Bilateral Persistent Fetal Vasculature Associated With Holoprosencephaly

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Abstract. A 3.26-kg neonate with a gestational age of 40 weeks presented with episodic hypothermia and seizures, but stable vital signs. Semilobar holoprosencephaly was seen on magnetic resonance imaging. Ocular examination revealed bilateral persistent fetal vasculature. As genetic testing was not contributory, toxic intrauterine environmental insulin causing neurologic maldevelopment was the presumed etiology. J Pediatr Ophthalmol Strabismus 2004;41:236-237.

INTRODUCTION

Holoprosencephaly is a malformation of the forebrain resulting in the failure of development of the cerebral hemispheres and neurologic dysfunction. Ocular persistent fetal vasculature results from the inability of the fetal hyaloid vascular system to regress. We describe a case of holoprosencephaly in combination with persistent ocular bilateral fetal vasculature, which, to our knowledge, has not been previously reported.

CASE REPORT

A 3.26-kg African American male neonate was delivered by a 19-year-old primigravida at 40 weeks' gestation. He had stable vital signs and blood parameters with the exception of episodic hypothermia, hyperbilirubinemia, and seizure-like activity. Magnetic resonance imaging of the head revealed the absence of distinct cerebral hemispheres with a small amount of residual frontal lobe, rudimentary thalami, and replacement of the missing hemispheres with cerebral spinal fluid, consistent with semilobar holoprosencephaly (Figure).

On postnatal day 18, an ophthalmic examination revealed poor fixation, minimal reaction to bright light, and 4-mm sluggish pupils. The corneal diameters measured 10 mm and the anterior segments showed no coloboma or lens opacity. Posteriorly, tractional retinal detachments on the temporal and nasal sides of the optic disc in the right eye were noted; these were less extensive in the left eye. There was an associated vitreous hemorrhage in the left eye. Glotic membranes were noted on the dome of the retinal elevations connecting to a common glial stalk extending anteriorly to insert on the equatorial posterior lens capsule nasally, consistent with the posterior form of persistent fetal vasculature. A ventriculoperitoneal shunt for the enlarged cystic cavity secondary to hydranencephaly
was performed. The neonate is stable and receiving supportive care.

DISCUSSION

Bilateral persistent fetal vasculature with holoprosencephaly is rare. Persistent fetal vasculature is a result of failure of regression of the fetal hyaloid vasculature and is usually unilaterial. In our patient, the glial network for the hyaloid vessels persisted despite the fact that the hyaloid vessels themselves had regressed. Persistent fetal vasculature has rarely been found in association with systemic diseases such as Warburg's syndrome, Aicardi's syndrome, ocular-palatal-cerebral syndrome, Norrie's disease, trisomy 13, fetal alcohol syndrome, and septo-optic dysplasia with schizencephaly.

Holoprosencephaly results from failure of cleavage of the prosencephalon into distinct cerebral hemispheres and failure of formation of the forebrain during the 5th and 6th weeks of gestation. The resultant area devoid of cerebral tissue is replaced by cerebrospinal fluid. This entity may be mistakenly reported as hydrocephalus, but is actually a form of hydranencephaly because there is replacement of missing brain hemispheres with cerebrospinal fluid and not a displacement of preexisting brain tissue. As with true hydrocephalus, a ventriculoperitoneal shunt may be performed to alleviate the associated morbidity of an enlarged head from hydranencephaly.

Holoprosencephaly represents a continuum of forebrain malformation with the anterior portions of the brain most severely affected. Less severe deficits may result in hypertelorism and varying degrees of inadequate midfacial and forebrain development such as a cleft lip or a single central incisor, whereas more severe deficits result in cyclopia. The incidence has been reported as 1 case per 15,000 live births. Associated conditions include trisomy 13 and 18, Meckel–Gruber syndrome, aberrations in chromosomes 2, 3, 7, and 21, and triploidy. It occurs in the offspring of diabetic women at a rate of 1% to 2%. In our patient, a normal 46,XY karyotype and the lack of both a family history and evidence of drug intake that could have had teratogenic effects supported a sporadic, nongenetic etiology. This neonate was born at term, his parents were nonconsanguineous, and he had no known family history of birth defects. Furthermore, the results of genetic testing, including chromosome 13q deletion syndrome, were negative, suggesting that the reported autosomal recessive transmission of children with lissencephaly and retinal dysplasia was unlikely. In addition, the presentation in our patient of intact limbs and facial bones together with the absence of a coloboma is evidence against a true histologically proven retinal dysplasia. Although retinal dysplasia should be considered in the diagnosis, the differentiation requires pathologic evaluation, which may fail even histologically to distinguish between retinal dysplasia and congenital retinal detachment. Further gene identification in holoprosencephaly, along with possible inciting environmental factors, remains to be elicited.

It is likely that our patient endured an unknown toxic environmental or genetic interaction resulting in an encephaloclastic process. This event occurred when the eye was fully developed, but the embryologic vascular hyaloid structures at the posterior pole had failed to regress totally with resultant bilateral persistent fetal vasculature.

It has been hypothesized that septo–optic dysplasia without hemispheric malformations, but with a central holoventricle, may represent one of the mildest forms of holoprosencephaly. If so, our case with the additional association of bilateral persistent fetal vasculature may represent an even more severe defect in forebrain development and may contribute to the understanding of this neurologic developmental disorder.

REFERENCES