Dandy-Walker syndrome in association with neurofibromatosis in monozygotic twins

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ABSTRACT

Dandy-Walker syndrome in monozygotic twins is reported. The twins reported, presented with delayed development, big head and dysmorphic features. In addition, there were significant cafe-au-lait spots on the trunk and other minor features consistent with the diagnosis of neurofibromatosis. To the best of our knowledge, Dandy-Walker syndrome in combination with neurofibromatosis in monozygotic twins has not been previously reported.

Keywords: Dandy-Walker syndrome, twins, neurofibromatosis.

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Dandy-Walker (DW) syndrome was delineated in 1914 by Dandy and Blackfan[1] and in 1942 by Taggert and Walker.[2] The syndrome was named by Benda[3] in 1954. The 2 essential features of the syndrome are hypoplasia or aplasia of cerebellar vermis and cystic dilatation of the 4th ventricle.[4] A posterior fossa cyst and mega-cisterna magna need to be differentiated from this syndrome. The DW syndrome has been seen in siblings[5,6] but is rare in identical twins.[4,7] We report DW syndrome in identical twins, in association with Neurofibromatosis type 1 (NF 1).

Case Report. Twin 1 and Twin 2, 3rd in birth order (both male) were born full term, vaginally on December 1995 to non-consanguineous parents. They were born in the hospital and at the time of delivery, the attending obstetrician had noted single placenta. There were no antenatal or perinatal complications. The parents noted delayed motor and mental development in both. At the age of 2 years and 8 months, they were referred to the University Hospital for neurological evaluation. The children could just stand with support. They had achieved head control at 9 months, and started sitting at 1 year. Speech had not yet developed. The head circumference was at the 50th centile in both, however, weight and height were below the 3rd centile. Both the children had prominent forehead, hypotelorism, low set ears and prominent occiput. There were many cafe-au-lait spots on the body, few of 5 cm^2 size, more on the trunk in both the children. In addition, a few depigmented spots were also seen. The routine blood counts, liver and renal function tests were normal. The nerve conduction studies and brainstem auditory evoked potentials were normal. The brain CT revealed typical features of DW syndrome in twin 1 (Figure 1) and in addition, associated hydrocephalus in twin 2 (Figure 2). Brain magnetic resonance imaging (MRI) was not carried out as the brain CT was typical of this condition.

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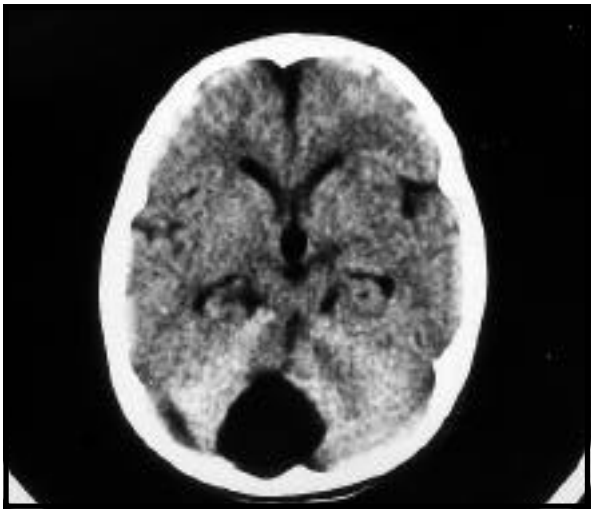

Figure 1 - Twin 1 showing cystic dilatation of the 4th ventricle with aplasia of cerebellar vermis.

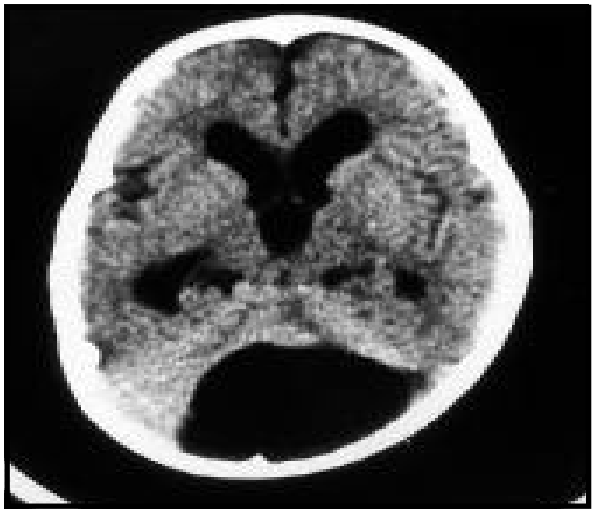

Figure 2 - Twin 2 showing cystic dilatation of 4th ventricle, aplasia of cerebellar vermis and dilatation of ventricles.

