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Original Article

Dandy–Walker syndrome

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الملخص

أهدف البحث: متلازمة داندي- والكر هي اعتلال نادر يتسم بعدم تكون كامل أو جزئي لدودة المخيخ، وتوسع كيسي للبطين المخي الرابع وتضخم الحفرة الدماغية الخلفية. ولا يعرف السبب الدقيق لحدوثه، على الرغم من وجود بعض التقارير التي ربطت بينه وبين عوامل الخطورة مثل العدوى الفيروسية للأمهات (الحصبة الألمانية، والتوكسوبلازما، والفيروس المضخم للخلايا) وتناول الكحول. تتراوح نسبة الإصابة بين واحد من كل 500,2 ولادة إلى واحد من كل 000,100 ولادة. قد يكون السبب في هذا الاختلاف الشاسع هو محدودية الحالات المنشورة، حيث أن معظم البيانات المتاحة هي تقارير أو سلسلة حالات متفرقة.

طرق البحث: أجريت هذه الدراسة الاستعادية على السجلات الطبية لحديثي الولادة المصابين بمتلازمة داندي- والكر الذين تم تنويمهم بوحدة الرعاية المركزة لحديثي الولادة بمستشفى جامعي في الفترة بين يناير 2001م وديسمبر 2010م.

النتائج: تنوم ثمانية رضع بمتلازمة داندي- والكر خلال فترة الدراسة، بمعدل عام 400/1 ولادة حية. وكانت نسبة الإناث إلى الذكور 7,1:1 (كان أحد الرضع ملتبس الجنس وتبين لاحقا أنه ذكر). كان متوسط عمر الحمل 39 أسبوعا (يتراوح بين 36-40 أسبوعا)، ومعدل الوزن عند الولادة 716,2 جرام (يتراوح بين 965,1 -335,3 جرام). تم تشخيص المتلازمة لنصف الرضع قبل الولادة. وكان لدى جميع الرضع استسقاء دماغي، وخمسة لديهم عيوب عصبية أخرى؛ أما عيوب خارج القحف فقد وجدت لدى 50% من الرضع. عاش جميع الرضع حتى خروجهم.

الاستنتاجات: على الرغم من أن العديد من نتائجنا تتفق مع البيانات المنشورة، فإن معدل متلازمة داندي- والكر في دراستنا كان أعلى بكثير من أي دراسة سابقة. وهذا يتطلب المزيد من البحوث لتفسير هذه النتائج غير المتوقعة.

الكلمات المفتاحية: متلازمة داندي-والكر; تضخم الرأس; تضخم البطين المخي

Abstract

Objectives: Dandy–Walker syndrome is a rare disorder characterised by complete or partial agenesis of the vermis, cystic dilatation of the fourth ventricle and an enlarged posterior fossa. The precise aetiology is unknown, although there have been reports of associations with risk factors like maternal virus infections (rubella, toxoplasma, and cytomegalovirus) and alcohol consumption. The reported incidence varies between one per 2500 births to one per 100,000 births. This huge difference may be due to the limited published case series, as most of the available data are sporadic case reports or series.

Methods: A retrospective review was conducted of medical records of neonates with Dandy–Walker syndrome admitted to the neonatal intensive care unit of a university hospital between January 2001 and December 2010.

Results: Eight infants with Dandy–Walker syndrome were admitted during the study period, giving an overall incidence of 1/400 live births. The female-to-male ratio was 1.7:1 (one infant had ambiguous gender but was later found to be male). The mean gestational age was 39.0 weeks (range, 36–40 weeks), and the mean birth weight was 2716 g (range, 1965–3335 g). The syndrome was diagnosed in half the infants prenatally. All infants had associated hydrocephalus, and five had other neurological anomalies; extra-cranial anomalies were seen in 50% of infants. All infants survived to discharge.

Conclusion: Although many of our results were consistent with published data, the incidence of Dandy–Walker syndrome in our study was much higher than any

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reported previously. Further research is required to elucidate this unexpected finding.

