Asian Journal of Current Research in Clinical Cancer
ISSN: 3062-4444
2024, Volume 4, Issue 1, Page No: 25-30

Available online at: www.galaxypub.co/page/journals

Galaxy Publication

Case Report on Persistent Fetal Vasculature Accompanied by Congenital Hydrocephalus

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Received: 05 February 2024; **Revised:** 17 April 2024; **Accepted:** 22 April 2024

ABSTRACT

Persistent fetal vasculature (PFV), or persistent hyperplastic primary vitreous (PHPV), is a rare condition involving abnormal development of the vitreous and retinal structures. This case report highlights a premature male infant, born at 35 weeks gestation weighing 2.135 kg, who presented with PFV, hydrocephalus, and developmental delay. The infant underwent an emergency cesarean section due to fetal distress. Antenatal ultrasound revealed significant ventriculomegaly (43 mm). Postbirth, the infant required brief positive pressure ventilation and was admitted to the NICU. Initial CT brain imaging revealed hydranencephaly, and ocular evaluations, including fundoscopy and B-scan ultrasound, revealed a hyperechoic mass in the left eye, which raised the suspicion of retinoblastoma. However, a later CT orbit study ruled out a mass or calcifications, confirming a diagnosis of PFV affecting the left eye, with no mass lesions or calcifications present. Whole exome sequencing (WES) identified a de novo mutation in the COL4A1 gene (c.1802G > T p.(Gly601Val)). The infant remained in the NICU for 65 days, where he remained hemodynamically stable and was able to tolerate full oral feeding. He was discharged home in stable condition. This case emphasizes the importance of considering PFV in the differential diagnosis in the presence of leukocoria or microphthalmia. Differentiating PFV from retinoblastoma can be difficult because PFV usually affects one eye and does not show calcification, whereas retinoblastoma often presents with calcified masses. Advanced imaging techniques, such as CT scans, play an important role in accurate diagnosis. A comprehensive ophthalmic examination and further diagnostic workup are essential in these cases.

Keywords: Diagnosis, CT brain, Persistent fetal vasculature (PFV), Management

How to Cite This Article: Osluf ASH, Shoukeer M, Almarzoog NA. Case Report on Persistent Fetal Vasculature Accompanied by Congenital Hydrocephalus. Asian J Curr Res Clin Cancer. 2024;4(1):25-30. https://doi.org/10.51847/0gjOEudJNr

Introduction

Persistent fetal vasculature (PFV), or persistent hyperplastic primary vitreous (PHPV), is a rare developmental anomaly of the vitreoretinal system. It arises due to incomplete regression of the primary vitreous during fetal development, resulting in a fibrovascular tissue mass behind the lens. PFV is a major cause of cataracts in infants, typically appearing in the first year of life [1-4]. It is predominantly unilateral and often sporadic, but when bilateral, it can be associated with systemic conditions such as Norrie's disease, Warburg syndrome, Patau syndrome, or retinal dysplasia. Hydrocephalus, a condition characterized by an abnormal accumulation of cerebrospinal fluid in the brain's ventricles, is a prevalent neurodevelopmental issue globally. It has substantial health implications, particularly in developing countries, and incurs significant treatment costs in places like the United States [5-8]. This report presents a case of PFV in conjunction with congenital hydrocephalus.

Case report

This case involves a preterm male neonate, born at 35 weeks of gestation, weighing 2.135 kg. The delivery occurred via emergency cesarean section due to fetal distress. The mother, a 28-year-old woman with a history of

hypothyroidism treated with oral thyroxine, had a prenatal ultrasound revealing severe ventriculomegaly (43 mm). The newborn's Apgar scores were 6 at 1 minute, 7 at 5 minutes, and 8 at 10 minutes. After delivery, he required brief positive pressure ventilation and was admitted to the neonatal intensive care unit (NICU).

