PHACE syndrome with parotid hemangiomas: a unique case report

Muhammad Umer Mukhtar 1*, Mahjabeen Kanwal 2, Adeel Qamar 2, Sadaf Arooj 2 and Samina Qamar 3

Abstract

Background: PHACE syndrome is a congenital disorder in infants characterized by the presence of large hemangiomas in the cervicofacial region along with congenital anomalies of the cardiovascular system, brain, and eyes. PHACE syndrome is an extremely rare condition, and PHACE syndrome with parotid hemangiomas has never been reported in the medical literature.

Case presentation: A 3-month-old female infant presented with cervicofacial plaques that later involved the left eyelids. The plaques blanched on application of pressure and were diagnosed to be hemangiomas. MRI and MRA studies of the brain showed extensive vascular malformations, agenesis of the left internal carotid artery, and hemangiomas in the parotid glands. A biopsy of the parotid glands confirmed the parotid hemangiomas. Bilateral cataracts and subclavian artery with an aberrant origin were also found. On the basis of the hemangiomas and the arterial, cardiovascular, and ocular abnormalities, PHACE syndrome was diagnosed. A multi-disciplinary treatment approach was begun, but the infant died 20 days after presentation to the hospital.

Conclusions: PHACE syndrome is an extremely rare condition that has only been described three hundred times in medical literature. It is usually associated with extensive structural, arterial, ocular, and cutaneous anomalies. However, PHACE syndrome with parotid hemangiomas has never been reported in the medical literature. Hemangiomas are the main diagnostic feature and the most common lesion of this disease. This strong association between PHACE syndrome and hemangiomas suggests the parotid hemangiomas seen in our case to be a new addition to the broad spectrum of anomalies associated with PHACE syndrome.

Keywords: PHACE syndrome, Infantile hemangioma, Vascular anomalies, Eye abnormalities, Magnetic resonance imaging, Case report

Background

PHACE syndrome is a congenital disorder characterized by the presence of large hemangiomas in the cervical and facial regions along with congenital anomalies of the cardiovascular system, brain, and eyes. The acronym PHACE stands for Posterior fossa malformations, Hemangiomas, Arterial abnormalities, Cardiac defects, and Eye anomalies. When developmental defects such as sternal clefting or supraumbilical raphe are also present, the acronym PHACES is used instead [1].
been reported previously in the literature as presenting along with PHACE syndrome [4]. The case is reported following the latest CARE guidelines.

**Case presentation**

A 3-month-old female infant presented with reddish plaques on both cheeks that had begun developing at the age of 1 month. These lesions had gradually spread to the cervical and temporal regions and had also involved the left eyelids. An examination confirmed the reddish plaques to be hemangiomas. MRI and MRA scans were obtained.

**MRI**

Multi-planner and multi-sequential MRI brain contrast studies of the patient were undertaken, and axial, coronal, sagittal, T1WI, T2WI, FLAIR, and SWAN images were acquired to evaluate intracranial abnormalities (Fig. 1). Axial images at the levels of temporal horns of the lateral ventricles exhibited mixed signal intensity foci on T1WI, T2WI, and FLAIR sequences in the left temporal lobe, quadrigeminal cistern, and left ambient cistern and gave blooming artifact on SWAN images that were consistent with vascular malformations (Fig. 1a). Susceptibility weighted images acquired at the level of the body of the lateral ventricles exhibited serpiginous blooming artifactual signals in the left cerebral hemisphere, showing dilated collateral vascular channels (Fig. 1b). Axial T1WI and T1W2 and coronal T1WI post-contrast images acquired at the level of the parotid glands exhibited bilateral symmetrically enlarged parotid glands that were isointense on T1WI and hyperintense on T2WI with diffuse post-contrast enhancement. Apart from the size and signal variability, multiple flow voids were noted within the parenchyma of both parotid glands. All these features indicated the presence of bilateral parotid hemangiomas (Fig. 1c).

**MRA**

A 3D reconstructed TOF MRA study was undertaken following the MRI studies of the brain (Fig. 2). MRA images revealed the absence of the left internal carotid artery throughout its course, while the intact left middle cerebral artery and the left anterior cerebral artery were being fed from the contralateral side via the anterior communicating artery (Fig. 2a, b). A tuft of serpiginous channels was noted in the left anterior ambient cistern being fed from the left posterior cerebral artery, and another such vascular nidus was noted in the quadrigeminal cistern being fed from the left vertebral artery (Fig. 2c, d). These findings confirmed the vascular malformations seen on correlative MRI images.

