by an MRI postnatally, satisfied the criteria for Posterior fossa abnormalities, Haemangiomas, Arterial abnormalities, Cardiac abnormalities and Eye abnormalities (PHACE) syndrome: a rare cutaneous neurovascular syndrome. This case highlights the diagnostic challenge posed by early phenotypes of haemangiomas as well as the importance of correctly diagnosing PHACE syndrome.

Cardiac abnormalities and Eye abnormalities (PHACE) syndrome.²

CASE PRESENTATION

An infant boy was born at 41+1 weeks by emergency caesarean section following failure to progress. The boy was noted to have a macular segmental vascular anomaly over the left face, initially diagnosed as a capillary malformation by the postnatal paediatric team.

An ultrasound scan at 24 weeks gestation had shown a large Dandy-Walker malformation with absent cerebellar vermis and large posterior fossa cyst. No other fetal malformations had been detected. He required a short stay on the Neonatal Unit due to hypoglycaemia, which soon resolved.

The vascular anomaly grew rapidly within the first few weeks of life and started to occlude the left eye, causing parental concern (figure 1 picture before treatment). This led to an attendance at the paediatric emergency department of our hospital, where he was admitted for observation and multi-disciplinary review, due to the rapid growth of the lesion. A dermatological opinion was sought, and the lesion was described as a large, vascular plaque extending from the left temporal scalp into the left orbit and zygoma. The clinical history and appearance of the lesion was in keeping with that of a segmental infantile haemangioma. An ophthalmology opinion established that the visual axis of the left eye was being affected, threatening the vision with risk of amblyopia.

Importantly, due to the additional presence of the Dandy-Walker malformation, a diagnosis of

BACKGROUND

Infantile haemangiomas (IH) are the most common benign childhood tumour with an estimated incidence of 4–5%.¹ IH in neonates are often misdiagnosed as capillary malformations (CM, syn. 'port-wine stain'), as they tend to be flat, before they start their rapid growth phase. Larger, segmental haemangiomas can be associated with structural abnormalities of the brain, cerebral vessels, eyes and heart in a disorder called Posterior fossa abnormalities, Haemangiomas, Arterial abnormalities,

Figure 1 Segmental haemangioma before treatment (left ptosis) with axial postgadolinium T1 MRI section demonstrating threat to vision (periocular haemangioma) and Dandy-Walker malformation.

To cite: Thomson J, Greig A, Lloyd C, et al. *BMJ Case Rep* Published online: [please include Day Month Year] doi:10.1136/bcr-2015-209889

Figure 2 Six months into propranolol treatment. Axial postgadolinium T1 MRI at 1 year.

PHACE syndrome was made. Through a multidisciplinary discussion it was decided that the patient would benefit from oral propranolol therapy.

INVESTIGATIONS

Prior to starting propranolol therapy the patient was worked up with the following investigations. An MRI brain and neck with MR angiography (MRA) was performed under general anaesthetic with appearances consistent with a haemangioma over the left face, extending into the orbit extraconally. The Dandy-Walker malformation was confirmed but no cerebral/carotid artery or cardiac abnormalities were seen. Routine bloods, an ECG and echocardiogram were all normal.

TREATMENT

The patient was started on oral propranolol initially at a dose of 1 mg/kg/day for 7 days. The dose was then increased to 2 mg/kg/day thereafter.

OUTCOME AND FOLLOW-UP

Our patient responded very well to treatment with flattening out of the lesion and no evidence of visual compromise. He continued propranolol therapy for a full year with no adverse effects and no evidence of regrowth after stopping the medication, also confirmed on repeat MRI scanning (figure 2). The Dandy-Walker malformation has caused minimal problems, and

Table 1 Diagnostic criteria for PHACE syndrome (adapted from Metry *et al* 2009)³

