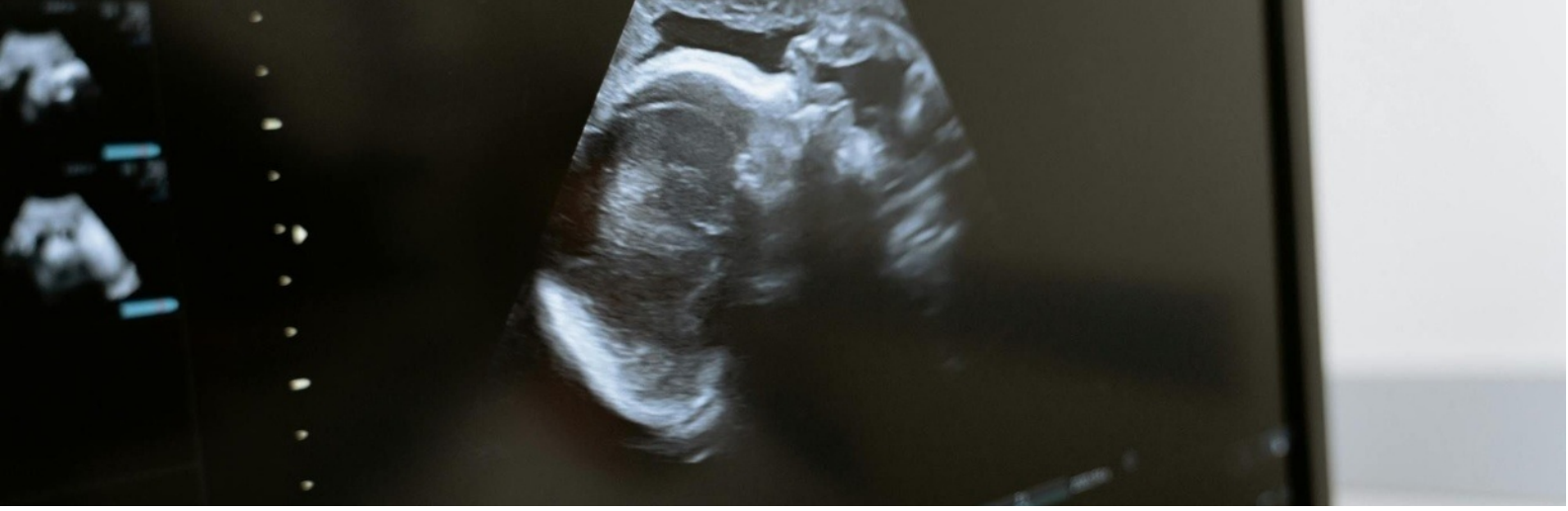

Dandy Walker Malformation Associated with Toxoplasmosis Infection in the Second Trimester: a Case Report

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Abstract:

Dandy-Walker Malformation (DWM) is a rare congenital brain disorder affecting the cerebellum and posterior fossa, occurring in 1 in 35,000 births. It is characterized by agenesis of the cerebellar vermis, fourth ventricle dilation, and an enlarged posterior fossa. Genetic factors, chromosomal abnormalities, and infections like rubella, CMV, and toxoplasmosis contribute to its etiology. This case describes a 16-year-old pregnant woman whose fetus was diagnosed with Dandy- Walker malformation (DWM) at 23.3 weeks. Prenatal findings included severe intrauterine growth restriction, absence of the cerebellar vermis, dysgenesis of the corpus callosum, and cardiac abnormalities. PCR confirmed Toxoplasma gondii infection. Despite treatment, fetal death occurred at 24 weeks. Karyotype analysis ruled out chromosomal abnormalities, suggesting a rare infectious etiology rather than a genetic cause. This case highlights the importance of prenatal toxoplasmosis screening, as its early detection can suggest an accurate diagnosis

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Dandy Walker Malformation Associated with Toxoplasmosis Infection in the Second Trimester: a Case Report

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Abstract

Dandy-Walker Malformation (DWM) is a rare congenital brain disorder affecting the cerebellum and posterior fossa, occurring in 1 in 35,000 births[1]. It is characterized by agenesis of the cerebellar vermis, fourth ventricle dilation, and an enlarged posterior fossa[1-3]. Genetic factors, chromosomal abnormalities, and infections like rubella, CMV, and toxoplasmosis contribute to its etiology[1]. This case describes a 16-year-old pregnant woman whose fetus was diagnosed with Dandy-Walker malformation (DWM) at 23.3 weeks. Prenatal findings included severe intrauterine growth restriction, absence of the cerebellar vermis, dysgenesis of the corpus callosum, and cardiac abnormalities. PCR confirmed *Toxoplasma gondii* infection. Despite treatment, fetal death occurred at 24 weeks. Karyotype analysis ruled out chromosomal abnormalities, suggesting a rare infectious etiology rather than a genetic cause. This case highlights the importance of prenatal toxoplasmosis screening, as its early detection can suggest an accurate diagnosis and timely treatment. It also broadens the understanding of DWM beyond its genetic origin, linking it to parasitic infections[8], in this case, caused by *Toxoplasma gondii.*[9]

