First-Trimester Diagnosis of Recurrent Meckel-Gruber Syndrome

Emel Ebru ÖZÇİMEN[1], Ali Sami GÜRBÜZ[2], Necati ÖZÇİMEN[3]

Konya, Turkey

ABSTRACT:

Meckel - Gruber syndrome (MGS) is a lethal autosomal recessive disorder characterized by occipital meningoencephalocele, postaxial polydactyly, and cystic dysplastic kidneys. Here, we present a case in which recurrent MGS was diagnosed in the first trimester.

Keywords: Meckel-Gruber syndrome, Polydactyly, Meningoencephalocele

Gynecol Obstet Reprod Med 2016;22:47-48

Introduction

Meckel-Gruber syndrome (MGS) is a lethal and rare autosomal recessive inherited disorder. It was first described by Meckel in 1822 and later by Gruber in 1934.[1] The characteristic MGS triad includes occipital meningoencephalocele, postaxial polydactyly, and cystic dysplastic kidneys.[1] Antenatal ultrasonographic examination can establish the correct diagnosis during the second or late first trimester. Here, we present a case in which MGS was diagnosed in the first trimester, and we discuss our findings with respect to those reported in the literature.

Case Report

A 22-year-old woman gravida 2, para 1 was seen at our clinic for a routine obstetric examination. The gestational age of the fetus, based on the mother's last menstrual period, was 9 weeks. There was no consanguinity between the parents, but according to the woman's medical history, the fetus in a previous pregnancy was malformed, and the infant was diagnosed postnatally with MGS.

An ultrasound study performed during the second pregnancy revealed a single, living fetus with crown–rump length (CRL) of 25 mm (9 weeks). An 8.5 × 6.5-mm cystic area was observed in the fetal calvarium (Figure 1). During the 11th week of gestation, fetal bradycardia and increasing nuchal translucency (Figure 2) were detected, and in the 12th week, occipital encephalocele and bilateral enlargement of the kidneys were observed. Chorionic villous sampling was not accepted by the family. As the results of the examination suggested MGS, termination of the pregnancy was offered, but not accepted, by the family at that time.

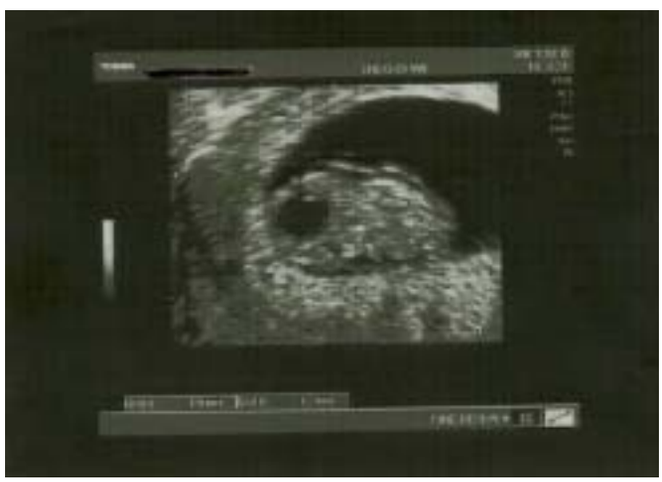

Figure 1: Ultrasound view of the cystic area in the fetal calvarium at 9 weeks of gestation

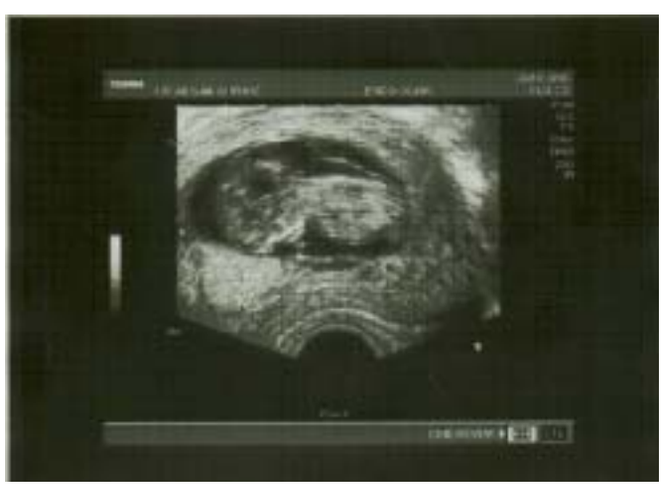

Figure 2: Ultrasound view of the increased nuchal translucency in the 11th week of gestation

