Congenital hydrocephalus due to aqueductal stenosis of probable autosomal recessive inheritance

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ABSTRACT

Hereditary stenosis of the aqueduct of Sylvius is known to be transmitted as an X-linked recessive trait, thus affecting only the male offspring. We describe a family of consanguineous marriage where 2 sons and 2 daughters were afflicted with congenital hydrocephalus associated with stenosis of aqueduct of Sylvius. The pattern of the disease in this family is consistent with autosomal recessive inheritance. The authors of this communication are not aware of any literature reporting a similar mode of inheritance regarding this condition. Perhaps this discordant genetic mode of inheritance could have been caused by the consanguinity between the parents.

Keywords: Hydrocephalus, aqueductal stenosis, autosomal recessive inheritance.

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Congenital hydrocephalus due to stenosis of the aqueduct of Sylvius can be associated with structural malformations, hemorrhage, infection, neoplasms or vascular malformations. In cases where more than one child in a family is affected, it should be considered as hereditary. Hereditary aqueductal stenosis is known to be transmitted as an X-linked recessive trait. This implies that a mother is the carrier of the abnormal gene and only her male offspring can be affected. The authors of this communication are not aware of any report of an inheritable type of this disorder which is of an autosomal recessive trait. The present report concerns a female infant born with hydrocephalus associated with aqueductal stenosis; her 3 older siblings, a sister and 2 brothers, had died of a similar congenital anomaly. The pattern of this disease in this family is consistent with autosomal inheritance and, therefore, at variance with what is known of this type of hydrocephalus, hence we find it worth reporting. The index infant was admitted into Assir Central Hospital which is the only tertiary referral health facility in Assir Region of Saudi Arabia.

Case Report. A female Saudi newborn was referred from a general hospital in Assir region to the neonatal intensive care unit of Assir Central Hospital (ACH) on the 3rd of October 1998 at the age of 3 days due to a large head size at birth. The mother had had regular antenatal care in the referring hospital and was not on any other medication except the routine hematins (ferrous sulphate and folic acid tablets) during the pregnancy which was uneventful. Due to the large fetal head size which was first detected by an abdominal ultrasonography at 36 weeks gestation, the mother was delivered by an elective lower segment Cesarean section at term.

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The infant had a normal Apgar score and was only offered the routine oropharyngeal suctioning and face mask oxygenation at birth. The anthropometric measures of the infant at birth were: weight 2500gm (10th centile); length 48cm (25th centile); head circumference 40.5 cm (> 95th centile).

The mother was gravida 8, para 8; all of her deliveries were conducted in the same hospital. Her 2nd child, a male, was also born with a large head, and a computerized tomographic (CT) scan, which was carried out in ACH, demonstrated hydrocephalus due to aqueductal stenosis. He also had a right talipes equinovarus deformity which was surgically corrected. No other congenital defects were observed. A ventriculo-peritoneal shunt was inserted in ACH but he died at home at the age of 6 months. According to the father, he was found dead in bed in the morning without any signs of an acute illness the previous evening. From the referral note and according to the father, 2 other siblings, the 4th and 6th, a male and female—respectively, were also born with big heads and proven by postnatal ultrasonography to be hydrocephalus (details on the ultrasound were not provided). The father consistently refused the transfer of any of these 2 infants to a higher centre for a CT scan and shunt procedure and each of them died at home before the ages of 3 months. The father volunteered that these 2 also had bilateral clubbed feet at birth and the 6th child additionally had clawed or flexed adducted thumbs and her course at home was complicated with several attacks of seizures but he declined to explain how these 2 died. The only additional information regarding them was that their heads had got enormously enlarged before they succumbed. Four of the siblings, the 1st, 3rd and 5th and 7th (all females), born without any congenital defects, are alive and healthy. The parents are 2nd cousins; the mother is a housewife, aged 28 years; the father is a soldier, aged 35 years.