Organ system	Major criteria	Minor criteria
Haemangioma >5 cm diameter PLUS Posterior fossa and structural brain	1 major criteria =PHACE syndrome ► Posterior fossa anomaly – Dandy-Walker complex or unilateral/bilateral cerebellar hypoplasia/dysplasia	2 minor criteria =PHACE syndrome ► Enhancing extra-axial lesion with features consistent with intracranial haemangioma – Midline anomaly – Neuronal migration disorder
Arterial lesions	► Anomaly of major cerebral arteries – Dysplasia of the large cerebral arteries – Arterial stenosis or occlusion with or without moyamoya collaterals – Absence or moderate to severe hypoplasia of the large cerebral arteries – Aberrant origin or course of the large cerebral arteries – Persistent trigeminal artery – Saccular aneurysms of any cerebral arteries	► Persistent embryonic artery other than trigeminal artery – Proatlantal intersegmental artery (types 1 and 2) – Primitive hypoglossal artery – Primitive otic artery
Cardiac abnormalities	► Aortic arch anomaly – Coarctation of aorta dysplasia – Aneurysm – Aberrant origin of the subclavian artery with or without a vascular ring	► Ventricular septal defect ► Right aortic arch (double aortic arch)
Eye abnormalities	– Posterior segment abnormality – Persistent fetal vasculature (persistent hyperplastic primary vitreous) – Retinal vascular anomalies – Morning Glory disc anomaly – Optic nerve hypoplasia – Peripapillary staphyloma – Coloboma	► Anterior segment abnormality – Sclerocornea – Cataract – Coloboma – Microphthalmia

he subsequently made adequate progress with speech and motor development.

DISCUSSION

'PHACE' is an acronym for Posterior fossa abnormalities, Haemangiomas, Arterial abnormalities (often in the brain), Cardiac abnormalities and Eye abnormalities (eg, microphthalmos).

The diagnosis of PHACE syndrome requires the presence of a facial segmental haemangioma larger than 5 cm plus one major diagnostic criterion (or two minor criteria).³ Table 1 below outlines the major and minor diagnostic criteria in the relevant organ systems. In our case, the presence of the Dandy-Walker malformation, a major criterion, satisfies the diagnostic criteria.

Recognition of a diagnosis of PHACE syndrome is important in terms of prognosis, as the association with cardiovascular and brain abnormalities may carry significant morbidity. If a diagnosis of PHACE syndrome is suspected, the workup should include: MRI brain and MRA of the head and neck vessels, an echocardiogram and eye examination.

Shortly after birth, segmental haemangiomas may have a unique, 'telangiectatic' appearance or present as a faintly erythematous plaque. It is these early phenotypes, before the rapid growth phase starts, that can easily be mistaken for CMs.³ It is important to be aware of the main differences between these two types of vascular malformations: Haemangiomas are benign proliferations of endothelial cells that grow rapidly in the first year of life and spontaneously involute in childhood, while CMs are composed of ectatic vessels in the papillary dermis and persist throughout a patient's life.⁴

Recognition of segmental IH is important, since up to 30% will also have a diagnosis of PHACE syndrome.⁵

The first published use of propranolol for complex IHs in 2008 has revolutionised their management, providing a safe, effective and usually well-tolerated alternative to oral prednisolone.⁶ Its use should be considered in cases where haemangiomas cause severe disfigurement or impair vital or sensory functions.⁶

Learning points

- ▶ Infantile haemangiomas (IH) can often be mistaken for capillary malformations (port-wine stains) in their early stages before the rapid growth phase.
- ▶ Larger, segmental facial haemangiomas of the face are associated with Posterior fossa abnormalities, Haemangiomas, Arterial abnormalities, Cardiac abnormalities and Eye abnormalities syndrome in up to 30% of cases.
- ▶ Propranolol is a safe and effective treatment for IH. Multidisciplinary team involvement and workup with MRI/ MR angiography head and neck vessels, an echocardiogram and eye examination is advised.

Contributors JT conceptualised and drafted the initial manuscript, revised it and approved the final manuscript as submitted. CF and AG conceptualised the manuscript, revised it and approved the final manuscript as submitted. CL contributed the MRI and reports and approved the final manuscript as submitted. DM conceptualised revised and approved the final manuscript as submitted.

Competing interests None declared.

Patient consent Obtained.

Provenance and peer review Not commissioned; externally peer reviewed.

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