

## Meckel-Gruber syndrome

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**Abstract** Meckel-Gruber syndrome is a congenital disorder characterized by occipital encephalocele, polydactyly and polycystic kidneys. This rare syndrome has been reported in

the literature as incompatible with life. We present the case of a newborn afflicted with the clinical triad of Meckel-Gruber syndrome. Appropriate treatment instituted in our case led to a good early outcome.

**Key words** Meckel-Gruber syndrome · Encephalocele · Hydrocephaly

### Introduction

Meckel-Gruber syndrome is an autosomal recessively transmitted [7, 11] fatal disorder probably first delineated by Meckel in 1882. Recently, Paavola et al. reported the locus, mapped to chromosome 17q21-q24 [9]. Most babies affected are either medically aborted or stillborn. The rest of the patients die shortly after birth [4, 6, 11].

Though the classic triad consists of encephalocele, polydactyly and polycystic kidneys, in 52% of cases the first two signs may be sufficient for the diagnosis of Meckel-Gruber syndrome [10]. Prenatal diagnosis of this syndrome with the aid of ultrasonography (US) is of great importance. Oligohydramnios and severe renal involvement may be evaluated by US as soon as 14 weeks, but it may not be reliably excluded until 20 weeks into the pregnancy. A high risk (almost 25%) of recurrence in subsequent pregnancies [3] is an important point for consideration.

### Case report

The patient was the first child of a healthy 26-year-old woman and a healthy 29-year-old man who had a first-degree consanguinity. No abnormality had been detected by US examination during pregnancy. A spontaneous vaginal delivery at term revealed a 3400-g malformed infant. He had a 3-cm occipital encephalocele mass with cerebrospinal fluid oozing over its surface (Fig. 1). He had an atypical facies with short palpebral fissures, left epicanthal fold, long filtrum, short nose and low-set ears (Fig. 2). He had a large fontanelle and open sutures, a head circumference of 36 cm, polydactyly of both upper extremities and polysyndactyly of the lower right extremity (Figs. 3, 4), bilateral inguinal hernias, global diminution of neonatal reflexes and hypotonicity in all extremities. No preliminary radiological work-up was done owing to the high risk of infection and the apnoeic respiration of the infant. The sac was excised with no peroperative complication. Histological examination revealed encephalocele. After the operation, he was taken to the neonatal intensive care unit for the following 7 days; during that time the patient had occasional apnoea attacks, with slight drops in O<sub>2</sub> saturation, cyanosis and bradycardia, especially in the prone position. Owing to the poor suction reflex, he was initially fed through a nasogastric tube. No other important medical



**Fig. 1** This photograph showing the encephalocele mass was taken in the first hours of life

problems or infections intervened. Soon he started to feed orally and gained weight; his motor activity also improved. Renal US and IVP demonstrated diffuse enlargement of both kidneys. Bilateral polycystic kidney disease (Fig. 5) was also noted. Renal function tests were found to be normal, and no hypertension was noted. Echocardiography revealed no pathology. The ventricles were dilated and the cerebellum was seen on cranial US to be hypoplastic. Cranial MRI was performed 30 days after birth, revealing ventricular dilatation, cerebellar hypoplasia, enormously

**Fig. 2** The facies of the patient in the third month of life

**Fig. 3** Polydactyly in our patient

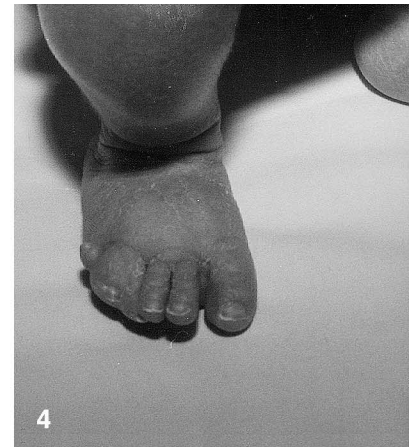
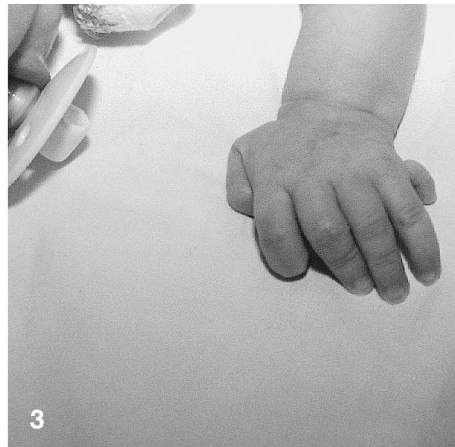
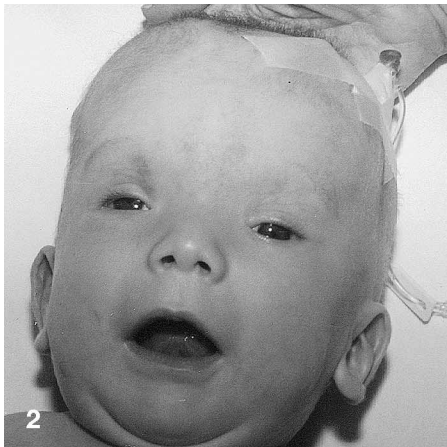
**Fig. 4** Syndactyly in our patient

