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Dandy-Walker Variant in A Fetus of an ICSI Twin Gestation: A Case Report

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ABSTRACT

Dandy-Walker variant (DWV) might be considered as one of the borderlines in the examination of fetal brain. We report the first case of a DWV in a fetus conceived by ICSI. A 34 year-old woman underwent assisted reproductive treatment due to male factor infertility. A twin gestation was achieved, one of the fetuses was diagnosed as DWV on 22 weeks' ultrasound examination. Fetal MRI confirmed the diagnosis. The couple did not allow fetal karyotyping. Pregnancy continued uneventfully. Associated cardiac and minor skeletal anomalies were seen in the postpartum examination of the affected newborn. She died six days after birth due to pulmonary insufficiency. Karyotype analysis of the affected infant performed after birth was reported to be partial trisomy 9. Parental karyotype analysis was further performed and balanced reciprocal translocation t(4;9) was found in the mother. A careful posterior fossa evaluation should be performed as part of routine anatomical survey in ICSI conceptions. Upon the detection of an anomaly, a comprehensive fetal ultrasound for associated abnormalities and karyotype analysis are vital for obstetric management and neonatal survival.

Key Words: Assisted reproductive treatment, congenital anomaly, Dandy-Walker variant, intracytoplasmic sperm injection (ICSI), partial trisomy 9

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Introduction

The incidence of fetal chromosomal or structural abnormalities after assisted reproductive treatment (ART) is one of the most intriguing topics. Specifically, the central nervous system anomaly rate was found to be 0.7% in fetuses and children conceived after ICSI, which is statistically similar to spontaneous conceptions (1).

A partial or complete cerebellar vermian defect may occur sporadically or as a component of the Dandy-Walker syndrome (DWS), Down syndrome or Joubert Syndrome (2). The Dandy-Walker malformation (DWM), Dandy-Walker variant (DWV), and mega cisterna magna (MCM) seem to represent steps on a continuum of developmental anomalies of the posterior fossa (3). Therefore, the Dandy-Walker complex (DWC) was suggested to be used to describe this continuum of aberrant development of the posterior fossa that might be associated with multiple congenital anomalies and radiographic abnormalities (3).

DWC is a rare abnormality of the central nervous system (CNS), usually observed during the prenatal period or early infancy. In a population-based study of posterior fossa anomalies, the incidence of DWM/V was reported to be 1/11574 births (4). On the other hand, in a recent study, DWM was reported to be relatively common, the incidence was given as 1 in 2500-3500 live births with a slight female predominance (5).

DWV forms one part of the spectrum of DWC and is a less severe posterior fossa anomaly than the classic DWM, however it might be associated with both extra-and intracranial anomalies with or without chromosomal abnormalities. The outcome is grim for DWM/V in the presence of concurrent anomalies (4). However, isolated DWV was reported to have a good developmental outcome (6). Previous studies reported additional fetal extracranial anomalies to be seen in 65% of DWV cases (7, 8). In a recent study evaluating associated anomalies in a case series of 24 pediatric patients with DWV, concurrent anomalies included cardiac (42%), gastrointestinal (21%), orthopedic (13%), and genitourinary (13%) abnormalities (6). Ventriculomegaly also has been reported to be one of the most common (27%) concurrent intracranial anomalies detected sonographically in DWV cases (9).

With this report we presented a DWV case in a pregnancy achieved with ART. To our knowledge, this is the first reported case of a DWV in a pregnancy conceived through ICSI.

Case Report

The couple was evaluated for primary infertility of 13 years duration. Female examination revealed a 34 years old woman with normal ovarian reserve and no other pathology, while male evaluation revealed azoospermia. The wife underwent ovulation induction with antagonist protocol and all the steps of the treatment were ordinary. For sperm retrieval, percutaneous sperm aspiration was performed, which demonstrated that the azoospermia was of obstructive origin. ICSI was the method of fertilization. On the third day after oocyte

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retrieval three embryos were transferred into the uterus and twelve days after the transfer procedure serum β-HCG value showed the presence of a pregnancy and, three weeks afterwards transvaginal ultrasound showed two gestational sacs with fetal heart activities in both of them. The follow-up was uneventful until 22 weeks. Nuchal translucency measurements were normal in both fetuses. The couple did not agree to an amniocentesis which was recommended at 15 weeks to reveal any possible chromosomal pathology in the twins.

