Meckel-Gruber syndrome associated with gastrointestinal tractus anomaly

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SUMMARY: Törel Ergür A, Taş F, Yıldız E, Kılıç F, Sezgin İ. Meckel-Gruber syndrome associated with gastrointestinal tractus anomaly. Turk J Pediatr 2004; 46: 388-392.

Meckel-Gruber syndrome (MGS) is rare autosomal recessive disorder characterized by occipital encephalocele, postaxial polydactyly and polycystic kidneys. A one – day-old girl was admitted to our clinic with occipital encephalocele, polydactyly, ulnar deviation of left hand and failure to thrive. Patient's parents were first-degree relatives. It was learned that the patient's two sisters had died from similar anomalies. In our case, prenatal sonographic examination revealed oligohydramnios and hydrocephaly in the 33rd week of gestation. At birth her weight was 2200 g. Both physical and radiological examinations diagnosed MGS. Cranial computed tomography (CT) showed agenesis of cerebellar vermis and corpus callosum, and cystic dilatation of the 4th ventricle and lateral ventricles. The case died due to severe respiratory distress in the Intensive Care Unit on day 38. In the postmortem examination, longitudinally located intestine-like stomach was determined without a fundus. In conclusion, intestinal malrotation and hepatic portal fibrosis have been reported in MGS in the literature. In this case, a longitudinally located intestine-like stomach in MGS is reported for the first time. No such association to our knowledge has been previously reported.

Key words: Meckel-Gruber syndrome, corpus callosum agenesis, Dandy-Walker malformation, gastrointestinal tract anomaly.

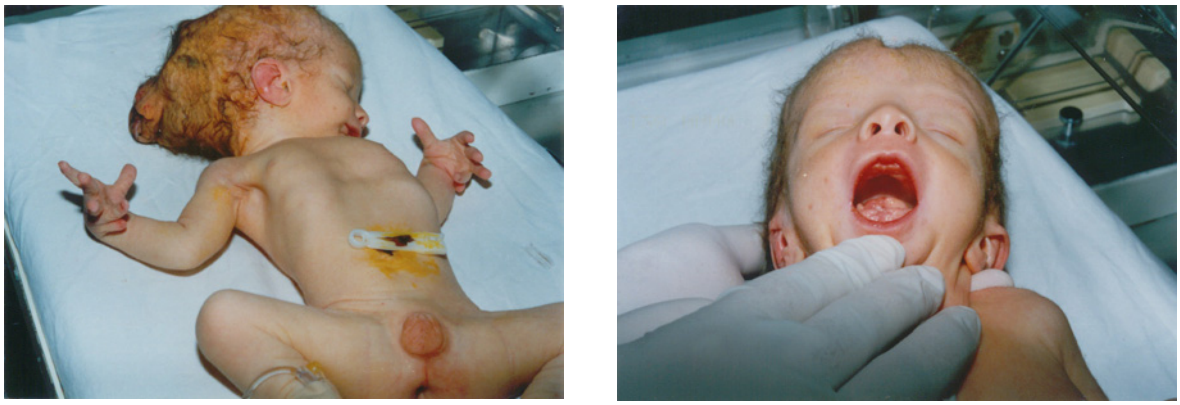
Meckel-Gruber syndrome (MGS) was first described by Meckel in 1822 and then in 1934 by Gruber, who gave the complex name "dysencephalia splanchnocystica"[1]. The classical triad is occipital encephalocele, polydactyly and cystic kidneys[2]. Antenatal ultrasonic examination can establish the final diagnosis by identifying at least two of the major features described previously[3]. Here, we report a case of MGS with gastrointestinal tract anomaly that previously has not been reported. The clinical, radiological and postmortem findings and related literature are reviewed.

