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Holoprosencephaly: About A Case and Ante-Natal Ultrasound Diagnosis.

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Abstract*: Holoprosencephaly is a rare and complex malformation that affects one case per 15,000 births and results from an abnormality in the cleavage of the prosencephal. It is often associated with chromosomal abnormalities in 50% of cases such as trisomy 13. This pathology is accessible to prenatal diagnosis by an antenatal ultrasound examination, there are essentially 3 forms of increasing severity whose diagnosis is easier in the more severe the form. The prognosis is generally poor and management is difficult. For the viable forms, psychomotor retardation, abnormal movements, spastic quadriparesis, epileptic seizures, endocrinological and olfactory and visual sensory anomalies are associated.*

Keywords: holoposencephaly; malformation; ultrasound diagnosis;

1. Introduction:

Holoprosencephaly is a rare and complex congenital malformation that consists of a total or partial cleavage defect of the prosencephalon or forebrain. It occurs between the 18th and 28th day of embryogenesis and its frequency is about 1/15000 births[1] . It can be isolated, but is often part of a trisomy 13.
It results in neurological and facial manifestations of variable degree depending on the type of holoprosencephaly. This pathology is accessible to antenatal diagnosis by ultrasound from T 1, and requires a very detailed morphological study in search of a malformative association.
The prognosis of this disease depends on the type of malformation, a fetal death in utero is possible, for those who survive a hydrocephalus, a psychomotor delay, endocrine disorders and other disorders may be present. The management is very variable, ranging from a medical termination of pregnancy to supportive treatments depending on the manifestations

2. Clinical case:

It is about Mrs. A.Y. 24 years old, primiparous with no notable pathological history, no notion of consanguineous marriage, no notion of known genetic abnormality in the family, the course of the current pregnancy is marked by the discovery of gestational diabetes based on a fasting blood sugar level made at the end of T1, Consulted in our training for the follow-up of her pregnancy, the patient benefited from a biological check-up of the 1st trimester which showed a gestational diabetes diagnosed on a positive fasting glycaemia, and from a T1 ultrasound showing a complete absence of visualization of the midline.

During the second trimester ultrasound showed an accolement of the thalami without visualization of the 3rd ventricle, nor of the cavum of the septum pellucidum, the inter hemispheric siscure visible on the posterior part not visible on the anterior part.
The corpus callosum was visible only on the splenic bone. A study of the facial morphology showed a double cleft lip and palate with hypotelorism. The cranial perimeter was decreased.
The rest of the ultrasound did not show intrauterine growth retardation or any other morphological abnormality.
During the course of the pregnancy, the patient was put on insulin therapy with hygionic and dietary measures, and delivered by vaginal delivery at 38 weeks of amenorrhea of a male infant, presenting neonatal respiratory distress, who died at D4 of life.

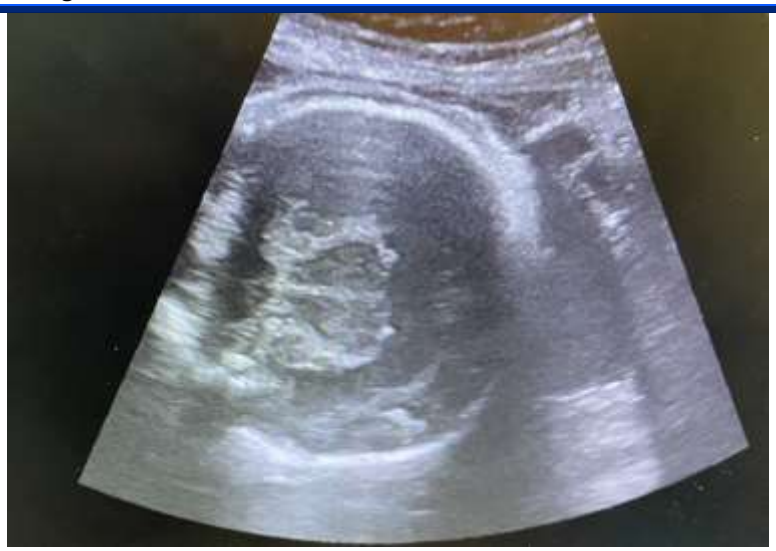

Figure 1: semilobar form visible on ultrasound: single ventricle with absence of the median line anteriorly, the two thalami appear joined, a posterior complex appears to be respected

