Case report

PHACE(S) syndrome: Report of a case with new ocular and systemic manifestations

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Abstract

Purpose: To describe an infant with PHACE(S) syndrome [posterior fossa anomalies (P), hemangiomas (H), arterial anomalies (A), cardiac abnormalities and coarctation of aorta (C), eye abnormalities (E), and the sternal defects (S)] with unusual strabismus, congenital glaucoma, and new systemic manifestations.

Methods: A 6-month-old girl was referred with large hemangiomas on the left side of the face.

Results: In the ocular examination, right esotropia and hypotropia, and limitation of elevation in adduction in the right eye were seen. Morning glory disk anomaly was seen in the left fundus. Intraocular pressure (IOP) was 28 mmHg in the right eye and 15 mmHg in the left eye. Brain computed tomography (CT) scan demonstrated Dandy-Walker malformation. In the CT angiography of the thoracic arteries, coarctation of aorta in descending part, the aberrant origin of the left subclavian artery from the end of the aortic arch, and anomalous origin of the left vertebral artery from the posterior aspect of the aortic arch were found. Therefore, the presence of large facial hemangioma, posterior fossa anomaly, aortic arch anomalies, and morning glory disk confirmed the diagnosis of PHACE(S) syndrome. Propranolol (0.5 mg/kg/day) was initiated to treat hemangioma and coarctation of aorta. Due to uncontrolled glaucoma, goniotomy was performed in the right eye 3 months after the first visit. One year after the initial visit, the hypotropia and esotropia of the right eye considerably decreased.

Conclusions: To our knowledge, this report was the first report of a pattern like Brown’s syndrome (may be called apparent Brown’s syndrome) and the second report of the congenital glaucoma in a case of PHACE(S) syndrome. In addition, the anomalous origin of the vertebral artery from the aortic arch has not been reported in the PHACE(S) syndrome. Thus, the clinicians should perform the glaucoma work-up for each patient with this syndrome.

Keywords: PHACE syndrome; PHACES syndrome; Facial hemangioma; Dandy-Walker malformation; Morning glory disk

Introduction

In 1996, Frieden and colleagues described an association of posterior fossa anomalies (P), hemangiomas (H), arterial anomalies (A), cardiac abnormalities and coarctation of aorta (C), and eye abnormalities (E) and named it PHACE syndrome.1 Boulinguez and colleagues added the sternal defects (S) to this acronym and changed the name to PHACES syndrome.2 Females were dominant in most series of this syndrome.1–10 Most reported cases were sporadic, but mutations in the X-linked genes were proposed to cause this syndrome in some patients.1–10

In this article, we report a case of PHACE(S) syndrome with unusual strabismus, congenital glaucoma, and new systemic manifestations.
Case report

A 6-month-old girl was referred to the strabismus clinic of Farabi Eye Hospital. She had mild developmental delay and a history of hospital admission because of respiratory distress two weeks earlier. Birth history and family history were unremarkable.

Physical examination revealed large infantile hemangiomas on the left side of the face (involving eyelids and lips) (Fig. 1), left arm and left side of the neck and chest. The otolaryngologic examination showed hemangioma in the buccal, nasal, and pharyngeal mucosa. The cycloplegic refraction showed +2.75 spheres in the right eye and +3.5 spheres in the left eye. Right esotropia and hypotropia was seen (Fig. 1, left). In the right eye, there was a limitation of elevation in adduction. Other ductions were normal. Slit-lamp examination was unremarkable. In the fundus examination, morning glory disk anomaly was seen in the left fundus (Fig. 2). The cup/disk ratio was 0.5 in the right eye. Other fundus details were normal in the right eye.

In the examination under anesthesia, forced duction testing for right superior oblique muscle showed severe restriction of elevation in adduction (like Brown’s syndrome). Intraocular pressure (IOP) with Tono-Pen (Reichert Inc., Depew, NY) was 28 mmHg in the right eye and 15 mmHg in the left eye. Central corneal thickness with PachPen (Accutome, Lynwood, WA) was 542 μm in the right eye and 553 μm in the left eye. The horizontal corneal diameter was 13.5 mm in the right eye and 11 mm in the left eye.

The orbital computed tomography (CT) scan showed enlargement of the right globe. Brain CT scan demonstrated Dandy-Walker malformation [posterior fossa cyst, partial absence of cerebellar vermis, and hypoplastic cerebellar hemispheres (Fig. 3)]. In the CT angiography of the thoracic arteries, coarctation of aorta in descending part, the aberrant origin of the left subclavian artery from the end of the aortic arch, and anomalous origin of the left vertebral artery from the posterior aspect of the aortic arch were found (Fig. 3). Thyroid and liver function tests, complete blood count, serum creatinine, and calcium were within normal limits.

