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Meckel Gruber syndrome, A case report (3 cases)

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Abstract : *Meckel Gruber syndrome is a rare autosomal recessive poly malformative syndrome defined by occipital encephalocele, polydactyly and cystic renal dysplasia. Ultrasound is currently the best tool for antenatal screening of this lethal poly malformation and its confirmation is done by karyotype study. We report three cases of Meckel syndrome discovered by ultrasound.*

Keywords : encephalocele, Meckel Gruber, polycystic kidneys, postaxial polydactly, ultrasound

Introduction :

Meckel Gruber syndrome (MGS) was described by Meckel in 1822, and Gruber in 1934, associating encephalocele, polydactyly and cystic dysplasia of the kidneys. MGS is a rare malformative syndrome of autosomal recessive transmission. The variability of the clinical pictures reported in the literature shows that the polymorphism of this syndrome is an essential characteristic. Ultrasound is currently the best tool of antenatal screening for this lethal poly malformation [1]. We report three cases of Meckel syndrome discovered by ultrasound during antenatal screening.

Observations

- 1st patient:A 26 years old patients, Primigravida, third degree of cosanguineous marriage, pregnancy not followed, having consulted for the first time at 20 amenorrhea weeks, in whom the ultrasound has objectified: an evolving monofetal pregnancy, occipital encephalocele(figure1), large dysplastic kidneys occupying the abdomen(figure2), polydactilia, and ventriculo-megalia(figure3)
- 2nd patient : Patient aged of 34 years, G2P1 (1 vaginal delivery), pregnancy not followed, having consulted at 21 amenorrhea weeks in whom we objectified: a microcephaly, with occipital encephalocele(figure4), large kidneys(figure5), a cleft lip and club foot(figure6)
- 3rd patient: 24 year old female patient, primigravida, first degree consanguineous marriage, unattended pregnancy, admitted at 30 amenorrhea weeks for menace of premature delivery, in whom the ultrasound showed: a mega large cistern with two large hyperechogenic kidneys with medullary cyst(figure 7 and 8) and polydactyly(figure 9).

In the first patient, the pregnancy was marked by fetal death in utero, in the second patient, a therapeutic termination of pregnancy was recommended, while in the third patient, the delivery was premature with death in the first hour of life.

Discussion

Meckel syndrome is an inherited syndrome characterised by a cluster of congenital malformations affecting the central nervous system and kidneys. It is usually fatal shortly after birth [2]. Meckel syndrome affects 1 of 13,250 to 1,140,000 people worldwide. It is most common in Finland, where the birth prevalence is 1 of 9,000 and the mutation frequency is 1%. Several genes have been mapped: MKS1, MKS2, MKS3, MKS4 MKS5 MKS6 MKS7 MKS8 MKS9 MKS10 MKS11 MKS12, TMEM 138 and TMEM 237[3]. Meckel's syndrome is generally defined by the triad of occipital encephalocele, cystic kidney dysplasia and polydactyly. Polydactyly is most often post-axial (6th finger), but can sometimes be pre-axial (thumb duplication). Other anomalies may be present: cleft lip and palate, anophthalmia or microphthalmia, urethral atresia, cardiac and genital malformations.

Diagnostic criteria : -major criteria: cystic renal dysplasia is a mandatory criterion for diagnosis in association with anamnios [4];
-minor criteria: hepatic fibrosis; occipital encephalocele; polydactyly; other central nervous system malformations: Dandy-Walker malformation and Arnold Chiari malformation

Prenatal diagnosis :Prenatal diagnosis can be made on the basis of an ultrasound image of an anechoic intracranial cyst and/or a cranial malformation at the end of the first trimester or in the presence of abnormally large kidneys [5]. Other features of the syndrome may be detected at a later stage on ultrasound. Amniocentesis may reveal an elevated amniotic alpha-fetoprotein level

due to encephalocele [9]. Karyotype remains the best way to confirm the diagnosis If the pregnancy is carried to term, the newborn dies perinatally.

Evolution Meckel's syndrome is lethal with an average survival time of less than 24 hours. However, Genuardi describes a case of Meckel syndrome with polycystic kidneys, Dandy-Walker, postaxial polydactyly and survived for 43 months before dying of renal failure [6].

Genetic counselling: aims to inform parents of an affected individual that the risk of recurrence is 25% for subsequent pregnancies.

Differential diagnosis: Trisomy 13 and 18 are ruled out by a normal karyotype [7]. Other poly malformative syndromes may pose greater diagnostic difficulties. Carpenter-Hunter syndrome associates encephalocele, renal cystic dysplasia, polydactyly, but also generalized bone lesions. Polydactyly can also be found in Ellis von Creveld, short rib polydactyly, Moon-Bardet-Biedl, holoprosencephaly-polydactyly (pseudotrisomy 13) syndromes. A great help in diagnosis will be the isolation of the Meckel syndrome gene.