Keywords: Dandy–Walker syndrome; Macrocephaly; Ventriculomegaly

Introduction

Dandy–Walker syndrome is a rare condition, which consists of hypoplasia of the cerebellar vermis, dilatation of the fourth ventricle and an enlarged posterior fossa. The syndrome is considered to be the commonest cerebellar malformation. It is poorly understood, and the incidence is unknown. Although this malformation can be diagnosed prenatally by neuroradiology, identifying patients is difficult, as there is no specific symptom or sign. It is not uncommonly detected from the associated hydrocephalus. The outcome is highly variable and ranges from normal or nearly normal development to profound disability or even early death. Data on this disease in Saudi Arabia are limited.

This study involved examination of the records of all infants with Dandy–Walker syndrome seen at our centre in the past 10 years and an analysis of the clinical and epidemiological aspects.

Materials and Methods

This retrospective study was carried out at the neonatal intensive care unit of the largest teaching hospital in the region and the only Government hospital that provides level III neonatal services in the city. The intensive care unit has a capacity of 18 beds.

All cases of Dandy–Walker syndrome born at or referred to the centre between January 2001 and December 2010 were reviewed. The information obtained from the files included gestational age, sex, Apgar score, birth weight, head circumference, place and mode of delivery, nationality, length of hospital stay, associated morbidity and mortality rate.

Microsoft Excel spreadsheets were used for data collection, and the data were analysed with SPSS version 15.0. Means, ratios and percentages were calculated. The study was authorised by the ethical committee.

Results

During the study period, eight infants with Dandy–Walker syndrome were admitted to the neonatal intensive care unit (Table 1), giving an overall incidence of 1/400 live births. Seven infants were Saudis. Three were born vaginally and five by caesarean section. Two infants were boys, five were girls, and one infant was born with ambiguous genitalia but was later found to be male, giving a female-to-male ratio of 1.7:1. The mean gestational age was 39.0 weeks (range, 36–40 weeks); one infant was borderline premature, but all the other infants were born at term. The mean birth weight was 2716 g (range, 1965–3335 g). The mean head circumference was 35.6 cm (range, 31–43.5 cm). The mean Apgar scores were 6 and 7 at the 1st and 5th minute, respectively.

Dandy–Walker syndrome was diagnosed in four infants prenatally. The diagnosis in six infants was confirmed by computerised tomography scan and in two by magnetic resonance imaging. All the infants were discharged home after a mean hospital stay of 26.5 days (range, 7–58 days).

Table 1: Overall findings in eight infants born with Dandy–Walker syndrome.

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5	Patient 6	Patient 7	Patient 8
Sex	F	F	M	F	F	F	M[a]	M
Mode of delivery	Vaginal	Caesarean section	Vaginal	Vaginal	Caesarean section	Caesarean section	Caesarean section	Caesarean section
Gestational age (weeks)	39	39	39	39	40	41	39	36
Nationality	Saudi	Saudi	Algerian	Saudi	Saudi	Saudi	Saudi	Saudi
Birth weight (g)	1965	3080	2500	2840	3125	2090	2795	3335
Length (cm)	45.0	45.5	46.0	50.0	47.0	46.0	47.0	51.5
Head circumference (cm)	30.5	37.0	31.0	35.5	40.0	30.5	37.0	43.5
Apgar score 1st min	7	5	7	6	6	3	5	2
Apgar score 5th min	8	8	8	7	9	6	7	2
Diagnosed by	CT	CT	CT	CT	MRI	MRI	CT	CT
Hydrocephalus	Present	Present	Present	Present	Present	Present	Present	Present
Other cranial findings	Encephalocoele and lisscencephaly	None	Multiple cysts and skull defect	Joubert's syndrome	Hydrancephaly	Lisscencephaly	None	Corpus callosum agenesis
Extra-cranial	Intrauterine growth restriction. micrognathia, microtia and patent ductus arteriosus	None	None	None	Patent ductus arteriosus	None	Hypospadias, ventricular septal defect and patent ductus arteriosus	Patent ductus arteriosus
Hospital stay (days)	25	41	58	7	27	18	15	21

[a] Ambiguous genitalia.

Table 2: Cranial and extra-cranial findings associated with Dandy–Walker syndrome in eight infants.

