An Unusual Case of Prenatal Ultrasound Diagnosis of Persistent Hyperplastic Primary Vitreous with Retinoblastoma

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Introduction

Fetal persistent hyperplastic primary vitreous (PHPV) and retinoblastoma (Rb) is rare congenital abnormal development of the vitreous body[1,2]. According to related manifestations after delivery, PHPV is clinically called "white pupil." It mainly manifests as vision loss and lens opacity and, in severe cases, as intravitreal hemorrhage and eyeball atrophy. The disease is possibly isolated or associated with congenital syndromes, such as Walker–Warburg syndrome and Norrie disease. Rb is the most common intraocular malignancy of childhood. The role of prenatal ultrasound screening for Rb has been discussed[3]. Here, we present a case of persistent primary hyperplasia vitreous diagnosed in the second trimester using prenatal ultrasonography. An echogenic band with an irregular surface was detected between the lens and the posterior wall of the left eye. No other system abnormalities were present in the fetus.

Case Presentation

The patient's mother is a 29-year-old female who had two pregnancies and one delivery. The prenatal ultrasound examination was performed at 24 weeks of gestation, and the following were detected: the bilateral orbits of the fetus are asymmetric, the left eyeball is smaller than the right, the lens and vitreous body of the right eye have no obvious abnormalities, and there is a band-shaped hyperechoic area between the left eye lens and posterior wall of the eyeball with a funnel-shaped appearance with calcification (Figure 1a). Three-dimensional (3D) imaging shows that the left eyeball is smaller than the right, and the left vitreous has a band-shaped hyperechoic area (Figure 1b). Color blood flow imaging showed a band-shaped hyperechoic area, and the blood flow signal continued in the posterior papillary artery (Figure 1c). Prenatal ultrasonography was diagnosed as PHPV, but retinoblastoma is suspected. After communicating with the pregnant woman and her family, the pregnant woman requested to induce labor, and a baby girl was born. Postpartum ocular ultrasonography showed that an echogenic band with calcification extends from the vitreous to the posterior wall of the eyeball, which was consistent with prenatal ultrasonography (Figure S1a). Computed tomography showed a fibrous band between the left vitreous and posterior wall of the eyeball (Figure S1b). The left eyeball was smaller than the right (Figure S1c). The specialized ophthalmology examination showed that bilateral eyeballs were unequal in size, and the left eyeball showed a typical "white pupil" (Figure S2a, S2b). The pathological examination showed that the left eyeball was smaller than the right (Figure S2c). PHPV with retinoblastoma diagnosis was confirmed by the pathological examination, showing a retrolental connective fiber-vascular tissue, hyperplasia of blood vessels, retinal detachment and Rb were also observed (Figure S3a, S3b, S3c)

Discussion

Fetal eye deformities are rare, including anophthalmia, microphthalmia, cataract, and PHPV, and clinical reports mainly focus on fetal cataracts. Eye diseases are more common in term children and men, and about 90% of patients have unilateral diseases[4]. However, bilateral onsets are mostly accompanied by other ocular and systemic abnormalities, including congenital trisomy 13, Walker–Warburg syndrome, or Norrie disease, which are clinically described during the postpartum period according to related manifestations. PHPV is often manifested as a "white pupil," accompanied by cataracts, glaucoma, vision loss, and lens opacity. In severe cases, intravitreal hemorrhage, congenital retinal detachment, and even eyeball atrophy may occur[5].

Normally, the primitive vitreous develops from the intercellular space between the lens vesicle and primitive optic vesicle at 6–12 weeks of the pregnancy. During the same period, the blood vessels in the primitive vitreous begin to shrink gradually, and the primitive vitreous is completely degenerated and absorbed after delivery. If the primitive vitreous body is not completely degenerated and absorbed during embryonic development, and the fibrovascular connective tissue is abnormally proliferated, it will form a persistent primitive vitreous hyperplasia.

Prenatal two-dimensional ultrasonography showed that the central part of the vitreous was hyperechoic with a "funnel" or "inverted triangle" shape[6]. The posterior wall of the lens was connected to the base, and the tip was connected to the optic disk. One side of the orbit is smaller than the other side. A three-dimensional surface imaging showed hyperechoic fibrous plaques in the vitreous inside the eyeball, and color Doppler blood flow detected blood flow signals in strip arteries[7].

