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MECKEL GRUBER SYNDROME: A CASE DIAGNOSED IN UTERO*

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SUMMARY: Balcı S, Önol B, Erçal MD, Beksaç S, Erzen C, Akhan O. (Departments of Pediatrics, Pathology, Obstetrics and Gynecology, and Radiology, Hacettepe University Faculty of Medicine, Ankara, Turkey). Meckel Gruber syndrome: a case diagnosed in utero. Turk J Pediatr 34: 179-185, 1992.

A case of Meckel Gruber syndrome is presented, diagnosed prenatally from the medical history of the mother which revealed a previous malformed stillborn with anencephaly, meningomyelocele, polydactyly and ambiguous genitalia. This was the first prenatally diagnosed case ever reported in Turkey. The clinical, computed tomography and postmortem findings and the related literature are reviewed. *Key words: Meckel Gruber syndrome, Dandy-Walker malformation, prenatal diagnosis.*

Meckel Gruber syndrome is a rare autosomal recessive disorder characterized by multiple central nervous system anomalies and gastrointestinal, genitourinary and skeletal system malformations. Most of the cases are either stillborn or die soon after birth. Genetic counselling is important for parents considering a future pregnancy who have had previous stillbirths with similar malformations[1,2].

We recently diagnosed a case of Meckel Gruber syndrome associated with Dandy-Walker malformation in utero. The mother of the infant had had a previous stillbirth with similar anomalies.

Case Report

A 28-year-old mother was admitted to the Obstetrics and Gynecology Clinic of the Hacettepe University Faculty of Medicine in the 33rd week of gestation for ultrasonographic examination which demonstrated a hydrocephalic fetus with an enlarged abdomen and oligohydramnios. The medical history revealed a previous stillbirth in the 38th week of gestation that had ambiguous genitalia, polydactly,

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anencephaly and meningomyelocele. This pregnancy was followed by the birth of three healthy children. The parents were unrelated. The alpha-fetoprotein level (AFP) was 55 ng/dl, which was considered to be within normal limits for this gestational age.

Meckel Gruber syndrome was suspected prenatally because of the past history of the mother and the ultrasonographic determinations. The pregnancy was terminated by the induction of labor, during which the malformed fetus died. The fetus was examined using ultrasonography and computed tomography (CT) prior to postmortem examination. Postmortem examination revealed a fetus with short, deformed ribs and an enlarged abdomen (Fig. 1). Computed tomography showed a dilated foramen magnum and an absence of the fourth ventricle. There was a cystic mass behind the location of the fourth ventricle having cerebrospinal fluid density which elevated the tentorium and displaced the mesencephalum anteriorly. These findings mimicked a Dandy-Walker malformation (Fig. 2). The cervical and thoracal vertebral canals were also dilated.

