AMERICAN ACADEMY™ OF OPHTHALMOLOGY

Combined Persistent Fetal Vasculature

A Classification Based on High-Resolution B-Mode Ultrasound and Color Doppler Imaging

Andina Hu, MD, PhD,[1,*] Xiaoqing Pei, MD, PhD,[2,*] Xiaoyan Ding, MD, PhD,[1,*] Jiaqing Li, MD, PhD,[1] Yonghao Li, MD, PhD,[1] Fang Liu, MD,[1] Zijing Li, MD,[1] Zongyi Zhan, MD,[1] Lin Lu, MD, PhD[1]

Purpose: The purpose of this study was to classify combined persistent fetal vasculature (PFV) on the basis of the ultrasonographic and Doppler characteristics. The potential clinical significance for both surgery design and prognosis determination was discussed.

Design: A cross-sectional case series.

Participants: The eyes of 54 children diagnosed with unilateral combined PFV were evaluated using B-mode ultrasound and color Doppler imaging (CDI).

Methods: Each participant's age at first presentation, diagnosis for referral, gender, family history, and systemic or other ocular anomalies were recorded. Retinal detachment, optic nerve abnormalities, and macular dislocation were also recorded in detail according to the RetCam (Clarity Medical Systems, Pleasanton, CA), ultrasound, and Doppler findings. The PFV eyes were divided into 4 groups on the basis of the ultrasound and CDI findings. Intergroup analysis was performed.

Main Outcome Measures: Overall and intergroup analyses of the demographic features of the children with PFV were performed. The axial length, depth of the anterior chamber, and lens thickness were compared between the affected eyes and the fellow healthy eyes among the 4 groups.

Results: Some 22.2%, 18.5%, 33.3%, and 25.9% of the eyes were grouped into type I ("I" shape), II ("Y" shape), III (inverted "Y" shape), and IV ("X" shape) combined PFV, respectively. The age at first presentation for type I was older than that for the other groups ($P = 0.014$). The axial length was reduced ($P = 0.012$) and the anterior chamber more shallow ($P = 0.011$) than in fellow healthy eyes for type IV eyes, but not for the other 3 groups.

Conclusions: Ultrasound and CDI are informative screening and diagnostic tools that show characteristic flow patterns in the 4 types of combined PFV. This novel classification system provides new and important information for the diagnosis of PFV and, if validated, may play a role in guiding treatment recommendations in the future. *Ophthalmology 2016;123:19-25 © 2016 by the American Academy of Ophthalmology.*

Persistent fetal vasculature (PFV), also known as "persistent hyperplastic primary vitreous," is a rare congenital ocular developmental malformation that is caused by the regression failure of the primary vitreous during the embryonic period.[1,2] The remnants of the fetal hyaloid system, extending from the optic disc to the lens to varying degrees, may hamper the proper development of the retina. It is usually associated with microphthalmia, cataract, retrolental fibrovascular mass, elongation of the ciliary processes, and retinal traction or detachment.[3]

Persistent fetal vasculature can be present in 3 forms: anterior, posterior, and combined (both anterior and posterior). Combined PFV is the most common and complicated form, accounting for approximately 60% of all cases.[4] When left untreated, PFV may develop into corneal opacification, secondary angle-closure glaucoma, or spontaneous intraocular bleeding.[5–8] The prognosis is poor, and the condition sometimes requires enucleation because of painful uncontrolled intraocular pressure elevation or phthisis bulbi.[5,6] Although some eyes with the anterior form of PFV exhibit a relatively good visual prognosis after surgery,[4,9] both the posterior and the combined form constrain the achievement of good vision.[5] However, the indications for surgery in combined PFV have changed over the years as knowledge of the disease together with surgical instrumentation and sophisticated microsurgical techniques have advanced. Early and appropriate surgical intervention may prevent the progressive, pathologic changes that occur in combined PFV, and so offer hope for a positive visual outcome.[4,6] Thus, the early diagnosis and assessment of the lesion before surgery are essential.

Recently, color Doppler imaging (CDI) has been reported to provide additional structural and vessel dynamic information in a number of adult orbital and ocular disorders.[10]

http://dx.doi.org/10.1016/j.ophtha.2015.09.001
ISSN 0161-6420/15

Presently, there is little information concerning the potential usefulness of CDI in characterizing ocular diseases during infancy or childhood. In this study, we use CDI and B-mode ultrasound as auxiliary but valuable tools in the evaluation of PFV in children. The purpose of this study was to classify combined PFV on the basis of the ultrasound and CDI characteristics to provide helpful information for both the surgery design and the prognosis determination for combined PFV.

