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Major megalencephaly in a15-day-old newborn with Fraser syndrome. One Malagasy case report

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Abstract
Fraser syndrome is a rare polymalformative genetic. The cryptophtalmia is the most common abnormality of this genetic disease. We report a case of Fraser syndrome presenting a complex symptomatology associating megalencephaly, bilateral cryptophthalmia with right microphthalmia and probable left coloboma with associated epidermoid cyst. The antenatal screening of this malformation syndrome remains precarious in Madagascar.

Keywords: cryptophtalmia, Fraser, megalencephaly, syndactily

1. Introduction
Fraser syndrome is a rare polymalformative genetic syndrome whose diagnosis associates the presence of two major criteria and a minor or one major criterion and four minor criteria [1]. The cryptophtalmia is the most common abnormality of this genetic disease. There are other abnormalities determining the diagnostic criteria (uro-genital, cardiac, musculoskeletal,...).
The antenatal screening of this malformation syndrome remains precarious in Madagascar. We report a case of Fraser syndrome presenting a complex symptomatology associating megalencephaly, bilateral cryptophthalmia with right microphthalmia and probable left coloboma with associated epidermoid cyst.

2. Materials and methods
This is a newborn male 12 day term, admitted to our service for polymalformative syndrome. No consanguineous marriage according to the family. But this is a 5th parity with another live child with hydrocephalus whose origin was not mentioned. Spontaneous miscarriage occurred during the first pregnancy, and 2 stillbirths with unspecified polymalformative syndrome. Pregnancy was followed by regular pre-natal consultations with four ultrasound examinations without morphological study. There were no complications during delivery.
The new-born had bilateral cryptophthalmia with ear malformation (otocephaly) and enlargement of the base of the nose, syndactyly of the fingers and toes; an umbilical hernia (Figure 1), a cleft palate, and small voice. No difficulty during breastfeeding.
The CT scan objectified a right microphthalmia, an eyeball left of normal size but connected to a rounded hypodense training sub-palpebral making evoke a dermoid cyst associated with a coloboma; hypertrophy of the cerebral hemispheres with predominant left pachygyrie with a mass effect on the tent of the cerebellum; agenesis of corpus callosum; widening of cranial sutures and absence of ethmoid bone and right parietal bone (Figure 2).
Transfontanellar ultrasound showed agenesis of the corpus callosum.
The abdominal and pelvic ultrasound revealed hyperechoic renal parenchyma, losing their fetal lobulation (Figure 3).
A cardiac ultrasound was performed but with normal result.
The child is hospitalized in the pediatric surgery department.

3. Discussion
Nowadays, more than 300 cases of Fraser syndrome have been reported; with different clinical and radiological aspects. It is a genetic disease with autosomal recessive inheritance [2] which, according to the literature, consanguinity of parents constitutes 15 to 24.8 % of the etiopathogenesis (2,). In our case, the absence of consanguinity between the two parents was confirmed by the family but not verified in the absence of a genetic test.
According to the diagnostic criteria, defined by Thomas *et al*. the Fraser syndrome diagnosis is affirmed by the presence of at least two major criteria and a minor or major criterion and three minor criteria [4]. The major criteria include cryptophthalmia, syndactyly, genital abnormalities and antecedents of the same symptoms in siblings [4, 5]. The minor criteria include skeletal abnormalities, umbilical hernia, renal agenesis, cleft lip and palate, mental retardation and more rarely brain abnormalities such as: hydrocephalus, abnormality of gyration, encephalocele..... (3, 4, 5). Our patient has two major criteria and six minor criteria that we have included ultrasound abnormality of the kidneys on ultrasound, otocephaly and megalencephaly on diffuse pachygyria.
In the antenatal diagnosis of this syndrome, oligoamnios is the

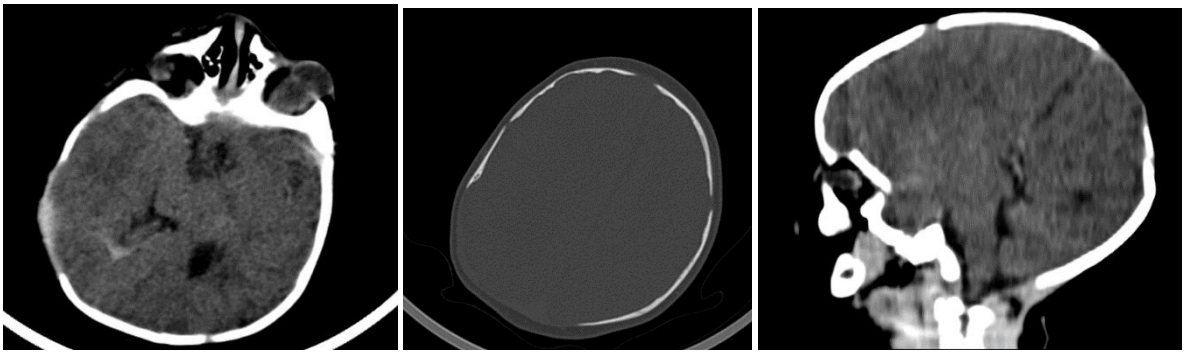
first sign to look for with hyperechogenicity of the lungs, then non-visualization of the kidneys, microphthalmia and syndactyly. This antenatal diagnosis is based on obstetrical ultrasound with fetal morphological study from 20 weeks of amenorrhea (5). Several ultrasonographic follow-ups were performed in our patient during the antenatal period, but no particular anomaly was reported.

The malformations associated with Fraser syndrome are multiple but the cardinal sign is cryptophthalmia. It is therefore essential to differentiate between other syndromes that have cryptophthalmia without syndactyly such as “blépharophimosis syndrome " which is a rare congenital orbito-palpebral malformation, characterized by depression and flattening of the orbit associated with malformations of the eyelids (epicanthus, telecanthus, ptosis) and characteristic eyebrows arched and hypertrichosic (6). There is also the palpebral coloboma, which is defined by a deficiency of the palpebral margin (6).

The treatment of Fraser syndrome, which has a clinical polymorphism, requires a multidisciplinary approach but is based on surgery (7). The therapeutic decision for our patient, still a problem in developing countries like ours, will depend on the technical and human resources of the hospital and especially the financial resources of the family.

4. Tables and Figures

Fig 1(A): bilateral cryptophtalmia, otocephaly, nasal droop and nostril enlargement. (B) Umbilical herniation, syndactyly.



A B C

Fig 2: CT scan without contrast agent injection showing (A) right microphthalmia, left normal sized left eyeball connected with a cystic palpebral structure, (B) right occipital bone defect with widening of the sutures, (C) agenesis of the corpus callosum

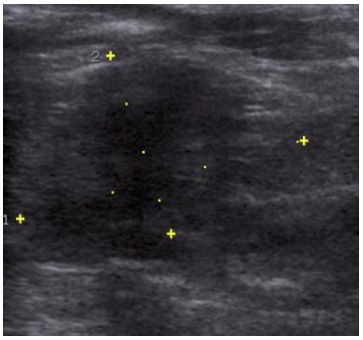


Fig 3: Renal ultrasound showing hyperechogenicity of the renal parenchyma and loss of foetal lobulation

5. Conclusions

Fraser syndrome is a rare polymalformative genetic syndrome that can be diagnosed in the antenatal period by some signs and in the postnatal period by clinical criteria. The prenatal diagnosis and treatment of this syndrome are still a challenge in developing countries like Madagascar.

6. References

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