CASE REPORT

Concomitant carotid aplasia and basilar artery occlusion in a child with PHACES syndrome

Noel Delgado,¹ Jason J Carroll,² Philip M Meyers²¹Columbia University College of Physicians and Surgeons, New York, USA²Department of Radiology, Columbia University College of Physicians and Surgeons, New York, USA**Correspondence to**
Noel Delgado,
nd2467@columbia.edu

Accepted 1 August 2017

SUMMARY

We report a case of an 8-year-old girl with posterior fossa abnormalities, haemangioma, arterial lesions, cardiac abnormalities or coarctation of the aorta and eye abnormalities syndrome with right carotid aplasia and complete basilar occlusion. The patient initially presented at 2.5 weeks of age with a growing right facial haemangioma involving segments 1, 3 and 4. Initial MRI at 2.5 weeks of age revealed an extraconal right orbital haemangioma without posterior fossa abnormalities and MR angiography (MRA) 3 weeks later showed right internal carotid aplasia. A follow-up MRA and cerebral angiography at 8 years of age revealed a complete occlusion of the basilar artery that was not appreciated on previous imaging. Neurological function remains normal, meeting all age-appropriate milestones.

BACKGROUND

Posterior fossa abnormalities, haemangioma, arterial lesions, cardiac abnormalities or coarctation of the aorta and eye abnormalities (PHACE) syndrome is a rare neurocutaneous disorder of unknown aetiology, characterised by facial haemangiomas plus one or more extracutaneous abnormalities involving the eyes, heart, major arteries and brain.¹ When sternal cleft or midline raphé is present, the extended acronym PHACES is used. While congenital and/or progressive craniocervical vascular abnormalities are common in cases of childhood PHACES syndrome, there is no current literature describing basilar arterial occlusion in these patients.

CASE PRESENTATION

A 2.5-week-old girl presented with a rapidly progressing right facial haemangioma involving segments 1, 3 and 4 that was not initially seen at birth (figure 1). She was born at 36.5 weeks gestation to a gestational surrogate, from an in vitro fertilisation with twin gestation. The pregnancy and delivery were uneventful, and her fraternal twin brother remains phenotypically normal. At birth, she was noted to have two small midline haemangiomas on her chest as well as a sternal cleft. These combined findings prompted further evaluation for PHACES syndrome.

Initial MRI of the brain at 2.5 weeks revealed an extraconal right orbital haemangioma but did not show any posterior fossa abnormalities. Follow-up MR angiography (MRA) 3 weeks later showed several vascular anomalies, including a dominant

Figure 1 Schematic representation of this patient's infantile facial haemangioma (involving segments 1, 3 and 4), as seen at birth. Red areas indicate haemangioma involvement.

left A1 segment, diminished calibre of the distal right posterior cerebral artery branches and right internal carotid aplasia (figure 2). Imaging of the posterior circulation showed a patent basilar artery at the time (figure 3).

Cardiological assessment via transthoracic echocardiogram (TTE) showed a patent foramen ovale with bidirectional flow but normal cardiac function and otherwise normal intracardiac anatomy. There was no evidence of aortic coarctation. A slight blood pressure differential was subsequently noted on Doppler ultrasonography of the right (75 mm Hg, systolic) and left (80–90 mm Hg, systolic) arms at 11 months of age, however, workup with TTE at the time was inconclusive for tortuosity or abnormal origin of the subclavian artery. Initial ophthalmological evaluation of the right eye showed normal visual acuity, without any structural abnormalities. Given the vision-threatening orbital involvement of the haemangioma, she was started on prednisolone 1.9 mg/kg/day and subsequently on propranolol 1 mg/kg/day divided three times daily.

Routine repeat MRA was performed at 8 years of age, which revealed interval occlusion of the

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To cite: Delgado N, Carroll JJ, Meyers PM. *BMJ Case Rep* Published Online First: [please include Day Month Year]. doi:10.1136/bcr-2017-221055

Figure 2 MR angiography at 5.5 weeks of age, demonstrating right internal carotid artery aplasia (arrow).

midbasilar artery in addition to the previously seen right internal carotid artery aplasia (figure 4). Postocclusion dilatation of the distal basilar artery with decreased flow-related signal in the bilateral posterior communicating arteries was seen as compared with the prior imaging performed at 5.5 weeks of age. Catheter cerebral angiography confirmed a complete midbasilar occlusion (figure 5) and newfound fusiform ectasia of the right subclavian artery with mild band-like narrowing, resulting in a right subclavian steal phenomenon. Furthermore, decreased relative cerebral blood flow in the right cerebral hemisphere was noted on arterial spin labelling (ASL) perfusion scan of the brain (figure 6), although the patient's neurological and cognitive functions remained normal.

Figure 3 Posterior circulation MR angiography at 5.5 weeks of age, showing a patent basilar artery.

Figure 4 MR angiography at 8 years of age of the circle of Willis (three-dimensional time-of-flight technique), demonstrating right internal carotid artery aplasia (arrow) and complete basilar artery occlusion (arrowhead).

OUTCOME AND FOLLOW-UP

The patient has remained clinically stable, without obvious neurological symptoms since last neurological imaging was performed. She is currently in second grade and is doing well in school. Moreover, she has many friends and is active in sports,

Figure 5 Conventional catheter-based angiogram at 8 years of age of the posterior circulation after contrast injection into the left vertebral artery, illustrating complete midbasilar artery occlusion (arrow).