Case Report

A one-day-old case was admitted to our hospital with failure to thrive and multiple congenital abnormalities. Patient's parents were first-degree relatives who were both healthy. Patient was born by cesarian section at term (38 weeks). At the 33rd week of gestation, ultrasonographic examination revealed oligohydramnios and hydrocephaly of fetus. At birth her weight was 2200 g and she had an Apgar score of eight at five minutes. It was learned that the patient's one month old sister had died with hydrocephaly and encephalocele, but not polydactyly. The patient's other sister, who had similar anomalies (hydrocephaly, encephalocele), had also died in the newborn period.

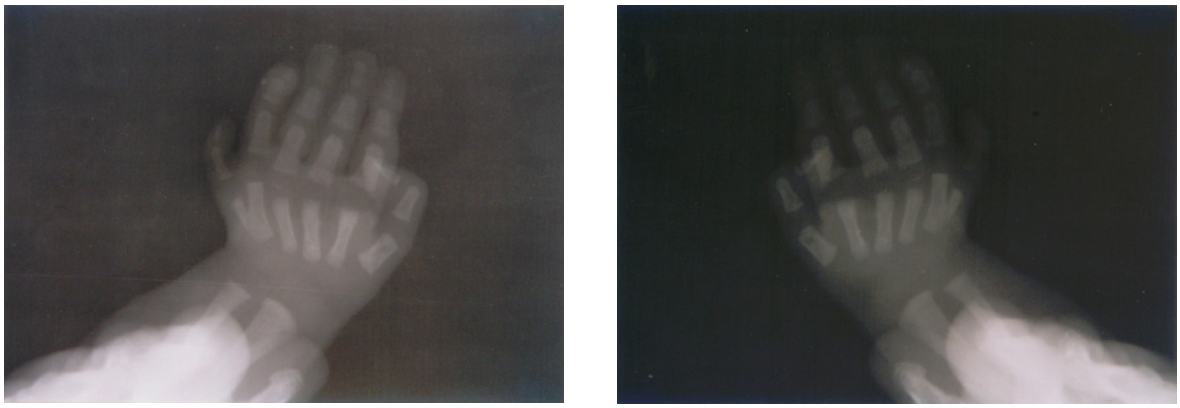
Physical examination revealed a small, hypoactive neonate with an occipital encephalocele and polydactyly. The patient had in addition micrognathia, hypertelorism, coloboma of iris, lobulation of tongue, bilateral ulnar deviation of hands, and ambiguous genitalia (Fig. 1a, 1b). On radiological examination, hand X-ray demonstrated bilateral ulnar deviation and ulnar polydactyly with duplication of 5th metacarp (Fig. 2a, 2b); foot X-ray demonstrated bilateral polydactyly and duplication of the left 5th metatars (Fig. 3a, 3b). Axial cranial computed tomography (CT) showed cystic dilatation of the 4th ventricle. The cyst was completely filling the enlarged posterior fossa, and cerebellar hypoplasia was present along with the vermis

agenesis. Additionally lateral ventricles were severely dilated and corpus callosum agenesis was observed. Cranial bone deformity was determined (Fig. 4a, 4b). In abdominal tomography, a posterior arc defect in lumbar and sacral vertebrae was detected (Fig. 5).



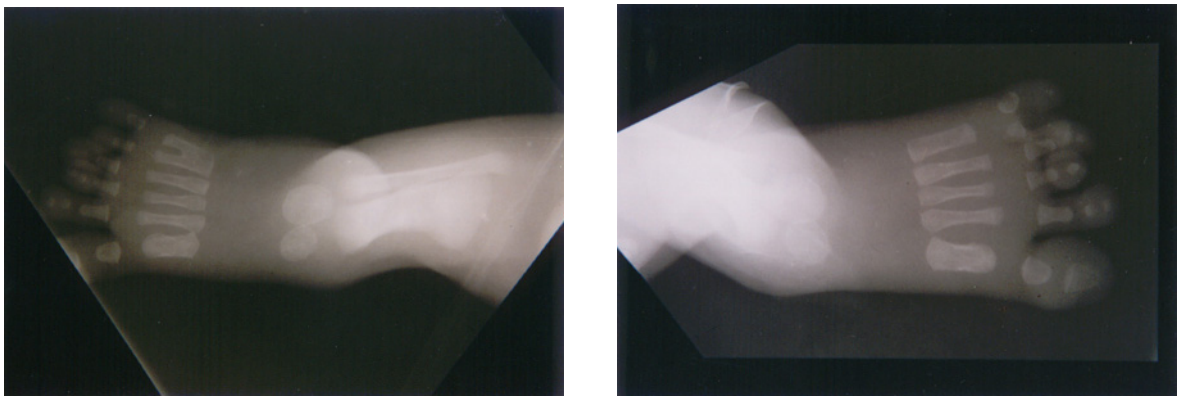
(a) (b)

