

Prenatal diagnosis of X linked hydrocephalus without aqueductal stenosis

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SUMMARY The outcome of four successive pregnancies in a woman heterozygous for X linked hydrocephalus is described. The last two were scanned by ultrasound. In one, a good prognosis was given; the fetus was male but there was no evidence of dilated cerebral ventricles. In the other, hydrocephalus was diagnosed. The absence of aqueductal stenosis in this case supports the hypothesis that in this X linked condition communicating hydrocephalus is the primary defect and aqueductal stenosis is secondary.

Since the original description of X linked inheritance in congenital hydrocephalus,¹ reports have nearly all confirmed that the syndrome is caused by stenosis of the aqueduct of Sylvius.²⁻⁴ Until recently, prenatal sex determination followed by selective termination of pregnancy in the case of a male fetus was the only procedure available to avoid term delivery of an affected child.⁵⁻⁶ Nowadays, early development of hydrocephalus can be diagnosed by ultrasound as early as the mid-trimester of gestation on the basis of dilatation of the cerebral lateral ventricles.⁷

At our Genetic Counselling Clinic we have seen six families with isolated hydrocephalus; four appeared to be transmitted through autosomal recessive inheritance and two through X linked recessive inheritance. One of the latter is the subject of this report, and the absence of aqueduct stenosis is demonstrated.

Case reports

In 1972, the proband (fig 1, II.2), at the age of 18, delivered a hydrocephalic male infant (III.1) at 37 week's gestation, weighing 3450 g, who died during the first week of life. According to her parents one of her two brothers was also hydrocephalic (II.3). A year later she delivered a stillborn hydrocephalic male weighing 3550 g (III.2). These two deliveries took place outside our Institute and no detailed necropsies were carried out.

She was referred to our genetic clinic in the 17th week of her third pregnancy. From her history, X linked congenital hydrocephalus was suspected. Ultrasound examination (Picker LS 2000) showed the biparietal diameter and the intracranial structure to be normal. At 20 weeks the biparietal diameter remained normal, no dilated ventricles were seen, and the fetus was seen to be male. Delivery was at term by Caesarean section. The infant, weighing 3100 g, showed no sign of hydrocephalus. However, his later development was slow and at the age of two years he has cerebral palsy but no hydrocephalus on ultrasound.

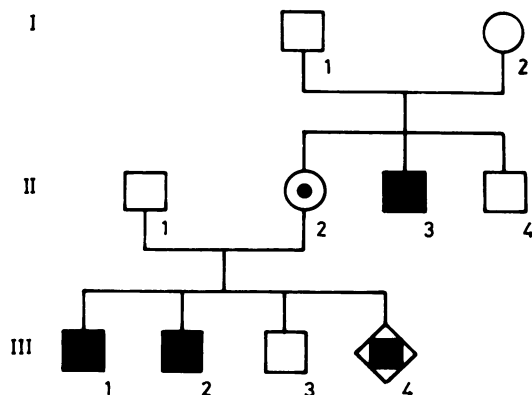


FIG 1 Family pedigree.

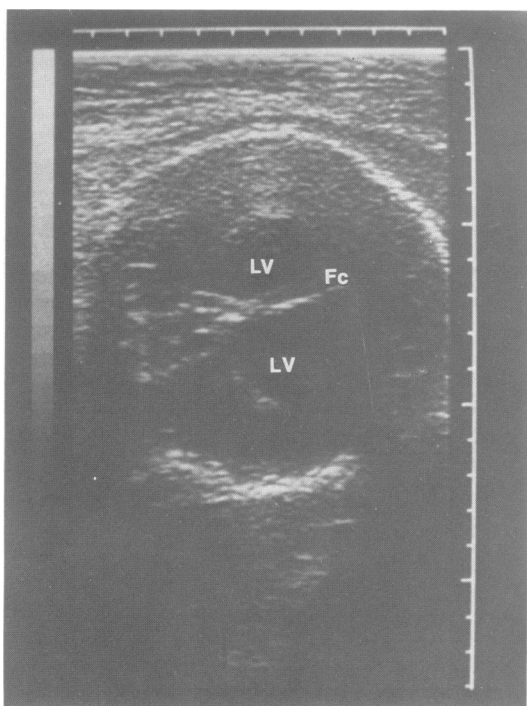


FIG 2 Falx cerebri (Fc) between the dilated ventricles (LV) of the 28 week old fetus with X linked hydrocephalus (Picker LS 2000).