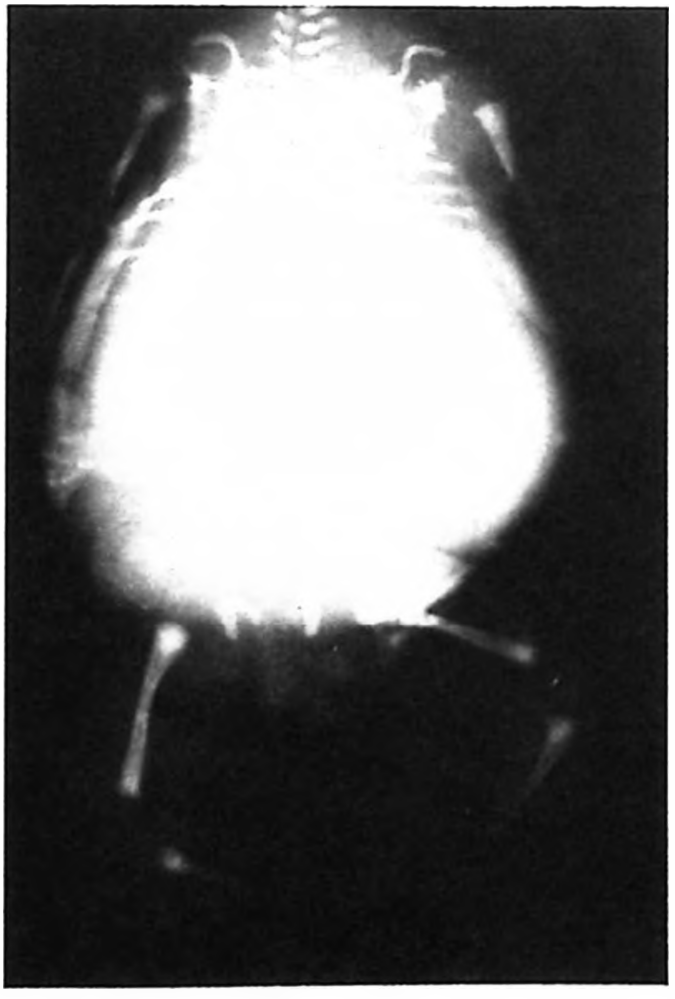

Fig. 1: Postmortem X-ray demonstrates deformed, short ribs on the right side of the fetus.

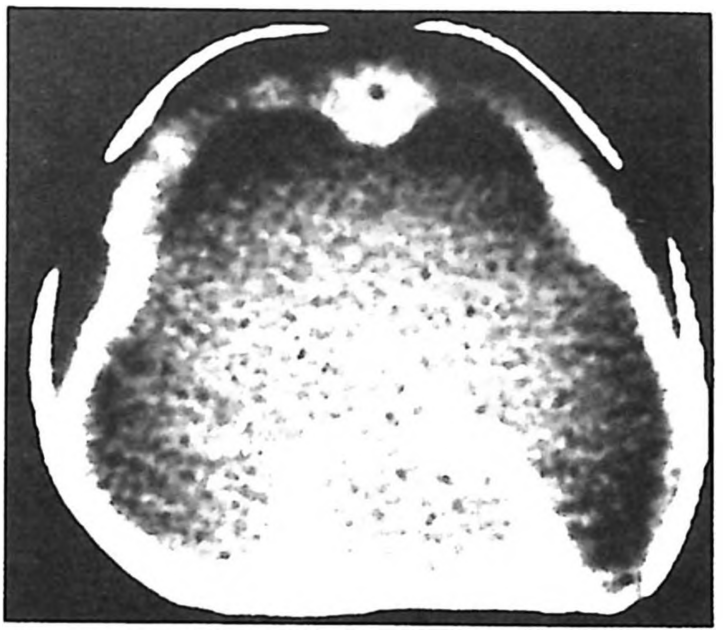

Fig. 2: CT reveals dilation of the lateral ventricles, hydrocephaly and an arachnoidal cyst in the posterior fossa.

Abdominal CT demonstrated hepatomegaly and bilateral polycystic kidneys with minimal ascites.

Postmortem examination revealed a fetus with a weight of 3400 g, length 51 cm, head circumference 39 cm, chest circumference 30 cm and abdominal circumference 41 cm. It had a macrocranium with edematous skull skin, a low set right auricule and the left side of the mandible was hypoplastic with micrognathia. It had a cleft palate and tongue, hypotelorism, a flattened nose and a fold rising up from the inner canthus sweeping downward and laterally below the eyes. The thorax was hypoplastic, the abdomen was enlarged with renal masses and hepatomegaly was present. The hands and feet had postaxial polydactyly and the left hand also had clinodactyly. Bilateral simian lines were also present (Fig. 3).

The gross appearance of the brain demonstrated flattened gyri, cerebellar hypoplasia and a cystic posterior fossa. Olfactory bulbs were absent (Fig. 4). Coronal sectioning showed an extreme dilation of the lateral and third ventricles, with the association of dilation of the aqueduct of Sylvius and agenesis of the corpus callosum. There was also cystic dilation of the fourth ventricle. The dorsal part of this particular cyst was covered only by a leptomeningeal covering which was about four cm in diameter in toto. Because of the compression of the cyst, the medulla was so distorted that it resembled a Dandy-Walker malformation in shape.