Fig. 1. Pathologic findings: a) General (occipital encephalocele, micrognathia, bilateral ulnar deviation and ambiguous genitalia). b) Facial features of case (micrognathia, hypertelorism and lobulation of tongue).



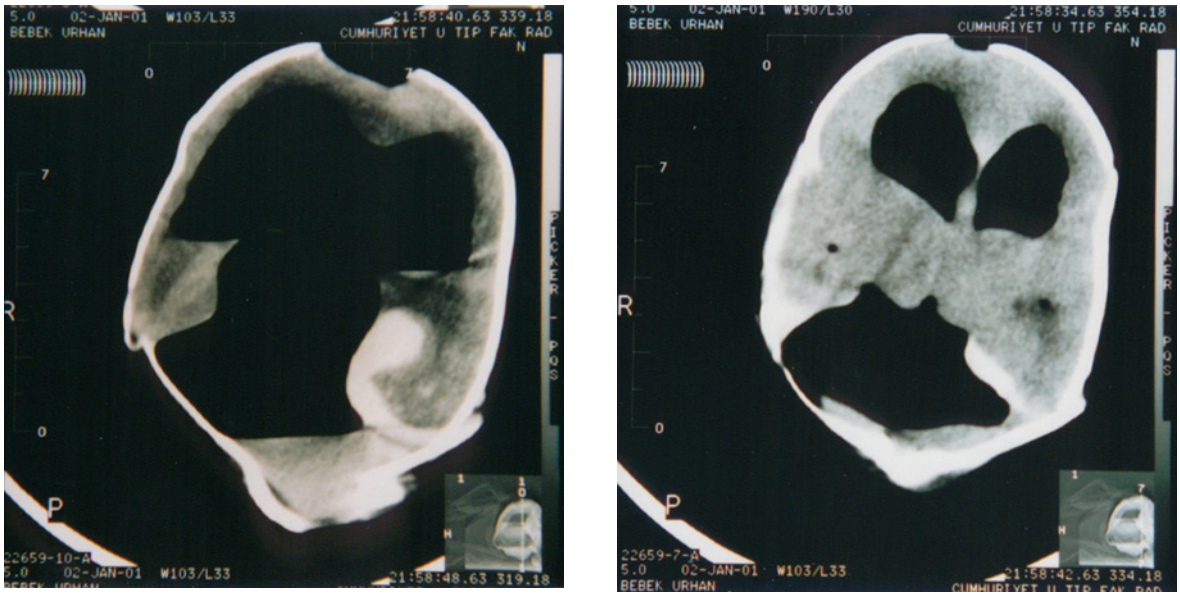
(a) (b)

Fig. 2. Hand X-ray: a) (Left), b) (Right); bilateral ulnar deviation, polydactyly and duplication of 5th metacarp.



(a) (b)

Fig. 3. Foot X-ray: a) (Left), b) (Right); Bilateral polydactyly and duplication of the left 5th metatars.



(a) (b)

Fig. 4. Axial cranial CT: a), b); Occipital encephalocele, cystic dilatation of the 4th ventricle, cerebellar hypoplasia, cerebellar vermis agenesis, hydrocephaly.