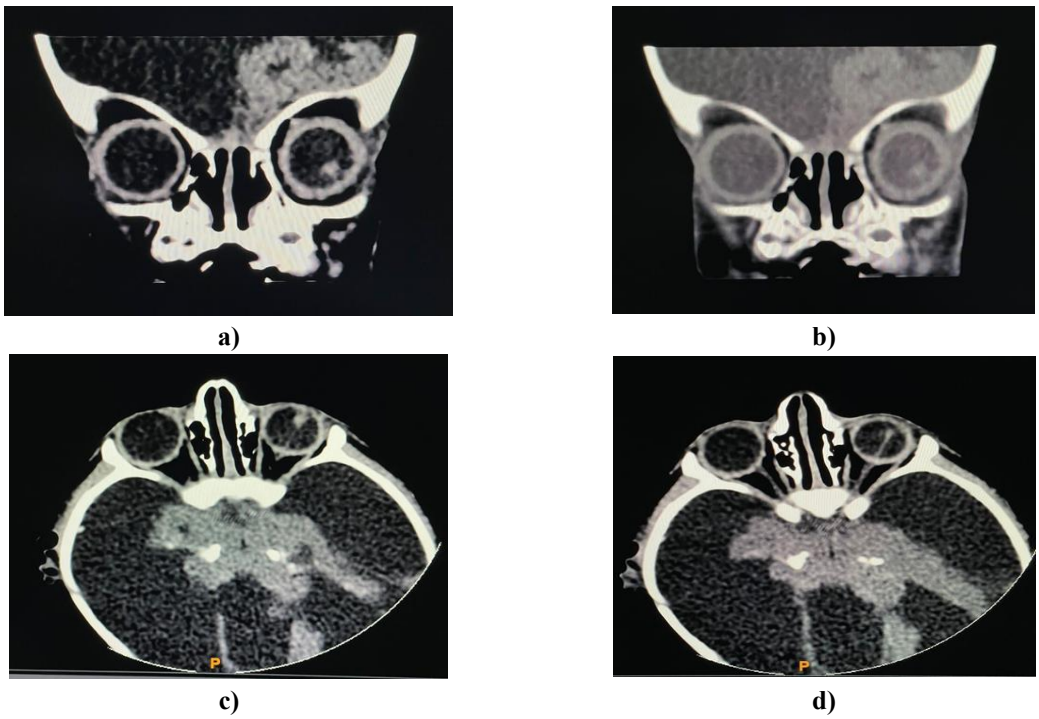
Upon physical examination, the baby was noted to have an abnormally large head with a circumference of 36 cm (below the 90th percentile). He also exhibited wide fontanels, spaced cranial sutures, and sunken eyes. His facial features were suggestive of a triangular face, and although he was alert with spontaneous eye movements, his pupils were sluggish. The baby showed poor muscle tone, with weak reflexes, and had significant head lag.

Initially, the baby experienced respiratory distress and required nasal continuous positive airway pressure (CPAP), but his condition improved, and he was eventually weaned to room air. No abnormalities were detected in the abdominal ultrasound, and his liver function tests indicated conjugated hyperbilirubinemia, with total bilirubin levels of 594 µmol/L and direct bilirubin at 349 µmol/L.

An ophthalmologic examination revealed a dilated pupil and a large preretinal hemorrhage in the right eye, accompanied by a pale optic disc. The left eye presented with microphthalmia and cataracts, and no retinal view was possible. A CT scan of the brain confirmed hydranencephaly **(Figure 1)**. In addition, a B-scan ocular ultrasound and fundoscopy raised the suspicion of retinoblastoma in the left eye due to a hyperechoic mass. However, a follow-up CT of the orbits revealed findings consistent with persistent hyperplastic primary vitreous in the left eye, both anterior and posterior forms, without mass lesions or calcifications **(Figure 2)**.

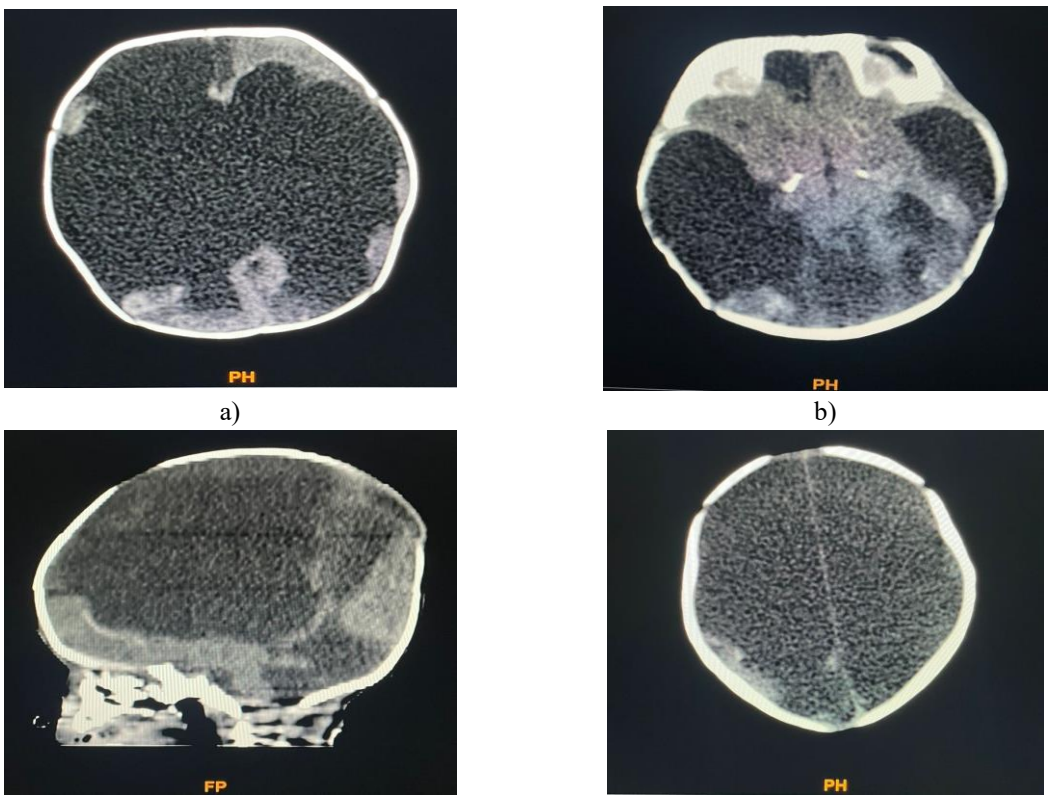
The infant was transferred to a specialized medical center for further care. Despite requiring oxygen supplementation and nasogastric tube (NGT) feeding, the baby's general condition remained stable. Genetic testing through whole exome sequencing (WES) identified a de novo heterozygous variant (c.1802G > T p.(Gly601Val)) in exon 26 of the COL4A1 gene.

