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Meckel Gruber Syndrome-An Autopsy Report of a Rare Case

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Abstract: Meckel Gruber Syndrome is a rare autosomal recessive disorder characterized by a typical clinical triad of meningo-encephalocele, polycystic kidneys and polydactyly. The worldwide incidence varies from 1 in 13250 to 1 in 140000 live births. Highest incidence was reported in Gujrati Indians. We report autopsy features of a Meckel Gruber Syndrome in a 22 weeks female fetus
Keywords: Meckel Gruber Syndrome, Clinical triad, Encephaolocele, Polycystic kidney, Polydactyly.

INTRODUCTION

Meckel Gruber Syndrome (MGS) is a rare autosomal recessive lethal malformation characterized by a clinical triad of occipital encephalocele, bilateral polycystic kidneys and post axial polydactyly [1]. The world wide incidence varies from 1 in 13250 live births to 1 in 140000 live births which are reported from the community originating from the Gujrat state in western India [2]. We report a case of MGS in a female fetus in which the diagnosis was made at 22 weeks of pregnancy based on the classical triad of this syndrome detected with ultrasonography.

CASE REPORT

A 23 years old lady presented with 22 weeks amenorrhoea with previous history of spontaneous abortion at 6th month pregnancy with fetal congenital malformation. There was no history of consanguinous marriage. Her antenatal ultrasonography revealed a single live intrauterine fetus of 22 weeks gestation with occipital encephalocele, cystic dysplasia of bilateral kidneys, polydactyly, type IV Arnold Chiari malformation with mild ventriculomegaly and severe oligohydraminos. Her complete blood count and urine examination was normal and seromarkers for HIV, HBsAg and VDRL were nonreactive. The termination of pregnancy was done as the malformation was lethal and the fetus was sent for neonatal autopsy.

AUTOPSY FINDINGS

A premature female abortus weighing 460 grams was received for autopsy. External examination revealed occipital defect with encephalocele, bilateral polydactyly of hands and feet, each limb having 6 fingers with abnormal facial features i.e. low set ears, depressed nasal bridge and hypertelorism (Fig 1,2). In situ examination of thoracic cavity revealed hypoplastic lungs (Fig 3). Abdominal cavity revealed enlarged kidneys with multiple small cysts on external surface and cut surface (Cystic renal dysplasia- fig. 3).

Microscopy of kidneys revealed multiple cysts lined by attenuated to cuboidal epithelium. Interstitium showed primitive tubules and glomeruli along with undifferentiated mesenchyme (Fig.4).

Cranial cavity revealed occipital encephalocele with incompletely developed cerebellum i.e. type IV Arnold Chiari malformation. Based on the above features, the diagnosis was made as Meckel Gruber syndrome.