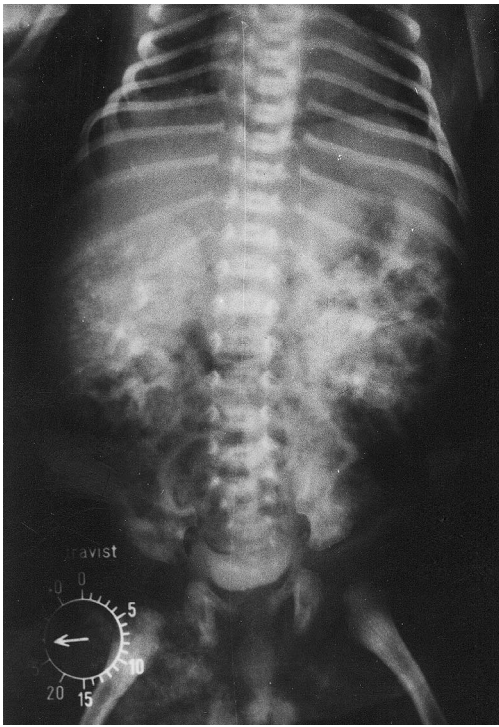
widened preoptine cisterna and posterior displacement of the brain stem structures (Fig. 6). Since the ventricular system was dilated and the fontanel were bulging and tight, a ventriculo-peritoneal shunt system was applied. Serial examinations following the second operation revealed normal-appearing fontanel and no important neurological deficit other than ocular divergence and mild facial paresis. Chromosomal analysis was found to be normal with 46, XY karyotype. At the time of the 7-month follow-up, it was learned from the family that the patient had died at home. No autopsy was allowed and the cause of death could not be explained.

## Discussion

The Meckel-Gruber syndrome has so far been reported as an autopsy finding in stillborn infants or abortuses. After Meckel introduced this syndrome to the medical literature in 1882, affected siblings were noted by Brucner and Calmann in 1893 and DeLange in 1930. In Turkey, the first prenatally diagnosed case was reported in 1992 [2]. Here we report a case of Meckel-Gruber syndrome in an infant who lived for 7 months.

The patients affected by this syndrome have facies characterized by microcephaly, microphthalmia and facial clefts. The central nervous system is affected to a significant extent by holoprosencephaly, internal hydrocephalus, occipital encephalocele (80%) or meningoencephalocele. Cysts of the kidney and, less often, of the liver or pancreas have been noted. In 75% of cases postaxial polydactyly is present. Some cases involve genital anomalies, such as hypoplastic penis, undescended testis, septate vagina and bicornuate uterus. Congenital heart anomalies are found in 5% of cases [4, 5, 6, 11]. Here we analysed a case of a newborn afflicted with polydactyly, syndactyly, atypical facies, renal cystic disorder, occipital encephalocele/exencephalocele and cerebellar hypoplasia. These clinical findings were consistent with the Meckel-Gruber syndrome. No genital or congenital heart anomaly

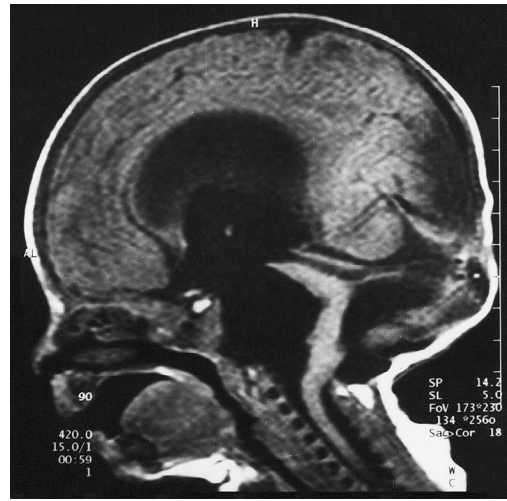




**Fig. 5** IVP of the patient revealed pelvicalyceal ectasy

lies were detected. Differential diagnosis of this syndrome should include trisomy 13 and Smith-Lemli-Opitz syndrome [11]. The normal chromosomal number and the absence of genital anomalies in our case exclude these diagnoses.

An autopsy study [1] of seven cases of this syndrome revealed a triad of central nervous system abnormalities: prosencephalic dysgenesis, occipital exencephalocele and rhombic roof dysgenesis. In this report and some others, occipital encephalocele was defined as a displacement of rhombic roof elements, including caudal III ventricle, cerebellar vermis and IV ventricle through an enlarged posterior fontanel rather than through an occipital cranium bifidum. The radiological findings of our case showed correlation with this definition (Fig. 6). This type of malformation is more precisely labelled an exencephalocele. Prenatal US examination around 14–16 weeks of gestational age is of the utmost importance for prompt



**Fig. 6** MRI of the patient before the placement of the VP shunt was typical of this syndrome

diagnosis of this syndrome. A finding of concurrent marked oligohydramnios and bilateral severe renal anomalies should initiate a search for the Meckel-Gruber syndrome. This allows medical abortion and avoids the birth of a malformed infant. At around 16 weeks of gestation the maternal serum also contains high levels of alpha fetoprotein in these pregnancies. A recent study [8] reported prenatal US findings of six fetuses with the syndrome. All demonstrated evidence of renal cystic dysplasia, oligohydramnios and occipital encephalocele. Our patient was allowed to be born owing to an inaccurate prenatal US examination. Physicians caring for obstetric patients should be alert to the aforementioned findings. Some authors tend to classify the hydrocephalus associated with congenital malformations as nontreatable disorders [7]. We operated on the patient twice. The first operation was performed in the very first hours of life, and the encephalocele sac was excised. In the second operation a ventricular shunt device was placed, and the infant was then hospitalized in a neonatal intensive care unit. The patient did well and showed clinical and neurological improvement. This exceptional outcome may be due in part to the early institution of surgical repair and intensive care facilities and to the relatively small size of the encephalocele mass.

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