Considering the combination of hydrocephalus and the poor visual prognosis, a do-not-resuscitate (DNR) status was established for the infant. After 65 days in the NICU, during which he stabilized on room air and was able to tolerate full oral feeding, the infant was discharged in stable condition.



a) **b)** **c)** **d)**

Figure 1. The CT scan of the orbits revealed a relatively smaller left eye globe with a hypoplastic lens and a shallow anterior chamber; a retro-lental soft tissue band was observed extending towards the posterior chamber, passing through the vitreous, and reaching the posterior choroidal layer; the vitreous in the left eye appeared denser than usual; no evidence of calcifications or mass formations was found; the right eye globe appeared normal; the muscle cones, central fat, optic nerves, preseptal and extra-conal spaces, and lacrimal glands all displayed consistent attenuation patterns and preserved structures bilaterally; no abnormal attenuation or localized lesions were identified; the bony orbital walls, orbital fissures, and optic foramina were intact; these imaging findings were indicative of persistent fetal vasculature (PFV).



a) b)

c) d)

Figure 2. The cranial CT scan demonstrates cerebrospinal fluid (CSF)-like density occupying the majority of the cranial cavity, with the absence of discernible cortical brain tissue lining the inner aspect of the skull; the falx cerebri remain intact and visible; small residual portions of brain parenchyma are identified in the parietal and occipital lobes, exhibiting signs of abnormal calcification; notable calcifications are also present in the basal ganglia region; structures of the posterior fossa, particularly the cerebellum, appear underdeveloped, and the fourth ventricle is prominently dilated; these radiologic findings strongly suggest a diagnosis of hydrocephalus.

Results and Discussion

During embryonic development, the eye is nourished by a network of blood vessels, which typically regress after maturation. When this regression fails to occur completely, a condition known as persistent fetal vasculature (PFV) may develop. PFV commonly presents with clinical features such as leukocoria, microphthalmia, and cataracts, and it must be considered in the differential diagnosis of retinoblastoma [9-15]. In the case we observed, retinoblastoma in the left eye was initially suspected. However, after conducting multiple detailed ophthalmologic and imaging evaluations, a diagnosis of PFV was established [1]. Identifying PFV can be challenging for both pediatricians and ophthalmologists due to its clinical resemblance to retinoblastoma. Nevertheless, PFV should be among the first considerations when examining cases of leukocoria or microphthalmia.

Computed tomography (CT) imaging can reveal the ocular and orbital anomalies associated with PFV, including signs like microphthalmia, buphthalmos, fibrotic tissue behind the lens near the Cloquet canal, and retinal detachment. Hyperreflective signals in the subretinal space can also be noted. Consistent with our findings and those in most PFV cases, intraocular or orbital calcification is usually absent [16]. To differentiate PFV from retinoblastoma via CT imaging, the lack of intraocular calcification and the presence of microphthalmia are key features. Typically unilateral, PFV frequently coexists with microphthalmia or cataracts, and the absence of calcification helps distinguish it from retinoblastoma [17].