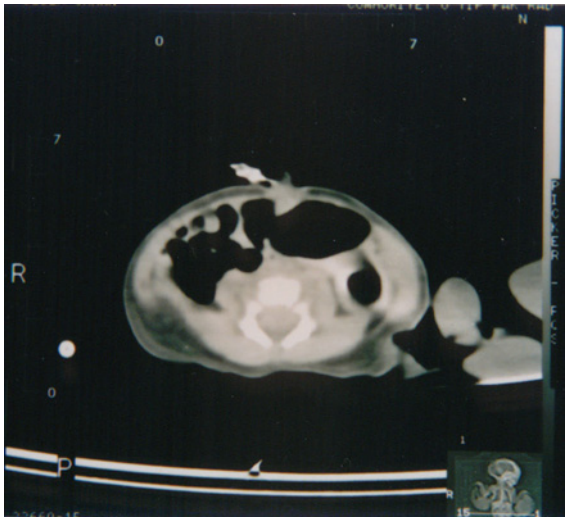


Fig. 5. Abdominal CT: Posterior arc defect in lumbar vertebrae.

Patient's chromosome analysis was performed on cultures of peripheral lymphocytes and was determined as 46XX.

We began intravenous fluid and electrolyte and antibiotic treatment. Cranial operation was delayed due to severe respiratory distress. The case died in the Intensive Care Unit at the age of 38 days. At necropsy the infant weighted 2200 g with crown-rump length of 38 cm (90% ↑) and crown-hell length of 50 cm (50%); multiple malformations were noted both externally and internally.

Postmortem examination revealed micrognathia, lobulation of tongue, short neck, coloboma of iris, hypoplasia of optic nerve, hypertelorism, and a flattened nose. The thorax was hypoplastic. Macroscopically, the stomach resembled the duodenum (intestine-like appearance), and there

was no fundus. Longitudinally localized parietal cells of stomach were shown histopathologically (Fig. 6a, 6b). The left kidney was heavier than the right kidney and contained multiple cysts. Immature scarce glomeruli in the cortices and dilated collecting tubules in the medulla were observed on microscopic examination. The hands and feet had postaxial polydactyly.

The gross appearance of the brain demonstrated hydrocephaly, and cerebellar and cerebral hypoplasia with Dandy-Walker malformation. Cerebellar vermis and corpus callosum agenesis were present (Fig. 7). Olfactory bulbs were absent.

Table I. Pathological Findings of the Patient

Findings
– Occipital encephalocele
– Cerebral/cerebellar hypoplasia
– Cerebellar vermis agenesis
– Hydrocephalus
– Dandy-Walker anomaly
– Corpus callosum agenesis
– Hypoplasia of optic nerve
– Hypertelorism
– Micrognathia
– Lobulation of tongue
– Coloboma of iris
– Short neck
– Postaxial polydactyly (hand and feet)
– Ambigiuous genitalia
– Multicystic kidney (left)
– Intestine-like longitudinally located stomach

Discussion

Meckel-Gruber syndrome is an autosomal recessive disorder characterized by occipital encephalocele, polydactyly and polycystic kidneys[4]. The diagnostic criteria for MGS require that at least two of the following three

