

CR

CASE REPORT

E. P. C. M. S.

A Case Report on Phaces Syndrome: Widespread Hemangiomas Associated with Arnold Chiari Malformation Type I, Right Middle Cerebral Anomaly and Supraumbilical Raphe

Marifi Cabaluna, M.D., PL-2
Mary Lillian Tocyap, M.D., PL-3
Benjamin Carcamo, M.D.

INTRODUCTION AND BACKGROUND

“PHACES syndrome” is the association of posterior fossa malformations, hemangiomas, arterial anomalies, coarctation of the aorta and other cardiac defects, eye anomalies and sternal malformations.^{1,2} We describe a case of a patient in our local population with PHACES syndrome. Our report contributes to the limited literature currently available on this rare condition and also emphasizes the approach to diagnosis of patients who present with these clinical features.

CASE PRESENTATION

This is the case of a 19 y.o. hispanic girl, born at 40 weeks of gestation to non-consanguineous parents without complications, who developed an enlarging strawberry hemangioma at the right side of her neck which was excised at 3 months of age. She had other hemangiomas that resolved spontaneously by 5 years of life. At 13 years of age she developed a small dural base hemangioma overlying the left temporal bone, multiple hemangiomas at the right intraorbital area, a large neck lymphangioma, and skin and muscle hemangiomas. No treatment was pursued at that time.

At 16 years of age she presented with progressive disease with right sided hemangiomas on the chin, upper eyelid, ear pinna, chest wall, right labia majora, and hemangiomas on the right and left flank areas. On physical examination, there was no heart murmur, her blood pressure was normal and abdominal exam revealed a supraumbilical raphe.

The head CT scan showed intracranial subdural hemangiomas in the right frontal convexity and left temporal lobe, Chiari Type I malformation in the posterior fossa, prominent branch of the right middle cerebral artery and intraorbital hemangioma with calcification. The neck CT scan showed a right intra-parotid hemangioma and left thyroid gland hemangioma displacing the carotid artery. An abdominal CT revealed a hemangioma in the left adrenal gland and in the right paraspinous musculature at L3 level.

The patient was treated with alpha-2a interferon and sclerosis treatment which reduced the hemangiomas and lymphangiomas. Her right intraorbital hemangioma caused proptosis, blurring of vision and headaches. She developed frequent gum bleedings, and chronic dysphagia from neck hemangiomas. She had mild shortness of breath with minor exercise which resolved

as her cervical hemangiomas responded to sclerotic therapy. She also developed sciatic pain presumably caused by her right gluteal hemangioma and depression due to her chronic illness. At present, her hemangiomas and lymphangiomas are still persistent. She is also currently treated for Glanzmann thrombasthenia.

DISCUSSION

Our patient presented with at 5 features of the syndrome: Chiari-type I malformation with downward tonsillar ectopy in the posterior fossa (P), extensive hemangiomas (H), prominent branch of the right middle cerebral artery (A), exophthalmos (E), and supraumbilical raphe (S).

The pathogenesis of the syndrome is unknown but Frieden reported an infant with PHACE syndrome of which a posterior fossa malformation was detected on prenatal ultrasound at 12 weeks gestation, suggesting its origin during the first trimester of pregnancy.³ Several authors postulated that sternal clefting and facial hemangiomas develop between 8 to 10 weeks of gestation.^{2,4} Bhattacharya suggest an abnormality of cell proliferation and apoptosis and further studies are awaited on possible genetic implication since extraordinary female predominance had been reported.⁴

Published literature reported cases with at least three of the features present in a patient; some reported a slight variation in the clinical presentation of a feature which could represent a milder form of the disease entity.^{5,6,7}

Structural and cerebrovascular brain malformations occur in over half of the reported PHACES patients. Dandy-Walker malformation is the most common. This is characterized by hypoplastic or absent cerebellar vermis and markedly dilated fourth ventricle/posterior fossa cyst. Frieden described 43 patients with extensive hemangiomas, 74% of which have Dandy-Walker.³ Metry reported 6 out of 14 patients with PHACE syndrome with Dandy-Walker malformation.⁸ Other malformations include agenesis of the corpus callosum, cerebellar atrophy, septum pellucidum, isolated frontal lobe calcification, microcephaly and arachnoid cysts.⁹

