Nigerian Journal of Paediatrics 1993; 20(4): 98-100

X-linked Hydrocephalus (Bickers-Adams syndrome) in Siblings.

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Summary

Okogbo ME and Amadin RO. X-linked Hydrocephalus (Bickers-Adams syndrome) in Siblings. *Nigerian Journal of Paediatrics* 1993; **20**:98. A family with three consecutive male children with prenatal hydrocephalus is reported. The proband had prenatal hydrocephalus, bilateral flexion-adduction deformity of the thumbs and spasticity. Exclusion of other causes of prenatal hydrocephalus on clinical grounds, implicated X-linked hydrocephalus (Bickers-Adams syndrome) as the most probable diagnosis. Since identification of an X-linked hydrocephalus has important consequences for genetic counselling, analysis of the family history of any male infant with overt hydrocephalus at birth, is therefore very important.

Introduction

THE first description of the syndrome of X-linked hydrocephalus was by Bickers and Adams in 1949.[1] There have been several subsequent reports of the syndrome which is estimated to account for two percent of all cases of congenital hydrocephalus.[2,3] The syndrome is characterized by prenatal hydrocephalus, severe enough to impede delivery, aqueductal stenosis. congenital flexion-adduction deformity of the thumbs (cortical thumbs), mental retardation and spasticity. Variable associated abnormalities include fusion of the thalami, small pons, absence of septum pellucidum, hypoplasia of corticospinal tracts, poroencephalic cysts and agenesis of the corpus callosum. The present report concerns a family with three consecutive male siblings who, on clinical grounds alone, were presumed to have an X-linked congenital hydrocephalus.

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Case Report

BP was delivered at the Murtala Muhammed Hospital, Kano, on February 16, 1981 by caesarean section, because of two previous sections. The birthweight of the baby was 4000gm and the Apgar scores were five, six and eight at one, five and 10 minutes, respectively. The head circumstance was 51cm (>98th centile) with inverted triangular head appearance. The anterior fontanelle was tense, while the sutures were widely separated. There was generalized hypertonia with

exaggerated muscle stretch reflexes. Bilateral flexion-adduction deformity of the thumbs was also present. There was no urinary or faecal incontinence. The spine was normal and spinal radiograph showed no evidence of dysraphism. No intracranial calcification were visible on plain skull radiograph. No other obvious malformations were present; pallor, jaundice, petechiae and hepatosplenomegaly were absent. Serological tests for toxoplasma and cytomegalovirus were not performed because of lack of facilities for these tests. Full blood count, including platelets was within normal limit. Examination of the cerebrospinal fluid (CSF) obtained from ventricular tap, revealed no pleocytosis; CSF protein was 80mg/dl and sugar 120mg/dl. The patient died on the fifth day of life and request for autopsy was not granted.

The father and mother who were 32 and 28 years old respectively, were not related. The father, with a head circumference of 57.5cm, had only primary school education and is a domestic servant, while the mother dropped out at primary three, because of poor school performance and she is a full time house wife. The height of the mother was 157cm; her fasting blood sugar was normal; the Hb-genotype was AA and VDRL was negative. Family history of macrocephaly, mental retardation or epilepsy was denied, but the present family had two previous hydrocephalic male infants delivered by caesarean sections in 1985 and 1986 respectively; they died at four days and 14 months of age, respectively. The mother denied any history of hydrocephalus in her own family. The first child of the present family was a male who was delivered vaginally in 1984; he had normal developmental milestones, but died at the age of 15 months from a febrile illness. The subsequent three male children including the present case, had congenital hydrocephalus. The only surviving child of the family, a normal female, was born in 1991.

Discussion

Prenatal, or foetal hydrocephalus may be caused by congenital malformations in the central nervous system (CNS), such as in spina bifida and in Dandy-Walker syndrome, [4] chromosomal anomalies, [5] or genetic disorders such as the Bickers-Adams syndrome,[1] an X-linked hydrocephalus and intrauterine infections.[6]

In the present study, the proband had foetal hydrocephalus that was associated with bilateral cortical thumbs and spasticity. Significant family history of this proband included a school drop-out mother with dull intelligence, a feature that has been observed in some mothers who are carriers of X-linked hydrocephalus,[2] two male siblings who were also delivered by caesarian section because of hydrocephalus. Thus, it may be presumed that these three siblings were cases of X-linked (Bickers-Adams) syndrome. Absence of spina bifida in the proband and in the hydrocephalic male siblings, is against the hydrocephalus being due to this congenital mal-formation. Neither the proband, nor the siblings had any dysmorphic features to suggest a chromosomal anomaly as the cause of hydrocephalus in the three siblings. Warburg's syndrome, a disorder of autosomal recessive inheritance [7] was considered as a differential diagnosis, but the absence of several eye defects in any of the siblings makes this condition most unlikely. Intrauterine infections [6] are also important causes of foetal hydrocephalus, but visceromegaly and disturbed hematopoiesis which are expected associated features of most intrauterine infections, were absent in the proband, nor was a plain radiograph of the skull supportive of infections in the absence of intracranial calcification.