Figure 6 Arterial spin labelling perfusion scan at 8 years of age with diffuse decreased relative cerebral blood flow to the right cerebral hemisphere.

practices gymnastics and plays the piano. The importance of avoiding contact sports and any other sports that risk vascular injury to her unaffected side has been discussed with the family and will be an important aspect of her care moving forward. She is currently scheduled for a follow-up MRI/MRA in 12 months.

DISCUSSION

Previous studies on cerebral vasculopathy in PHACES syndrome suggest that up to 77% of cases exhibit cerebral vascular anomalies.² In most reported cases, the cerebral and cervical arterial anomalies occur ipsilateral to the facial haemangiomas or bilaterally.³ Examples of carotid dysgenesis in PHACES syndrome are common and have been reported in the literature.^{4–6} Our case of concomitant carotid aplasia with subsequent basilar occlusion has not been previously reported in children with PHACES syndrome.

The underlying pathophysiology of PHACES syndrome remains uncertain. However, several mechanisms have been proposed, including early neural crest cell damage, vascular growth factor deregulation, improper signalling mechanisms and genetic insult.^{2–10} As suggested by Bhattacharya *et al*,¹⁰ inappropriate vascular apoptotic and proliferative signalling may reconcile the often-coexisting aplasia and progressive steno-occlusive vascular disease seen in PHACES syndrome. In the ‘improper signalling’ model, vascular aplasia occurs due to inappropriate regression and apoptotic signalling cascades during early embryogenesis. Meanwhile, progressive arterial occlusion may result from centripetal proliferation and luminal reduction from unrepressed proliferation and delayed apoptosis of persistent vascular cells.⁹

While an early neural crest cell insult affecting neural crest cell migration may explain the carotid aplasia seen in this patient, it

would not account for delayed occlusion of the mesoderm-derived basilar artery.^{11 12} The coexisting carotid artery aplasia and late-onset occlusion of the basilar artery, in this case, is more consistent with a model of inappropriate or poorly timed apoptotic and proliferative signals. Although speculative, we suspect that the same improper signalling that led to aplasia of the right carotid artery is responsible for the failure of the basilar artery in this patient. In particular, we postulate that early dysgenesis and non-fusion or normal fusion with subsequent vascular proliferation of the primitive right basilar artery may have led to occlusion of the basilar artery (figure 7).

Aplasia, hypoplasia or occlusion of a major cerebral artery is associated with significant increase in risk for developing acute ischaemic stroke (AIS) in children with PHACES syndrome, especially when more than one vessel is involved.¹³ Moreover, high-grade stenosis in these patients increases the risk for development of moyamoya-like pial and meningeal vascular collaterals. Simultaneous carotid aplasia and basilar occlusion place this patient at significant risk for developing AIS. Decreased relative cerebral blood flow of the right hemisphere seen on ASL perfusion imaging in this patient is concerning for possible future ischaemic events in that region. However, given the lack of neurological symptoms in this patient, the ASL findings may likely represent a delay in transit time rather than true cerebral hypoperfusion.¹⁴

Prevention and management of AIS in patients with PHACES and multiple arterial anomalies present a distinct challenge to physicians. Direct methods of vascular revascularisation such as middle meningeal or superficial temporal artery to middle cerebral artery bypass are technically difficult in children due to small donor and recipient vessels and have not been reported in PHACES. Indirect revascularisation procedures, such as pial synangiosis, on the other hand, have been more successful in symptomatic patients.^{15 16} Intervention for primary stroke prevention can be performed in patients with progressive vaso-occlusive disease. However, surgical intervention was not pursued in this case due to overriding concerns that adequate compensatory flow and lack of frank ischaemia could prevent successful vascular collateral formation. Furthermore, it was deemed that an early failed synangiosis procedure with subsequent scarring might hinder or preclude the feasibility of future intervention. Literature on the ideal timing of surgery and the indications for prophylactic revascularisation in these cases remains lacking, however, and further studies are necessary to

Figure 7 Right internal carotid artery aplasia and basilar artery occlusion, due to non-fusion or occlusion of an absent or abnormal primitive right basilar artery. BA, basilar artery; ICA, internal carotid artery.

Learning points

- ▶ Vascular dysgenesis is not static in posterior fossa malformations, haemangiomas, arterial anomalies, cardiac defects, eye abnormalities, sternal cleft and supraumbilical raphe (PHACES) syndrome and continued imaging in childhood may be needed.
- ▶ Although involvement of multiple major cerebral arteries increases the risk for acute ischaemic stroke in patients with PHACES syndrome, vaso-occlusive disease may be compensated, so immediate intervention may not be required.
- ▶ Indirect revascularisation has been successful in these patients, although indications and best timing for intervention have not been established.
- ▶ Imaging of cerebral blood flow to guide treatment remains in development.

better understand the ideal management of this difficult population.

Acknowledgements The authors would like to thank Dr. Pallavi S. Utukuri and Dr. Prachi Dubey for their help with imaging acquisition and their invaluable insight.

Contributors All persons who meet authorship criteria are listed as authors, and all authors certify that they have participated sufficiently in the work to take public responsibility for the content, including participation in the concept, design, analysis, writing or revision of the manuscript. Conception and design of study: PMM. Acquisition of data: ND, JJC. Analysis and/or interpretation of data: ND, JJC, PMM. Drafting the manuscript: ND, JJC, PMM. Revising the manuscript critically for important intellectual content: ND, PMM. Approval of the version of the manuscript to be published: ND, JJC, PMM.

Competing interests None declared.

Patient consent Obtained from guardian.

Provenance and peer review Not commissioned; externally peer reviewed.

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