During the routine antenal sonographic examination at 22 weeks, vermis agenesis was observed in one of the fetuses. Fetal magnetic resonance imaging (MRI) was ordered which reported mild enlargement of the posterior fossa, partial dilatation of the fourth ventricle and agenesis of the inferior part of the middle cerebellar vermis, identified as DWV. A detailed sonograpic examination performed accordingly did not reveal any other associated abnormality. Fetal karyotype analysis was offered to the couple in order to delineate any chromosomal pathology, however they did not agree and opted to give birth to both the twins after extensive counselling. The follow-up of the affected fetus was normal, no further intracranial pathology or growth retardation were observed. The contractions started at 33 weeks gestation and, despite the application of tocolysis with nifedipine, they could not be stopped, and ultimately led to the normal vaginal birth of the twins. With the appearance of the contractions at 33 weeks gestation, immediate parenteral steroid administration was performed.

Both the newborns were females and taken to the neonatal intensive care unit (NICU). The healthy infant was 1950 gr and removed from NICU one day afterwards. The affected infant was 1330 gr and died in NICU six days after the birth due to pulmonary insufficiency. The affected infant was seen during the initial postpartum examination to have brachycephaly, hypertelorism, low-set ears, camptodactyly in three digits of the right hand and two digits of the left hand and bilateral simian lines. Postpartum cranial sonography was performed and showed vermian agenesis. Postpartum echocardiography was also performed and revealed subaortic ventricular septal defect (VSD) and patent ductus arteriosus (PDA). Karyotype analysis was done in the affected infant and she was found to have partial trisomy 9. With this result, karyotyping of the parents and the healthy infant was also performed. The investigation revealed a balanced reciprocal translocation t (4;9) in the mother and normal karyotypes in the father and the healthy infant. Since the couple were unwilling, autopsy examination of the affected infant could not be performed.

Discussion

DWV is hypoplasia of the cerebellar vermis with cystic dilatation of the fourth ventricle, but without significant enlargement of the posterior fossa. Although DWM is an obvious posterior fossa defect, DWV was reported to be difficult to detect as it was suggested to be one of the situations in which intracranial malformation occurred with normal ventricular atrial measurement (10). This pathology might be considered as one of the borderlines in the examination of the fetal brain. We report the first case of a pregnancy conceived through ICSI of which DWV was diagnosed in one of the dizygotic twin fetuses. In our case also, no ventriculomegaly, hydrocephalus or other intracranial pathology were observed apart from vermian agenesis.

In the diagnostic workup of posterior fossa anomalies, ultrasound is reliable and accurate for making the diagnosis, fetal MRI can be used to confirm the diagnosis. However, diagnostic uncertainties while describing fetal cerebellar disorders still exist in daily clinical practice, mainly because of anatomically overlapping conditions (11). Autopsy might be considered the gold standard for accurate diagnosis of the fetal abnormality. However, even neuropathological examinations of some cases with cerebellar vermian abnormalities were confusing when differentiating between different vermian pathologies like DWV, vermian hypoplasia and vermian agenesis (12). Furthermore, although the sonographic diagnosis of fetal DWM is accurate, significant discrepancies exist in prenatal and postnatal diagnosis of DWV (7). Therefore, postnatal imaging should be performed in all fetuses with DWC. Postnatal cranial ultrasound confirmed the diagnosis in our case.

The prognosis is uncertain for an infant born with the prenatal diagnosis of DWV since chromosomal, intracranial and extracranial abnormalities might be associated. Isolated inferior vermian defect was reported to be associated with a good prognosis (2). Obstetric management and also the neonatal outcome depends on the gestational age at diagnosis, karyotype analysis and associated intracranial or extracranial abnormalities. In the present case, a detailed ultrasound study was performed to reveal any concurrent anomaly which showed no major abnormality. In the postpartum period, echocardiography was performed, which demonstrated subaortic VSD and PDA and minor skeletal anomalies with facial dysmorphism were observed in the examination.

DWC was reported to be associated with various chromosomal abnormalities such as chromosomes 3, 9, 13 and 18 (13). Therefore, evaluation of the cisterna magna as part of a routine anatomical survey should be supported. In our case, fetal karyotype analysis was offered to the couple, however, they did not agree and opted for the continuation of the pregnancy. After birth, karyotyping was performed which revealed partial trisomy 9. Upon obtaining this result, parental karyotypes were also analyzed, which showed balanced reciprocal t (4;9) translocation in the mother.