Genetic counselling: Meckel syndrome is autosomal recessive. The frequency of the Meckel syndrome gene in the general population is approximately 1:400. At present, it is not possible to accurately screen for the Meckel syndrome gene. However, the recent localisation of the responsible locus on chromosome 17 with three genes potentially involved shows that research is close to the goal. Therefore, in the absence of formally defined criteria for Meckel syndrome, it is essential to preserve fatal tissues for gene and molecular analysis to enable a precise diagnosis. Indeed, if in the case of an isolated Dandy Walker, genetic counselling should be reassuring, as the risk of local recurrence is 1%, in the case of Meckel syndrome with Dandy Walker this risk is 25% [8].

Conclusion

The most common malformations found in Meckel syndrome are polycystic renal dysplasia, encephalocele, polydactyly, and hepatic fibrosis, none of which are constant. The polymorphism of this syndrome can be considered an essential feature, but one that complicates access to a diagnosis of certainty. Advances in genetics with the precise isolation of the gene responsible for Meckel syndrome will be the next step towards a diagnosis of certainty, and its application to antenatal diagnosis.

References

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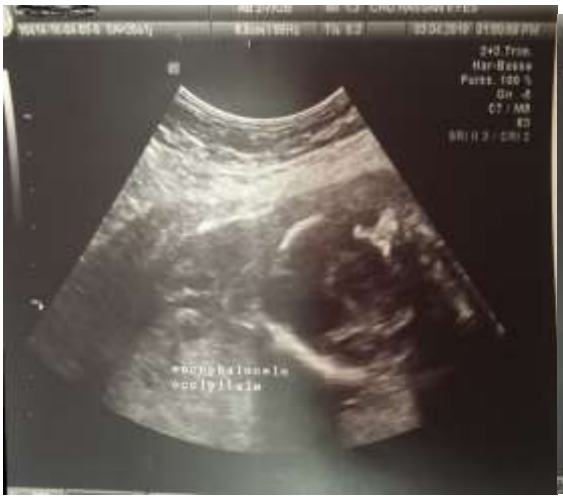

