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Case Report

Phace Syndrome in Children: Two Case Reports [☆]

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ABSTRACT

PHACE(S) syndrome combines: posterior fossa brain malformations, face hemangioma, arterial cerebrovascular abnormalities, cardiovascular abnormalities, eye abnormalities, and ventral developmental defects (Sternal defects or supra-umbilical rope). The diagnosis is based on the association of an infant hemangioma exceeding 5cm in size on the face, neck, scalp with 1 major criteria or 2 minor criteria. Imaging, especially Gadolinium MRI and MRA of the brain, neck, and aortic arch, transthoracic echocardiography, or even cardiac MRI play a key role in the detection of associated neurological and cardiovascular abnormalities.

We report 2 cases of PHACE syndrome revealed by 2 different clinical presentations.

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Introduction

The PHACE syndrome should be evoked in facial hemangioma of the child. This syndrome combines posterior fossa brain malformations, face hemangioma, arterial cerebrovascular abnormalities, cardiovascular abnormalities, eye abnormalities, and ventral developmental defects. Neurovascular abnormalities must be systematically detected which can cause strokes. Imaging, especially Gadolinium magnetic resonance imaging, magnetic resonance angiography of the brain, neck, and aortic arch, transthoracic echocardiography, or even cardiac MRI should look for associated neurological and cardiovascular abnormalities [1].

Case Presentation N° 1

A 12-year-old girl, without any pathological medical history, presented acute left hemiplegia associated with headaches. The clinical examination found motor deficit with angiomatous lesion of the left cervical and temporal region (frontotemporal distribution (S1), Fig. 1).

The patient had no sternal deformation and the cardiovascular examination was normal. Brain CT scan was initially performed (Fig. 2), then brain MRI was realized. It showed an acute ischemic stroke in the right middle cerebral artery territory and a sequela left occipital ischemic stroke (Fig. 3). Cerebral angiography showed a distal stenosis of the right internal

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Fig. 1 – Case 1: angiomatous lesion of the left cervical and temporal region (frontotemporal distribution (S1)).

carotid artery with the development of collateral vascularization giving an appearance as a ‘puff of smoke’ in the context of Moya-moya syndrome (Fig. 4). The diagnosis of PHACE syndrome was retained based on the association of the angiomatous lesion with cerebrovascular manifestations.

Case Presentation N° 2

A 6-month-old female infant, with a neonatal respiratory distress, was presented to the emergency department with shortness of breath.

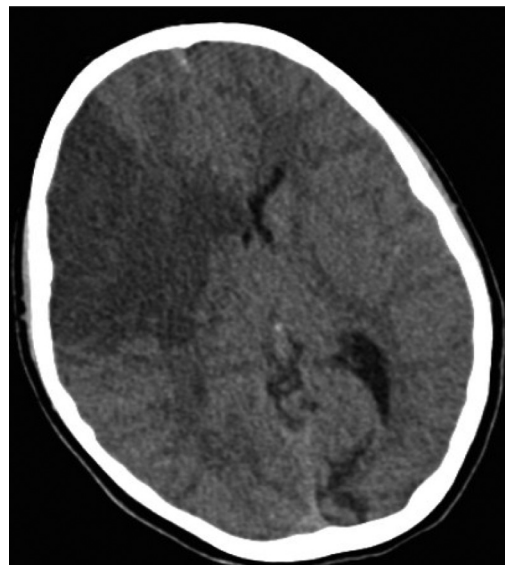


Fig. 2 – Case 1: Brain CT scan showing an acute ischemic stroke in the right middle cerebral artery territory and a sequela left occipital ischemic stroke.

The clinical examination found cyanosis of the extremities with a mandibular angioma (S3). Cardiovascular examination found a left parasternal heave radiating to the axilla. A coarctation of the aorta was suspected. A cervicothoracic CT angiography was performed showing subglottic hemangioma, a narrowing of the horizontal aorta and the left carotid artery, a posterior birth of the subclavian artery from the isthmus, and a dilated and tortuous brachiocephalic arterial trunk (Fig. 5). There was also a hepatic angioma.

All clinical and paraclinical elements were in favor of PHACE syndrome.