Cranial finding	%	Extra-cranial finding	%
Hydrocephalus	100	Patent ductus arteriosus	50
Lisscencephaly	25	Ventricular septal defect	12.5
Encephalocoele	12.5	Intrauterine growth restriction	12.5
Multiple cysts	12.5	Micrognathia	12.5
Skull defects	12.5	Microtia	12.5
Joubert's syndrome	12.5	Hypospadias	12.5
Hydrancephaly	12.5		
Corpus callosum agenesis	12.5		

The incidence of extra-cranial anomalies was 50%, and all were cardiac: two were isolated cardiac defects, and the other two were associated with urinary anomalies or dysmorphism. One infant had associated Joubert syndrome. No chromosomal abnormalities were observed. All the infants had hydrocephalus, and five had other neurological anomalies (encephalocoele, lissencephaly, agenesis of the corpus callosum, hydrancephaly or brain cysts) (Table 2).

In five infants, a ventriculo-peritoneal shunt was inserted before they left hospital to relieve the intracranial pressure, while the remaining infants were discharged to be followed-up if shunting became indicated.

Discussion

Dandy–Walker syndrome (Figure 1) has been known for more than a century[1]; however, many aspects (aetiology, biology, types and outcome) are not well understood. Thus, the data vary in the medical literature.[2] The reported incidence also varies, ranging from one per 2500[3] to one per 100,000 births[4]; however, our cohort showed an incidence of 1/400 live births, which is much higher than any reported previously. This figure remains high even if the cases diagnosed prenatally are omitted in order to eliminate referral bias (1/800 live births).

Unless the syndrome is detected prenatally, by ultrasound or magnetic resonance imaging[5] or increased head circumference (prenatally or postnatally), the diagnosis is challenging because of a lack of specific symptomatology.[6] In our study, the diagnosis was made prenatally in 50% of the infants. Although the remaining 50% were found to have ventriculomegaly on prenatal ultrasound, Dandy–Walker syndrome was not diagnosed.

The aetiology is unclear, although its association with risk factors like maternal viral infection (e.g. rubella, toxoplasma, cytomegalovirus) and alcohol ingestion have been proposed.[7] Genetic and chromosomal abnormalities have also been found.[8,9] We found none of these risk factors, except in the case associated with Joubert's syndrome, in which there was a family history of this syndrome.

The pathogenesis is also unknown, although several theories have been proposed. One is embryonic arrest of the rhombencephalon, with failure of cerebellum fusion in the midline between weeks 7 and 10 of gestation. This leads to persistence of the anterior membranous area, which expands and interposes itself between the hypoplastic vermis and the choroid plexus. Furthermore, the roof of the fourth ventricle expands upward through an agenetic corpus callosum.[10] The clinical presentation can be variable. Hydrocephalus is common prenatally or during the neonatal period, although this is a complication rather than part of the disease. Most cases are diagnosed during infancy.[11] In our cases, hydrocephalus was observed prenatally in all the infants.

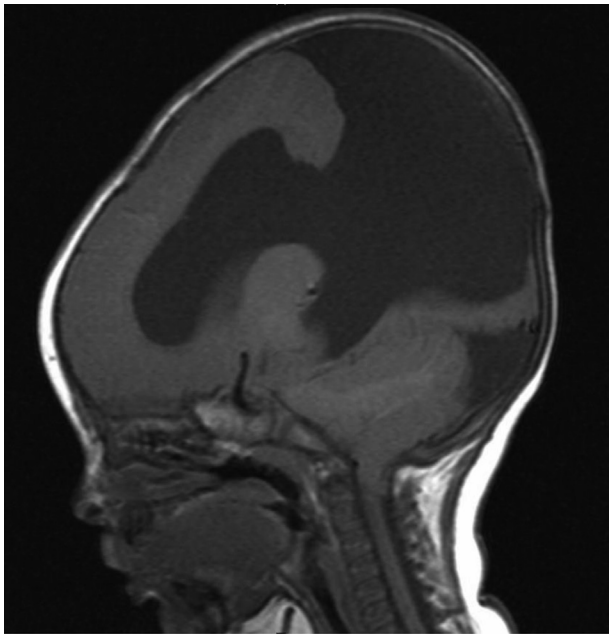

Figure 1: Radiological view of an infant with Dandy–Walker syndrome.