On physical examination (on first admission), the infant was generally stable, pink and active. The head was large, circumference 40.5 cm. The anterior and posterior fontanelles were markedly wide and all the cranial sutures were widely separated; transillumination test on the skull was positive. The eyes intermittently rotated to an extreme downward position producing a ‘setting sun’ sign, but the fundi were normal. There were no other dysmorphic features and no skeletal anomalies involving any of the limbs. The other systems were within normal limits. Computerized tomographic scan of the head was reported as showing normal posterior fossa and brain stem; huge dilatation of the lateral and 3rd ventricles but normal sized 4th ventricle; loss of both fronto-temporal cerebral cortex. The report was concluded as being consistent with a non-communicating hydrocephalus due to stenosis of the aqueduct of Sylvius. Complete blood count and blood chemistry results were within normal limits. Chromosomal studies were not conducted on any member of the family due to lack of facilities. No autopsy was undertaken on any of the deceased siblings.

The patient had a ventriculo-peritoneal shunt inserted at the age of 4 days. The drain was placed in the right lateral ventricle and connected with a low-pressure valve. Her post-operative period was uneventful and she was therefore discharged home on the 7th post-operative day. The infant has been readmitted twice: first at the age of 2 months for reinsertion of the VP shunt which got displaced from the lateral ventricle; and the 2nd for ventriculitis and meningitis caused by coagulase negative Staphylococcus. She was in coma with decorticate posturing and ventilator dependent at the time of reporting (aged 4 months).

**Discussion.** If 4 out of 8 children in a family have been afflicted with congenital hydrocephalus, it strongly suggests that the underlying disorder is genetically inherited. Since 2 of these infants were found by computerized tomography to have had aqueductal stenosis as the related cause of their hydrocephalus, it can be rightly assumed that this was most probably also the underlying cause in the other 2 affected siblings whose hydrocephalus was identified by ultrasonography only.

Hereditary aqueductal stenosis is known to be transmitted as an X-linked recessive trait, hence it is supposed to be limited only to the male offspring of a given family. In the family here reported, 2 sons and 2 daughters had been affected by the disease, a picture that is inconsistent with an X-linked transmission but at par with autosomal inheritance pattern. In X-linked hydrocephalus associated with aqueductal stenosis, adduction-flexion deformity of the thumb is characteristic but not invariably; it is found in about one 4th of cases. In the present series, only one of the 4 affected children had flexed adducted thumbs (together with clubbed feet), and 2 had clubbed feet with normal hands. Sovik et al reported on a family of 8 affected children in which thumb contracture was not noted. To our knowledge, a combination of adducted thumbs and clubbed feet that was encountered in the present series has not previously been documented in association with aqueductal stenosis. Perhaps this feature is peculiar to this unusual type of inheritance. Nevertheless, clubbing of the feet at birth can be quite non-specific.

The consistency in the birth order, by which the normal children of this mother alternate with hydrocephalic ones, is worth noting. Perhaps this arrangement is purely a mere coincidence, but it could also be a feature of this unusual autosomal
recessive syndrome. The exact cause of death among these children cannot be accurately determined since none of them died in hospital. This could possibly have been due to progressively raised intracranial pressure which must have impacted on the vital centers in the brain.

We postulate that the unusual genetic pattern of hereditary aqueductal stenosis observed in this family might have been influenced by the consanguinity between the parents who are cousins. Consanguineous marriage is an important correlate of congenital malformation.6,7 A study in the Al Qassim area of Saudi Arabia has revealed that consanguineous marriages (54%) were associated with a high incidence of birth defects.8 In a study conducted on 3103 Saudi families, consanguinity rates in different provinces of Saudi Arabia ranged from 52% to 68% with the highest prevalence for 1st cousin marriages.8 Across various provinces, the frequency ranged from around 40% in some areas to 80% in others; that of Assir province (population, 2 million) is 54%.8 Since high rates of inbreeding influence the frequency of genetic defects and congenital malformation, it becomes paramount to mount a genetic counseling campaign in this environment.

References