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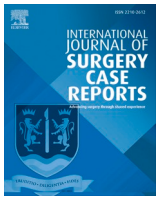

Case report

Concurrent Dandy-Walker malformation and persistent fetal vasculature: A case report

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ABSTRACT

Introduction and importance: Dandy-Walker malformation (DWM) is a rare cerebellar condition, and persistent fetal vasculature (PFV) is a congenital eye anomaly. This report presents the first known case of DWM with PFV.
Case presentation: A 31-day-old male infant presented with right eye discharge, lethargy, and breath-holding spells. He was born at 37 weeks with respiratory distress. Examination and CT scan revealed DWM and PFV. Due to financial constraints, recommended treatments were limited. Follow-up at seven months showed developmental delays but no hydrocephalus.
Clinical discussion: The co-occurrence of DWM and PFV is exceptionally rare and may be linked to TUBA1A gene mutation. Similar cases in the literature support this genetic association.
Conclusion: This study emphasizes the importance of early diagnosis and multidisciplinary management for optimizing outcomes in patients with DWM and PFV. Genetic investigations could further elucidate the underlying pathophysiology.

1. Introduction

Dandy-Walker malformation (DWM) is a rare condition involving the cerebellum and posterior fossa, with an incidence rate of 1 in 10,000 to 30,000 births [1]. It is primarily characterized by a triad involving partial or complete agenesis/hypoplasia of the cerebellar vermis, enlargement of the posterior fossa, and cystic dilatation of the fourth ventricle.

Persistent fetal vasculature (PFV), previously known as persistent hyperplastic primary vitreous (PHPV), is a congenital developmental anomaly of the eye caused by the failure of regression of the primary vitreous. It is divided into anterior, posterior, or mixed types, characterized by the presence of a vascular membrane behind the lens [2].

Several previous reports have described ophthalmic manifestations associated with DWM, including congenital cataracts, macular edema, microphthalmos, and buphthalmos [3,4]. In this report, we describe the first case, to our knowledge, of DWM with PFV. This case report has been reported in line with the SCARE Criteria [5].

2. Case presentation

A 31-day-old male infant presented to the emergency department with a 15-day history of watery discharge from his right eye, reduced feeding, and lethargy for one week. For five days, he had yellowing of the skin and eyes, and for two days, he experienced bluish discoloration of the lips with breath-holding spells occurring up to twice a day. He was born at 37 weeks via emergency cesarean-section due to meconium-stained amniotic fluid and developed grade 2 respiratory distress shortly after birth. His APGAR scores were 6 at 1 min and 8 at 5 min. He was admitted to the neonatal intensive care unit, placed on oxygen (bubble CPAP 5/5), and discharged after five days of intravenous (IV) antibiotics. There were no prenatal checkups or follow-up visits after discharge. He weighed 2.4 kg at birth and at presentation (below the 5th percentile). He is the child of a consanguineous marriage.

On examination, the infant appeared ill and lethargic, with petechiae on his chest. His weight remained at 2.4 kg since birth and had not changed, neither increasing nor decreasing. Neurologically, he had an incomplete Moro reflex, poor sucking and rooting reflexes, and decreased muscle tone in all four limbs with brisk reflexes. He also had

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bilateral clubbed feet and a soft anterior fontanelle. Lab tests revealed elevated total bilirubin, direct bilirubin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), and procalcitonin (Table 1). An ophthalmological exam revealed a white pupillary reflex (leukocoria) in the right pupil, microphthalmia, and retinal detachment in the right eye.

A CT scan of the orbit and brain revealed contour deformity of the right eye, and the globe appeared smaller than normal, confirming microphthalmia (Fig. 1a). A linear high-density structure was identified extending from the head of the optic nerve to the posterior surface of the lens in the right eye globe (Fig. 1b). Additionally, high density was noted in the right vitreous chamber compared to the left (Fig. 1a). The lack of calcification ruled out retinoblastoma, and the fundoscopic findings, coupled with the CT scan, raised suspicion of PFV.

A brain CT scan showed an enlarged posterior fossa (Fig. 2a and c) with hypoplastic cerebellar vermis and hemispheres (Fig. 2b, c, and d). The retrocerebellar cerebrospinal fluid space, which communicated with the fourth ventricle, was enlarged (Fig. 2e). Mild dilation of the bilateral lateral ventricles was also noted (Fig. 2f). The scan indicated flattening of sulci and gyri, suggesting possible lissencephaly, but this could not be confirmed due to financial constraints and lack of parental consent for an MRI scan.