Hemangiomas are frequent in childhood but their association with other anomalies is rare.^{5,10} The hallmark of PHACES syn-

Continued on page 7

A Case Report of Phaces Syndrome: Widespread Hemangiomas Associated With Arnold Chiari Malformation Type I, Right Middle Cerebral Anomaly and Supraumbilical Raphe (Continued)

drome is a large, segmental, plaque-like hemangioma which may involve one to several facial dermatome. Metry reported predominance of left-sided facial hemangiomas among patients with the syndrome.⁸ Extracutaneous location of the hemangioma can occur¹¹ and there is a high risk for the hemangiomas to develop in the airway (22% of reported cases by Metry) which poses significant airway compromise.^{8,12}

Arterial anomalies include bilateral agenesis of the internal carotid arteries,¹³ persistent fetal vasculature,¹⁴ transcranial collaterals from the external carotid arteries and agenesis of the vertebrobasilar system.¹⁵ The cerebrovascular anomalies are concerning due to progressive arterial occlusion, stroke and other neurologic complications. Drolet reported 5 infants with PHACE syndrome who suffered arterial stroke.¹⁶

Metry reviewed 130 patients with PHACE syndrome; more than one third of these cases have cardiac anomalies. Coarctation of the aorta is the most common defect reported. Other anomalies seen include PDA, VSD, ASD, tricuspid and aortic atresia.⁸

Eye anomalies include optic nerve atrophy, exophthalmos, microphthalmos, colobomas, strabismus, congenital cataracts and glaucoma.^{17,18}

Sternal clefting and/or supraumbilical abdominal raphe complete the spectrum of the syndrome. Sternal cleft, is a rare congenital malformation caused by failure of the sternum to fuse during the third month of embryologic development.^{7,19} Metry reported 43 out of 130 PHACES patients with ventral development defect, 12 patients with both sternal cleft and supraumbilical raphe, and 2 patients have supraumbilical raphe alone.⁸

In patients with large facial and multiple hemangiomas, it is important to conduct detailed neurological examination to look for posterior fossa malformations,^{2,20} do an extensive cardiovascular exam to look for cardiac and arterial anomalies, refer to an ophthalmologist to rule out eye defects; special attention should be given to sternal examinations as well as search for hemangiomas in airway localization.^{10,13}

Glanzmann thrombasthenia was also an incidental finding on our index patient. This is an inherited disorder of platelet function, characterized by a defect in the platelet glycoprotein IIb/IIIa complex, causing abnormal bleeding. Whether this is an isolated event or could be a variant or part of the association is undetermined and further investigation should be done. To our knowledge, there had been no case reported of a patient with PHACES syndrome and Glanzmann thrombasthenia.

REFERENCES

1. Wendelin G, Kitzmuller E, Salzer-Muhar U. PHACES: a neurocutaneous syndrome with anomalies of the aorta and supraaortic vessels. *Cardiology Young*. 14(2):206-09, April, 2004
2. Rossi A and Paolo Tortori-Donati. Agenesis of bilateral internal carotid arteries in the PHACE syndrome. *AJNR Am J Neuroradiol*. 27(8):1602, September, 2006

