

Meckel Gruber Syndrome: occurrence in non-consanguineous marriages

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(Index word: Meckel Gruber syndrome)

Abstract

Meckel Gruber syndrome is an uncommon, lethal, autosomal recessive disorder, associated consistently with polycystic kidneys, posterior encephalocoele and polydactyly. We report three cases in non-consanguineous marriages, suggesting that the single gene defect occurs more commonly in non-consanguineous marriages than mutant genes associated with other autosomal recessive disorders that are usually related with consanguineous marriages. The usefulness of prenatal diagnosis is discussed.

Introduction

Congenital polycystic kidneys occur due to a variety of causes such as autosomal recessive or autosomal dominant polycystic kidney disease, cystic renal dysplasia and lower urinary tract obstruction. Correct diagnosis is essential for appropriate management. Meckel Gruber syndrome is also associated consistently with polycystic kidneys [1]. Awareness and diagnosis of this syndrome will enable counselling of parents regarding the 25% recurrence risk.

Case reports

The clinical features and necropsy findings are given in Table 1. All three fetuses were products of non-consanguineous marriages. Only the sibling of case 2 had limb deformities and a posterior encephalocoele, and died seven days after birth. A necropsy examination was not done. An ultrasound scan done at 17 weeks of gestation in case 2 showed an abnormal skull shape and dilated lateral ventricles.

All three fetuses had posterior encephalocoeles (Figure 1) and polycystic kidneys (Figure 2), and two had polydactyly. In all three the renal cysts involved the cortex and medulla. All three had hypoplastic lungs and Potter's facies (Figure 1) comprising a sloping forehead, beak-shaped nose and micrognathia. Case 1 had a right-sided aortic arch.

Discussion

Infants with Meckel Gruber syndrome die soon after or within a few days of birth or survive at the most a few weeks. Death is usually due to renal defects or nervous system abnormalities [2]. Other abnormalities described

Table 1. Clinical features and necropsy findings

Parity	Gestational age*	Sex	Birth weight (grams)	Age at death (hours)	CNS anomalies	Kidney anomalies	Limb defects	Liver anomalies
1 P ₁ C ₀	32	Male	2230	One	Posterior encephalocoele, holoprosencephaly	Polycystic kidneys	Polydactyly	None
2 P ₂ C ₀	34	Female	2000	Stillbirth	Posterior encephalocoele	Polycystic kidneys	None	None
3 P ₁ C ₀	34	Female	1800	<1	Posterior encephalocoele	Polycystic kidneys	Polydactyly	Fibrotic liver

*Expressed as period of amenorrhoea, CNS = Central Nervous System

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Figure 1. Case 2: Posterior encephalocele and Potter's facies.



Figure 2. Case 2: Cystic kidneys.

include fibrosis of liver, cerebellar hypoplasia, holoprosencephaly, and Arnold–Chiari and Dandy–Walker malformations [2, 3]. Although malformations of the cardiovascular system such as septal defects, pulmonary stenosis, patent ductus arteriosus and coarctation of the aorta have been reported previously [2], the occurrence of a right-sided aortic arch (case 1) has not been reported.

Although Meckel Gruber syndrome has been reported in consanguineous marriages [4] it is also known to occur in children from non-consanguineous marriages [5] suggesting that the single gene defect occurs more commonly in the latter population than mutant genes associated with other autosomal recessive disorders that are usually related with consanguineous marriages.

This condition can be suspected when there is an elevated alpha fetoprotein level together with a sonographic diagnosis of oligohydramnios associated with encephalocele, enlarged kidneys and polydactyly at 11 to 14 weeks [6, 7]. Prenatal diagnosis will enable the parents to consider termination of pregnancy. Even if abortion is illegal, unnecessary caesarian section can be avoided if the diagnosis is known. Postnatally, once the syndrome is recognised, parents should be offered the choice of no medical intervention for the infant. Neonates who die due to encephalocele and polydactyly should be subjected to necropsy examination to detect the presence of polycystic kidneys. In the ensuing pregnancies prenatal diagnosis must be attempted late in the first trimester [7], since second trimester diagnosis is made difficult by the development of oligohydramnios.

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