CASE REPORT

DOWN SYNDROME WITH DANDY WALKER MALFORMATION - RARE ASSOCIATION

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Abstract:
The association of Down syndrome with Dandy Walker malformation (DWM); one of the variation in Dandy Walker Syndrome (DWS) is extremely rare. Till now only 5 cases have been reported. Out of these, the first patient died, the second was severely handicapped; the third patient showed greater deficit in gross motor skills and one case had successful endoscopic hydrocephalus treatment with poor qualitative fine motor development and mild cerebellar dysfunction, and in one case the association between Down syndrome and Dandy walker malformation had been shown but the developmental profile was not reported. The present case reveals the possibility of relatively good prognosis with relatively uncommon co-occurrence of Down syndrome and Dandy walker malformation.

Key words: Dandy-Walker malformation; Down syndrome.

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Introduction:

Down syndrome (DS), Trisomy 21 is the most common genetic cause of mental retardation with a prevalence of 1 in 700 live births, or 6000 births yearly in the United States [1]. The coexistence of DS and DWS previously reported in few cases, suggests that it is relatively uncommon in both conditions to occur simultaneously. While the case reported by Constantini et al. [2] died at 2 weeks of age, Estroff et al. [3] described a 4-month old infant with Trisomy 21 and Dandy Walker variant (DWV) as severely handicapped, Kaitilin Love et al described 37 month old male child with DS and DWM with poor motor development [4]. We would like to report a similar association after taking consent from grandmother of the child to conclude that the developmental outcome of DS–DWM association may separately depending on the severity of the clinical and neurological involvement of each malformation

Case Report

A 7 year old female patient was referred to our pediatric unit with the complaint of delayed speech. This girl was born to 22 year old mother and 25 year old father who are non-consanguineous couple. The antenatal, natal and post natal period was uneventful. On taking history it was revealed that all the developmental milestones of the child were delayed. Child started sitting without support at 4 year of age and walking without support at the age of 5.5 years, and now the child's gross motor skills compared to 4 year old child as she can go up and down stairs with one foot per step but not able to skip. Her fine motor skills compared to 3 year old child as after training at home by caregivers; she was able to hold the pen and was able to scribble and was able to drink from the cup without spillage after the age of 4 years. Now she is able to copy circle but is not able to draw cross or square and she can't button clothes fully. In the language domain she attained monosyllabus at 5 years of age and now she can speak at least 6 words with meaning but not able to make sentences which is compared to 15 month of age and her social skills were those of a 4 year old child as she is able to go to the toilet alone and can play imaginatively with doll but is unable to tie shoe laces and unable to help in household tasks and repeating 4 digits. At the age of 2 years child underwent surgery for Patent Ductus Arteriosus.

On clinical examination the weight of the child 14 kg (<3rd percentile), height 103 cm. (<3rd percentile) head circumstance 44 cm (<3rd percentile). General physical examination showed features of Down syndrome and on neurological examination hypotonia was recognized and there are no signs of raised intracranial pressure. Karyotype analysis confirmed Trisomy-21 Figure-1.

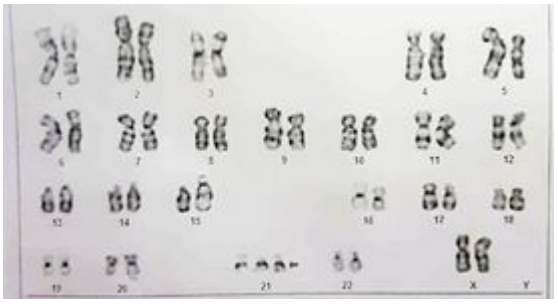

Fig 1: Karyotype showing Trisomy21

Post operated 2D echocardiography was normal. Complete Hemogram and ultrasonography abdomen was normal. Thyroid function tests were normal. Hearing assessment showed bilateral mild hearing loss for which brainstem evoked response audiometry was advised. Intelligent Quotient assessment according to Wechsler intelligence scale for children showed mild mental retardation. Child's

left wrist and hand X-ray AP view gives estimation of six carpal bones and distal end of Ulna bone ossification but it is not showing ossification of pisiform bone which corresponds to 6 to 7 years of age. X-ray cervico-thoracic spine was normal and MRI brain showed Hypoplasia of inferior vermis, Superior vermis is elevated and rotated, Cyst like dilation of the fourth ventricle, enlarged posterior fossa, suggestive of Dandy walker malformation and No hydrocephalus Figure-2.

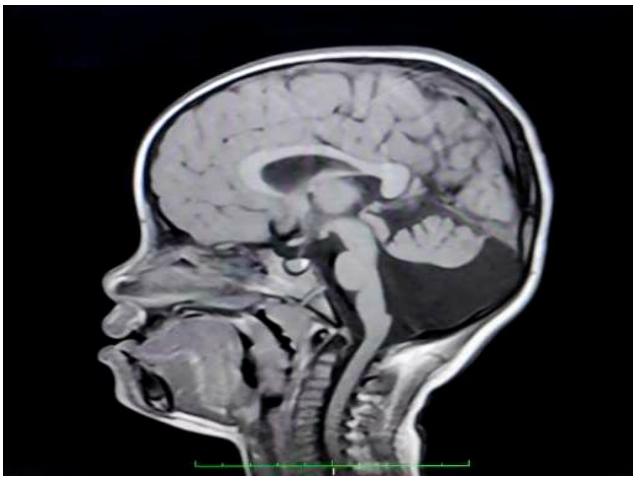

Figure 2: MRI showing Dandy Walker malformation in posterior fossa.