Thus, to summarize, the MRI and MRA showed vascular malformations in the brain in the form of agenesis of the left internal carotid artery, dilated collateral vascular channels being fed from the contralateral vessels, serpiginous channels in the anterior ambient cistern, and a vascular nidus in the quadrigeminal cistern. MRI also showed the presence of parotid hemangiomas. Biopsies from both parotid glands were sent for histopathological examination. The biopsies confirmed the presence of hemangiomas in both parotid glands (Fig. 3). Further investigations were carried out with a CT angiogram showing a
subclavian artery with an aberrant origin. The child also had congenital cataracts in both eyes. The cervicofacial hemangiomas, combined with the arterial, cardiovascular, and ophthalmic anomalies, indicated an unmistakable diagnosis of PHACE syndrome. A multidisciplinary treatment approach was begun, but the patient died 20 days after her presentation to the hospital due to unsettled shortness of breath.

Discussion

PHACE syndrome affects girls nine times more frequently than boys [2]. It is an under-diagnosed syndrome that can be diagnosed by the presence of facial hemangiomas greater than 5 cm, along with the presence of one of several major criteria or two of several minor criteria. However, facial hemangiomas are the primary criteria considered in the diagnosis of PHACE syndrome. The hemangiomas are plaque-like lesions occurring in a geographic pattern unrelated to the facial dermatomes. In our case, facial hemangiomas involved a portion of the neck, both cheeks, the temporal region, and the left eyelids. The literature so far reports mostly cutaneous hemangiomas; extracutaneous hemangiomas are rare but have been reported in organs such as the brain, bowels, and lungs [5]. To our knowledge, our case is the first one to report hemangiomas in the parotid glands. Hemangiomas in PHACE are often considered to be a relatively benign part of the spectrum, but if they occur on important areas like the eyelids, ears, airways, they can interfere with vision, hearing, and breathing and can thus cause serious distress to the infant.

Oza et al [6] showed a relationship between large facial hemangiomas and brain structural and arterial malformations. A wide range of structural brain anomalies have been observed in patients with PHACE syndrome, including posterior fossa brain malformations, hypoplasia/dysplasia of the midbrain or hindbrain, and cerebellar abnormalities. Less common brain structural malformations include abnormal cortical development and absence of the pituitary gland. The most common cardiovascular anomaly in PHACE syndrome is the aberrant origin of the subclavian artery, followed by aortic coarctation. Of patients with cardiac involvement, 92% have cerebrovascular anomalies that include stenosis, hypoplasia, aberrant origin, course or absence of the main vessels of the brain (especially cerebral, vertebral, basilar, or internal carotid arteries) with the presence of collateral channels, and persistence of embryonic vessels.

The many structural and cerebrovascular malformations just described are associated with a high risk of cerebrovascular accidents and neurological sequelae that may include epilepsy, headaches, and developmental delays. Recent studies have highlighted that some patients of PHACE syndrome are at risk for developing a progressive vasculopathy in which vessels become further dilated and tortuous, develop moyamoya-type collaterals,
and may eventually undergo complete occlusion [7, 8]. In our case, the infant had agenesis of the left internal carotid artery. Collateral channels and vascular nidi were present in various locations throughout the brain to compensate for the absent vessel. The collateral channels were dilated and serpiginous and were being fed from the vessels on the opposite side.

The association of PHACE syndrome and parotid hemangiomas, as reported in the present case, has never been described before. The review of literature on PHACE syndrome revealed that only one other gland has been reported to be affected by hemangiomas: the thyroid gland [5]. Other than that, no gland—either endocrine or exocrine—has been reported to be affected by the hemangiomas present in PHACE syndrome.

Conclusion
Hemangiomas are the main feature and the most common lesion of PHACE syndrome, being present in 98% of the cases. The parotid hemangiomas reported in our case might simply have been a coincident pathology, but the strong association between PHACE syndrome and hemangiomas suggests the parotid hemangiomas to be a new addition to the broad spectrum of anomalies associated with PHACE syndrome.

Abbreviations
MRI: Magnetic resonance imaging; MRA: Magnetic resonance angiography

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None