Unfortunately, the patient died within days of diagnosis.

Discussion

In 1996, Frieden et al. created the acronym PHACE(S) to define a syndrome that combines: P: Posterior fossa malforma-

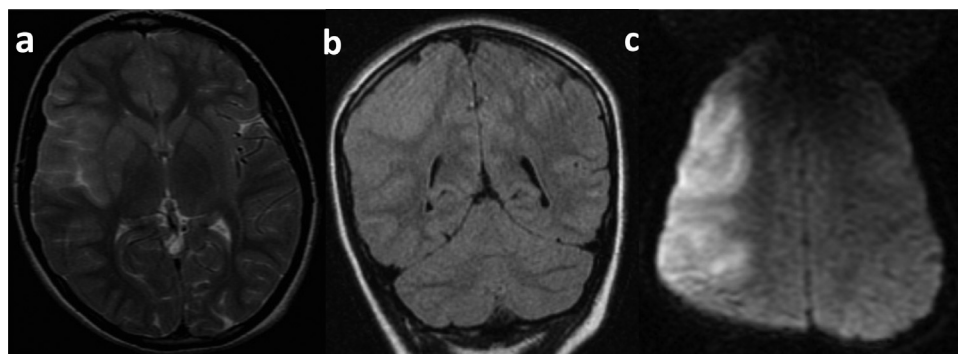


Fig. 3 – Case 1: Brain MRI in T2 weighted sequences (a); Flair (b) and diffusion weighted sequences (c) showing an acute ischemic stroke in the right middle cerebral artery territory.

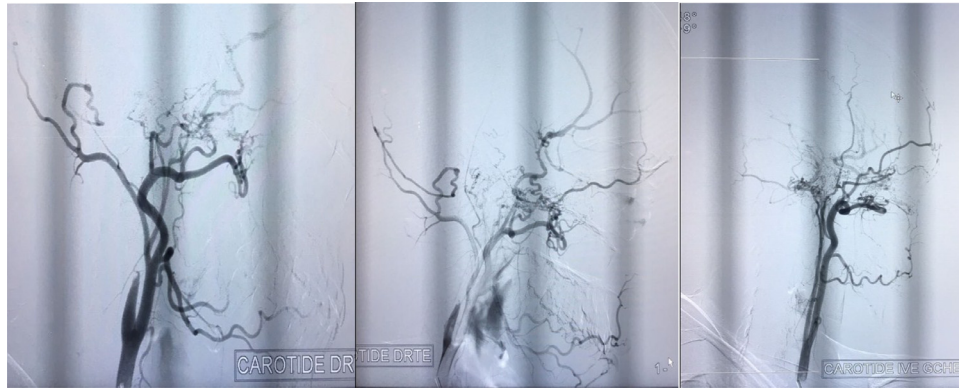


Fig. 4 – Case 1: Cerebral angiography showing a distal stenosis of the right internal carotid artery with the development of collateral vascularization giving an appearance as a ‘puff of smoke’ in the context of Moyamoya syndrome.

