

Meckel-Gruber syndrome: report of an affected Papua New Guinean family

JOHN D. VINCE¹, MARY BAKI² AND PRITHWIS CHAKRAVARTI²

Faculty of Medicine, University of Papua New Guinea, Port Moresby and
Port Moresby General Hospital, Papua New Guinea

SUMMARY

We present the first case report of a Papua New Guinean family affected by Meckel-Gruber syndrome. Of six children, five of whom died, three definitely and two possibly were affected.

Case report

The proband, a male baby weighing 3 kg at birth, was born by spontaneous vaginal delivery at a rural health centre in the Bereina area of the Central Province in Papua New Guinea. His mother, in her sixth pregnancy, had booked at 28 weeks of gestation, and had a lowest antenatal haemoglobin of 6.3 g/dl. Major abnormalities were noted at birth and transfer of mother and baby to the Port Moresby General Hospital was arranged.

The baby was noted to have an occipital encephalocele and had an occipito-frontal circumference of 33 cm with a pronounced sloping forehead. The palate was felt to be rather high and arched, the eyes were noted to be small, and the penis also was noted to be small.

The mother had a striking and highly unfortunate obstetric history (Table 1), with only one of her previous 5 children surviving.

In the light of this history, with two previous children affected by occipital encephalocele and polydactyly, a diagnosis of Meckel-Gruber syndrome was made. Ultrasonography of the kidneys showed hypoechogenicity with no corticomedullary differentiation, consistent with bilateral renal dysplasia.

The child initially fed well, but became febrile on the third day of life. Since no surgical or major medical intervention was planned, the mother decided to take the baby home. Just before her intended discharge, however, the baby developed fits associated with hypoglycaemia and died at the age of 5 days.

Discussion

There seems little doubt that 3 of this family's 6 children had Meckel-Gruber syndrome. This condition, first described by Meckel in 1822 (1), again by Gruber 112 years later (2) and more recently characterized by Opitz and Howe (3) and by Salonen (4), is a multisystem disorder with autosomal recessive inheritance (5). The gene locus has recently been mapped to chromosome 17q21-q24 (6). Affected children most frequently exhibit the triad of occipital encephalocele, postaxial polydactyly and polycystic kidneys. Hypoplastic kidneys and microphthalmia are also common (7). There is a wide spectrum of phenotypic expression, even within the same family (8,9), and heterozygotes may also manifest mild phenotypic abnormalities such as polydactyly (10). Unfortunately, because the family was living in a rural village, we did not have access to the written records of the family's first 5 children although the fifth child had been admitted to the hospital. In the light

¹ Division of Child Health, Department of Clinical Sciences, Faculty of Medicine, University of Papua New Guinea, PO Box 5623, Boroko, NCD 111, Papua New Guinea

² Departments of Paediatrics and Radiology, Port Moresby General Hospital, Free Mail Bag, Boroko, NCD 111, Papua New Guinea

TABLE 1

DETAILS OF OFFSPRING IN THE AFFECTED FAMILY

Child	Outcome	Information
Female	Died at 2 days	? Neonatal infection
Female	Died at 1 week	? Neonatal infection
Female	Alive and well 5 years	
Male	Died at 1 hour	Encephalocele + other abnormalities including polydactyly
Male	Died at 4 months	Encephalocele + polydactyly
Male	Died at 5 days	Encephalocele + hypoplastic kidneys

of the known phenotypic variation it is, however, not unreasonable to suggest that the first two children, who died in the first week of life, may also have been affected.

Both parents were from the same village. Extensive discussion in their own language failed to reveal any consanguinity, though gene clustering within what was until relatively recent times a fairly isolated community is likely.

Early antenatal diagnosis with ultrasound is now available where such facilities exist (11). Whilst obstetric ultrasonography is available at Port Moresby General Hospital, it is, perhaps, unlikely that this rural family, from a strongly traditional Roman Catholic area, would wish to avail themselves of it. The concept of autosomal recessive inheritance is alien to most rural - and indeed to many urban - dwellers, for whom other traditional explanations relating to personal or family matters are far more comprehensible and relevant. Most likely, the still relatively young mother will become pregnant again and, hopefully, even if not next time, will at some stage successfully and safely deliver a normal child to expand her family.

We believe this to be the first documented Papua New Guinean family affected by Meckel-Gruber syndrome.

REFERENCES

- 1 **Meckel JR.** Beschreibung zweier durch sehr ähnliche Bildungsabweichung enstelter Geschwister. *Dtsch Arch Physiol* 1822;7:99.
- 2 **Gruber GB.** Beitrage zur Frage 'gekoppelter' missbildungen (Akrocephalosyndactilie und Dysencephalia splanchnocystica). *Beitr Pathol Anat* 1934;93:459.
- 3 **Opitz JM, Howe JJ.** The Meckel syndrome (dysencephalia splanchnocystica, the Gruber syndrome). *Birth Defects* 1969;5:167.
- 4 **Salonen R.** The Meckel syndrome: clinicopathological findings in 67 patients. *Am J Med Genet* 1984;18:671-689.
- 5 **Hsia YE, Bratu M, Herbordt A.** Genetics of the Meckel syndrome (dysencephalia splanchnocystica). *Pediatrics* 1971;48:237-247.
- 6 **Paavola P, Salonen R, Weissenbach J, Peltonen L.** The locus for Meckel syndrome with multiple congenital anomalies maps to chromosome 17q21-q24. *Nat Genet* 1995;11:213-215.
- 7 **Smith DW.** Meckel-Gruber syndrome (dysencephalia splanchnocystica). In: Jones KL, ed. *Smith's Recognisable Patterns of Human Malformation*, 5th edition. Philadelphia: WB Saunders, 1997:184-185.
- 8 **Wright C, Healicon R, English C, Burn J.** Meckel syndrome: what are the minimum diagnostic criteria? *J Med Genet* 1994;31:482-485.
- 9 **Summers MC, Donnfeld AE.** Dandy-Walker malformation in the Meckel syndrome. *Am J Med Genet* 1995;55:57-61.
- 10 **Nelson J, Nevin NC, Hanna EJ.** Polydactyly in a carrier of the gene for the Meckel syndrome. *Am J Med Genet* 1994;53:207-209.
- 11 **Sepulveda W, Sebire NJ, Souka A, Snijders RJ, Nicolaidis KH.** Diagnosis of the Meckel-Gruber syndrome at eleven to fourteen weeks' gestation. *Am J Obstet Gynecol* 1997;176:316-319.