After these evaluations, propranolol (0.5 mg/kg/day) was initiated to treat hemangioma and coarctation of aorta. This drug has also some IOP-lowering effects. The dose of the propranolol was increased to 1 mg/kg/day after 1 month. Similarly, the cardiologist considered treatment with the same dosage of propranolol for vascular problems. The dorzolamide eye drop, three times daily, was also initiated in the right eye to treat glaucoma. Due to uncontrolled glaucoma, goniotomy was performed in the right eye 3 months after the first visit.

In the last follow-up (1 year after the initial visit), the hypotropia and esotropia of the right eye considerably decreased (Fig. 1, right). Also, the size of the facial hemangioma was decreased (Fig. 1, right). In the examination under anesthesia, IOP with Tono-Pen (Reichert inc., Depew, NY) was 12 mmHg in the right eye and 14 mmHg in the left eye. The cup/disk ratio decreased to 0.3 in the right eye. The patient is now under treatment of propranolol (1 mg/kg/day).

Discussion

Approximately one-third of the PHACE(S) syndrome cases have eye involvements. In a recent study on 23 cases of PHACE(S) syndrome, 14% of the cases showed ocular involvement. The reported ocular manifestations of this syndrome could be divided into posterior segment abnormalities (morning glory disk anomaly, persistent fetal vasculature, peripapillary staphyloma, retinal vascular anomalies, optic nerve hypoplasia and atrophy, choroidal
hemangioma,8,9 and retinal coloboma3), anterior segment abnormalities (cataract,3,5,6,8,10 microphthalmia,3,5,6,8 conjunctival hemangioma,8 posterior embryotoxon,8,9 Mitten-dorf dots,5 corneal opacity,3 sclerocornea,2,9 iris coloboma,9,11 iris heterochromia,8,9,11 and iris vessel hypertrophy,3,6), and miscellaneous ocular abnormalities (congenital glaucoma,8 cryptophthalmos,8,9 proptosis,3,8,9 Horner syndrome,5,8,9 congenital 3rd or 4th nerve palsies,3,11 strabismus,5,8,9,11 and ptosis5,8).

The diagnosis of the PHACE(S) syndrome was based on the presence of a facial hemangioma with the area of more than 5 cm² plus one major or two minor criteria.8 Among ocular manifestations, the posterior segment abnormalities were included in the major criteria category, and the anterior segment abnormalities were included in the minor criteria category.8 Therefore, the presence of large facial hemangioma, along with posterior fossa anomaly, aortic arch anomalies, and morning glory disk (three major criteria) in this patient confirmed the diagnosis of PHACE(S) syndrome.

To our knowledge, this report was the first report of a pattern like Brown’s syndrome (may be called apparent Brown’s syndrome) and the second report of the congenital glaucoma in a case of PHACE(S) syndrome. The original report of PHACE(S) syndrome considered absence of congenital glaucoma as a sign to differentiate PHACE syndrome from other neurocutaneous syndromes.1 In 1999, Coats and colleagues reported a case with PHACE syndrome and congenital glaucoma.8 Like their report, in our case, the congenital glaucoma was found in the eye opposite to the side of hemangioma. Similarly, in the Lasky and colleagues’ report of a case with PHACE syndrome and higher cup/disk ratio in the right eye, the hemangioma was more in the left side of the infant’s face.8 These three reports might suggest an association between PHACE(S) syndrome and congenital glaucoma in the eye opposite to the side of hemangioma. However, this association might be merely an incidental finding.

The history of breathing difficulty in this infant may be due to the hemangiomas in the neck and pharynx or arterial anomalies. As we know, the anomalous origin of the vertebral artery from the aortic arch (seen in our patient) has not been reported in the PHACE(S) syndrome. The consequences of this anomaly are not known and require longer follow-up of this patient.

Propranolol,10 topical, intralesional, and oral steroid,3,5,8 interferon z²a,3,6,8,9 aminocaproic acid,3 and partial resection were used to treat facial hemangioma in the literature. Propranolol had beneficial effects in coarctation of aorta and glaucoma. Thus, the initiation of this drug in our patient was logical. Similar to Coats and colleagues’ report,9 our case underwent surgery for congenital glaucoma in the course of follow-up.

In conclusion, patients with large facial hemangioma must be evaluated for other manifestations of the PHACE(S) syndrome, including eye diseases. In addition, the clinicians must be aware of the probable association between this syndrome and congenital glaucoma and perform the glaucoma work-up for each patient with this syndrome.

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