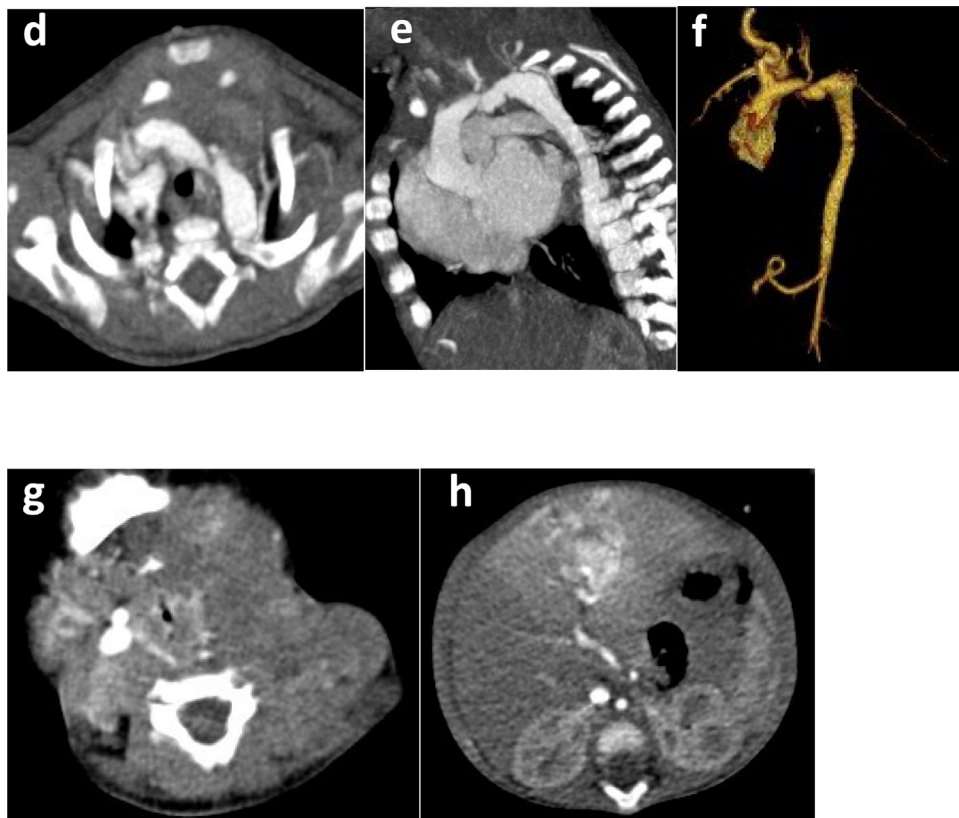


Fig. 5 – Case 2: Cervicothoracic angioscanner showing a narrowing of the horizontal aorta and the left carotid artery, a posterior birth of the subclavian artery from the isthmus, and a dilated and tortuous brachiocephalic arterial trunk (a,b,c) with cervical angiomas (g) and hepatic angioma (h).

tions, H: Hemangiomas of the face, A: Arterial cerebrovascular anomalies, C: Cardiovascular anomalies, E: Eye anomalies, and S: Ventral developmental defects (Sternal defects or supraumbilical raphe). The syndrome PHACE is present in 2% to 3% of infantile hemangiomas with a feminine preference [1,2].

When PHACE syndrome is suspected, clinical examination should look for ocular, sternal, neurological, and cardiac abnormalities. The clinical presentation is polymorphic, variable from one patient to another, and may be incomplete. In

PHACE syndrome, facial hemangioma is broad and usually tuberous. It can be unilateral or bilateral, segmental or inter-segmental. Haggstrom et al. described four facial segments: frontotemporal (S1), maxillary (S2), mandibular (S3), and frontonasal (S4). Hemangiomas in distribution S1 and S4 were more likely to be associated with cerebrovascular, cerebral, or ocular abnormalities while the S3 distribution of hemangiomas are often associated with cardiac abnormalities, of aortic arch and with ventral developmental defects.

Table 1 – Major and minor criteria of PHACE syndrome diagnosis.

Major criteria	
→anomalies of larger brain vessels (Dysplasia, arterial stenosis or occlusion with or without moya-moya collaterals, absence or hypoplasia, aberrant origin, persistent trigeminal artery and saccular aneurysm)	→Persistent embryonic artery
→posterior fossa anomaly (Dandy walker complex or cerebellar hypo/dysplasia)	→Enhancing extra axial lesion consistent with intracranial hemangioma/ Midline anomaly/ Neuronal migration disorder
→aortic arch anomaly/Coarctation/aortic aneurysm/Aberrant origin of the subclavian artery with or without a vascular ring	→Ventricular septal defect/right aortic arch
→ocular posterior segment anomalies/retinal vascular anomalies/persistent fetal vasculature/Optic nerve hypoplasia/Peripapillary staphyloma/Morning Glory disc anomaly	→ocular anterior segment abnormality/Sclerocornea/cataract/coloboma/microphthalmia
→Ventral or midline anomaly : sternal defect/sternal cleft/Supraumbilical raphe	→Hypopituitarism/Ectopic thyroid[2,5].