Based on the ophthalmological examination and CT scan findings, the differential diagnoses included mega cisterna magna, Arnold-Chiari Malformation, arachnoid cyst, Walker-Warburg Syndrome, and DWM. Mega cisterna magna was ruled out due to the lack of isolated posterior fossa cyst without cerebellar vermis hypoplasia. Arnold-Chiari Malformation was excluded because there was no downward displacement of the cerebellar tonsils. An arachnoid cyst was ruled out due to the absence of cystic structures in the subarachnoid space. Walker-Warburg Syndrome was unlikely due to the lack of muscle weakness or dystrophic changes. Findings from the ophthalmological examination coupled with the imaging helped narrow down the differential to include PFV as a concurrent working diagnosis alongside DWM.

Due to the high procalcitonin levels (Table 1), coupled with signs and symptoms pointing towards an ongoing bacterial infection, IV antibiotics were initiated. The ophthalmologist recommended surgery for the retinal detachment, but the parents declined due to cost. The neurosurgeon did not recommend immediate intervention for DWM as the infant had not developed hydrocephalus. The patient was discharged with instructions to continue IV antibiotics for 14 days and follow up in five days and again at seven months. At seven months, the infant had not developed hydrocephalus, and surgery was still not advised. He weighed at 3.5 kg (below 5th percentile), was 61 cm long (below 5th percentile), and had a head circumference of 38 cm (15th to 50th percentile). Developmental delays were noted, including failure to hold his neck while lying down. Long-term management was advised, including regular follow-ups with a neurosurgeon to monitor for hydrocephalus, ongoing ophthalmologic evaluation, developmental assessments, and monitoring for recurrent infections.

3. Discussion

DWM was first identified by Dandy and Blackfan in 1914. Taggart and Walker provided descriptive information in 1942, and Benda introduced the term “Dandy-Walker Malformation” in 1950 [6]. It is a nonspecific brain malformation that occurs due to single-gene disorders, chromosomal aberrations, or sporadic environmentally induced cases, either isolated or in conjunction with other abnormalities. Early signs of DWM may present as a range of symptoms, including vomiting, sleepiness, irritability, convulsions, unsteadiness, and lack of muscle coordination [7].

The anomaly may have genetic or environmental predispositions, with the latter involving prenatal exposure to viruses including *CMV* or *Rubella*, maternal diabetes, medications, alcohol, or other teratogenic substances [1]. Radiological imaging is diagnostic of DWM. The prognosis of DWM is variable, with children exhibiting cognitive impairment, while studies have shown up to one-third can also develop normally [1]. Intellectual outcome is highly dependent on associated central nervous system (CNS) anomalies, with poorer outcomes in this group. In the absence of CNS malformation, detection and treatment of hydrocephalus is the single most critical factor in normal intellectual development [6].

PFV commonly presents with leukocoria, microphthalmia, cataract, and elongated ciliary process, although amblyopia, glaucoma, and retinal detachment are associated with poor prognosis. The retinal detachment in PFV is a congenital nonattachment of the retina, believed to result from the traction of the persistent components of the fetal intraocular vasculature [2].

Our patient and his siblings did not present with any additional congenital abnormalities, making chromosomal aberrations or Mendelian disorders such as Warburg or Meckel-Gruber syndromes unlikely. Due to the heterogeneity of ocular clinical presentations reported in cases of DWM, including this case, an early ophthalmic examination should be performed in evaluating children presenting with DWM. The progression of posterior PFV and its associated complications can be mitigated by early conservative or surgical intervention, potentially restoring visual function to some degree.

Both the posterior subtype of PFV and DWM are rare anomalies, and their co-occurrence in this patient is exceptionally uncommon, with only one other case report linking the two to TUBA1A gene mutation in our literature search [8]. The TUBA1A gene has been associated with many congenital brain malformations, including DWM, lissencephaly, malformation of the corpus callosum, cerebellum and basal ganglia, and cerebellar vermis hypoplasia [9].

