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Cerebro-Oculo-Facio-Skeletal (COFS) Syndrome: Case Report

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Abstract **Case Report**

Cerebro-oculo-facio-skeletal (COFS) syndrome is an autosomal recessive genetic degenerative disorder of the brain and spinal cord that begins before birth. The originality of our clinical case is that the diagnosis of COFS was made in a 25 weeks and 5 days, on the basis of antenatal imagery data (ultrasound and specific MRI), namely an overall atrophy of the cerebral parenchyma and Ponto-cerebella under arachnoidians with cataract.

Keywords: COFS syndrome, antenatal diagnosis, ultrasound, MRI, brain atrophy.

INTRODUCTION

Congenital cataract is a rare disease with an estimated incidence of 0,5 % birth. This is an anomaly in the transparency of the cristallin existing at birth. It is an obstacle to visual development that can lead to amblyopia and binocular vision impairment. It can affect psychomotor acquisitions.

According to World Health Organization (WHO) estimates, about 80 % of cases of blindness are preventable and congenital cataracts account for a large proportion. It is responsible for 10% of the blindness of the child and 4 % of that of the adult. Systematic rubella vaccination decreased the rate of congenital cataract caused by this maternal infection by 20 % to 1 % [1]. Knowledge of the various personal and family, pre- and perinatal risk factors is crucial in attempting to reduce the incidence of this condition.

The diagnosis of congenital cataract can be made in antenatal during fetal ultrasound surveillance during pregnancy. The ultrasound shows an increase in the echogenicity of the center of the lens. This is supplemented at best by a fetal cerebral magnetic resonance imaging (MRI) and a serological check-up.

Different clinical forms may occur, ranging from isolated cataracts without ocular or systemic anomalies to cataracts with ocular anomalies and/or polymalformative syndromes, to skeletal diseases, dermatological, neurological, metabolic, genetic or chromosomal abnormalitie. Here we report a case of congenital cataract in the cerebro-oculo-Facio-Skeletal (COFS) syndrome diagnosed in antenatal.

CASE REPORT

Mrs B.S, 26 -year-old patient, primipara, was referred to us for reference ultrasound at 25 weeks and 5 days following the discovery in morphological ultrasound of a fetal hypotrophy with left wrist fixed in bending. There was no personal or family history in the couple, except for second-degree inbreeding. For the prenatal check-up, the patient was immunized against rubella but not toxoplasmosis, hepatitis B and syphilis serologies were negative. The triple test for chromosomal removal was not done. Early ultrasound was consistent with term with nuchal clarity at 1, 2 mm.

The ultrasound control recovered a harmonious growth retardation of 5 weeks, clubfeet and left hand stretched, hydramnios with an unobserved stomach and finally, a hyperechogenic and thickened appearance of both lens in favour of congenital cataracts with no other abnormalities of the face **(Figure1-2-3).**

A fetal Magnetic Resonance Imaging (MRI) was requested and that objectified a global atrophy of cerebral parenchyma and Ponto-cerebellar subarachnoid with cataract and clubfeet **(Figure 4-5).**

The decision was to complete with an amniocentesis and then make a therapeutic termination of the pregnancy by misoprostol. The amniocentesis

showed a normal karyotype 46, XX. The delivery took place at 29 weeks by cesarean section for failure to trigger. The examination at birth found a newborn female, Apgar 1/1/1, with hypotrophy (400 gr), bilateral cataract, arthrogryposis and microcephaly **(Figure 6).** The death occurred 40 minutes ago.

