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Developmental outcomes of Down syndrome and Dandy-Walker malformation

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Abstract

Dandy-Walker syndrome (DWS), or Dandy-Walker complex, is a congenital brain malformation of the posterior fossa, typically resulting in developmental delay and cognitive disability. The co-occurrence of Down syndrome (DS) and DWS is relatively uncommon; thus, its impact on developmental outcomes has not been fully elucidated. Herein, we report a case of a 37-month-old child with DS and DWS, who is functioning at the following age-equivalent: gross motor at a 9-mo level, fine motor 6 mo, expressive language 14 mo, receptive language 9 mo. As such, it is important to determine how the DWS influences developmental outcomes, and appreciate the importance of early interventional therapy.

Keywords

Down syndrome; Dandy-Walker syndrome; developmental outcomes

1. Introduction

Trisomy 21, leading to Down syndrome (DS), is the most common genetic cause of mental retardation with a prevalence of 1 in 733 live births, or 5400 births yearly in the United States [1]. The coexistence of DS and Dandy-Walker syndrome (DWS) has been previously reported in two cases, suggesting that it is relatively uncommon for both conditions to occur simultaneously [2,3]. While the case reported by Constantini et al. [2] died at 2 wk of age, Estroff et al. [3] described a 4-month-old infant with trisomy 21 and Dandy-Walker variant (DWV) as severely handicapped. Our report is the first to detail the developmental course of a child with DS and DWS.

2. Case report

A 37-month-old male was born to a 27-year-old Caucasian mother (G2, P2) and a 22-year-old Caucasian father of German descent, who are non-consanguineous. The pregnancy was complicated by gestational diabetes and hyperemesis, which were controlled with diet and prednisone, respectively. At approximately 36 wk gestational age, hypertension with proteinuria was present and labor was induced shortly thereafter. The boy's birth weight was 2.63 kg (25–50th percentile), length 47 cm (25–50th percentile), and head circumference 33.7 cm (50–75th percentile). Immediately after delivery, DS facies and hypotonia were

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recognized, and a chromosomal karyotype confirmed the diagnosis of 47,XY+21. Other than the presence of an extra chromosome 21, a microarray comparative genomic hybridization showed no additional duplications or deletions. Array comparative genomic hybridization was carried out using a commercially available whole genome oligonucleotide microarray (Agilent Technologies, Santa Clara, CA). This oligonucleotide array contains ~ 44,000 (60 mers) probes spaced at ~ 75 kb with high-density coverage in known disease genes.

Cranial ultrasound at day 4 of life revealed asymmetry of the ventricles with excess fluid in the posterior portion of the brain and agenesis of the corpus callosum (Fig. 1). Magnetic resonance imaging displayed a superior vermis but absence of the mid and inferior vermis. In addition, there was a wide communication of the fourth ventricle and a posterior fossa retrocerebellar cerebrospinal fluid collection. Furthermore, agenesis of the corpus callosum was confirmed (Fig. 2). The magnetic resonance imaging showed no frank hydrocephalus although the temporal horns of the lateral ventricles were mildly prominent. The prominence of the rostral portion of the cerebral aqueduct could indicate a degree of aqueductal stenosis or web. The results suggested the possibility of DWV initially; however, follow-up head computed tomography scans at 7, 9, 12, 18, and 32 mo of age showed no evidence of ventricular dilation or ventriculomegaly (Fig. 2). The scans showed an essentially stable ventricular system with no evidence of hydrocephalus and thus supported the diagnosis of Dandy-Walker malformation (DWM).

