

Meckel Gruber Syndrome diagnosed in two consecutive pregnancies

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Abstract

Meckel Gruber syndrome is a lethal, autosomal recessive, multisystemic disorder that is associated with a mutation affecting ciliogenesis. In this report, we present two consecutive pregnancies of a woman complicated with MKS. In the first pregnancy with MKS, the amniotic fluid index was under 1 cm with bilateral polycystic fetal kidneys. Post-abortion macroscopic examination of the first fetus revealed multiple congenital anomalies including occipital encephalocele, axial polydactyly and pes equinovarus. Ultrasound examination during the second gestation revealed a singleton pregnancy complicated by MKS. There were multiple congenital anomalies including an occipital encephalocele, polycystic and horseshoe shaped kidneys, axial polydactyly, cleft lip and palate.

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Introduction

Meckel Gruber Syndrome (MKS) is a rare and lethal, autosomal recessive disease first described by the German

anatomist Johann Friedrich Meckel in 1822. Although it is classically characterized by the triad of occipital encephalocele, large polycystic kidneys, and postaxial polydactyly, there may be associated multiple anomalies such as oral clefting, genital anomalies, central nervous system (CNS) malformations, including Dandy-Walker and Arnold-Chiari malformations, and liver fibrosis.¹⁻⁴

In this report we present two consecutive pregnancies of a woman complicated by MKS.

Case Report

First pregnancy with MKS

A twenty seven year old woman presented at 18 weeks gestation in her second pregnancy. Physical examination and routine laboratory workup findings were unremarkable. She had a three-year-old healthy male child. Her medical and family histories were unremarkable.

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Ultrasound findings: Fetal biometry confirmed the 18-week pregnancy using biparietal diameter, abdominal circumference and femur length measurements. The amniotic fluid index was less than 10 mm and bilateral fetal kidneys were polycystic. Parents did not want to proceed with further antenatal diagnostic tests and pregnancy was terminated with induced abortion.

Post-abortion macroscopic examination revealed multiple congenital anomalies including occipital encephalocele, axial polydactyly and pes equinovarus (Figure 1). The kidneys were enlarged, horseshoe shaped and polycystic. Post-abortion findings were consistent with MKS. The parents were informed about MKS and the risk of recurrence.

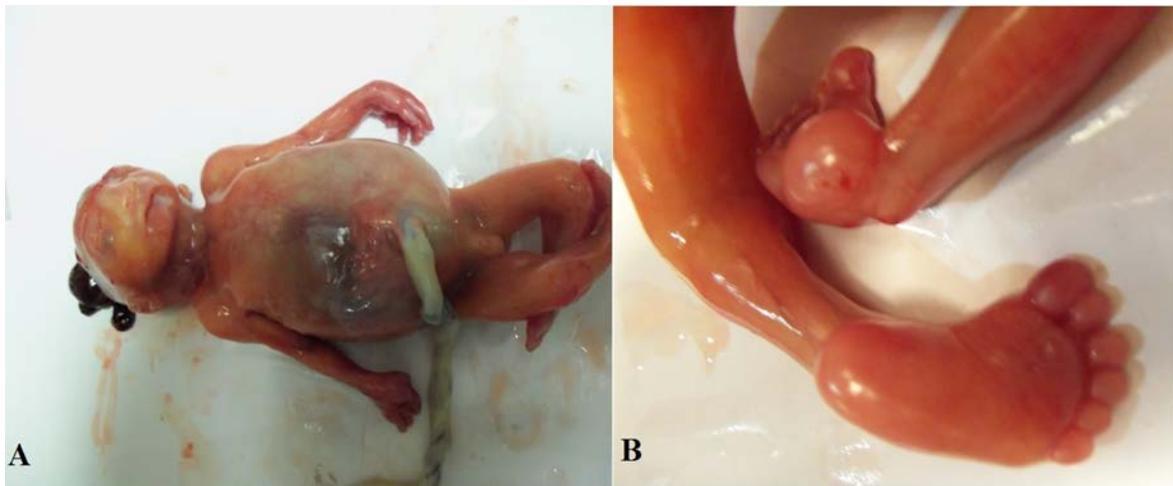


Figure 1. Post-abortion view of the first pregnancy complicated with Meckel Gruber Syndrome.