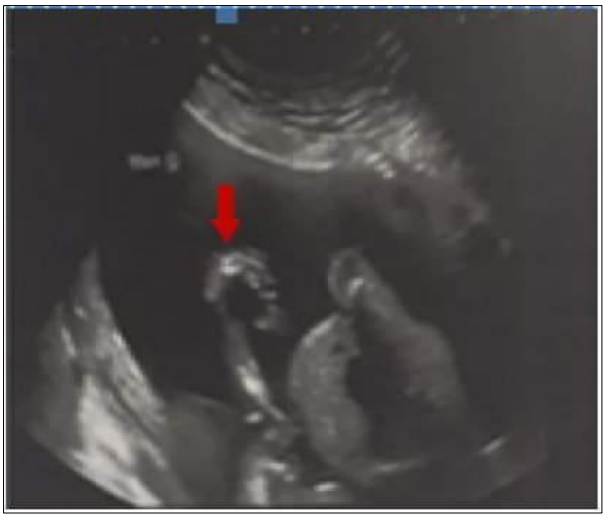

Figure 1

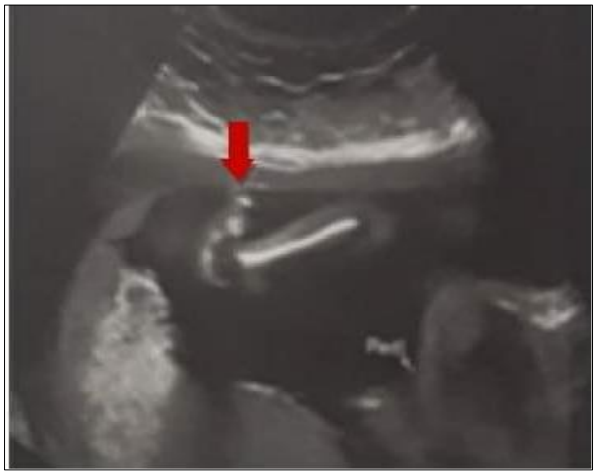

Figure 2: Left hand is motionless and stretched on ultrasound

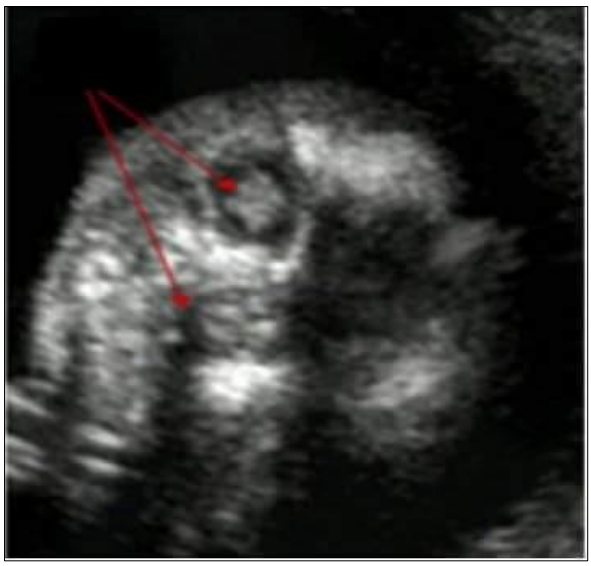