Partial trisomy of chromosome 9 and DWS association was noted in a few case reports in the literature. Trisomy 9 is one of the most frequent autosomal anomalies compatible with long survival rate. The spectrum of clinical severity roughly correlates with the extent of trisomic chromosome material. Craniofacial dysmorphism, brain malformations, dilated ventricles with hypogenesis of corpus callosum, agenesis of corpus callosum and DWM might be seen in cases with trisomy 9 (14, 15). Dosage effect of genes located on chromosome 9 has been suggested to contribute to the abnormal development of the CNS in patients with partial or complete trisomy 9 (16).

In conclusion, posterior fossa evaluation should be an essential part of routine ultrasound examination. If an anomaly is detected, fetal MRI should be ordered to confirm the diagnosis. Subsequently, a comprehensive fetal ultrasound examina-

tion for associated extracranial abnormalities and karyotype analysis which are vital both for the obstetric management and the neonatal survival should be performed.

Conflict of Interest

No conflict of interest was declared by the authors.

References

1. Ludwig M and Katalinic A. Malformation rate in fetuses and children conceived after ICSI: results of a prospective cohort study. RBM Online 2002;5:171-8.
2. Keogan MT, DeAtkine AB, Hertzberg BS. Cerebellar vermian defects: antenatal sonographic appearance and clinical significance. J Ultrasound Med 1994;13:607-11.
3. Barkovich AJ, Kjos BO, Norman D, Edwards MS. Revised classification of posterior fossa cysts and cystlike malformations based on the results of multiplanar MR imaging. Am J Roentgenol 1989;153:1289-300.
4. Long A, Moran P, Robson S. Outcome of fetal posterior fossa anomalies. Prenat Diagn 2006;26:707-10.
5. Lavanya T, Cohen M, Gandhi SV, Farrell T, Whitby EH. A case of a Dandy-Walker variant: the importance of a multidisciplinary team approach using complementary techniques to obtain accurate diagnostic information. Br J Radiol 2008;81:e242-5.
6. Sasaki-Adams D, Elbabaa SK, Jewells V, Carter L, Campbell JW, Ritter AM. TheDandy-Walker variant: a case series of 24 pediatric patients and evaluation of associated anomalies, incidence of hydrocephalus, and developmental outcomes. J Neurosurg Pediatr 2008;2:194-9.
7. Harper T, Fordham LA, Wolfe HM. The fetal Dandy-Walker complex: associated anomalies, perinatal outcome and postnatal imaging. Fetal Diagn Ther 2007;22:277-81.
8. Has R, Ermis H, Yüksel A, Ibrahimoglu L, Yildirim A, Sezer HD, et al. Dandy-Walker malformation: a review of 78 cases diagnosed by prenatal sonography. Fetal Diagn Ther 2004;19:342-7.
9. Ecker JL, Shipp TD, Bromley B, Benacerraf B. The sonographic diagnosis of Dandy-Walker and Dandy-Walker variant: associated findings and outcomes. Prenat Diagn 2000;20:328-32.
10. McGahan JP. The fetal head: borderlines. Semin Ultrasound CT MR 1998;19:318-28.
11. Malinger G, Lev D, Lerman-Sagie T. The fetal cerebellum. Pitfalls in diagnosis and management. Prenat Diagn 2009;29:372-80.
12. Russo R, Fallet-Bianco C. Isolated posterior cerebellar vermal defect: a morphological study of midsagittal cerebellar vermis in 4 fetuses- early stage of Dandy-Walker continuum or new vermal dysgenesis? J Child Neurol 2007;22:492-500.
13. Imataka G, Yamanouchi H, Arisaka O. Dandy-Walker syndrome and chromosomal abnormalities. Congenit Anom 2007;47:113-8.
14. Temtamy SA, Kamel AK, Ismail S, Helmy NA, Aglan MS, El Gammal M, et al. Phenotypic and cytogenetic spectrum of 9p trisomy. Genet Couns 2007;18:29-48.
15. Vanlandingham M, Nguyen TV, Abdul-Rahman OA, Parent A, Zhang J. Phenotypical manifestations of partial trisomy 9 and monosomy 4 in two siblings. Neurol Sci 2008;29:467-70.
16. Chen CP, Chang TY, Shih JC, Lin SP, Lin CJ, Wang W et al. Prenatal diagnosis of the Dandy-Walker malformation and ventriculomegaly associated with partial trisomy 9p and distal 12p deletion. Prenat Diagn 2002;22:1063-6.