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CASE REPORT

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Meckel-gruber syndrome: About an evocative case in French Guiana—When ultrasound is insufficient for accurate diagnosis in a complex syndrome

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Abstract

In modern medicine, prenatal diagnosis can no longer be sufficient by ultrasound examination.

The genetic technical progress and its contribution may remain a challenge in isolated sites with the consequences that this implies in perinatal health.

KEYWORDS

Differential diagnosis, Genetic screening, Meckel-Gruber syndrome, Prenatal diagnosis

French Guiana is the only French department located on the South American continent. It covers an area of approximately 84,000 km^2, the largest department in France. It is 90% composed of a dense equatorial forest at the origin of health disparities with access to health care made difficult for some populations in this department (access in places exclusively by river or air for 12% of the population)[1]

In the case described below, ultrasound signs suggest Meckel-Gruber syndrome combining a triad of anomalies:

- The occipital encephalocele,
- Bilateral renal cystic dysplasia,
- And polydactyly often postaxial.[2]

Other signs include fibrosis-type polycystosis of the liver and hyperplasia of the bile ducts.[2]

MKS is a rare, lethal autosomal recessive ciliopathy with near-zero survival rates at birth.[3 4]

MSK (MIM 249 000) is caused by a dysfunction, due to genetic mutations, of the primary cilia during early embryogenesis. Several genes, encoding ciliary proteins, of which 15 currently have been identified (MSK1, MSK2, MSK3, MSK4, MSK5, MSK6, MSK7, MSK8, MSK9, MSK10, MSK11, MSK12, MSK13, and TMEM138, TMEM237). [5 6 2 7]

However, no genetic investigation was carried out due to the lack of resources and anatomo-pathological examinations that deprived us of informed genetic counseling.

This work reminds us that in "isolated" structures with limited resources, it is by no means possible to be satisfied with ultrasound screening, which although "early" despite health isolation, can be a source of confusion both in medical diagnosis, and in the subsequent care and genetic counseling, whose parents are too often amputated.

Mrs XX is a 15-year-old primigest. She was born and lives in a small isolated commune in French Guiana, accessible only by water or air.

An early dating ultrasound was performed, but without morphology and nuchal translucency measurement. Mrs XX did not benefit from the triple test for Trisomy 21 (ultrasound examination performed at the Prevention and Care Center, CDPS).

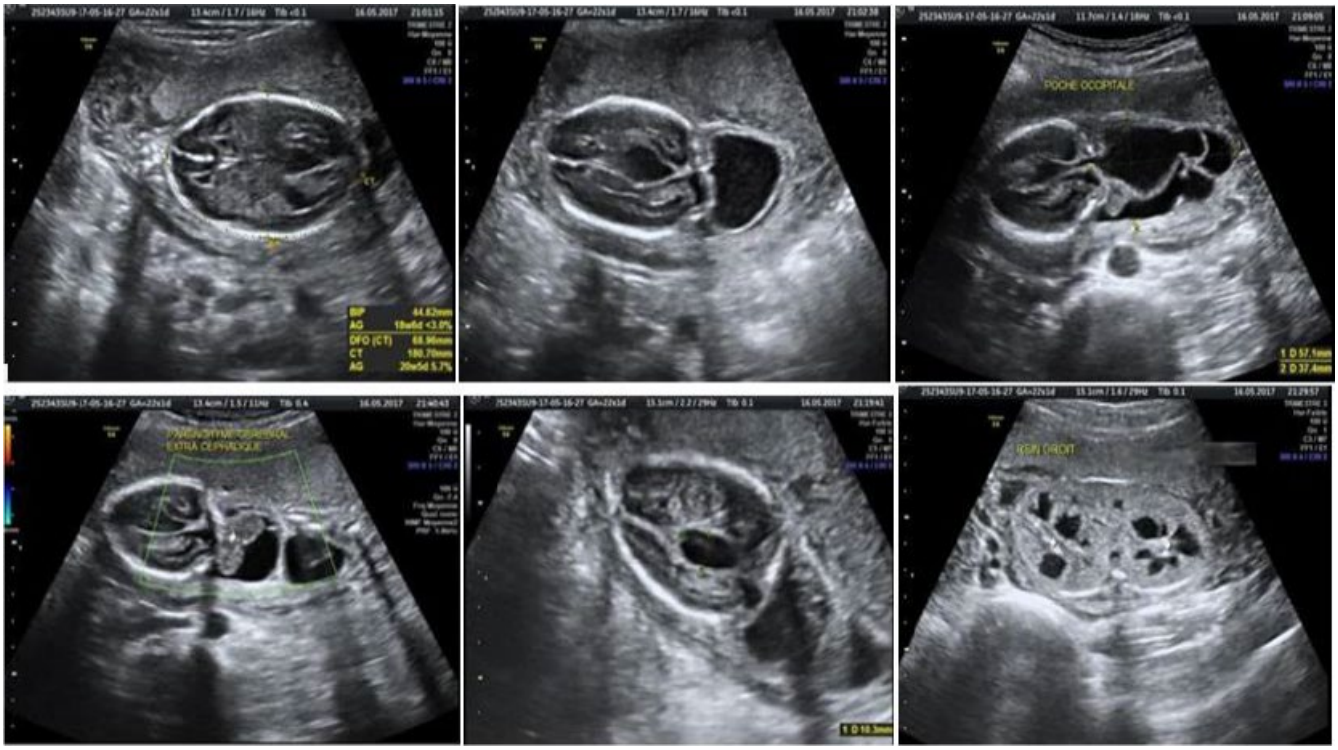

FIGURE 1 Ultrasound Signs

Her 20-year-old husband is also her cousin. Apart from this notion of inbreeding, there is no significant family history.