Due to financial constraints, genetic testing to confirm the association of the two anomalies with TUBA1A could not be carried out. However, the findings associated with DWM and PFV in the CT scans suggest the possibility of tubulinopathy. TUBA1A (OMIM #605529) is a de novo gene mutation which encodes for tubulin alpha 1-A, a microtubule protein responsible for functioning and stability, expressed in both the retina and the brain. Since both the eye and brain arise from the ectoderm, it is not surprising to find these anomalies together [10]. While ocular manifestations of this gene defect are still emerging, we believe our case has findings similar to those of the reports that confirm the two anomalies with TUBA1A mutation.

Ramirez’s case report shared similarities with our case in terms of DWM and PFV [8], but their findings included optic nerve hypoplasia, whereas our case reports retinal detachment and microphthalmia. Similarly, Myer’s case reported bilateral congenital cataracts, microphthalmia, and PFV in a patient with complex brain malformations, including a hypoplastic cerebellar vermis, similar to our case [10]. The TUBA1A gene mutation in the eyes has been reported with a range of malformations, including but not limited to optic nerve hypoplasia, extraocular muscle fibrosis, microphthalmia, congenital cataracts, and PFV [8]. Their case reports the findings of microphthalmia, PFV, and retinal detachment. While Jordan and Montezuma reported a case of PFV with retinal detachment and microphthalmia, their case was associated with De Morsier syndrome and gastroschisis, involving gene defects in Sox2, Sox3, and Hexsl [11].

Table 1
Results of the laboratory investigations.

Laboratory test	Result	Normal range
Total bilirubin	11.63 mg/dL	<2 mg/dL for 1 month to <12 months
Direct bilirubin	0.36 mg/dL	<0.2 mg/dL for >1 month
ALT	133 units/L	12–45 units/L for 1–12 months
AST	371 units/L	9–80 units/L for 8–12 months
Procalcitonin	0.198 ng/mL	0.046 ng/mL

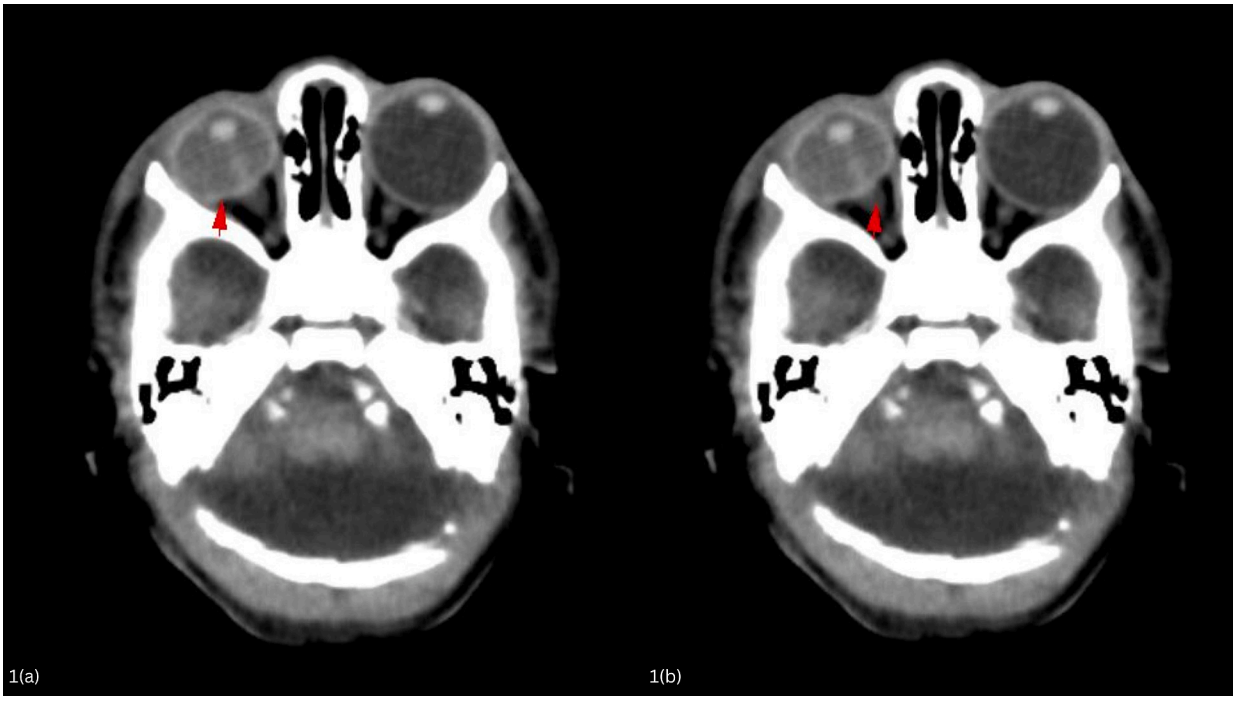

Fig. 1. (a) illustrates microphthalmia (arrow). (b) depicts a linear high-density structure extending from the head of the optic nerve up to the posterior surface of the lens (arrow).