2.1. Developmental outcome

The patient was born with muscular hypotonia and ligamentous hyperlaxity. Cerebellar dysfunctions, such as, nystagmus, ataxia, tremor were not noted. In terms of development, the patient rolled over at 6 mo, sat independently at 12 mo, and has not yet begun crawling. He said his first word at 10 mo, and currently has approximately 5 words. Developmental outcomes were assessed at a chronological age of 37 mo of age using the *Vineland Adaptive Behavior Scales, Second Edition* [4]. The Vineland Scales assess personal and social sufficiency across three domains of functioning (mean score of 100 and Standard deviation +15): Communication, Daily Living Skills, and Socialization. The Vineland Scales also assess motor skills. Results from the Vineland Scales revealed communication score of 59 (expressive language age-equivalent of 14 mo, receptive language age-equivalent of 9 mo), Daily Living Skills 55, Socialization 65, Motor 49 (gross motor age-equivalent of 9 mo, fine motor age-equivalent of 6 mo), and Adaptive Behavior 54. Notably, socialization was an area of strength when compared to communication, daily living skills, and motor skills. The motor score is the lowest as the patient continues to have muscular hypotonia and ligamentous hyperlaxity, and is unable to crawl or ambulate independently.

3. Discussion

DWS, or Dandy-Walker complex, is a congenital brain malformation encompassing a continuum of disorders characterized by cystic posterior fossa anomalies [3,5]. The continuum varies in degree of cerebellar vermis malformation and has previously been differentiated as DWM, in the presence of a posterior fossa enlargement, and DWV in the absence of posterior fossa enlargement [3,6,7]. Recently, several authors have suggested that the term DWV inappropriately consists of variable definitions, so the term should be abandoned [8,9]. Variable neurological abnormalities associated with DWS include hydrocephaly, microcephaly, ventriculomegaly, and agenesis of the corpus callosum [8,10,11]. Anomalies outside of the central nervous system described in association with DWS include cardiac defects, craniofacial abnormalities, gastrointestinal abnormalities, genitourinary abnormalities, respiratory aberrations, and musculoskeletal dysmorphisms [5]. Sasaki-Adams et al. [5] suggest that mild vermian hypoplasia and a normal-sized posterior fossa is associated with a good developmental outcome; however, the co-occurrence of the

aberration with another neurological syndrome increases the potential for developmental delay [5].

Although there is no direct estimate of isolated DWS incidence, DWM has an estimated incidence of 1/2500 to 1/3500 births from the conclusion that DWS comprises 3% of hydrocephalus cases [9]. Both teratogenic and genetic factors have been implicated as the cause of this cerebellar developmental disorder, consistent with a multifactorial inheritance pattern [12]. Genetic causes are variable, and various abnormalities of chromosomes 3, 5, 8, 9, 13, and 18 have been associated with DWS [3,5,12–14]. Grinberg et al. [15] isolated a region on 3q24-25.1 commonly deleted in individuals with DWM.

Neurodevelopmental outcomes in typically developing children with DWM have been described [16]; however, there have been no reports examining the neurodevelopmental challenges experienced by children with DS and DWM. The coexistence of DS and DWS have been previously reported in only two cases [2,3]. The case reported by Constantini et al. [2] died at 2 wk of age, and Estroff et al. [3] described a 4-month-old infant with trisomy 21 and DWV as "severely handicapped". In both cases, the developmental profile was not reported. We describe a case of a 37-month-old male with DS and DWM, with no evidence of ventricular dilation, ventriculomegaly, or hydrocephalus on follow-up computed tomography scans.

Although the co-occurrence of DS and DWM is relatively uncommon, it is important to determine how DWM influences developmental outcomes, and appreciate the importance of early interventional therapy with emphasis in all developmental domains including gross motor, fine motor, communication, and social skills. Children with DS have muscular hypotonia, joint hyperlaxity, and delayed gross motor skills. Motor milestones for children with DS include rolling between ages 5.0 and 6.4 mo, sitting independently between 8.5 and 11.7 mo, crawling between 12.2 and 17.3 mo, and walking independently between 15 and 74 mo [17,18]. At the age of 37 mo, our patient is able to verbalize 5 words and sits independently, but is unable to crawl. The Vineland scales show the following age-equivalent: gross motor at a 9-mo level, fine motor 6 mo, expressive language 14 mo, receptive language 9 mo for a chronological age of 37 mo. Motor skills are the most delayed with the lowest score compared to other domains.