Patients with PHACE(S) syndrome are at high risk of developing subglottic hemangioma, particularly in cases of facial hemangiomas of mandibular localization [3,4]. Ophthalmological abnormalities often occur on the homolateral side of facial hemangioma. These are often microphthalmias. Other abnormalities may be encountered such as buphthalmias, glaucoma, congenital cataracts, retinal hypervascularizations, and optic nerve hypoplasia [1,3]. Imaging, especially Gadolinium MRI and MRA of the brain, neck, and aortic arch, Transthoracic echocardiography, or even cardiac MRI should look for associated neurological and cardiovascular abnormalities. Computed tomography scanning is not performed in first intention because it does not perform well in the detection of cortical dysplasia in addition to the risk of radiation. Central neurological malformations are the most common and involve the posterior fossa. Most often, it is a Dandy-Walker syndrome, which consists of an enlargement of the posterior cerebral fossa, an ascension of the tent of the cerebellum, and a cystic dilation of the fourth ventricle. Other abnormalities of the posterior cerebral fossa have been reported such as arachnoid cyst and mega cisterna magna. The supratentorial cerebral malformations are less common and they include cortical dysplasia, grey matter heterotopia, hypoplasia or absence of the corpus callosum or septum pellucidum, frontal lobe calcifications, absent foramen lacerum, polymicrogyria, and microcephaly. Intracranial hemangiomas are rare but they are increasingly found [1,3].

MRA of the brain, neck and aortic arch often show the absence, hypoplasia or dysplasia (tortuousness, stenosis and aneurysm) of an internal carotid artery and/or vertebral artery. External carotid arteries are rarely affected. The persistence of a trigeminal artery has also already been reported. Arterial stenosis and tortuosities can lead to ischemic strokes that are very rare in PHACE syndrome (such as our first observation). Coarctation of the aorta or cardiac malformations may also be present, corresponding to tricuspid or aortic valve atresia, abnormalities of pulmonary venous return, persistence of the arterial canal and interventricular communications [1,2,3]. Endocrine abnormalities affecting the thyroid and pituitary gland have also been reported recently in patients with PHACE syndrome. Ventral developmental defects were not described initially by Frieden, but can be associated with PHACES syndrome which includes sternal clefting and supra-umbilical abdominal rope malformations [3].

The diagnostic criteria for PHACE syndrome were established in 2009 and revised in 2016 by G Table 1 arzon et al. There are two categories: PHACE syndrome associating an infantile haemangioma exceeding 5cm in size on the face, neck, scalp with 1 major criteria or 2 minor criteria, and the possible PHACE syndrome associating a hemangioma of more than 5cm and 1 minor criteria: Table 1.

In our first case, the diagnosis was made based on the association of hemangiomas exceeding 5cm in size on the neck and scalp with anomalies of larger brain vessels (major criteria), while in the second case the diagnosis was established based on the association of facial hemangiomas and aortic arch anomaly, coarctation of the aorta and aberrant origin of the subclavian artery.

When cerebrovascular abnormalities are detected, repeat brain MRI and MR angiography must be performed. The absence of radiological progression after 1 year reduces the risk of further progression. The place of imaging examinations is not clearly codified in the literature. Regular clinical follow-up is still recommended throughout life [1,5].

Specialized management of associated malformations is discussed on a case-by-case basis based on their functional impact. Oral corticosteroid therapy was the first-line treatment of hemangiomas, but currently, studies have shown the effect of propranolol in stopping their proliferation or even their involution. It should be administered gradually starting with 0.5 to 1mg/kg/day in the first week, increasing progressively to 2 to 3mg/kg up to optimum dose so as not to disturb blood pressure. The treatment duration will depend on the progression of each IH. In the case of cerebral vascular disease, neurosurgical treatments should be appropriate [5,6].

Conclusion

After cutaneous manifestations, brain vascular malformations and cardiovascular abnormalities are the most common manifestations of PHACE syndrome. Imaging, especially Gadolinium MRI and MRA of the brain, neck, aortic arch, and transthoracic echocardiography play an important role in their detection. The specialized management of associated

malformations is discussed on a case-by-case basis according to their functional impact.

Patient consent statement

Written informed consent for publication was obtained from the patient.

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