Case Report

Meckel-Gruber syndrome: Antenatal diagnosis and ethical perspectives

Sarar Mohamed (1,2), Fatima Ibrahim (2), Kameel Kamil (3), Satti A. Satti (3)
1) Department of Pediatrics, College of Medicine, King Saud University, Riyadh, Saudi Arabia
2) Department of Pediatrics, Shargelneel Hospital, Khartoum State, Sudan.
3) Department of Obstetrics, Shargelneel Hospital, Khartoum State, Sudan.

ABSTRACT

Meckel-Gruber syndrome (MGS) is an autosomal recessive disorder characterized by occipital encephalocele, polycystic kidneys and variable other congenital malformations. We report on a Sudanese patient with MGS diagnosed by antenatal ultrasound scan. Pregnancy was terminated at 25 weeks of gestation.

Key words:
Meckel-Gruber syndrome; Encephalocele; Polydactyly; Cystic kidneys.

INTRODUCTION

Meckel-Gruber Syndrome (MGS) is a rare, genetically heterogeneous and lethal autosomal recessive disorder characterized by occiptal encephalocele, postaxial polydactyly, and bilateral dysplastic cystic kidneys [1-3]. The incidence of MGS is 1:140,000 [2]. This disorder is hypothesized to be caused by defects in primary cilia. MGS can be associated with anomalies including cleft lip and palate, anopthalmia, micropthalmia, ductal plate malformation of the liver, cardiac and genital anomalies [2-5] The diagnosis of MGS is considered when antenatal ultrasound shows associated findings [5]. Recently, several mutations defining novel MGS loci were identified [6-8]. We here report on a Sudanese baby with MGS.

CASE REPORT

A twenty six years old gravida 2 para 0+1 presented at 12 weeks of gestation with a previous history of a baby with congenital malformations including occipital encephalocele. The parents are first degree cousins on both maternal and paternal sides. There was no other family history of congenital malformations. The mother denied taking any medications during pregnancy other than folic acid, which was started

Correspondence to:
Sarar Mohamed,
Department of Pediatrics (39),
College of Medicine,
King Saud University,
P.O. Box 2925, Riyadh11461,
Saudi Arabia
Email: sararmohamed@hotmail.com

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early in pregnancy.

Ultrasound scan, done at 15 weeks gestation revealed encephalocele. Detailed ultrasound scan was repeated at 24 weeks gestation which confirmed posterior encephalocele, bilateral cystic kidneys, talipes, and polydactyly. The possibility of MGS was raised, the natural course and the prognosis was explained to the parents who opted to terminate the pregnancy. Following further extensive genetic counseling and approval of the hospital ethics committee, termination of pregnancy was carried out at 25 weeks gestation. The baby was born alive but gasping and died in 15 minutes, no resuscitation was offered. The birth weight was 1 kg, length was 32cm, and head circumference was 20cm all <3rd centile. Clinical examination revealed occipital encephalocele, microcephaly, cleft palate, post axial polydactyly, bilateral talipes, short limbs, and grossly enlarged abdomen with bilaterally palpable kidneys (Figures 1 and 2). The genitalia were undetermined with 1 cm phallus with a single opening, labioscrotal folds and no palpable inguinal mass. Chromosomal analysis of the baby revealed 46 XY karyotype. Further detailed DNA study was not available.

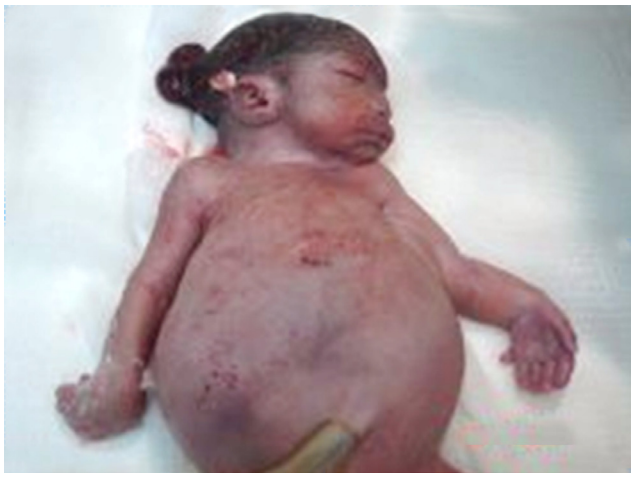

Figure 1- Occipital encephalocele, microcephaly, post axial polydactyly, short limbs, and grossly enlarged abdomen.