Keywords: Dandy Walker malformation; Toxoplasmosis; Hydrocephalus; FISH karyotype; Fetal growth restriction (FGR); Prenatal ultrasound; Cerebellar vermis.

RESUMEN

La malformación de Dandy-Walker (MDW) es un trastorno congénito raro del cerebro que afecta el cerebelo y la fosa posterior, con una incidencia de 1 en 35,000 nacimientos[1]. Se caracteriza por la agenesia del vermis cerebeloso, dilatación del cuarto ventrículo y agrandamiento de la fosa posterior[1-3]. Su etiología incluye factores genéticos, anomalías cromosómicas e infecciones como rubéola, CMV y toxoplasmosis[1]. Este caso describe a una mujer embarazada de 16 años cuyo feto fue diagnosticado con MDW a las 23.3 semanas. Los hallazgos prenatales incluyeron restricción severa del crecimiento intrauterino, ausencia del vermis cerebeloso, disgenesia del cuerpo calloso y anomalías cardíacas. La PCR confirmó infección por *Toxoplasma gondii*. A pesar del tratamiento, ocurrió la muerte fetal a las 24 semanas. El cariotipo descartó anomalías cromosómicas, sugiriendo una etiología infecciosa rara en lugar de genética. Este caso resalta la importancia del cribado prenatal de toxoplasmosis, ya que su detección temprana puede sugerir un diagnóstico y tratamiento oportuno. También amplía la comprensión de la MDW más allá de su origen genético, vinculándola con infecciones parasitarias[8], en este caso por *Toxoplasma Gondii*[-9].

Palabras clave: Malformacion de Dandy Walker; Toxoplasmosis; Hidrocefalia; Cariotipo FISH; Restricción del crecimiento intrauterino (RCIU); Ecografía prenatal; Vermis cerebeloso.

Introduction

Dandy-Walker malformation (DWM) is a congenital condition affecting brain structures, particularly the posterior fossa and cerebellum, and can be diagnosed during gestation. Its incidence is estimated at approximately 1 in 35,000 births. The most common finding associated with this malformation is hydrocephalus, present in 80% of reported cases; however, only 4% of hydrocephalus cases are attributable to DWM[1].

DWM is characterized by a classic triad: complete or partial agenesis of the cerebellar vermis, enlargement of the posterior fossa with upward displacement of the tentorium, transverse sinus, and torcular, and cystic dilation of the fourth ventricle[1-3]. The underlying pathology involves an anomaly in the development of the cerebellar vermis, preventing the closure of the fourth ventricle, subsequently displacing the vermis upwards. This process halts the development of the tentorium, straight sinus, and torcular, resulting in an enlarged posterior fossa[1-3].

Prenatal diagnosis of DWM should not be made before 15 weeks of gestation, as cerebellar vermis development is still incomplete during this period, increasing the likelihood of false positives[3]. Ultrasound characteristics include enlargement of the cisterna magna (>10 mm) visualized in the axial plane at the transcerebellar diameter level[3].

Central nervous system anomalies associated with DWM include ventriculomegaly, agenesis of the corpus callosum, holoprosencephaly, and encephalocele. Chromosomal abnormalities such as trisomies 9, 13, 18, and 21; triploidy; and deletions of 6p and 3q22-q24 have been associated with the condition. Non-chromosomal syndromes linked to DWM include Meckel and Walker-Warburg syndromes[1]. Environmental factors may also contribute, though less frequently, such as congenital infections with rubella, cytomegalovirus (CMV), and toxoplasmosis during the first and second trimesters of gestation[1].

Dandy-Walker malformation occurs more frequently in females than in males[2]. Its most relevant clinical manifestations include hydrocephalus, delayed psychomotor development, ataxia, hypotonia, seizures, and craniofacial malformations, among others[2]. Early identification and proper follow-up are essential for managing complications associated with this congenital malformation.

