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Case Report

CASE REPORT

Meckel Gruber syndrome associated with anencephaly—an unusual reported case

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Abstract

Meckel–Gruber syndrome (MGS) is a rare and lethal ciliopathic disorder, with the incidence ranging between 1 in 13 000–400 000 live births. MGS is characterized by multisystem developmental malformations with the classical features of renal cystic dysplasia, occipital encephalocele and post-axial polydactyly. Except for occipital encephalocele, the CNS abnormalities associated with MGS that are less frequently reported include hydrocephaly, anencephaly or malformation of cerebellum. Our presented case of MGS is associated with anencephaly and other facial abnormalities. This kind of ailment is infrequently reported in literature.

INTRODUCTION

Meckel–Gruber syndrome (MGS) is a rare and lethal ciliopathic disorder, with the incidence ranging between 1 in 13 000–400 000 live births. It is a congenital autosomal recessive condition and carries a 25% risk of recurrence in each pregnancy [1,2].

MGS is characterized by multisystem developmental malformations with the classical features of renal cystic dysplasia, occipital encephalocele and post-axial polydactyly. The criteria for the diagnosis of MGS is the presence of at least two of the three classic features such as dysplastic cystic kidney, occipital encephalocele and polydactyly, which are commonly observed with the frequency of 100, 90 and 83.5% respectively [3,4].

Except for occipital encephalocele, the CNS abnormalities associated with MGS that are less frequently reported include hydrocephaly, anencephaly or malformation of cerebellum. Our presented case of MGS is associated with anencephaly and other facial abnormalities. This kind of ailment is infrequently reported in literature [5].

CASE REPORT

A 40-year-old grand multiparous woman gravida 9 para 8 was referred to our hospital at 24 weeks of gestation for a detailed anatomy scan because of a foetus with bilateral enlarged cystic kidneys, oligohydramnios, and microcephaly. Her obstetric history revealed that she had given birth to seven healthy babies in her previous pregnancies, but the last pregnancy had history of early neonatal death due to suspected MGS (bilateral dysplastic kidney, anencephaly, cleft lip and palate, occipital encephalocele). She has history of a first degree consanguineous marriage. Our antenatal ultrasonographic scan revealed multicystic dysplastic kidneys (Fig. 1), absence of bladder, marked oligohydramnios, anencephaly and occipital encephalocele. The patient was counselled in detail regarding the poor foetal prognosis. A termination of the pregnancy was not offered as an option because of cultural and religious constraints.

At 30.2 weeks of gestation, she experienced labour pains. Five hours after admission, she had a spontaneous vaginal

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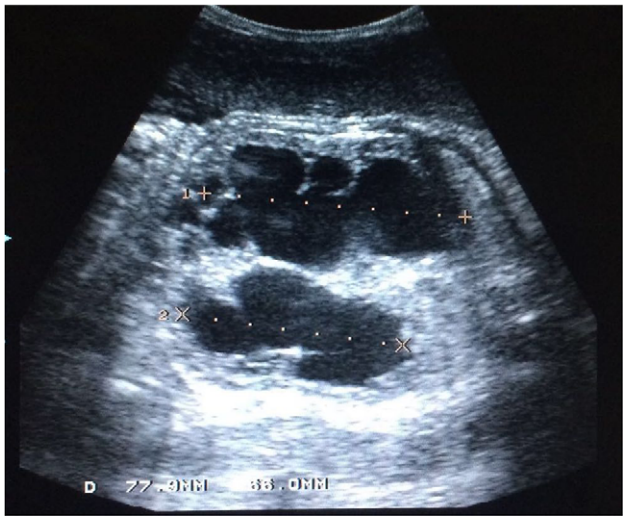

Figure 1: Ultrasound image shows bilateral dysplastic cystic kidneys.

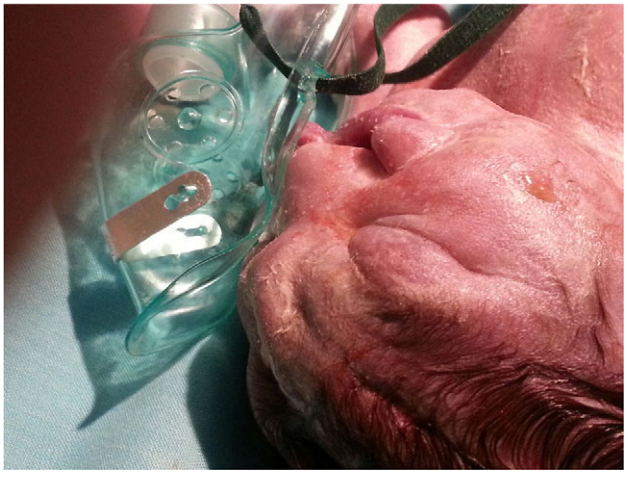

Figure 2: New-born with anencephaly, cleft lip, upper slanting of eyes.

delivery of a male foetus with an Apgar score of 1 in 1 min and 1 in 5 min and a weight of 2.4 kg. The new-born was examined by our neonatologist, and the external examination revealed anencephaly (Fig. 2) with head circumference 25.5 cm, occipital encephalocele (Fig. 3), cleft lip and cleft palate (Fig. 2), upper slanting of eyes (Fig. 2), low set ears, huge distended abdomen due to bilateral renal mass (Fig. 4), flexion of both wrist joint and post-axial hexadactyly on both feet. We kept the new-born under human care after counselling the parents. Approximately 1 h after delivery, the baby expired.