Figure1: occipital encephalocele

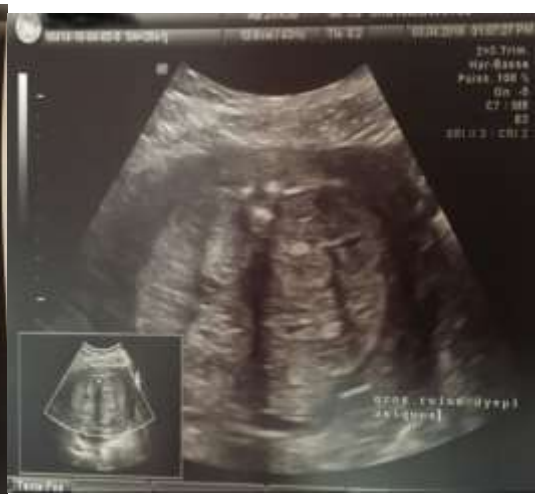

Figure2 :large dysplastic kidneys occupying the abdomen

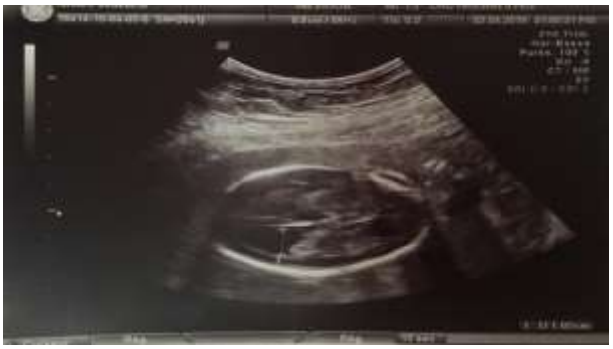

Figure3 :ventriculo-megalia

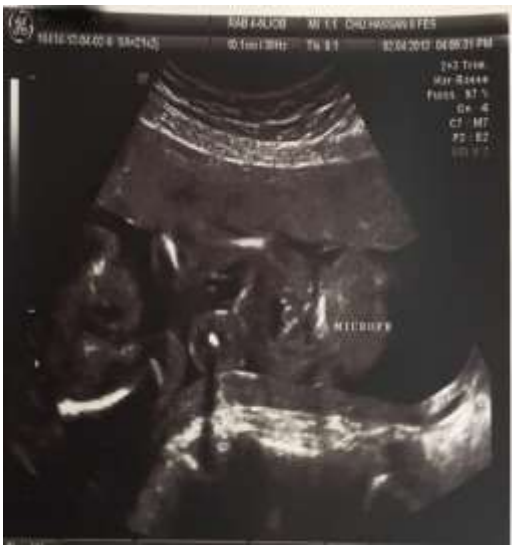

Figure4 : a microcephaly, with occipital encephalocele

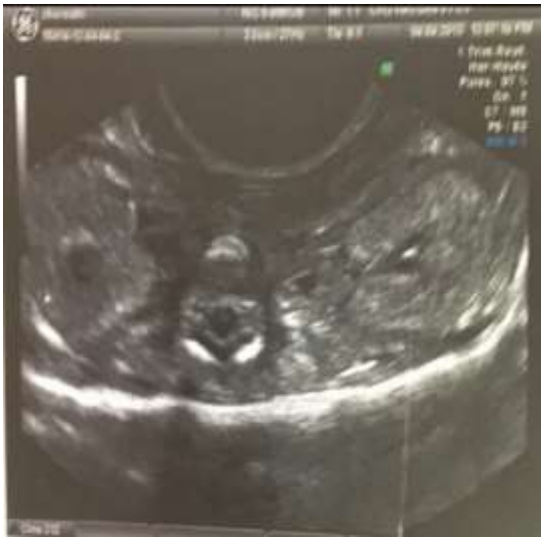

Figure 5 : Large Kidney

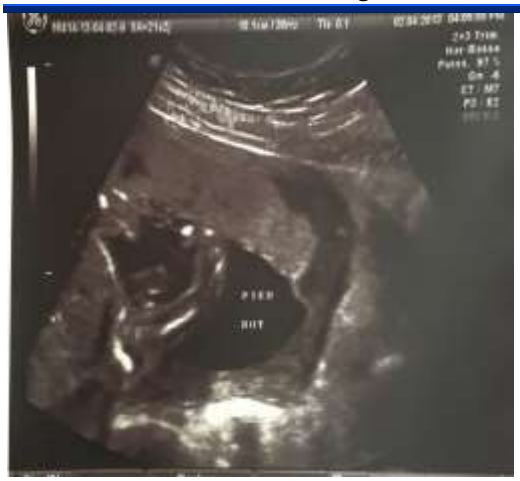

Figure6 :a cleft lip and club foot

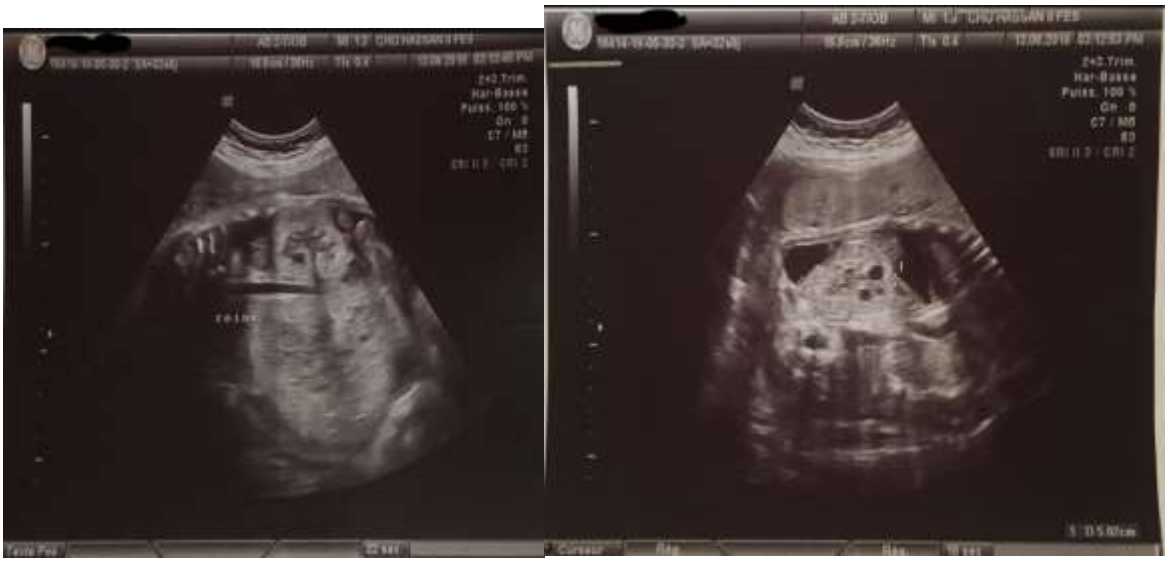

Figure 7 and 8 : two large hyperechogenic kidneys with medullary cyst

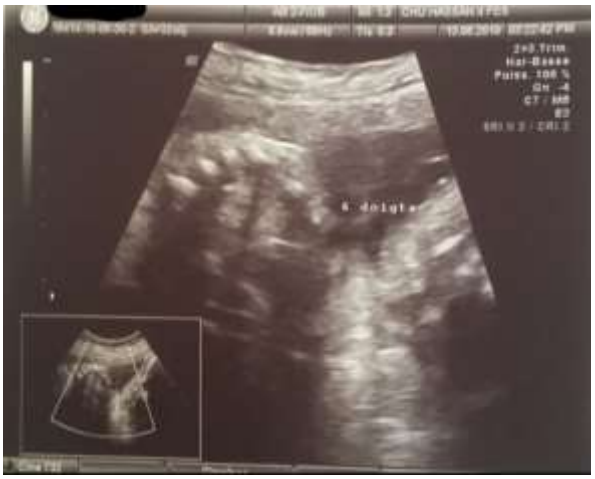

Figure 9:polydactyly