Fig-1: Occipital Encephalocele

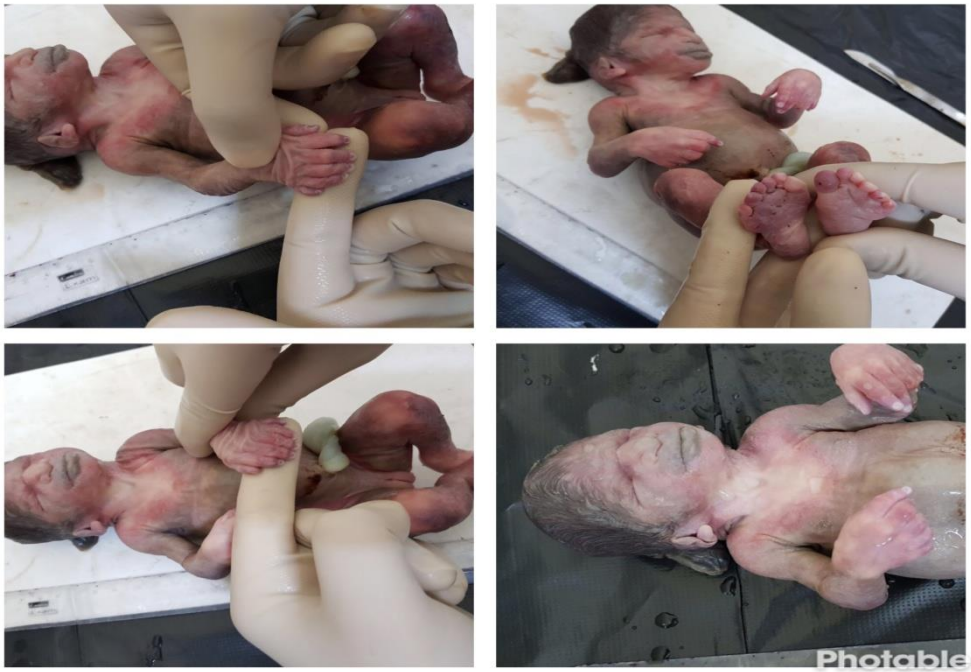

Fig-2: Bilateral Polydactyly of hands and feet with abnormal facial features

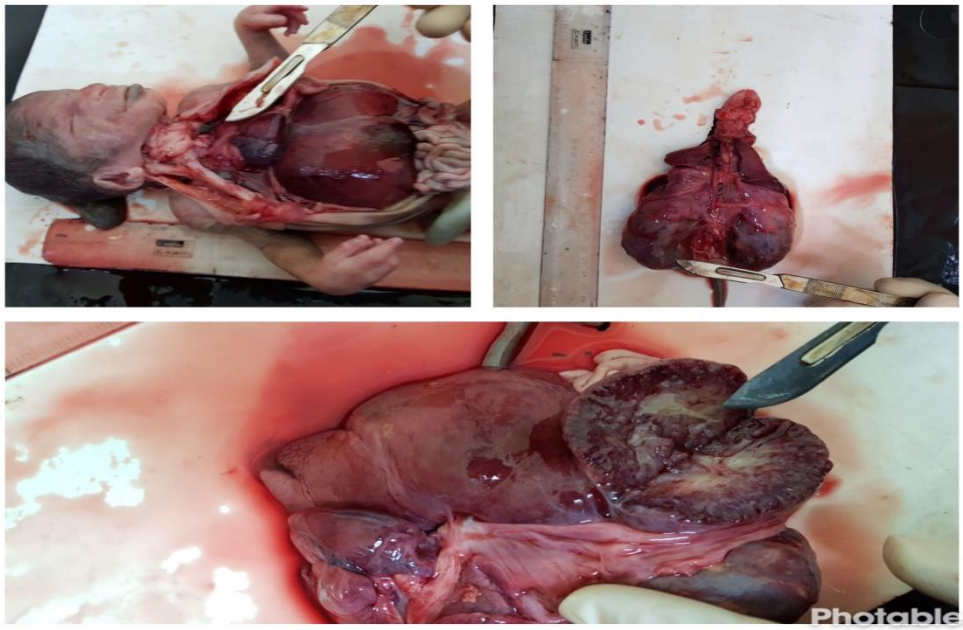

Fig-3: Hypoplastic Lungs and Enlarged kidneys with multiple small cysts on external surface and cut surface (Cystic renal dysplasia)

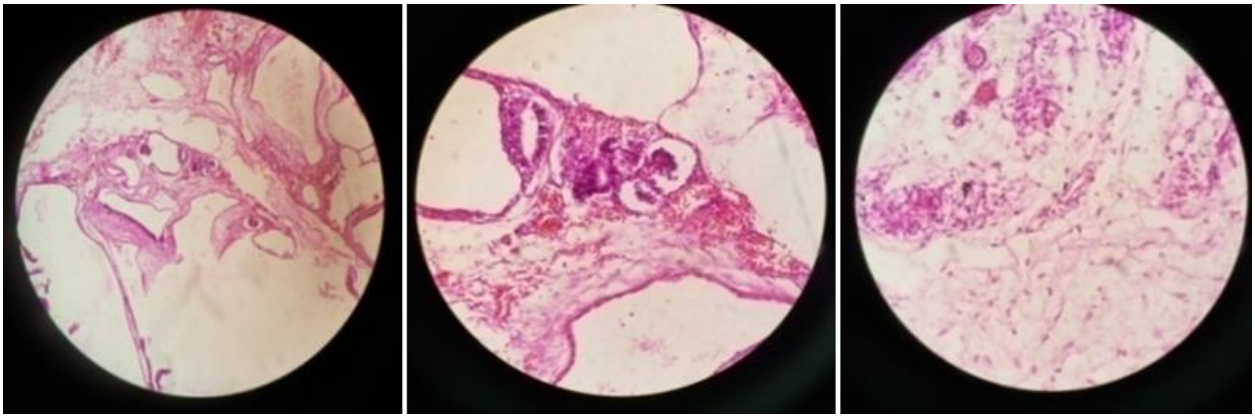

Fig-4: Microscopy of Kidneys- Multiple cysts lined by attenuated cuboidal epithelium. Interstitium showed primitive tubules and glomeruli along with undifferentiated mesenchyme

DISCUSSION

MGS was first described by J.R. Meckel in 1822 in 2 neonatal babies who died because of encephalocele, polycystic kidneys and polydactyly[3]. In 1934, George B. Gruber reported familial cases with similar features [4]. The disease is rare and affects all races with equal prevalence in males and females. The chance of MGS in subsequent pregnancy is 25% [3,5,6]. Our case also revealed previous history of spontaneous abortion with congenital malformation.

Though consanguinity has been reported as important factor in genetic basis, the syndrome is also detected in children from non-consanguinous marriages [7]. In our case, the fetus was a product of nonconsanguinous marriage. The single gene defect occurs commonly in case of non- consanguineous marriages while mutant genes are associated with consanguinity. The mutations are mapped to 6 different loci in different chromosomes [1]. MGS has been suggested to be caused by failure of mesodermal induction leading to ciliopathies caused by dysfunction of cilia [8].

The neonatal mortality rate is 100% in cases of MGS[5]. The major diagnostic criteria of MGS include cystic renal dysplasia, polydactyly and occipital encephalocele. The associated other malformation include facial abnormalities, ambiguious genitalia ,cardiac and gastrointestinal anomalies and CNS malformations like agenesis of corpus callosum, Dandy Walker cyst and Arnold Chiari malformations [9].

In our case, the associated anomalies were abnormal facial features i.e. low set ears, depressed nasal bridge, hypertelorism and Arnold Chiari malformation (type IV). Perinatal diagnosis of MGS can be made by routine ultrasonography for fetal

anomalies at 11 to 14 weeks of pregnancy and by estimation of alfa- fetoprotein levels in the maternal serum. However, alfa- fetoprotein levels are not raised when the encephalocele contains a closed sac [10, 11]. As this case was the recurrence after first pregnancy, the patient was adviced genetic study before planning next pregnancy.

CONCLUSION

Meckel Gruber Syndrome is a rare and lethal syndrome with neural tube defects associated with wide variety of malformations. Ultrasonography and maternal serum alfa-fetoprotein levels can be used to access the recurrence in next pregnancy. Neonatal autopsy and genetic studies play important role in the diagnosis of this syndrome.

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