[1] Baskent University Hospital Obstetrics and Gynecology Department, Perinatology Unit, Konya, [2]Novafertil IVF Center, Konya, [3] Medicana IVF Center, Konya

Address of Correspondence: *Emel Ebru Özçimen*
Başkent University Hospital Obstetrics and Gynecology Department Konya, Turkey
eparlakyigit@yahoo.com

Submitted for Publication: *17. 10. 2014*
Accepted for Publication: *03. 11. 2014*

In the 16th week of gestation, the amniotic fluid level decreased. Genetic amniocentesis showed a normal female karyotype, 46XX. On ultrasound, bilateral polycystic kidneys, encephalocele, and short lower limbs were seen. The pregnancy was terminated by vaginal misoprostol.

Autopsy findings

The fetus weighed 160 g, and the CRL was 15 cm. Macroscopic examination revealed dolicocephaly, short lower extremities, occipital encephalocele, polydactyly of both the lower and upper extremities, and polycystic kidneys. On microscopic examination, fibrosis in the stroma of the lungs and liver, mild edema in the brain, hydrocephalous, and polycystic changes in the kidneys were observed. The umbilical cord had three vessels. The macroscopic and microscopic abnormalities supported the diagnosis of MGS.

Discussion

MGS is a rare and lethal ciliopathic genetic disorder characterized by renal cystic dysplasia, central nervous system malformations (occipital encephalocele), polydactyly (postaxial), hepatic developmental defects, and pulmonary hypoplasia due to oligohydramnios.[2] MGS has been estimated to occur in 1 of 12,000–14,0000 births.[3] It was first described in the 19th century, with the various components of the syndrome increasingly recognized over time. The syndrome has an autosomal recessive pattern of transmission, and seven genes, all associated with ciliary functions, have been implicated in its etiology.

The fetus described in this study had encephalocele, polydactyly, hydrocephalus, and polycystic kidneys. The finding of abnormally short lower extremities, as occurred in this case, is rare and was first reported by Malguria.[2]

In addition to MGS, the differential diagnosis should include trisomy 13, Zellweger syndrome, Agostino syndrome, and Jeune syndrome.[4] The diagnosis of MGS is based on the detection of oligohydramnios and the morphological features seen on ultrasound in a fetus with a normal karyotype. Ultrasonography performed at the end of the first trimester can detect encephalocele and enlarged cystic kidneys. Additionally, high-resolution ultrasound can detect pathologies such as a cystic area in the fetal calvarium, allowing the diagnosis to be made during the first trimester, as was possible in this case.

Given its autosomal recessive mode of transmission, the risk of recurrence of MGS is high (25%) and is thus an important consideration in subsequent pregnancies. Lu et al. described a pre-implantation genetic diagnosis (PGD) performed in a Chinese family who had four fetuses with MGS type 3.[2] In families with a history of fetal death due to MGS, counseling regarding future pregnancies should include the options of PGD and an early detailed ultrasonography examination.

References

1. Henkel KE, Pfeiffer RA, Stoss H. Meckel-Gruber Syndrome. Pathologe 1993;14(1):32-35.
2. Lu Y, Peng H, Jin Z, et al. Preimplantation genetic diagnosis for a Chinese family with autosomal recessive Meckel-Gruber Syndrome type 3 (MKS3). PloS One 2013;8(9): e73245.
3. Ramadani HM, Nasrat HA. Prenatal diagnosis of recurrent Meckel Syndrome. Int J Gynaecol Obstet 1992;39(4): 327-32.
4. Ickowicz V, Eurin D, Maugey-Laulom B, et al. Meckel-Gruber Syndrome: sonography and pathology. Ultrasound Obstet Gynecol 2006;27:296-300.