Figure 3: Ultrasound appearance of a clubfoot

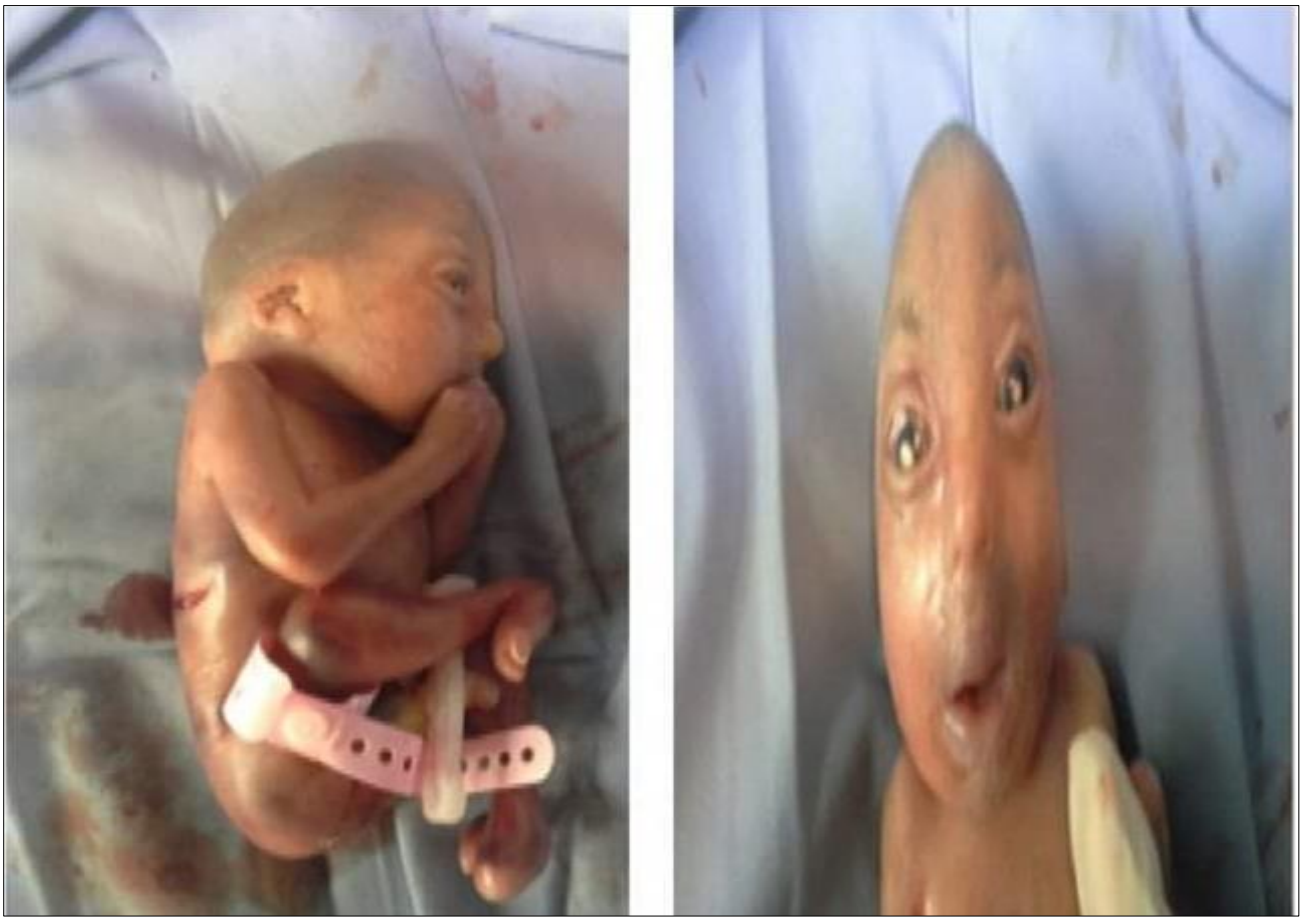

Figure 4: Aspect of global atrophy of the cerebral parenchyma and the ponto-cerebellar subarachnoid parenchyma in fetal magnetic resonance imaging.