Clinical case

A 16-year-old female, mestizo, student, non-user of alcohol or drugs, weighing 70 kg and measuring 1.57 m, with no family, pathological, or surgical history, presented for her first prenatal visit on 11/29/2024 with a 17-week pregnancy based on a reliable last menstrual period (08/02/2024). Initial prenatal tests included a positive pregnancy test, blood typing (O+), normal complete blood count, negative hemoparasites, negative HIV, TORCH screening with reactive rubella IgG and non-reactive IgM, non-reactive herpes virus IgM, non-reactive toxoplasmosis IgG and IgM, non-reactive hepatitis B antigen, and non-reactive CMV IgG and IgM. Additionally, an infectious profile showed bacterial vaginosis caused by *Gardnerella vaginalis*, which was treated intravaginally. The patient started prenatal vitamins and was scheduled for a second prenatal check-up, including a new TORCH panel and an anatomical ultrasound.

On 12/30/2024, she returned for follow-up, reporting no symptoms and positive fetal movements. Her new TORCH panel showed reactive IgM for toxoplasmosis, and an anatomical ultrasound performed on 12/26/2024 at 20.6 weeks of gestation revealed an estimated fetal weight of 209 g (<3rd percentile), small bones for gestational age, and an enlarged cisterna magna (25 mm). Due to these findings, an urgent referral was made to gynecology and perinatology, with a repeat toxoplasmosis IgM in 15 days and treatment initiation with pyrimethamine/sulfadoxine.

On 01/13/2025, at 23.3 weeks of gestation, a perinatology evaluation included an anatomical ultrasound showing severe intrauterine growth restriction (IUGR) (<1st percentile), micrognathia, hypoplastic nasal bone, absent cerebellar vermis, hydrocephalus, corpus callosum dysgenesis *(Figure 1)*, pericardial effusion, cardiomegaly, perimembranous ventricular septal defect, intrahepatic calcifications, and hepatosplenomegaly. Doppler studies showed pathological uterine artery indices (PI >95th percentile), absent umbilical artery flow, and middle cerebral artery vasodilation. Perinatology recommended continued treatment for gestational toxoplasmosis. Based on ultrasound features, a diagnosis of Dandy-Walker syndrome possibly related to toxoplasmosis versus aneuploidies was made. Additional tests, including karyotyping via FISH, chromosomal microarray (CMA), and PCR for *Toxoplasma gondii* and cytomegalovirus (CMV), were ordered.On 01/16/2025, the amniotic fluid FISH karyotype returned as XY ***(normal male),*** with no evidence of trisomies 13, 18, or 21. PCR for CMV was negative, while PCR for

Toxoplasma gondii was **positive.** CMA results also showed a **normal male karyotype**.

A week later, the patient presented to the emergency department due to absent fetal movements. A transabdominal obstetric ultrasound confirmed fetal demise, with no fetal heartbeat or movements. The pregnancy was managed with misoprostol, and 12 hours later, expulsion of a 536 g **male** fetus was documented. A posterior cranial protrusion was noted, with no other apparent phenotypic malformations.

Dandy-Walker malformation is classically characterized by a triad of findings: complete or partial agenesis of the cerebellar vermis, an enlarged posterior fossa with upward displacement of the tentorium, transverse sinus, and torcular, and cystic dilation of the fourth ventricle[1-3].

In this case, an anatomical ultrasound at 23.3 weeks showed an absent cerebellar vermis *(Figure 3)*, an enlarged cisterna magna (25 mm, normal <10 mm) *(Figure 2-3)*, fourth ventricle dilation, and additional cerebral and cardiac anomalies, all consistent with DWM.

DWM is a rare condition, with an incidence of 1 in 35,000 births, and among hydrocephalus cases, fewer than 5% are attributed to DWM. The malformation occurs more frequently in female fetuses[4-5]. However, in this case, the fetus was male, confirmed by FISH karyotype and external genital examination.

Although this pregnancy resulted in utero fetal death, newborns with DWM often present with motor development delays, macrocephaly due to hydrocephalus, cranial nerve paralysis, and cognitive impairment[6]. Autopsy findings help confirm phenotypic features, including craniofacial, intracranial, and cardiac malformations, previously described in ultrasound reports[7].

In most cases, DWM is attributed to genetic disorders, chromosomal anomalies such as trisomies 9, 13, 18, and 21; triploidy; and deletions of 6p and 3q22-q24[10-11]. However, infectious causes are rare. In this case, no genetic abnormalities were found, but primary *Toxoplasma gondii* infection was confirmed serologically and via PCR, strongly suggesting a parasitic etiology. Literature indicates that fetal infection risk increases with advancing gestational age[8-9].