The right kidney weighed 300 g and measured 13 × 7 × 5 cm. On cross section, it contained several cysts, the most prominent one being 0.5 cm in diameter. The

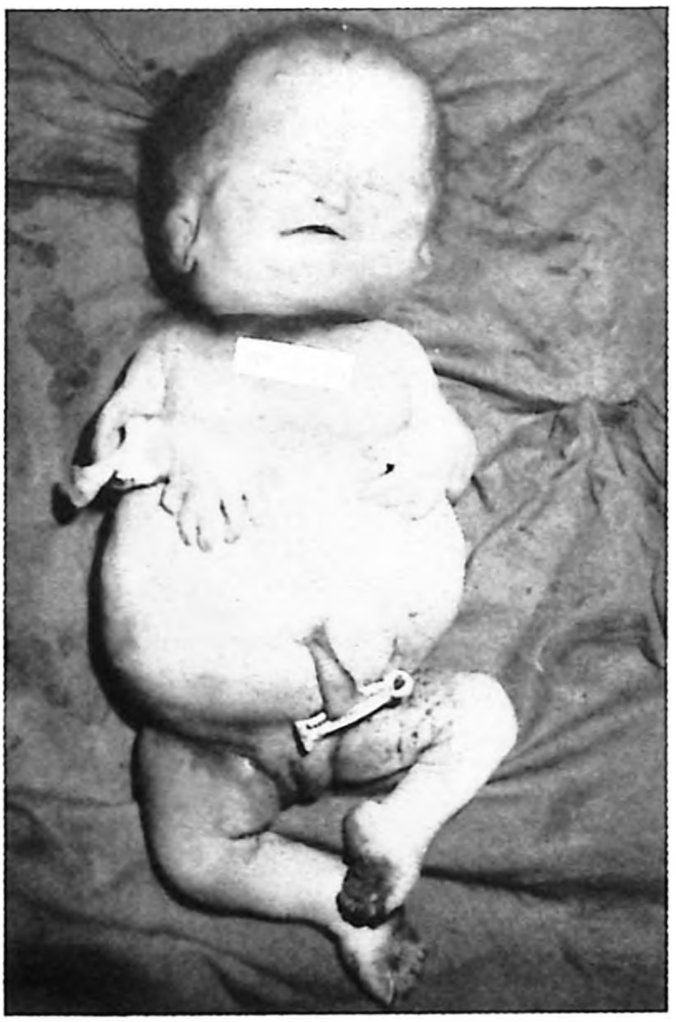

Fig. 3: Note large head, low set ears, inner canthal folds, micrognathia, polydactyly of the hands and feet, and a large abdomen.