Mental retardation that is associated with the X-linked hydrocephalus varies from moderate to severe and is reported to be independent of the hydrocephalus [8] Therefore, the retardation cannot be a consequence of the hydrocephalus *per se*. In

some families, other male relatives on the maternal side have been mentally retarded without any evidence of hydrocephalus, thus suggesting limited expression of the gene.[9] A recent study of five mentally-retarded normocephalic male relatives of three bydrocephalic male infants, has shown that, of these five children, three had moderate ventricular dilation, while two had normal-sized ventricles.[10] There is thus, inter-family and intra-family variability in the expression of this X-linked gene. Identification of X-linked hydrocephalus has important consequences for genetic counselling because there is a 25 percent risk for each subsequent pregnancy and a 50 percent risk that any subsequent male infant will be affected.[11]

Advances in diagnosis and treatment have renewed interest in foetal hydrocephalus. The findings that intrauterine decompression of hydrocephalus is beneficial and that *in-utero* ventriculi-amniotic shunt is feasible, have made antepartum diagnosis of foetal hydrocephalus attractive. [12-15] Prognosis of congenital hydrocephalus depends, however, on its aetiology and the presence of associated congenital anomalies. Prenatal shunting of the hydrocephalus in X-linked cases with high frequency of associated anomalies, is of doubtful benefit. Indeed, less than 10 percent of all cases of foetal hydrocephalus have isolated hydrocephalus and potential candidates for antenatal neurosurgical intervention are therefore, few.[16]

Acknowledgement

We wish to thank Miss Patience Ezeh for secretarial assistance.

References

1 Bickers DS and Adams RD. Hereditary stenosis of the aqueduct of Sylvius as a cause of congenital hydrocephalus. *Brain* 1949;**72**: 246-61.

2 Smith's Recognizable Patterns of Human Malformation. Philadelphia: WB Saunders 1988: 156-7.

3 Editorial. Sex-lined Hydrocephalus with several mental defect. *Br Med J* 1962; **1**: 168.

4 Hirsch J F, Pierre-Kahn A, Renieri D, Sainte-Rose C and Hoppe-Hirsch E. The Dandy-Walker malformation. *J Neurosurg* 1984; **61**: 515-22.

5 Aicardi J. Diseases of the Nervous System in Childhood. Mackeith Press 1992: 298.

6 Volpe JJ. Neurolgy of the Newborn. 2nd Ed. Philadelphia: WB Saunders 1987: 548-95.

7 Bordarier C, Aicardi J and Goutieres F. Congenital hydrocephalus and eye abnormalities with severe developmental brain defects: Warburg's syndrome. *Ann Neurol* 1984; **16**: 605.

8 Jansen J. Sex-linked hydrocephalus. *Dev. Med Child Neurol* 1975; **17**: 633-40.

9 Fried K. X-linked mental retardation and/or hydrocephalus. *Clin Genet* 1972; **3**:258-63.

10 Willems PJ, Brouwer OF, Dijkstra I and Wllmink J. X-linked hydrocephalus. *Am J Med Genet* 1987; **27**:921-8.

11 Holmes LB, Mash A, Zu Rhein GM, Levin M and Optiz JM. X-linked aqueductal stenosis: clinical and neuropathological findings in two families. *Pediatrics* 1973;**51**:697-704.

12 Michejda M and Hodgen GD. In-utero diagnosis and treatment of non-human primate fetal skeletal anomalies I. Hydrocephalus. *JAMA* 1981; **246**: 1093-7.

13 Michejda M, Patronas N,Di Chiro G and Hodgen GD. Fetal hydrocephalus II. AMelioration of fetal porencephaly by in-utero therapy in nonhuman primates. *JAMA* 1984: **251**:2548-52.

14 Clewell WH, Johnson ML, Meier PR, Mewkirk JB, Zied SL, Hendee RW, Bowes WA Jnr, Hecht F, O'keef D, Henry GP and Shikes RK. A surgical approach to the treatment of fetal hydrocephalus. *N Engl J Med* 1982; **306**: 1320-5.

15 Bannister CM. Fetal neurosurgery - a new challenge on the horizon. *Dev Med Child Neurol* 1984; **26**:827-30.

16 Gukk A and Volpe JJ. Fetal Neurology. New York: Raven Press: 1989:253-6.