The mother became pregnant for the fourth time in 1981. Despite these distressing experiences she did not attend the antenatal clinic until the 28th week of pregnancy. On ultrasound the fetus was found to be male and the lateral ventricles were seen to be widely dilated (fig 2). At 30 weeks' gestation a 2050 g stillborn male infant was delivered.

At necropsy the cerebral ventricles were markedly dilated and the surrounding cerebral substance was very thin. On examination of the brain stem in serial segments, the aqueduct of Sylvius was found to be patent. It was covered with a normal ependyma (fig 3). No obstruction or narrowing was observed. The lumen of the duct was a little elongated dorso-ventrally. Small hamartomatous hyperplastic nodules consisting of ependyma and glial cells were seen at the end of the canal (fig 4).

Discussion

X linked hydrocephalus comprises about 2% of all cases of isolated congenital hydrocephalus.⁸ The presence of stenosis of the aqueduct of Sylvius has

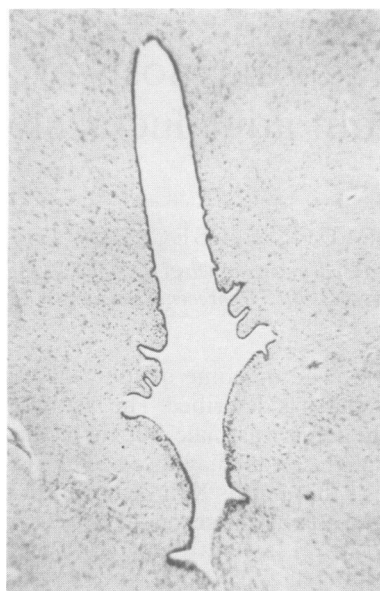


FIG 3 The aqueduct of Sylvius is patent and covered with a regular ependyma. (Haematoxylin and eosin.)



FIG 4 On the ventral side of the aqueduct there is a hamartomatous nodule with ependyma and glia cells. (Haematoxylin and eosin.)

been shown in most of the previously reported cases of X linked hydrocephalus.²⁻⁴ Observations both in animal experiments⁹ and in man¹⁰ suggest that the development of stenosis of the aqueduct may be secondary to communicating hydrocephalus. Absence of aqueductal stenosis has been reported in only three previous cases.^{7 11 12} The authors suggested that communicating hydrocephalus is the primary defect and that aqueductal stenosis is secondary.

In our case the aqueduct was elongated. Ventricular dilatation could have been caused by lateral compression of the brain stem. If the fetus had survived beyond 30 weeks' gestation, increasing compression could have caused complete stenosis. Reports of aqueductal stenosis published so far are based on necropsies carried out at term, while in the case presented here the fetus was delivered during the 30th week of gestation. Our results support the hypothesis that X linked congenital hydrocephalus is primarily a communicating hydrocephalus and that aqueductal stenosis arises later.

In the family presented here the mode of inheritance of hydrocephalus is likely to be X linked recessive. Because of our experience in prenatal ultrasound diagnosis of hydrocephalus, we did not carry out amniocentesis for fetal sexing during the proband's third pregnancy, and because of the absence of dilated cerebral ventricles a good prognosis was given. According to criteria set by previous authors,^{5 6} the pregnancy might have been terminated. The newborn child did not have hydrocephalus and his cerebral palsy appears to be coincidental.

During her fourth pregnancy, late referral delayed the diagnosis of hydrocephalus until the 28th week. We do not know at what stage of gestation the dilated ventricles could have been shown by ultrasound.

It must be emphasised that a normal biparietal diameter does not exclude the diagnosis of hydrocephalus, as the first sign is the dilatation of the cerebral ventricles. Failure to apply this parameter may lead to an incorrect diagnosis.¹³

Prenatal ultrasonic diagnosis of ventricular enlargement should be available to all women at risk for hydrocephalus. At present, the range of gestational

age in which X linked hydrocephalus may become manifest is not fully known, so caution should be exercised with respect to normal ultrasound findings of ventricular size in male fetuses at risk for X linked hydrocephalus.⁷ Supposing the onset of hydrocephalus within one family occurs at almost the same time, serial ultrasonic studies of cerebral ventricular size should lead to correct diagnosis of developing hydrocephalus in the second trimester of pregnancy. In these cases fetal sexing by amniocentesis or chorionic villus sampling is not required. However, in cases where ventricular enlargement may occur much later in pregnancy the only preventive measure at present remains sex determination of the fetus.

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