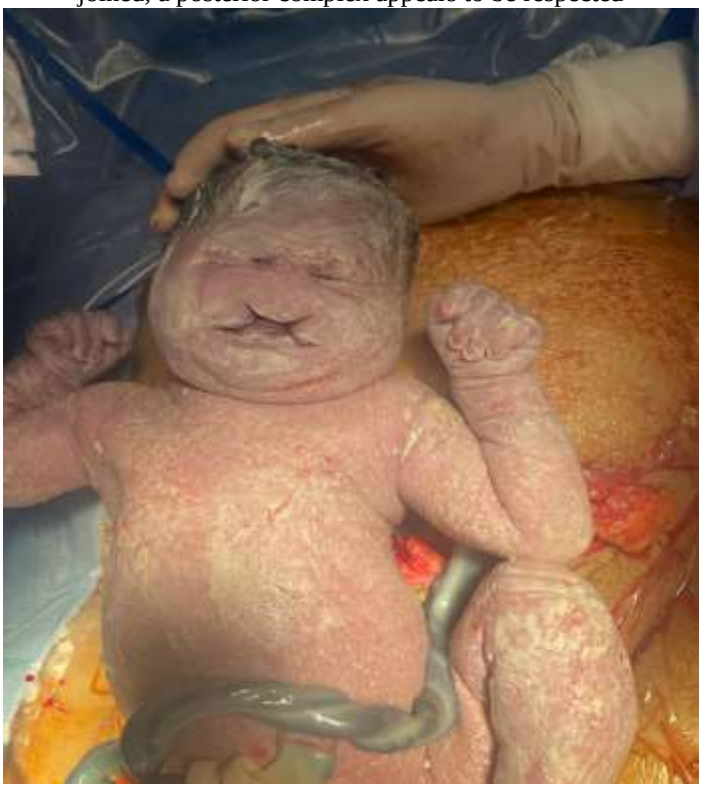

figure 2: semi-lobar form: double cleft lip with nasal agenesis and hypotelorism with microphthalmia.

3. Discussion:

Holoprosencephaly is secondary to a disorder of embryogenesis that results in the absence of cleavage of the forebrain [2]. The level of this cleavage defect will define 3 major forms, which are both prognostic forms. It can be associated with other malformations in a syndromic framework or isolated (non-syndromic) [3]. In the first case, it results from environmental causes and inherited or de novo chromosomal abnormalities (diabetes, fetal alcoholization, trisomies 13 and 18 ...). In the second case, inherited or de novo autosomal dominant mutations have been identified in 14 genes [8]. However, only 30% of non-syndromic HPE are explained by these mutations[4]. The genetic etiology remains unknown in about 70% of cases.

A distinction is made between the lobar form, which is the most severe form, where only one ventricle is present and the two cerebral hemispheres are not completely separated. The semi-lobar form in which the frontal and parietal lobes are fused with an inter-hemispheric sulcus only present in the posterior part of the brain. The lobar form is a crude form where only the central part of the two hemispheres is fused.

Depending on the type, this anomaly will be associated with variable craniofacial anomalies. In the major alobar form, we note the presence of a cyclopia with proboscis which corresponds to a nasal remnant located above the cyclopia, an agenesis of the maxilla, a cleft lip and palate.
In the semi-lobar form there is a microphthalmia with hypotelorism which is always constant, the other anomalies of the face are present in variable degree.
In the lobar form the facial anomalies are frustrated and rare, only the hypotelorism is visible.
The ante-natal diagnosis is of great interest in this pathology [5], it can be made in the first trimester for the major alobar form. No midline is seen and the choroid plexuses are fused forward. In the 2nd trimester of pregnancy, the fusion of the thalami is visible. A facial scan shows a single orbit above which a proboscis is implanted, a median and maxillary facial cleft, and the absence of a nose. In the semi-lobar form, the diagnosis in the first trimester is difficult and is often made in the second trimester where one finds to varying degrees, a single ventricle which is prolonged posteriorly by occipital horns which are separated and dilated, thalami which seem to be joined without visualization of the 3rd ventricle. The midline is visible on the posterior complex with a cerebellum of normal morphology. The cavum of the septum pillucidum is not visible, the realization of a sagittal section shows the partial absence of the corpus callosum. The morphological study of the face finds a hypotelorism with a cleft lip, this is the case of our patient.
The search for other malformations is necessary [6] [7], so the holoprosencephaly can be isolated or integrated in a syndromic framework. The search for an anomaly of the urinary tree such as a multi-cystic renal dysplasia. Post axial polydactyly with intrauterine growth retardation pointing to trisomy 13 [9].

The prognosis is variable depending on the severity of the malformation; the prognosis is life-threatening and in children who survive, many associated manifestations are described such as developmental delay, hydrocephalus, motor deficits, feeding and swallowing disorders, epilepsy, hypothalamic dysregulation, endocrine disorders of pituitary origin (diabetes insipidus). There are familial forms with a high variability of phenotype within the family.
The treatment consists in proposing an IMG for the forms diagnosed in the 1st trimester,
For the children who survive, the treatment is mainly symptomatic with a short life expectancy.

4. Conclusion

Holoprosencephaly is a rare malformation with a generally poor prognosis, accessible to prenatal diagnosis, by performing an antenatal ultrasound. The signs of which are all the more alarming as the form is rare, after diagnosis an enlightened information must be delivered to the patient with a foetal and maternal follow-up especially psychic.

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