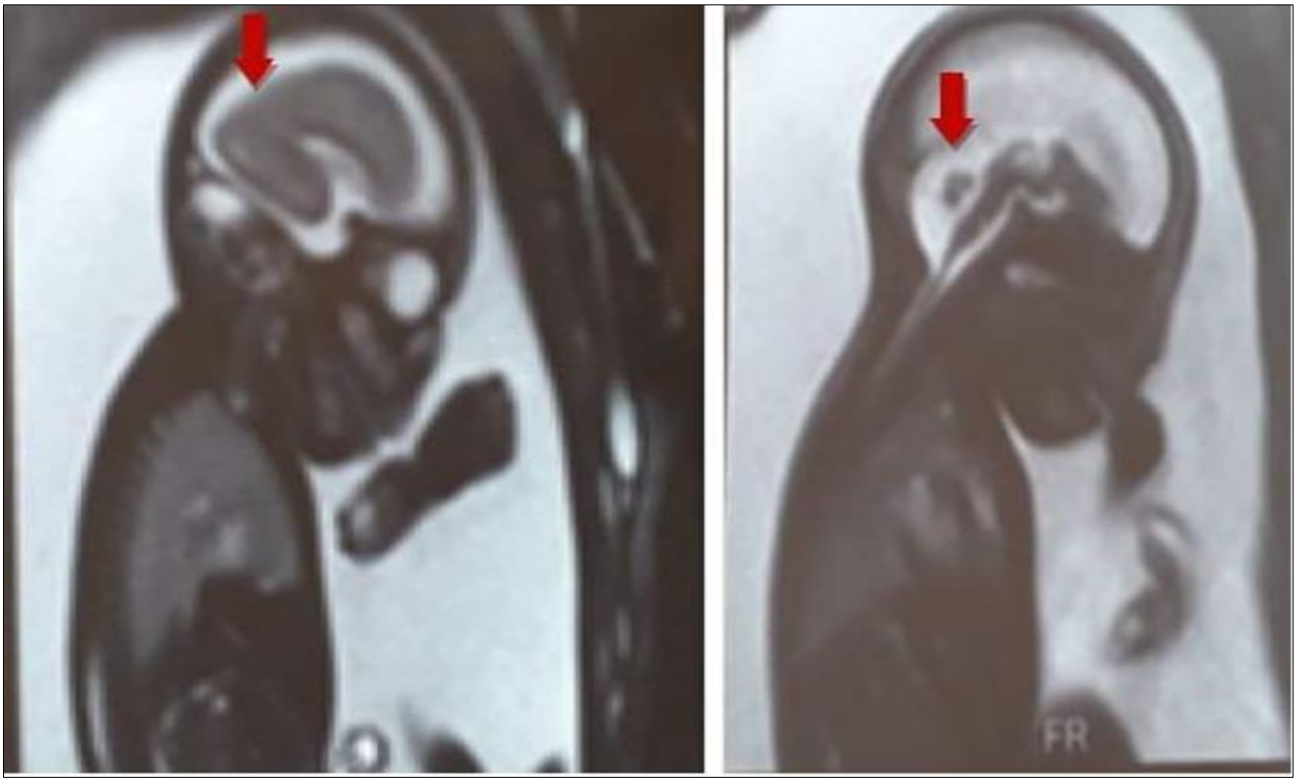

Figure 5: Cataract imaging in fetal MRI

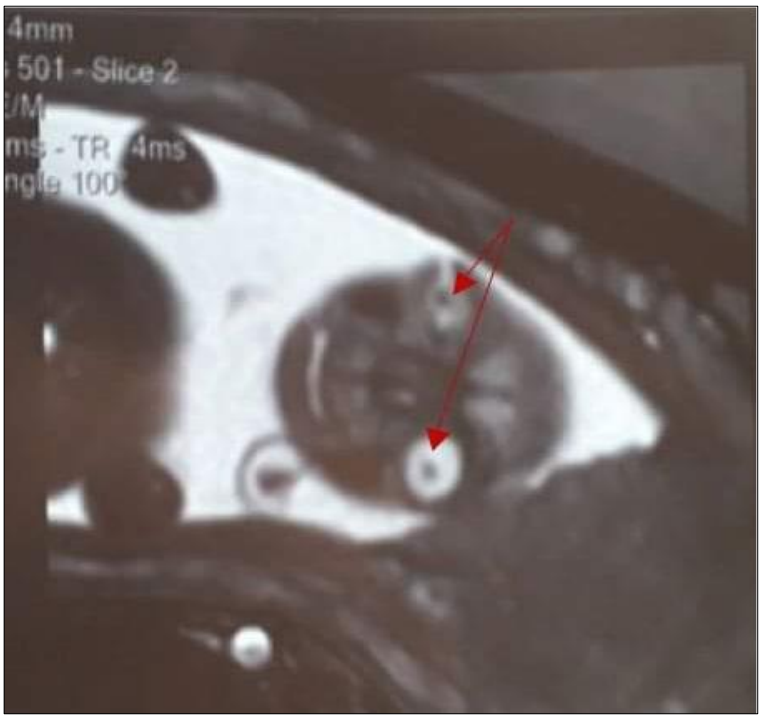

Figure 6: Neonatal aspect of a malformed fetus with arthrogryposis, microcephaly and cataracts

