Brief Communication: Possible X-Linked Anencephaly and Spina Bifida—Report of a Kindred

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Causal heterogeneity of anencephaly and spina bifida has been demonstrated; in rare families the neural tube defect may be caused by a single gene. We report a family in which four cases of anencephaly or spina bifida may represent X-linked inheritance.

Key words: anencephaly, spina bifida, X-linked inheritance

INTRODUCTION

A number of causes of anencephaly and spina bifida (ASB) have been postulated, including multifactorial determination, environmental factors, maternal factors, intrauterine factors, and, in rare cases, single gene inheritance. However, no one seems to have reported an instance of apparent X-linked inheritance as possible cause of this condition. We report here a kindred with apparent X-linked ASB.

The propositus (IV-1) was a male with anencephaly; in addition, a maternal first cousin (IV-3), mother's first cousin (III-2), mother's nieces' son (V-1) and mother's uncle (II-6) had anencephaly or spina bifida (Fig. 1).

CLINICAL REPORTS

The propositus was born to a gravida 1, para 0, 23-year-old woman. During the first prenatal visit she was found to have cirrhosis of the liver and splenomegaly thought to be caused by organic solvents. The child was born at 33–34 weeks of gestational age, and the pregnancy was complicated by polyhydramnios. The child died minutes after birth, and no autopsy was performed, although the death certificate gives the cause of death as anencephaly and prematurity.

A male cousin (IV-3) born to the propositus' mother's sister was the result of the first pregnancy of a 22-year-old woman. The pregnancy was described as uneventful, and the child was born at 40 weeks and had anencephaly, phimosis, and clubfoot.
Fig. 1. Pedigree of the kindred.

Mother's niece's son (V-1) was the first born and had anencephaly noted at birth. The maternal cousin (III-2) was born to a gravida 3, para 2 woman and had a myelomeningocele and hydrocephalus; he died at eight days of age. The maternal great-uncle (II-6) was the fifth child in a sibship of nine and died of an open spine, according to the death certificate.

Two miscarriages (IV-5, 8) and one stillbirth (IV-7) were also reported in this family. The cause of the stillbirth was intrauterine death with no associated anomalies; the cause of one miscarriage was tubal pregnancy; and the cause of the other miscarriage was unknown.

DISCUSSION

An enormous amount of research has been done on the causes of ASB. Environmental factors are likely to be involved, since epidemiological studies have found fluctuations in incidence occurring with changes in season, parity, maternal age, social class, and nationality [Leck, 1974; Carter, 1973]. Among some of the possible environmental factors are influenza A [Wilson and Stein, 1969], hyperthermia [Miller et al, 1978], water softness [Crawford et al, 1972], maternal zinc deficiency [Sever and Emanuel, 1973], and organic solvents [Holmberg, 1979]. Intrauterine and maternal physiological factors have also been examined as possible causes of ASB, with some of them being twin-twin interaction [Knox, 1974], previous abortion [Rogers, 1976], subfertility [Ahlgren et al, 1976], and pituitary dysfunction [Janerich, 1974]. However, none of these factors alone can account for most or all of the cases of ASB.

Holmes [1976] has raised the point that causal heterogeneity exists for ASB. He performed a study in which he discovered that whereas most of the infants had ASB due to presumed multifactorial determination, others had ASB because of single gene disorders such as the Meckel or the Robert syndrome, chromosomal abnormalities, aberrant tissue bands, cloacal extrophy, and teratogenic factors. The infants in the multifactorial category were those who had either ASB alone or ASB with other anomalies that did not represent a specific syndrome.

Christakos and Simpson [1969] and Fuhrmann et al [1971] have described families in which multiple cases of ASB could be attributed to a single autosomal recessive gene. James [1979] postulates that many of the female ASBs are caused by environmental fac-
tors, whereas most males and the rest of the females represent primarily genetic causes. His theory is supported by Rogers and Morris [1973], who found that as the incidence of ASB fell, the sex ratio approached one, with the fall in incidence being accounted for almost entirely by a fall in the incidence among females.

Rarely, ASB may be caused by an X-linked gene such as the one that seems to be present in the family reported here. It is interesting that hydrocephalus due to stenosis of the aqueduct of Sylvius is frequently caused by an X-linked recessive mutation [Edwards et al, 1961].

Other support for X-linked inheritance of some ASB cases comes from the finding that mothers' sisters' children are more likely to have ASB than are other relatives [Lippman-Hand, 1978].

REFERENCES


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