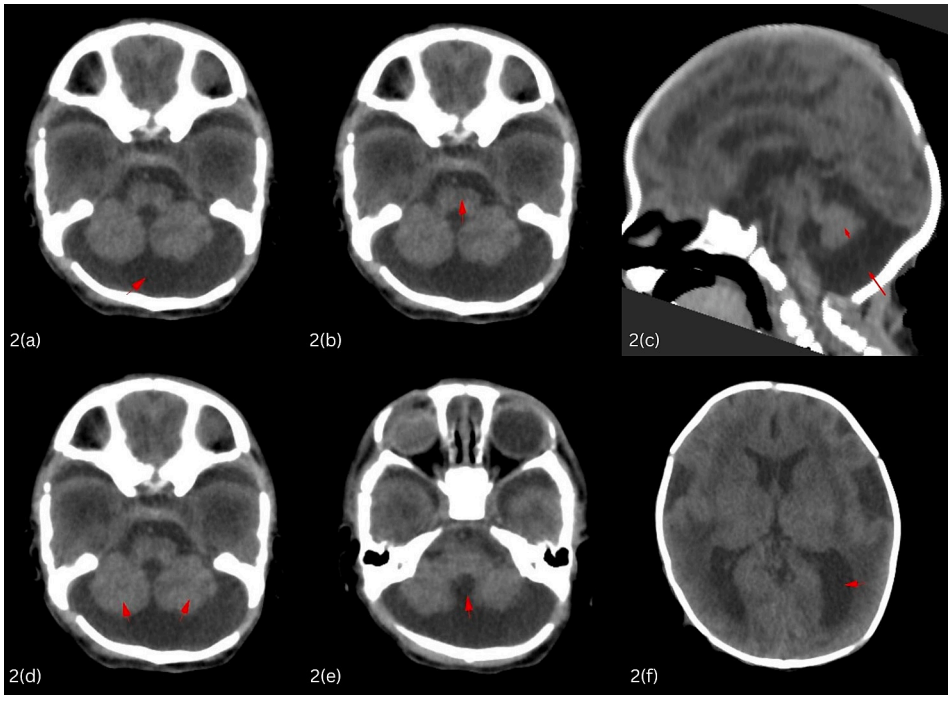

Fig. 2. (a) displays enlargement and cystic dilatation of the posterior fossa (arrow). (b) Shows cerebellar vermis hypoplasia (arrow). (c) Depicts both cystic dilatation of the posterior fossa and cerebellar vermis hypoplasia (arrow). (d) Exhibits cerebellar hemisphere atrophy (arrow). (e) Illustrates enlargement of the retrocerebellar space communicating with the fourth ventricle (arrow). (f) Demonstrates mild dilation of the lateral ventricle (arrow).

4. Conclusion

Our case depicts the rare coexistence of PFV and DWM in a neonate, likely associated with a genetic mutation like TUBA1A. Early recognition and multidisciplinary management are crucial for optimizing patient outcomes, including ophthalmological intervention for PFV-related complications and vigilant neurosurgical follow-up for potential hydrocephalus in DWM. Further genetic investigation could provide deeper insights into the underlying pathophysiology and aid in genetic counselling for families facing similar challenges.

Authorship

All authors had access to the data and a role in writing this manuscript.

Disclaimer

None to declare.

Patient consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Ethical approval

Our study is a case report of a single patient does not require an ethical approval in accordance with Sir Ganga Ram Hospital's policies (ethical approval requirement is waived at Sir Ganga Ram Hospital for case reports involving a single patient).

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Author contribution

Farwa Nisa: conceptualization, data curation, software, writing – original draft preparation.

Hala Nisa: supervision, software, writing – reviewing and editing.

Arsalan Nadeem: software, writing – reviewing and editing.

Maira Anwer: writing – reviewing and editing.

Guarantor

Farwa Nisa, MBBS.

Research registration number

Not applicable.

Conflict of interest statement

None.

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