The first trimester serological checkup is normal, it is not immune to toxoplasmosis.

Fetal morphologic ultrasound of 21 weeks of gestation, performed in CDPS, reveals polycystic kidneys and anamnios. Mrs XX is therefore transferred to French Guiana's only Type III Hospital Center with ICU (intensive care unit).

Ultrasound performed at 22 weeks of gestation in Level III Center reveals (Figure 1):

*At the level of the cephalic pole:

- An occipital encephalocele of 30.3×30.2 mm,

- A cerebellar engagement in the occipital "pocket" with meningoencephalocele type,

- A disorganization of the intracranial cerebral parenchyma with a cystic formation 10.3 mm wide.

*At the abdominal level:

- Two large polycystic kidneys that appear to occupy the entire abdominal cavity. The right kidney measuring 67.5×41 mm.

The operator concludes that there is a polymalformative syndrome with an anamnios and suggests a probable Meckel-Gruber syndrome. An opinion is requested from the CPDP who accepts, in view of the iconography, the request for medical interruption of pregnancy requested by the parents. An amniocentesis was not possible because there is an anamnios.

The expulsion of a male fetus of 1 300 grams occurs at 26 SA + 4 J. The morphological examination of the fetus objective encephalocele, abdominal distention probably related to renal dysplasia. Examination of the limbs reveals clubfoot and hexadactyly in both hands.

The autopsy could not be performed due to the lack of an anatomo-pathologist on site and could not confirm the syndrome.

Meckel-Gruber syndrome, however, has with ultrasound signs common to other syndromes. A differential diagnostic table of chromosomal abnormalities and Joubert's syndrome, Carpenter-Hunter syndrome, Bardet-Biedl syndrome highlighted the clinical ultrasound signs common to Meckel-Gruber syndrome. (Table 1).

This work shows that ultrasound alone is not sufficient to confirm MSK, as the differential diagnosis of MKM remains important. Indeed, the characteristic ultrasound signs of Meckel-Gruber syndrome are found in Joubert's syndrome, Carpenter-Hunter, and Bardet-Biedl.

An anatomo-pathological examination, in the absence of amniocentesis depriving us of a karyotype, would have contributed to the expulsion of the fetus to certify the diagnosis. According to the literature, the karyotype of a Meckel syndrome may be quite normal; the genotype with regard to the genetic mutation of the pathology would be more appropriate.

This article reminds us that in French Guiana, a French overseas department, suffers from limited access to genetic testing. In modern medicine, prenatal diagnosis can no longer

TABLE 1 Differential diagnosis with the ultrasound signs detected

	Possible ultrasound/clinical signs		Possible ultrasound/clinical signs
Joubert's syndrome [2,8]	Agenesis or hypoplasia of cerebellar vermis Renal cystic dysplasia Encephalocele Hepatic fibrosis Hydrocephaly Polydactyly Situs inversus Sign of the "molar tooth"	Carpenter-Hunter syndrome [9]	Renal cystic dysplasia Encephalocele Bone lesions Polydactyly *Skeletal abnormalities reported for short limb type*
Bardet-Biedl syndrome [3]	Renal dysplasia/ Liver fibrosis Polydactyly/Situs inversus		
Achieved ZIKA [10]	Callous body agenesis Arthrogryposis Brain calcifications Microcephaly Ventriculomegaly	Dandy-Walker syndrome [2 11]	Cystic dilation of the 4th ventricle Overall enlargement of the brain pit in connection with an ascent of the cerebellum and torcular tent Malformation of the vermis *The MSK can sometimes be associated with a Dandy-Walker*
Trisomy 13 [12]	Craniofacial anomalies Holoprosencephaly Hypertelorism Micro or anophthalmia Oligo or hydramnios Postaxial polydactyly RCIU	Smith-Lemli-Opitz syndrome [6]	Cerebellar agenesis Callous body agenesis Extremity abnormalities (polydactyly, syndactyly) Facial dysmorphia Microcephaly RCIU
Trisomy 18 [12 13]	Arthrogryposis Hydramnios Equine varus feet RCIU	Ellis Van Creveld syndrome [2 14]	Heart abnormalities (septal defects) Short ribs Cleft lip, palate Polydactyly RCIU *Reported cases of heart defects in MSK* [15]

Note: The elements in bold are the characteristics common to MSK [16]

be sufficient by ultrasound examination and that genetic technical progress and its major contribution may remain a challenge in isolated sites with the medical and psychological consequences that this implies in the field of perinatal health.

CONFLICTS OF INTEREST

The authors declare no conflict of interest regarding this study.

AUTHORS' CONTRIBUTIONS

MLD: wrote the article and did the literature review; PAN and J.D: performed the diagnostic ultrasound.

ETHICAL APPROVAL

On 13 September 2019, the Local Ethic Committee of the Hospital Center has reviewed and approved the article.

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