3. Frieden IJ, Reese V, Cohen D.. PHACE syndrome. The association of posterior fossa brain malformations, hemangiomas, arterial anomalies, coarctation of the aorta and cardiac defects, and eye abnormalities. *Arch Dermatol*. 132:307-11. 1996
4. Bhattacharya JJ, Luo CB, Alvarez H. PHACES syndrome: a review of eight previously unreported cases with late arterial occlusions. *Neuroradiology*. 46(3): 277-33, March 2004
5. Boulinguez S, Teillac-Hamel D, Bedane C, Bennaceur S, De Prost Y. Cervicofacial hemangioma and a minor sternal malformation: inclusion in PHACES syndrome? *Pediatric Dermatology*. 15(2):119-21. Mar-Apr, 1999
6. Slavotinek AM, Dubovsky E, Dietz HC, Lacbawan F. Report of a child with aortic aneurysm, orofacial clefting, hemangioma, upper sternal defect, and marfanoid features: possible PHACE syndrome. *Am J Med Genet*. 110(3):283-8. July 1, 2002.
7. Vermeer S, van Oostrom CG, Boetes C, Verrips A, Knoers NV. A unique case of PHACES syndrome confirming the assumption that PHACES syndrome and the sternal malformation-vascular dysplasia association are part of the same spectrum of malformations. *Clinical Dysmorphology* 14(4):203-06. October, 2005
8. Metry DW, Hawrot A, Altman C, Frieden JJ. Association of solitary, segmental hemangiomas of the skin with visceral hemeangiomatosis. *Arch Dermatol* 140 (5): 591-6. May, 2004
9. Drosou A, Benjamin L, Linfante I, Mallin K, Trowers A, Wakhloo AK, Thaller SR, Schachner LA. Infantile midline facial hemangioma with agenesis of the corpus callosum and sinus pericranii: another face of the PHACE syndrome. *J Am Acad Dermatol* 54(2):348-52. February, 2006
10. Buzenet C, Hamel-Teillac D, Acar P, Becquet F, Curan D, Michaud V, Sidi D, De Prost Y. [Facial hemangioma associated with arterial anomalies, coarctation of the aorta, and eye abnormalities: PHACES syndrome]. *Ann Dermatol Venereol* 127(3):292-95. March, 2000
11. Ersoy S, Mancini AJ. Hemifacial infantile hemangioma with intracranial extension: a rare entity. *Pediatr Dermatology* 22(4):309-13. July-August, 2005
12. Smith DS, Lee KK, Milkzuc, A. Otolaryngologic manifestations of PHACE syndrome. *Int J Pediatr Otorhinolaryngology* 68(11):1445-50. November, 2004.
13. Rossi A, Bava GL, Biancheri R, Tortori-Donati P. Posterior fossa and arterial abnormalities in patients with facial capillary hemangioma: presumed incomplete phenotypic expression of PHACES syndrome. *Neuroradiology* 43(11): 834-940. November, 2001.
14. Lasky JB, Sandu M, Balashanmugan A. PHACE syndrome: association with persistent fetal vasculature and coloboma-like iris defect. *J AAPOS* 8(5):495-8. October, 2004
15. Weon YC, Chung JI, Kim HJ, Byun HS. Agenesis of bilateral internal carotid arteries and posterior fossa abnormality in a patient with facial capillary hemangioma: presumed incomplete phenotypic expression of PHACE syndrome. *Am J Neuroradiol* 26(10):2635-9. November-December, 2005
16. Drolet BA, Dohil M, Golomb MR, Wells R, Murowski L, Tamburro J,



A Case Report of Phaces Syndrome: Widespread Hemangiomas Associated With Arnold Chiari Malformation Type I, Right Middle Cerebral Anomaly and Supraumbilical Raphe (Continued)

Sty J, Friedlander SF. Early stroke and cerebral vasculopathy in children with facial hemangiomas and PHACE association *Pediatrics* 117(3):959-64. March, 2006.

17. Kronenberg A, Blei F, Ceisler E, Steele M, Furlan L, Kodsi S. Ocular and systemic manifestations of PHACES (Posterior fossa malformations, Hemangiomas, Arterial anomalies, Cardiac defects and coarctation of the Aorta, Eye abnormalities, and Sternal abnormalities or ventral developmental defects) syndrome. *Journal of AAPOS* 9(2):169-73. April, 2005

18. Schwartz SR, Blei F, Ceisler E. Risk factors for amblyopia in children with capillary hemangiomas of the eyelids and orbit. *J AAPOS* 10 (3):262-8. June, 2006

19. Durusoy C, Mihci E, Tacoy S, Ozaydin E, Alpsoy E. PHACES syndrome presenting as hemangiomas, sternal clefting and congenital ulcerations on the helices. *J Dermatol* 33(3):219-22. March, 2006

20. Ioannidis AS, Liasis A, Syed S, Harper J, Nischal KK. The value of visual evoked potentials in the evaluation of periorbital hemangiomas. *American Journal of Ophthalmology* 140(2):314-16. August, 2005

Marifi Cabaluna, M.D., PL-2, Department of Pediatrics, Texas Tech University Health Sciences Center, El Paso.

Mary Lillian Tocyap, M.D., PL-3, Department of Pediatrics, Texas Tech University Health Sciences Center, El Paso, Texas.

Benjamin Carcamo, M.D., Clinical Assistant Professor, Department of Pediatrics, Texas Tech University Health Sciences Center, El Paso, Texas.