Methods

Subjects

A total of 68 children (42 boys, 26 girls) with PFV who were consecutively referred to the pediatric retina unit of Zhongshan Ophthalmic Center, SunYat-sen University, from January 2014 to June 2015 were included in this study. The diagnosis of combined PFV was based on the presence of persistent retrolental fibrovascular membrane and stalks extending from the optic nerve, with or without retinal traction or detachment. All of the protocols followed the tenets of the Declaration of Helsinki, and the study was approved by the ethical committee of Zhongshan Ophthalmic Center, Sun Yat-sen University. Comprehensive examinations were performed for all patients, including slit-lamp examination, indirect ophthalmoscopy, intraocular pressure measurement using a Schiotz tonometer, and anterior segment and retina wide-angle photography with a RetCam (Clarity Medical Systems, Pleasanton, CA) for infants or fundus photography for children (Topcon TRC 50DX; Topcon Corp. Tokyo, Japan). Fundus fluorescein angiography (FFA) was performed in some patients with visible fundus (Clarity Medical Systems). High-resolution B-mode ultrasound and Doppler examination (iU22; Philips Medical Systems, Royal Philips Electronics, Amsterdam, The Netherlands) were performed for each patient. All of the children who were unable to follow instructions were sedated using chloral hydrate (0.6 ml/kg; upper limit dose: 10 ml) before the examinations.

The exclusion criteria for our study were as follows: individuals who were diagnosed with only posterior PFV or anterior PFV; children who had bilateral involvement because familial exudative vitreoretinopathy or other genetic disease could not be excluded; children who had an intravitreal mass accounting for 50% of the vitreous cavity or more in B-mode ultrasonography; patients who demonstrated the presence of phthisis bulbi or anterior chamber and vitreous hemorrhage that make diagnosis difficult; patients with possible retinoblastoma; and patients with a history of prematurity or prior ocular surgery. In some cases, FFA of the fellow eye was performed and comprehensive examination of the patients' first-degree relatives was conducted to rule out the possibility of familial exudative vitreoretinopathy and other genetic diseases. Finally, 54 combined subjects with PFV (35 boys, 19 girls) were enrolled.

RetCam and Fundus Photography

The images of the anterior segment of the eyeball in all patients were captured after pupil dilation. The wide-field fundus photography (RetCam III imaging) for infants and children younger than 4 years old was performed by the same experienced retinal doctor (A.H.). Digital fundus photography was performed for all the children older than 4 years of age.

B-mode Ultrasound and Color Doppler Imaging

The B-mode ultrasound and CDI were performed by an expert sonographer (X.P.) using a color Doppler unit and a 9- to 12-MHz linear-array transducer (model G-60; Siemens, Erlangen, Germany). First, gray-scale ultrasound was performed, which demonstrated anatomic details and sonographic characteristics. Next, the Doppler examination was conducted, which revealed the existence of vascular flow. All of the patients were examined in the supine position to avoid any pressure on the eye. An abundant quantity of gel was applied over the closed eyelid, with the examiner's hand resting on the borders of the orbits to minimize the pressure on the globe.

All relevant clinical information, including age at first presentation, age at referral, diagnosis for referral, gender, family history, and systemic and other ocular anomalies, was collected. The depth of the anterior chamber, lenticular changes, lens thickness, retinal detachment, optic nerve abnormalities, and macular dislocation were also recorded in detail according to the RetCam, ultrasound, and Doppler findings.

Statistical Analysis

All of the analyses were performed using the Statistical Package for the Social Science software version 16.0 (SPSS Inc., Chicago, IL). The normality of the continuous variables' distribution was checked using the Kolmogorov−Smirnov test. The independent samples t test was used for the normally distributed continuous variables, and the Kruskal−Wallis H test was used for the non-normally distributed continuous variables. The Pearson chi-square test and Fisher exact test were used for the categoric variables. A P value <0.05 was considered statistically significant.

Results

In total, 54 subjects (54 eyes), 35 male and 19 female, were enrolled in this study. None of the subjects had a positive family history. The intraocular pressures of all subjects were normal (range, 7−18 mmHg). The median age at referral to our clinic was 24 months (range, immediately after birth to 264 months), whereas the median age at first presentation before referral was 3.5 months old (range, immediately after birth to 120 months). The main symptoms reported by caregivers were leukocoria, microphthalmia, strabismus, and poor vision. The demographic and clinical details of all the subjects are listed in Table 1.

Subtle structural abnormalities, including the lens-vitreous surface and vitreous-optic nerve surface, were investigated on the basis of ultrasonography and the presence or absence of blood flow, and characteristic flow patterns were noted in CDI. According to the ultrasound and Doppler results, all of the affected eyes could be grouped into 4 types (Table 1, Fig 1).

Type I ("I" shape) was found in 12 of 54 eyes (22.2%). It presented as a linear narrow band extending from the optic disc to the posterior lens capsule. Blood flow could be detected in the band in all 12 eyes (100%) (Fig 1A−D).

Type II ("Y" shape) was detected in 10 of 54 eyes (18.5%). It manifested as a membranous septum with a narrow base extending from the optic disc. However, the posterior lens capsule was widely covered. Ciliary detachment and traction or dense ciliary membranes were noted with ultrasonography. The CDI showed