All test results normal or abnormal pertinent to the case are mentioned in Table-1 & Table-2 respectively.

TABLE-1 : TESTS SHOWING NORMAL RESULTS IN INDEX PATIENT

Test	Result	Units	Normal Range
T3	1.86	ng/ml	0.87-1.87
T4	11.31	micro g/dl	6.32 - 12.23
TSH	2.31	micro lu/ml	0.34-5.36
Hb	12.4	gm/dl	11.5-15.5
Total counts	8200	cells/cumm	5000-13000
Platelet count	2.34	Lakhs/cu.mm	1.5-4.1
Peripheral smear	Normocytic normochromic blood picture		
USG Abdomen	No sonological abnormality.		
2D Echo	Showed Situs solitus, levocardia, normal RA, LA, RV, LV. Intact IAS/IVS. No PDA/COA.		
Bone age estimation	left wrist and hand X-ray AP view gives estimation of six carpal bones and distal end of alna bone ossification but it is not showing ossification of pisiform bone which corresponds to 6 to 7 years of age		

TABLE-2 : TESTS SHOWING ABNORMAL RESULTS IN INDEX PATIENT

Test	Result
Karyotype	Trisomy 21
Hearing assessment	Mild hearing loss
IQ Assessment	Around 60 (mild mental retardation)
MRI brain	MRI brain showed Hypoplasia of inferior vermis, Superior vermis is elevated and rotated, Cyst like dilation of fourth ventricle, enlarged posterior fossa, suggestive of Dandy walker malformation and No hydrocephalus

In view of MRI findings suggestive of DWM, neurosurgery opinion was taken and since the child did not have any symptoms or signs of raised intracranial tension it was advised to follow the child every six months and no immediate intervention was needed. Child was advised for rehabilitation and speech therapy and was advised to come for followup.

Discussion

Dandy walker malformation is a brain malformation that occurs during embryonic development of the cerebellum and fourth ventricle and is one of the variants of Dandy walker syndrome or Dandy walker complex which are frequently characterized by triad of, a) partial or total vermian agenesis; b) cystic dilatation of the fourth ventricle; c) an enlarged posterior fossa[3,6]. The Dandy Walker malformation is characterized by the presence of posterior fossa enlargement [3,6,7]. It can be associated with hydrocephalus and usually requires surgery. The various neurological abnormalities which are associated with Dandy walker malformation are hydrocephaly, microcephaly and ventriculomegaly [6,9,10] and the children with Dandy walker malformation may have intellectual disability, delayed development, spastic paraplegia and seizures. Other non-neurological malformations of heart, face, limbs, digits, gastrointestinal and genitourinary abnormalities can be a part of genetic syndromes with Dandy walker

malformation[5]. The estimated frequency of Dandy walker malformation is of 1/ 25000 to 1 / 35000 live births and it is of multifactorial in nature. It probably results due to genetic and environmental factors (teratogens). The genetic causes include various chromosomal abnormalities of 3, 5, 8, 9, 13, and 18 associated with Dandy walker malformation [3,5,11,12]. Grinberg et al. [13] isolated a region on 3q24-25.1 commonly deleted in individuals with Dandy walker malformation [14]. For the children having typically Dandy walker malformation; the neuro developmental outcomes have been described [13] but there are no reports on the neuro developmental challenges experienced by children with DS and DWM. The case reported by Constantini et al. [2] died at 2 weeks of age, Estroff et al. [3] described a 4-month old infant with trisomy 21 and Dandy Walker variant (DWV) as severely handicapped, Kaitilin Love et al described 37 month old male child with Down syndrome and Dandy Walker malformation with poor gross motor skills [4]. We describe a case of 7 year female child with Down syndrome and Dandy Walker malformation with no evidence of ventricular dilation or hydrocephalus with relatively good prognosis. Sasaki-Adams et al. 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 the co-occurrence of Down syndrome and Dandy walker malformation is relatively uncommon but it is important to know the influence of Dandy walker malformation on the neurodevelopmental outcome so that early interventional therapy can be given. Children with Down syndrome have muscular hypotonia, joint hyperlaxity, and delayed gross motor skills. At the age of 7 years, our patient's gross motor skills and social skills correspond to 4 year old child, fine motor skills are equivalent to 3 year old child, and her language corresponds to 15 month of age. Similar to children with Down syndrome who do not have Dandy walker malformation; this patient has strengths in social skills but there is weakness in communication. Hence, with early speech therapy communication skills can be improved. Because of muscular hypotonia our patient shows greater deficit in fine motor skills compared to the children with Down syndrome who do not have Dandy walker malformation. Hence, occupational therapy should be begun in the early years of life. With early interventional therapy and appropriate guidance and support the children with Down syndrome and Dandy walker malformation can show progress in their developmental milestone for a better future.

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