Meckel's syndrome (dysencephalia splanchno-cystica) in two Pakistani sibs

SUMMARY A Pakistani couple, who were first cousins once removed through their fathers, and whose mothers were also related, had two live-born children, a boy and a girl. Both children died within 2 hours of birth with occipital encephalocele, microcephaly, polycystic kidneys, and cystic distension of intrahepatic bile ducts. Both children had normal karyotypes. These abnormalities constitute Meckel's syndrome (dysencephalia splanchno-cystica); this is the fifth report of parental consanguinity, adding further support to the evidence for autosomal recessive inheritance of the disorder.

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Sibs with microcephaly, occipital encephalocele, and polycystic kidneys were first reported by Meckel in 1822. Both patients had, in addition, polydactyly and cleft palate. Numerous case reports in both this and the last centuries have appeared, including a review by Gruber (1934), who added one case of his own observation and proposed the name dysencephalia splanchno-cystica. Opitz and Howe (1969) described a further case and called the disorder Meckel's syndrome; they suggested that it was inherited in an autosomal recessive manner. Hsia et al. (1971) reported 7 patients including 2 pairs of concordant monozygotic twins in 1 family and 3 sibs in another. Fried (1973) has drawn attention to the relatively high prevalence among oriental Jews. Sibs, born to consanguineous Pakistani parents, are presented here; they provide additional supporting evidence for autosomal recessive inheritance.

Fig. 1 (a) First case (IV.14). (b) Second case (IV.15).
Case reports

Case report

A 27-year-old Pakistani woman gave birth to her first child in July 1973. She had been married in 1967 but her husband had then emigrated to the UK, and she only rejoined him in 1972. She was first seen when in labour. Her dates were unknown but the fundal height corresponded to 34 weeks' gestation. The infant was a liveborn male weighing 1510 g, who died at 1½ hours. On external examination (Fig. 1a) he showed pronounced microcephaly; a ruptured occipital encephalocele; Potter's facies and shovel hands; loose dry skin and lax abdominal muscles; and bilateral talipes. At necropsy the above findings were confirmed. There was no cleft palate and no polydactyly. The positive findings were small unaerated lungs (right 6.9 g, left 6.1 g); large thymus (12.6 g); a firm granular liver (92.0 g) which on histological examination showed dilatation of bile ducts (Fig. 2a); enormously enlarged kidneys (right 67.0 g, left 59.0 g, against an expected combined weight of 14.0 g); widely patent cranial sutures, large fontanelles, and cerebellar tissue within the occipital encephalocele. Histologically the kidneys showed polycystic change resembling adult polycystic disease (Potter’s type III) (Fig. 2b). Chromosomal analysis on blood taken before death showed no detectable abnormality (karyotype 46,XY).

In the following year, the mother was seen again in her second pregnancy. Progress initially appeared normal, but from 30 weeks onwards the fundal height was persistently less than expected by her dates. An ultrasonic biparietal diameter measurement at 33 weeks was 5.8 cm, and at 36 weeks 6.6 cm, suggesting microcephaly. At 37 weeks labour started spontaneously and resulted in breech delivery of a female infant of 1740 g, who died at the age of 2 hours.

Again there was microcephaly, an occipital encephalocele, containing necrotic cerebellar tissue, Potter's facies and hands, and bilateral talipes (Fig. 1b). The internal organs showed abnormalities similar to those of the first infant: small unaerated lungs (right 8.7 g, left 8.6 g), a finely lobulated liver weighing 104 g showing great increase in the number and mild distension of interlobular ducts on microscopical examination, a large polycystic left kidney (25.6 g), and a small dysplastic right kidney (2.4 g). Histologically both kidneys showed changes resembling adult polycystic kidneys (Potter's type III). These microscopical changes were identical to those in the first child.

Fig. 2  (a) Microscopical appearance of liver from IV.14 (×115). (b) Microscopical appearance of kidney from IV.14 (×32).
The karyotype was that of a normal female (46,XX).

The parents were subsequently seen for genetic counselling when a family history showed that they were first cousins once removed, the paternal grandfather of the affected infants being a brother of the maternal great-grandfather. The two grandmothers were also related, though the relation is not known (Fig. 3).

The mother became pregnant for the third time at the end of 1975. Amniocentesis at 16 weeks showed a normal level of alphafetoprotein in the fluid (0.025 g/l) and a normal 46,XY karyotype. Pregnancy progressed normally and at 39 weeks a healthy-looking male infant, weighing 2890 g, was born by the vertex; no abnormality was detected and he was allowed to go home with his mother on her discharge from hospital in the normal way.

Discussion

There have now been numerous reports of two or more sibs affected with Meckel’s syndrome. Hsia et al. (1971) reviewed such cases published up to the time of their paper. These authors reported normal karyotypes in 4 of their 7 infants and in several cases among the reviewed publications. In fact, no instance of a proven abnormal karyotype in a case of Meckel’s syndrome is known to the present authors.

The evidence for an autosomal recessive inheritance of this malformation is supported by the findings of 3 pairs of concordant monozygotic twins in 2 families (Stockard, 1921; Hsia et al., 1971) and by previous reports of parental consanguinity (Kanzow, 1859; Tucker et al., 1966; Walbaum et al. 1967; Fried et al., 1971). In the family of Tucker et al. (1966) the affected child was born of an incestuous father–daughter mating. Fried et al. (1971) included 2 families with first cousin parents in a report of 10 cases in 4 families.

Although the children reported here lacked polydactyly, cleft palate, and congenital heart disease, they did have microcephaly, encephalocoele, and polycystic kidneys and would be accepted by most, if not all, authorities as examples of Meckel’s syndrome. The diagnosis is supported by the histological findings in the liver and kidneys, namely proliferation of bile ducts with minimal dilatation in the liver, and cysts of variable size and shape surrounded by dense connective tissue in the kidney resembling adult polycystic kidneys. These appearances resemble those reported by Adams et al. (1974). This family thus provides a further instance of Meckel’s syndrome in sibs with consanguineous parents and thereby strengthens the evidence for autosomal recessive inheritance of this disorder.

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Addendum

At the 23rd annual meeting of the Paediatric Pathologists Society, A. A. M. Gibson, J. M. Scott, and H. A. Tait described 7 cases of Meckel’s syndrome occurring in Glasgow; they belonged to 4 different families, and all but one of the cases were Caucasians.

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