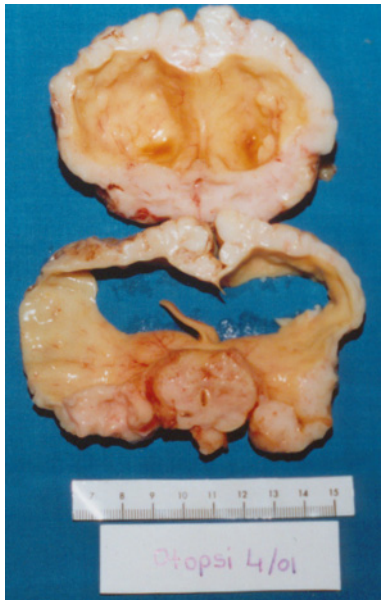
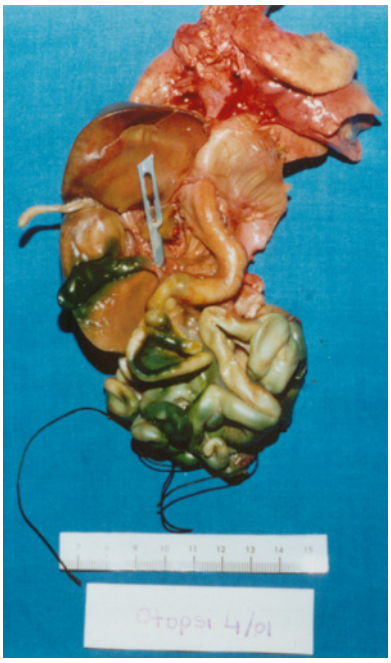
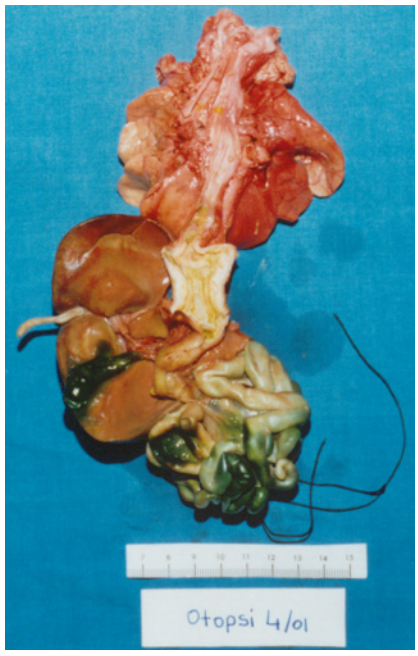


Fig. 7. The gross appearance: cerebellar and cerebral hypoplasia, cerebellar vermis and corpus callosum agenesis and lateral ventricle dilatation.

(a)





(b)

Fig. 6. The gross appearance: longitudinally located stomach.

conditions be present: occipital encephalocele, polydactyly, and cystic kidneys[5]. Occipital encephalocele and postaxial polydactyly were present in our case. There were multiple cysts in left kidney on necropsy.

In MGS, in addition, many of the other well known accompanying abnormalities were present. From rare anomalies, Malguria et al.[6] described MGS associated with short-limbed dwarfism. De Chalain et al.[7] described MGS associated with vertebral fusion. Several gastrointestinal anomalies have also been described, such as intestinal malrotation and hepatic portal fibrosis. However, the longitudinally localized intestine-like stomach demonstrated in our patient has not been previously reported.

In MGS, antenatal ultrasonographic examination can establish the correct diagnosis by identifying at least two of the major features described[3]. In our case at the 33rd gestational week, hydrocephaly was demonstrated, but the mother did not accept therapeutic abortion. When a mother has suffered previously from a pregnancy with MGS, the recurrence risk in 25%. With the present technology, a targeted ultrasound in the late embryonic or early fetal stages of pregnancy has the potential to diagnose this syndrome[8]. Balcı et al.[9] reported very early diagnosis (22 weeks) of MGS in four affected consecutive siblings[9].

The presence of elevated amniotic fluid α-fetoprotein (AFP) has permitted the diagnosis of MGS in the second trimester on several occasions. Elevated AFP levels are associated with other abnormalities including neural tube defects[3]. Our case's parent did not accept amniocentesis.

Diagnosis of Dandy-Walker malformation in MGS has been reported more frequently in recent years. In Turkey, the first case of MGS associated with Dandy-Walker malformation which was diagnosed in utero was reported in 1992[10]. Düzcan et al.[11] showed Dandy-Walker malformation in a stillborn MGS case. Yapar et al. also reported two cases of MGS with Dandy-Walker malformation diagnosed sonographically during the prenatal period[12]. The occurrence of a Dandy-Walker malformation in MGS confirms a disturbance in rhombencephalon development, and it should be included among the central nervous anomalies representative of the syndrome.

In conclusion, MGS is a rare autosomal recessive disorder with major characteristic features, and is best diagnosed prenatally by ultrasonography early in the second trimester. A number of additional malformations are commonly associated with varying degrees of frequency. We report a newborn case with MGS associated with longitudinally located intestinal-like stomach.

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