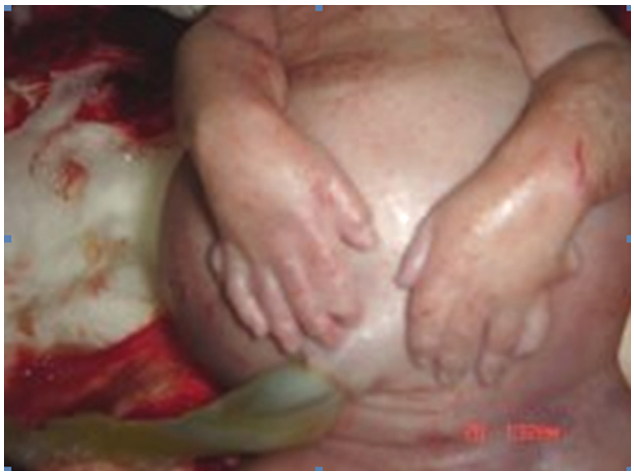

Figure 2- Close-up showing bilateral post axial polydactyly and the grossly enlarged abdomen.

DISCUSSION

Meckel-Gruber syndrome is a fatal, autosomal recessive disorder characterized by malformation of central nervous system, particularly occipital encephalocele, bilateral renal dysplasia, and polydactyly. As an autosomal recessive disorder, the risk of recurrence of Meckle Gruber syndrome is 25% [1-4]. The present family we report on is unlucky to have 2 babies with MGS in 2 consecutive pregnancies. Our patient showed most of the clinical signs reported in previous studies [1-5]. Renal disorder is noted in 95-100% of patients, occipital encephalocele in 60-80%, and postaxial polydactyly in 60-80% [1, 2, 5]. Facial anomaly, ambiguous genitalia, cardiac septal defect and gastrointestinal anomalies like omphalocele also occur in varying combinations [6]. The diagnosis of MGS is usually suspected with early prenatal ultrasound showing typical findings [9-11]. It was suspected in our patient at 15 weeks gestation and confirmed by the second ultrasound scan at 24 weeks of gestation. Recently, Kheir et al [12] described a Saudi newborn baby with MGS who was diagnosed at birth and expired in early neonatal period.

This case report highlights the importance of antenatal scan in diagnosis of inherited diseases such as MGS. This helps physicians and parents to plan further management of pregnancy. Following extensive genetic counseling the parents opted to terminate this pregnancy. Termination of pregnancy raises complex ethical, legal, social and religious issues. As MGS is not compatible with life, the opinion of parents was adhered to [13-14]. The Hospital Ethics Committee approved termination of pregnancy in this case as it is legal, ethical, and respect religious perspectives [13-14]. In Sudan, termination of pregnancy is allowed if three physicians anticipated that the unborn fetus is affected by a condition which is not compatible with life. The right of the unborn fetus should be strictly defended by physicians. In cases of unborn babies affected by conditions leading to developmental delay and other morbidities which are not lethal, termination of pregnancy is generally not indicated [13-14].

Recently, primary prevention of genetic diseases became a reality by introduction of preimplantation genetic diagnosis (PGD) [15-16]. In order to help families to make use of PGD, physicians need to confirm the diagnosis of the genetic disease at the DNA level in the index case. We were unable to perform mutation analysis for our patient because of lack of facilities. It was a missed opportunity to prevent possible recurrence of MGD for the third time in this unfortunate family.

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