In a study on 80 children with DS ranging in age from 1.08 to 11.5, with a mean age of 6.08 yr, the Vineland Scales revealed weakness in communication compared with daily living and social skills [19]. Similar to children with DS who do not have DWM; this patient has strengths in socialization and weaknesses in communication. The deficits in communication may be masked by strengths in socialization. Hence, it is important to receive early speech therapy to improve communication skills. As a consequence of muscular hypotonia and joint hyperlaxity, children with DS have delayed gross motor skills. However, this patient revealed greater deficits in gross motor skills compared to peers with DS who do not have DWM. As such, physical therapy should begin shortly after birth. Children with DS and DWM are capable of making progress in their developmental milestones with early interventional therapy and appropriate guidance and support.

References

1. Canfield MA, Honein MA, Yuskiv N, et al. National estimates and race/ethnic-specific variation of selected birth defects in the United States, 1999–2001. Birth Defects Res A Clin Mol Teratol. 2006; 76:747–756. [PubMed: 17051527]

2. Constantini S, Pomeranz S, Hoffman B, Martin O, Rappaport ZH. Coexistence of Dandy-Walker syndrome and Down's syndrome. Neurochirurgia (Stuttg). 1989; 32:56–57. [PubMed: 2524010]

3. Estroff JA, Scott MR, Benacerraf BR. Dandy-Walker variant: prenatal sonographic features and clinical outcome. Radiology. 1992; 185:755–758. [PubMed: 1438757]

4. Sparrow, S.; Cicchetti, D.; Balla, D. Vineland Adaptive Behavior Scales. 2. Minneapolis: Pearson; 2005.

5. Sasaki-Adams D, Elbabaa SK, Jewells V, Carter L, Campbell JW, Ritter AM. The Dandy-Walker variant: a case series of 24 pediatric patients and evaluation of associated anomalies, incidence of hydrocephalus, and developmental outcomes. J Neurosurg Pediatr. 2008; 2:194–199. [PubMed: 18759601]

6. Bolduc ME, Limperopoulos C. Neurodevelopmental outcomes in children with cerebellar malformations: a systematic review. Dev Med Child Neurol. 2009; 51:256–267. [PubMed: 19191827]

7. Tolmie, J. Clinical genetics of neural tube defects and other congenital central nervous system malformations. In: Rimoin, DL.; Connor, JM.; Pyeritz, RE.; Korf, BR., editors. Emery and Rimoin's Principles and Practice of Medical Genetics. Vol. 3. London: Harcourt Publisher Limited; 2002. p. 2985-2986.

8. Bolduc ME, Limperopoulos C. Neurodevelopmental outcomes in children with cerebellar malformations: a systematic review. Dev Med Child Neurol. 2009; 51:256–267. [PubMed: 19191827]

9. Brain, HA. Human Malformations and Related Anomalies. Stevenson, R.; Hall, J.; Goodman, R., editors. Vol. 2. New York: Oxford University Press; 1993. p. 89-95.

10. 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; 20:328–332. [PubMed: 10740206]

11. Has R, Ermi H, Yuksel A, et al. Dandy-Walker malformation: a review of 78 cases diagnosed by prenatal sonography. Fetal Diagn Ther. 2004; 19:342–347. [PubMed: 15192294]

12. Imataka G, Yamanouchi H, Arisaka O. Dandy-Walker syndrome and chromosomal abnormalities. Congenit Anom (Kyoto). 2007; 47:113–118. [PubMed: 17988252]

13. Ulm B, Ulm MR, Deutinger J, Bernaschek G. Dandy-Walker malformation diagnosed before 21 weeks of gestation: associated malformations and chromosomal abnormalities. Ultrasound Obstet Gynecol. 1997; 10:167–170. [PubMed: 9339523]

14. Witters I, Vandecruys H, Devlieger R, Fryns JP. Dandy-Walker malformation in a male fetus with mosaic 45,X/46,X,del(Y)(q11). Genet Couns. 2008; 19:439–441. [PubMed: 19239090]

15. Grinberg I, Millen KJ. The ZIC gene family in development and disease. Clin Genet. 2005; 67:290–296. [PubMed: 15733262]