Older patients might be asymptomatic, with normal or near-normal neurological examinations. They usually present with neurological manifestations such as developmental delay, spasticity, poor head control and seizures.[12] Some children present with symptoms suggestive of increased intracranial pressure and posterior fossa tumour, like nystagmus, cranial nerve palsy or truncal ataxia.[2,13]

The severity of Dandy–Walker syndrome depends on the presence of associated anomalies. Two thirds of patients have associated central nervous system abnormalities, the most important being brain-stem dysplasia and absence of the corpus callosum, as in our study. About one-third have non-neurological problems, including cleft lip and palate, cardiac and urinary problems or associated syndromic disorders,[14] such as were found in our study.

The treatment of Dandy–Walker syndrome consists of dealing with hydrocephalus by various approaches, although this is still controversial.[2] The prognosis depends largely on the associated anomalies. The mortality rate ranges from 27% to 50%, and hearing and/or visual problems are associated with poor intellectual development.[12]

Conclusion

Dandy–Walker syndrome is a rare yet serious disorder. Many aspects of this malformation remain poorly

understood. There are few local published case series, and more publications are required in order to explore the demographic and environmental factors that might influence different aspects of this anomaly. Although the number of infants in our study was small, most of our findings were consistent with the current literature. The incidence was, however, significantly higher than any reported previously. This important finding warrants a detailed search to elucidate the reasons, probably in a larger study with a prospective approach.

Conflict of interest

None declared.

References

1. Dandy WE, Blackfan KD. Internal hydrocephalus: an experimental, clinical and pathological study. **Am J Dis Child 1914**; 8: 406–482.
2. Parisi MA, Dobyns WB. Human malformations of the midbrain and hindbrain: review and proposed classification scheme. **Mol Genet Metab 2003**; 80: 36–53.
3. Kaiser G, Schut L, James HE, Bruce DA. Problems of diagnosis and treatment in the Dandy-Walker syndrome. **Neurology 1977**; 22: 771–780.
4. Ohaegbulam SC, Afifi H. Dandy-Walker syndrome: incidence in a defined population of Tabuk, Saudi Arabia. **Neuroepidemiology 2001**; 20: 150–152.
5. Donkelaar HJ, Lammens M, Wesseling P, Thijssen HOM, Renier WO. Development and developmental disorders of the human cerebellum. **J Neurol 2003**; 250: 1025–1036.
6. Maria BL, Zinreich SJ, Carson BCM, Rosenbaum AE, Freeman JM. Dandy-Walker syndrome revisited. **Pediatr Neurosci 1987**; 13: 45–51.
7. Altman NR, Naidich TP, Braffman BH. Posterior fossa malformations. **AJNR Am J Neuroradiol 1992**; 13: 691–724.
8. Akgul A, Babaroglu S, Bahar I, Bokesoy I, Birincioglu L, Cobanoglu A. An unusual combination: aortic arch coarctation associated with Dandy-Walker variant. **Int J Cardiol 2006**; 113: 258–260.
9. Cavalcanti DP, Salomao MA. Dandy-Walker malformation with postaxial polydactyly: further evidence for autosomal recessive inheritance. **Am J Med Genet 1999**; 85: 183–184.
10. Friede RL. *Developmental neuropathology*. 2nd ed. Berlin: Springer-Verlag; 1989. pp. 347–371.
11. Hirsch JF, Pierre-Kahn A, Renier D, Sainte-Rose C, Hoppe-Hirsch E. The Dandy-Walker malformation: a review of 40 cases. **J Neurosurg 1984**; 61: 515–522.
12. Jalali A, Aldinger KA, Chary A, Mclone DG, Bowman RM, Le LC, et al. Linkage to chromosome 2q36.1 in autosomal dominant Dandy-Walker malformation with occipital cephalocele and evidence for genetic heterogeneity. **Hum Genet 2008**; 123: 237.
13. Tal Y, Freigang B, Dunn HG, Durity FA, Moyes PD. Dandy-Walker syndrome: analysis of 21 cases. **Dev Med Child Neurol 1989**; 22: 189–201.
14. Hart MN, Malamud N, Ellis WG. The Dandy-Walker syndrome: a clinicopathological study based on 28 cases. **Neurology 1972**; 22: 771–780.