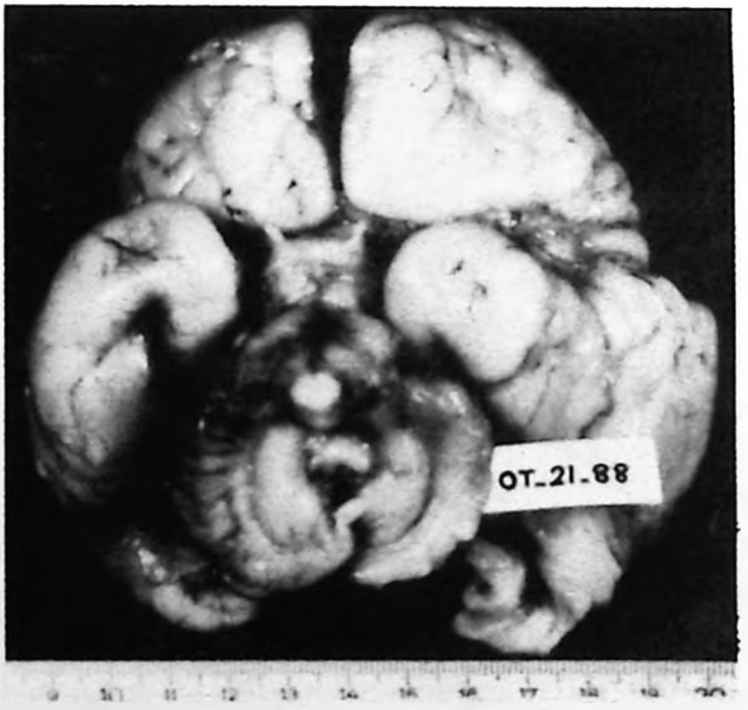

Fig. 4: Postmortem examination of the brain reveals the absence of olfactory bulbs; cerebellar hypoplasia, vermis agenesis and a dilated cystic fourth ventricle were noted.

medulla was so distorted that it resembled a Dandy-Walker malformation in shape.

The right kidney weighed 300 g and measured 13 × 7 × 5 cm. On cross section, it contained several cysts, the most prominent one being 0.5 cm in diameter. The left kidney weighed 270 g and also contained several cysts, the most prominent one being 0.6 cm in diameter (Fig. 5). Microscopically, tubules with very scanty glomeruli were detected in the cortices of both kidneys. The cystic collecting tubules of varying sizes surrounded by dense fibrous stroma were observed in the medulla. The ureters and bladder were normal.

Chromosome analysis was performed on cultures of peripheral lymphocytes and it was determined that the fetus was a normal female, 46 XX.

Fig. 5: Note hepatomegaly and enlarged cystic kidneys.

Discussion

This syndrome, first described by Meckel in 1822, is characterized by the presence of polycystic kidneys, polydactyly and occipital encephalocele. Gruber in 1934 referred to it as "dysencephalica splancho cystica" because of the additional central nervous system, somatic and splanchnic malformations[1-3]. The mode of transmission of this rare syndrome is an autosomal recessive gene[3]. The affected fetus is either stillborn or dies soon after birth. A careful examination should be made of every affected fetus keeping in mind this autosomal recessive condition so as to advise parents regarding future pregnancies. This syndrome is considered to be rare, and is more prevalent among Jews (1 in 50,000). However it has also been recorded in the Turkish medical literature[4-6].

The diagnostic criteria for Meckel Gruber syndrome requires that at least two of the three following conditions be present: occipital encephalocele, polydactyly, cystic kidneys in addition to a normal chromosome constitution. Fifty-seven percent of patients have all three major abnormalities[2].

Polycystic dysplasia is the most common and constant entity in Meckel Gruber syndrome[7]. Cystic changes in the renal parenchyma can be seen in all cases. Some patients only have microscopic cysts while others have huge polycystic kidneys. Histologically, the cysts are variably of the proximal and distal tubules or in the medulla. Ultrasonographic examination is a noninvasive method for prenatal detection of kidney anomalies[8].

The major CNS anomalies are occipital encephalocele and microcephaly. Encephalocele exists in four out of five cases. Various degrees of hydrocephaly and arrhinencephaly, and the absence of olfactory bulbs and optic nerves may accompany the CNS features. Cerebellar hypoplasia, hydrocephaly with Dandy-Walker malformation and agenesis of bulbus olfactorius were the CNS malformations observed in the patients we studied. Three cases of hydrocephaly associated with Meckel Gruber syndrome have been reported by Simopoulos[9], and two cases by Walbaum[10]. After a search of the literature, we were unable to find a report of a case that had CNS anomalies similar to our patient.

This syndrome is being increasingly recognized prenatally in the mid-second trimester because of an increase in amniotic fluid and maternal serum AFP levels[11,12]. The maternal AFP was normal because in the presented case there was no open neural tube defect.

As far as we know, this is the first case of Meckel Gruber syndrome associated with Dandy-Walker malformation (hydrocephalus, cyst of the posterior fossa and cerebellar hypoplasia) diagnosed in utero and published in Turkey.

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