Discussion. The 2 essential features of the DW syndrome are hypoplasia or aplasia of the cerebellar vermis and cystic dilatation of the 4th ventricle. The other 4 abnormalities include elevation of the tentorium cerebelli and lateral transverse sinuses and torcula; lack of patency of foramina of Magendie and Luschka, enlargement of the posterior fossa and hydrocephalus. Not all of these 6 features are present in a given patient. In our patients, twin one had cerebellar aplasia, cystic dilatation of the 4th ventricle and enlarged posterior fossa while twin 2 had, in addition, associated hydrocephalus. In a typical patient, there is no differential diagnosis; however in atypical presentations posterior fossa cyst and mega-cisterna magna need to be excluded. In both these latter conditions, the cerebellum is preserved, thus hypoplasia of cerebellar tissue favours DW syndrome.

Several series of DW patients, with life time follow ups, associated nervous system and other systemic anomalies have been reported in a manual on 'Congenital Malformations of the Brain' including pathologic, embryologic, clinical, radiologic and genetic aspects.[4] No consistent chromosomal abnormalities have been recognised. Two cases of Trisomy 21, and an abnormality of chromosomes 5 amongst 40 patients have been reported.[8] Trisomy 18, 13, and partial trisomy of chromosome 11q have also been seen.[8-10] An adult onset presentation of DW syndrome in siblings, was reported recently.[5] There are only 2 reports of DW syndrome in identical twins,[4,7] our patients, being the 3rd pair of twins. Murray et al[6] calculated the prevalence of DW malformation among siblings to be 2% and the recurrence risk in subsequent pregnancies to be 1 to 5%. These numbers suggest that single gene forms of the syndrome may exist. Some dysmorphic features are not unusual in these children.[4] An apparently new autosomal recessive syndrome with facial dysmorphism, macrocephaly, myopia and DW malformation has been reported.[11] Our patients had few dysmorphic features like hypotelorism, low set ears and depressed nasal bridge which did not fit in any known syndrome. The karyotyping was normal.

The diagnoses of NF 1 & 2 are based on established clinical criteria by the National Institute of Health (NIH) concensus development conference on NF.[12] Two or more of the NIH criteria are required to diagnose NF 1. However, in children aged less than 6 years other minor features like macrocephaly, short stature, hypotelorism and thoracic deformity have significant value in diagnosis.[13] The macrocephaly is reported in 53% children and short stature in 25%.[13] Both these features were present in our patients. Single or few small cafe-au-lait spots may be seen normally in children. Our patients had big cafe-au-lait spots of more than 5 cm^2 on the trunk and few small ones at other places, significant enough criteria for diagnosis of NF 1. According to Crowe,[14] 6 cafe-au-lait spots with some exceeding 1.5 cm in diameter, favours the diagnosis of NF 1. In younger children 5 or more cafe-au-lait spots of at least 0.5 cm diameter, suggest the diagnosis of NF 1, even in the absence of cutaneous neurofibromas.[15] Korf[16] showed that 24 of 41 (58%) children, went on to develop NF 1, according to NIH criteria, after an initial visit during which only cafe-au-lait spots were observed. Our patients were aged less than 3 years and there were cafe-au-lait spots - few more than 5 cm^2 in diameter, had macrocephaly and short stature; features significant enough to make diagnosis of NF 1. Medline search revealed only one report in German

literature of a combination of NF and DW syndrome.[17] The association of DW syndrome in twins with NF 1 has not been reported previously. We feel, this association may have an underlying genetic basis. An association of DW syndrome and chronic polyneuropathy has been reported.[18] Associated abnormalities in the brain and visceral anomalies determine the prognosis in these children. Mortality varies between 12.6% to 57%, though intelligence could be normal in upto 75% of them.[4] MRI is the best preferred diagnostic tool, because its multiplanar capability permits identification of malplaced vermian tissue. Available good antenatal ultrasound technique can diagnose the condition as early as 20 weeks of gestation. The presentation of DW syndrome in monozygotic twins, a rarity, and the association with NF is reported, in this communication.

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