PHPV has a poor prognosis, and if left untreated, it can cause repeated intraocular hemorrhage and secondary glaucoma, which may, eventually, require enucleation. However, the disease should be differentiated from Walker–Warburg syndrome and congenital cataract[6]. Congenital cataracts have a good prognosis and can be treated after birth. On ultrasound, cataracts are mainly detected in the lens, mostly in both eyes, with typical oval ring echoes. Walker–Warburg syndrome is an autosomal recessive syndrome. Its main features are congenital muscular dystrophy, hydrocephalus, cerebellar vermis hypoplasia, cerebellar hemisphere hypoplasia or corpus callosum hypoplasia, encephalocele, and ophthalmia with microscopic ocular malformations, including persistent primary vitreous hyperplasia. Norrie disease is another X-linked recessive disease that causes bilateral PHPV, and its features include early childhood leukocytosis, deafness, mental retardation, and loss of retinal ganglion cells. Glaucoma and cataracts can coexist. The phenotypic features include growth restriction, narrow nasal bridge, large ears, hypogonadism, and undescended testes. Since no other systemic abnormalities were present in our patient, she was diagnosed with isolated persistent vitreous hyperplasia.

Retinoblastoma, the most common malignant intraocular neoplasm of childhood is the most common cause of leukocoria which is a cose mimic of PHPV[3,8]. There have been very rare reports detailing in utero imaging of retinoblastoma. However, retinoblastoma is often associated with normal globe size and a calcified mass. PHPV is the second most common cause of leukocoria after retinoblastoma. Prenatal ultrasound reveals reduced eyeball and shows an echogenic band extending from the posterior surface of the lens capsule to the optic disc without any evidence of calcification.

In conclusion, PHPV with Rb is an important disease that can be diagnosed prenatally. This case illustrates the value of prenatal screening for persistent hyperplastic primary vitreous with retinoblastoma. However, it should be noted that the eyes may appear normal in the second trimester and abnormal in the third trimester. Additionally, for intrauterine diagnosis in subsequent pregnancies, it is recommended that prenatal genetic testing be performed at an early stage.

Ethical Approval

This study has been granted an exemption from the Medical Ethics Committee of Gansu Provincial Maternity and Child-Care Hospital. Participants provided their written informed consent to publish their cases (including publication of images).

Acknowledgments

Not applicable.

Conflicts of Interest

The authors have no conflicts of interest.

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Data Availability

The data and material in the current study are available from the corresponding author on reasonable request.

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Figure legends

Figure 1: Prenatal ultrasonography image of PHPV. (a) Two-dimensional ultrasound demonstrating PHPV, with a band-shaped hyperechoic between the left eye lens and posterior wall of the eyeball showing funnel-shaped (Red Arrow) with calcification (Yellow Arrow). (b) 3D imaging mode shows the left small eyeball and the left vitreous with band-shaped hyperechoic (Red Arrow). (c) Color blood flow was detected in the band-shaped hyperechoic area (Red Arrow). PHPV: Persistent hyperplastic primary vitreous. 2D: two-dimensional; 3D: three-dimensional.

Figure S1: Postpartum image of PHPV. (a) Two-dimensional ultrasound demonstrated the strong vocal cords in the vitreous were connected with the posterior wall of the eyeball (Red Arrow) with calcification (Yellow Arrow) . (b) CT showed a fibrous band between the vitreous and the posterior wall of the eyeball (Red Arrow). (c) CT showed the left eyeball smaller than the right. PHPV: Persistent hyperplastic primary vitreous. CT: Computed tomography.

Figure S2: Postpartum image of ophthalmology examination. (a-b) Postnatal ophthalmology examination shows bilateral eyeballs were unequal in size, and the left eyeball showed a typical “white pupil.”. (c) The pathological examination showed that the left eyeball was smaller than the right.

Figure S3: Postpartum image of pathological examination. (a) Pathological examination showed the right eye is normal. (b) Fibrous bands in the vitreous of the left eye and hyperplasia of blood vessels (Blue Arrow). (c) Pathological examination showed retinal detachment and retinoblastoma (Blue Arrow).

Supporting information

Additional supporting information is provided online at the end of the article.

Video 1. Prenatal ultrasound demonstrating persistent hyperplastic primary vitreous with retinoblastoma.

Video 2. Posterior ultrasound demonstrated persistent hyperplastic primary vitreous with retinoblastoma, which was consistent with the prenatal ultrasound.