For live-born infants with DWM, clinical manifestations like hydrocephalus and posterior fossa symptoms are managed surgically through ventriculoperitoneal and

cystoperitoneal shunting to reduce intracranial pressure[11-12]. In this case, no intervention was possible due to in utero fetal death.

CONCLUSIONS

This case report highlights the rarity of DWM and its high perinatal mortality risk. The three main ultrasound criteria for DWM diagnosis were present. Unlike most reported cases, this malformation was not linked to genetic abnormalities but to primary *Toxoplasma gondii* infection, a rarely documented finding.

This suggests that DWM may arise from parasitic infection rather than genetic mutations, expanding the understanding of its etiology.

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I extend my gratitude to the gynecologists and obstetricians who supported my medical practice.

CONFLICT OF INTEREST

The author declares no conflict of interest.

ATTACHED FILES

Figure 1. Hydrocephalus demonstrated in this section

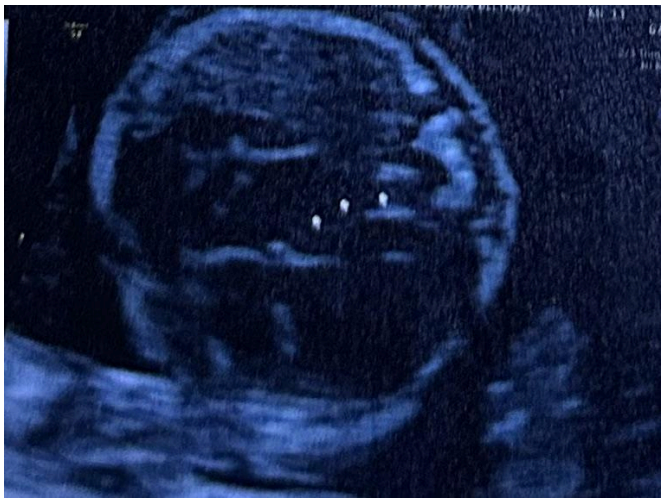


Figure 2. Bilateral ventriculomegaly, it is more accentuated on the left laterality in this section. **Arrow orange**: absence corpus callosum.

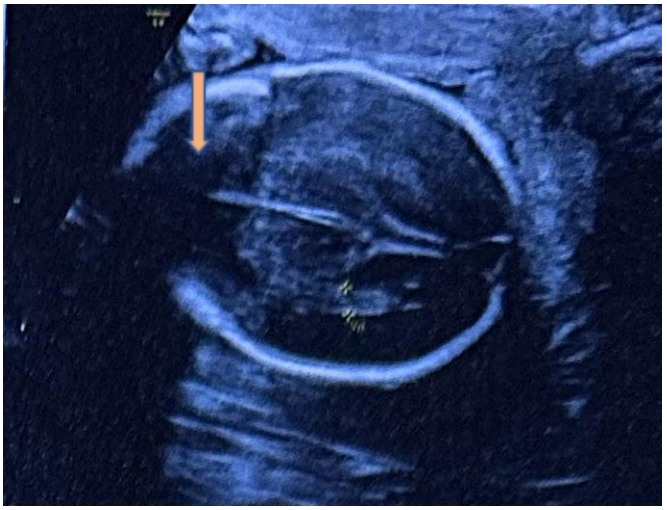
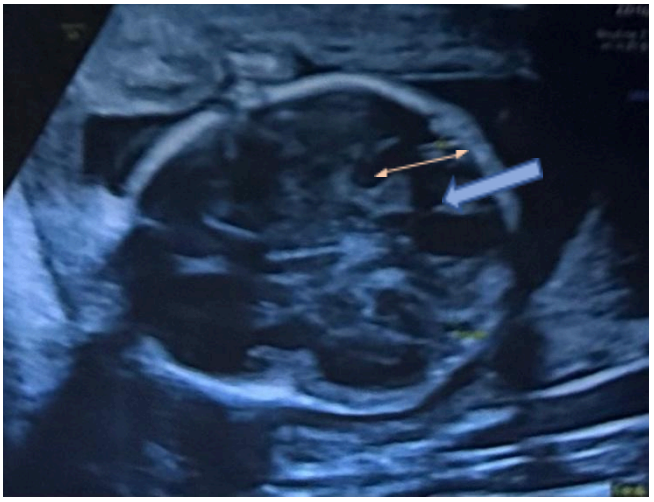


Figure 3. Orange arrow: Cisterna magna 25mm (normal <10mm)**. Blue arrow:** Absence of cerebellar vermis



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