DISCUSSION

There are four etiological forms of congenital cataracts: idiopathic cataract, genetic cataract, cataract following intrauterine infection and cataract following intrauterine toxic exposure. The genetic form includes isolated cataracts with a family history and cataracts associated with a genetic disease. The form of cataract associated with genetic disease is represented by trisomy 21, Lowe's syndrome, aniridia, Conradi's syndrome, Nance Horan's syndrome, galactosemia, Cockayne's syndrome, trisomy3 syndrome, Marfan's syndrome, Turner's syndrome and COFS syndrome [2]. The latter is the case of our patient. COFS syndrome is a very rare disorder present at birth with about 50 cases reported in theliterature. It affects men and women and affects many ethnic groups. It is an autosomal recessive genetic disorder [1].

This syndrome was first described by Pena and Shokeir in 1974. It is a rapidly developing neurological disorder that results in brain atrophy, with calcifications, cataracts, microcornea, optic atrophy, progressive joint contractures and growth retardation [3].

The appearance of people affected by COFS syndrome is relatively characteristic and includes the following major diagnostic criteria: Microcephaly; ocular anomalies including cataracts, microphthalmia, optic atrophy, and blepharophimosis [3], dysmorphic facies with a high and wide nasal bridge, large ears, overhanging upper lip and micrognathia; and lastly, musculoskeletal anomalies, including contractures of flexion of the limbs (arthrogryposis), scoliosis, dysplasia or dislocation of the hip, narrow pelvis, short waist, osteoporosis, dysplastic acetaphas, and the lower feet of the pendulum with proximal displacement of the second metatarsals and longitudinal grooves in the soles along the second metatarsal [4-5].

Neuropathology studies published in the first publications on COFS syndrome revealed generalized subcortical gliosis and a decrease in white matter with reduced myelin content [3].

Other features of this disorder include broad nipples, stunted growth, hypotony, feeding difficulties and a line in the palm of the hand formed by the fusion of the two usual lines (simian fold). Children with COFS syndrome have an increased vulnerability to respiratory infections. They show progressive deterioration and rarely survive beyond seven years [1].

The relationship between COFSS and differential diagnoses, Cockayne syndrome (CS), Pena-Shokier phenotype (PSP) and Neu-Lexova syndrome (NLS) are discussed. Pre-natal diagnosis followed by appropriate management in time may be helpful to reduce its incidence in the community [6]. Currently, the diagnosis of COFS syndrome is based on a phenotypic description coupled with a skeletal study and a neuroradiological check-up.

It is important to emphasize that since contractures, microphtalmia and micrognathia can all be detected by ultrasound, it is possible to makecorrect

differential diagnosis between complex related syndrome. This can be done by considering the major ultrasound findings, comparing them with the specific phenotypes of the disorders contributing to the differential diagnosis, and returning to ultrasound to look for possible minor anomalies wich would support the final diagnosis [7].

Fetal MRI has its place in cases of evocative ultrasound abnormalities due to greater specificity and precision.The originality of our clinical case is due to the fact that the diagnosis of COFS was made on the basis of specific fetal MRI data, namely an overall atrophy of the cerebral parenchyma and Ponto-cerebella under arachnoidians with cataract. MRI is valuable in identifying and following cerebral and cerebellar atrophy and loss of white matter [8]. Magnetic resonance spectrometry (MRS) has been used to demonstrate atrophy and hypo- or demyelination of white matter in affected patients [9].

DNA repair studies on fibroblast skin cells can help confirm a diagnosis of COFS syndrome but it will be a post-natal diagnosis. Molecular genetic tests to identify mutations in excision repair genes are available on a research basis only [7]. Treatment of COFS syndrome is symptomatic and supportive. Genetic counselling is recommended for families of affected children.

CONCLUSION

This case represents the interest of MRI for prenatal diagnosis of COFS syndrome suspected on ultrasound. This case demonstrates the feasibility of such a diagnosis by ultrasound and MRI identifies the malformations already present and detectable at mid-gestation.

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