A diagnosis of MGS was suggested, based on the presence of the classical features. The patient denied consent for a genetic analysis and autopsy of the infant.

DISCUSSION

MGS is a lethal syndrome, causing anomalies of the central nervous system (CNS), cystic dysplasia of the kidneys, and malformations of the extremities. Other anomalies associated with MGS are intrauterine growth retardation (IUGR), single umbilical artery, cardiovascular defects, cleft palate, several genital abnormalities, and oligohydramnios and hepatic periportal fibrosis [6].

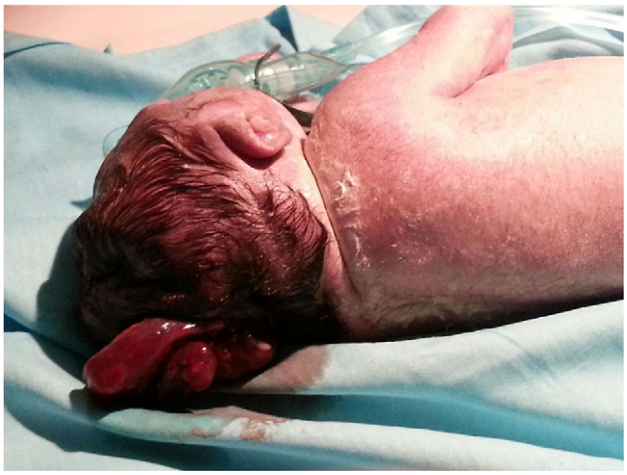

Figure 3: Occipital encephalocele.

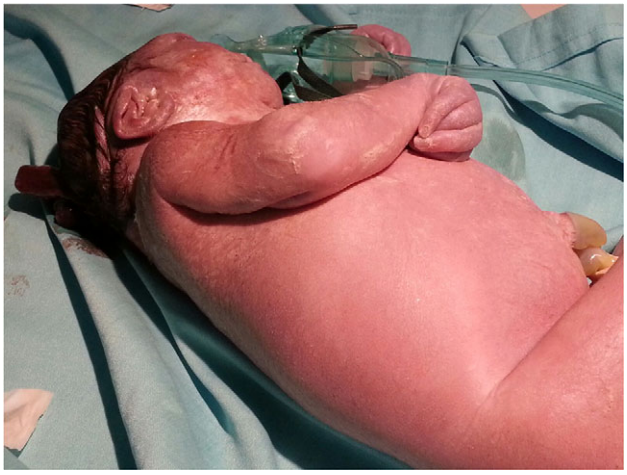

Figure 4: Distended abdomen due to bilateral renal mass.

Previous studies state that 57% of MGS cases had the three cardinal features, 16% had only polycystic kidney and polydactyly, and the rest exhibited other variations [7].

The phenotypic variability of MGS might be due to several gene mutations. Genetic mapping of the syndrome is still incomplete, and the most frequently responsible genes are MKS1 on chromosome 17, MKS2 on 11 and MKS3 on 8 [1,6,8].

Commonly encountered CNS abnormalities associated with MGS previously reported in the literature include occipital encephalocele, microcephaly, Dandy–Walker malformation and holoprosencephaly [6]. The less frequently reported CNS anomalies of MGS include anencephaly and hydrocephaly [5].

In a recent population-based study of MGS, it was found that among 173 cases of MGS, only 3.5% cases were associated with anencephaly. In another study of 67 cases of MGS, only one case was found with anencephaly [3,5].

In our case, we found the foetus with anencephaly along with other cardinal features of MGS.

The differential diagnosis of MGS includes trisomy 13, trisomy 18, Joubert syndrome, Bardet–Biedl syndrome and Smith–Lemli–Opitz syndrome [4]. Trisomy 13 is the most likely syndrome to be confused with MGS. Enlarged kidneys, severe oligohydramnios and the presence of an occipital cephalocele favours the diagnosis

of MGS, whereas holoprosencephaly or other midline CNS anomalies favors trisomy 13 [9].

MGS is best diagnosed prenatally by ultrasonography early in the second trimester. No specific biochemical and chromosomal studies indicate the presence of the MGS. Therefore, the prenatal ultrasonography detection of MGS is important for the diagnosis, which can be confirmed later by genetic analysis and careful post-mortem examination to establish the diagnosis. Clinical diagnosis is suggested on the basis of the presence of classical clinical features and when the syndrome recurs in subsequent pregnancies [2,9].

Although in our case, genetic analysis and post-mortem examination were not performed, prenatal USG findings, the presence of cardinal features and history of recurrence of similar anomalies that were clinically felt to represent MGS were used to establish the diagnosis.

MGS is inherited in an autosomal recessive manner so, the chance of giving birth to another child with MGS is 1 in 4 (25%) for each pregnancy [1,10].

MGS is a fatal disorder resulting in intrauterine or early neonatal death, thus prenatal diagnosis is important for the counselling of the parents regarding the poor foetal prognosis and to explain the chances of recurrence in subsequent pregnancies [2].

ACKNOWLEDGEMENTS

None.

CONFLICT OF INTEREST STATEMENT

None declared.

ETHICAL APPROVAL

Not applicable.

CONSENT

Informed written consent was taken from the patient.

GUARANTOR

Principal investigator.

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