A: Occipital encephalocele. B: Postaxial polydactyly and pes equinovarus

Second pregnancy with MKS

The following year, the woman presented at 20 weeks gestation in her third pregnancy. Her medical, physical and laboratory examinations were unremarkable.

Ultrasound examination revealed a singleton pregnancy complicated with multiple congenital anomalies

consistent with MKS again. There were multiple congenital anomalies including an occipital encephalocele, polycystic and horseshoe shaped kidneys, axial polydactyly (Figure 2), cleft lip and palate. The parents refused to proceed with further antenatal diagnostic tests, once again and the pregnancy was terminated with induced abortion.



Figure 2. Ultrasound findings of the second pregnancy complicated with Meckel Gruber Syndrome: (From left to right) Encephalocele, postaxial polydactyly and polycystic horseshoe shaped kidneys.

Post-abortion examination confirmed the antenatal ultrasound findings (Figure 3). The woman was discharged

uneventfully and the parents were referred to genetic consultation.



Figure 3. Post-abortion view of the second pregnancy complicated with Meckel Gruber Syndrome demonstrating encephalocele, oral clefting and postaxial polydactyly.

Discussion

MKS is associated with multiple anomalies; however, it can still be diagnosed antenatally with an ultrasound examination. Its incidence varies from 1 in 13,250 to 1 in 140,000 live births.⁵ Since the disease is transmitted in an autosomal recessive pattern the chance of a subsequent

gestation complicated with MKS is 25%.

MKS is associated with multiple anomalies; the major diagnostic criteria include polycystic dysplastic kidneys, occipital encephalocele, or other anomalies of the central nervous system and polydactyly.⁶ Anomalies classified within the minimal diagnostic

criteria include facial abnormalities, ambiguous genitalia, cardiac septal defects, gastrointestinal anomalies like omphalocele and CNS abnormalities like agenesis of corpus callosum, Dandy–Walker and Arnold–Chiari malformations.^{4,7}

In the present case report, occipital encephalocele, bilateral polycystic kidneys with axial polydactyly were present in both of the gestations. In addition to these findings, in the second gestation there was also cleft lip and palate.

MKS is one of a group of inherited disorders, including Joubert Syndrome, NPHP and Bardet-Biedl, that result from defects in the function of cilia and are therefore referred to as ciliopathies. Mutations in at least 10 different genes can result in MKS, making the genetic evaluation of this condition complex and expensive.^{8,9,10}

There are many severe malformations present in MKS so early antenatal diagnosis is possible. But since it has an autosomal recessive pattern of transmission, preimplantation genetic diagnosis (PGD) and in vitro fertilization (IVF) or intrauterine genetic analysis can be used. In our case the family has a 3 years old healthy child and they had a very low income. So they did not go further for genetic diagnosis. We think that it is more acceptable to perform genetic analysis after termination of the pregnancy since there are many severe accompanying malformations which are usually incompatible with life. PGD and IVF can be used for families with subsequent effected gestations and those who do not conceive a healthy child.

Although, commonly associated, severe oligohydramnios decreases the

clarity of the ultrasound images, in most cases the components of the entity can be determined by early ultrasound findings at 11-14 weeks gestation.^{5,11,12}

Differential diagnosis of the disease is important since there is a risk of recurrence in the subsequent pregnancies as in our case. Since most of the diseases with similar clinical presentations (Trisomy 13, Trisomy 18, Joubert Syndrome, Bardet-Biedl syndrome) have an underlying genetic pathology, neonatal autopsy and genetic analysis are crucial for the final diagnosis.^{6,13,14}

Conclusion

MKS is a lethal disorder and most affected fetuses die during pregnancy or shortly after birth. Thus, antenatal diagnosis provides the chance of early termination of the affected pregnancy. Genetic analysis and confirmation of the diagnosis of MKS is a vital tool that may be used in the counseling of the family for the future pregnancies.

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