Since PFV is one of the most common conditions mimicking retinoblastoma, it is identified in roughly 20% of suspected retinoblastoma presentations, making its recognition critical in clinical assessment [17]. Core clinical signs of PFV include leukocoria, lens opacity, elongation of the ciliary processes, a shallow anterior chamber, the presence of a fibrovascular membrane behind the lens, and a smaller-than-normal eye [18]. Under normal

physiological circumstances, fetal vasculature regresses, but persistence of these vessels can occur in approximately 3% of full-term neonates and as many as 95% of preterm infants, contributing to a variety of ocular pathologies [19]. PFV is typically diagnosed using ophthalmoscopy, but due to its clinical similarity to retinoblastoma, accurate diagnosis can be complicated. Co-occurrence of PFV and retinoblastoma is highly rare, with only two such cases documented in the literature [20, 21]. As a result, ophthalmologists must conduct comprehensive diagnostic investigations to ensure precise identification.

In the present case, both anterior and posterior forms of PFV were identified. PFV is categorized into three main types depending on which parts of the eye are involved [22, 23]. The anterior subtype, accounting for about a quarter of PFV cases, is characterized by lens opacities, fibrous tissue growth behind the lens, and elongation of the ciliary body. Posterior PFV, seen in approximately 12% of cases, involves attachments between vascular membranes and the optic disc, as well as abnormalities such as eye shrinkage and underdevelopment of the retina, macula, and optic nerve head. The mixed type, which our patient had, combines features of both anterior and posterior PFV and is observed in nearly 63% of cases.

Genetic analysis through whole exome sequencing (WES) in our case revealed a de novo heterozygous mutation c.1802G > T p.(Gly601Val) in exon 26 of the COL4A1 gene. This gene encodes the alpha-1 chain of type IV collagen and is known to be implicated in autosomal-dominant conditions such as porencephaly and infantile hemiparesis [24, 25]. Porencephaly is a rare neurological condition characterized by cerebrospinal fluid accumulation within the brain's cavities. Mutations in COL4A1 are associated with small vessel disease affecting cerebral circulation. Such mutations have also been identified in adults diagnosed with small vessel disease of the brain [25, 26]. Clinical features of this genetic alteration include ischemic stroke, intracerebral bleeding, and radiologic evidence of lacunar infarcts, white matter changes (leukoaraiosis), and microbleeds [26]. The brain CT scan of our patient demonstrated cerebrospinal fluid density occupying the cranial vault, with an absence of cerebral mantle tissue adjacent to the inner table of the skull.

Hydrocephalus, marked by an excessive buildup of cerebrospinal fluid in the brain's ventricles, is a serious neurological disorder that can arise at any age but is more common in children. It is associated with a broad spectrum of underlying causes, such as hemorrhage, neoplasm, infection, or stroke. In pediatric patients, hydrocephalus is often accompanied by ocular abnormalities and can significantly impair both neurological and visual functions [27]. If left untreated, hydrocephalus leads to progressive ventricular enlargement and elevated pressure inside the skull. In our case, congenital hydrocephalus was present along with congenital eye malformations. Notably, hydrocephalus can also directly influence vision, causing complications such as optic nerve atrophy. Mechanisms involved include degeneration across neuronal pathways, compromised blood flow to the optic nerve, or physical stress on optic structures. Visual problems such as optic atrophy may even be an early indicator of shunt failure, and prompt surgical intervention can reverse some visual deficits. The proximity of visual pathways to the lateral ventricles makes them particularly susceptible to damage caused by hydrocephalus-induced dilation. Consequently, children with hydrocephalus frequently exhibit ophthalmologic issues including decreased visual acuity, strabismus, limitations in eye movement, and visual field abnormalities [13, 27].

Conclusion

When evaluating patients presenting with leukocoria or microphthalmia, persistent fetal vasculature (PFV) should always be included as a possible diagnosis. Although distinguishing PFV from retinoblastoma may pose a diagnostic challenge for both pediatricians and ophthalmologists, certain features can assist in this differentiation. PFV characteristically affects only one eye and is commonly associated with microphthalmos or cataracts, typically without the presence of calcifications. Advanced imaging, particularly computed tomography (CT), plays a critical role in distinguishing PFV from retinoblastoma. A meticulous clinical and radiological assessment by ophthalmologists is essential in confirming the diagnosis.

Hydrocephalus in pediatric patients is frequently accompanied by a spectrum of ocular abnormalities. If left untreated, this condition may contribute to significant visual deficits and related complications.

Acknowledgments: The authors extend their appreciation to the Research Supervisor for their valuable guidance and support.

Conflict of Interest: None

Financial Support: None

Ethics Statement: None

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