16. Klein O, Pierre-Kahn A, Boddaert N, Parisot D, Brunelle F. Dandy-Walker malformation: prenatal diagnosis and prognosis. Childs Nerv Syst. 2003; 19:484–489. [PubMed: 12879343]

17. Melyn MA, White DT. Mental and developmental milestones of noninstitutionalized Down's syndrome children. Pediatrics. 1973; 52:542–545. [PubMed: 4270249]

18. Vicari S. Motor development and neuropsychological patterns in persons with Down syndrome. Behav Genet. 2006; 36:355–364. [PubMed: 16505965]

19. Dykens EM, Hodapp RM, Evans DW. Profiles and development of adaptive behavior in children with Down syndrome. Downs Syndr Res Pract. 2006; 9:45–50. [PubMed: 16869374]

Fig. 1.
Sagittal (left) magnetic resonance image demonstrating asymmetry to the ventricles with excess fluid in the posterior portion of the brain and agenesis of the corpus callosum.
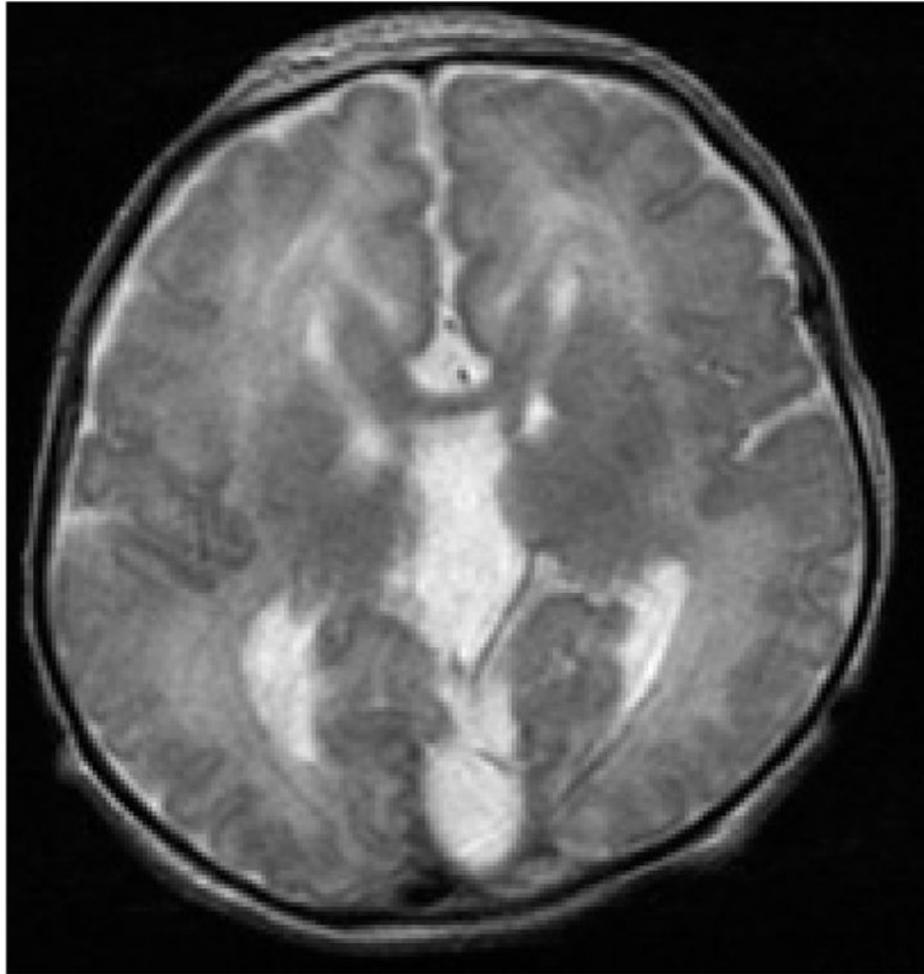
Fig. 2.
Axial (axial) magnetic resonance image showing agenesis of the corpus callosum.