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SOFT MARKERS IN THE PRENATAL SONOGRAPHIC DIAGNOSIS OF EDWARDS SYNDROME: A CASE REPORT

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ABSTRACT: Trisomy 18, also known as Edwards syndrome, is the second most common autosomal trisomy after trisomy 21. It is a severe syndrome with a high neonatal and infant mortality and the management of the affected babies is usually challenging. With the advent of prenatal screening for congenital anomalies, some sonographic findings termed soft markers have been linked with the syndrome. If these soft markers are detected during ultrasound scanning, further scanning should be done to rule out other structural anomalies and karyotyping should be offered to the mother for confirmation. Once the diagnosis is made and the mother counselled on the severity of the syndrome, an informed decision could then be made. We present a foetus with ultrasound findings of two soft markers- choroid plexus cysts and echogenic bowel - with associated congenital heart disease during prenatal ultrasound screening. Genetic studies after delivery confirmed trisomy 18.

KEYWORDS: Soft Markers, Prenatal Sonographic Diagnosis, Edwards Syndrome

INTRODUCTION: Soft markers are sonographic findings with little or no pathological significance, and they are not usually associated with any handicaps, unless there are associated structural abnormalities pointing to aneuploidy. [1,2]

The commonly studied soft markers include mild ventriculomegaly, choroid plexus cyst, absent or hypoplastic nasal bone, a thickened nuchal fold, intracardiac echogenic focus, echogenic bowel, short long bones, pyelectasis, and single umbilical artery. Some recent studies have proposed that these soft markers should be called normal variants if there are no associated anomalies. [2] However, the presence of more than one soft marker with or without major anomalies should make the sonologist suspect an aneuploidy. [2,3]

Choroid plexus cyst (CPC) has been associated with the risk of trisomies 18 and 21, while echogenic bowel (EB) is commonly associated with trisomy 21 but rarely with trisomy 18. [2,3] We present a foetus with ultrasound findings of CPC, EB and congenital heart disease during prenatal ultrasound screening. Genetic studies after delivery reportedly confirmed trisomy 18.

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CASE STUDY

A 35-year-old G4P3+0 (3 alive) was referred to the ultrasound unit of the antenatal clinic of University College Hospital, Ibadan, at gestational age of 21weeks, for anomaly ultrasound scan on account of suspicion of bilateral ventriculomegaly in the foetus from an ultrasound scan from a private facility.

She booked for antenatal care in the index pregnancy at 8-week gestation. There was no exposure to any known teratogenic agent, and there is no previous history of a child with congenital anomaly. She is not a known diabetic or hypertensive patient. She has had two previous caesarean sections.

Ultrasound scan done at 20 and 24 weeks revealed bilateral choroid plexus cysts (figure 1) and echogenic bowel loops (figure 2) respectively. Foetal echocardiogram was done by 23 weeks and it showed an inlet Ventricular Septal Defect (VSD). A diagnosis of a possible chromosomal abnormality was made, but this could not be confirmed because karyotyping is not readily available to confirm chromosomal disorder.

The foetus developed intrauterine growth retardation at 32 weeks' gestation. Mother developed severe preeclampsia at 34 weeks' gestation and she had an emergency lower segment caesarian section of which she delivered a live female baby weighing 1.2kg. Examining the baby, she had clenched fingers and low set ears. Echocardiography done confirmed the VSD.

Baby was admitted into the special care baby unit of the hospital on account of recurrent apneic attacks. She had an open-heart surgery for the VSD at 3 months old outside Nigeria and genetic study done during her management outside the country confirmed Edwards syndrome. Baby failed to thrive, at 3 years of age when this case report was written, she had only achieved neck control and sat with support.

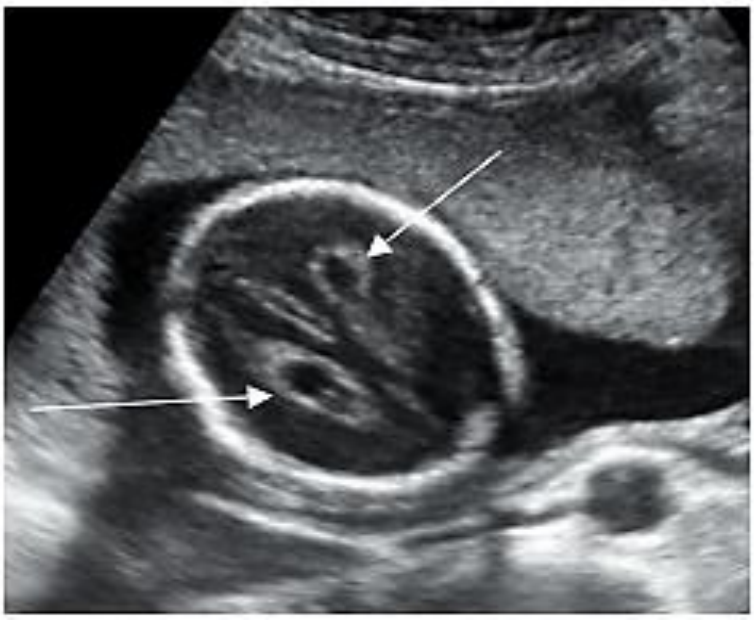

Figure 1: Transabdominal ultrasound of the head of the fetus at 20 weeks showing cysts (arrows) within the choroid plexus bilaterally

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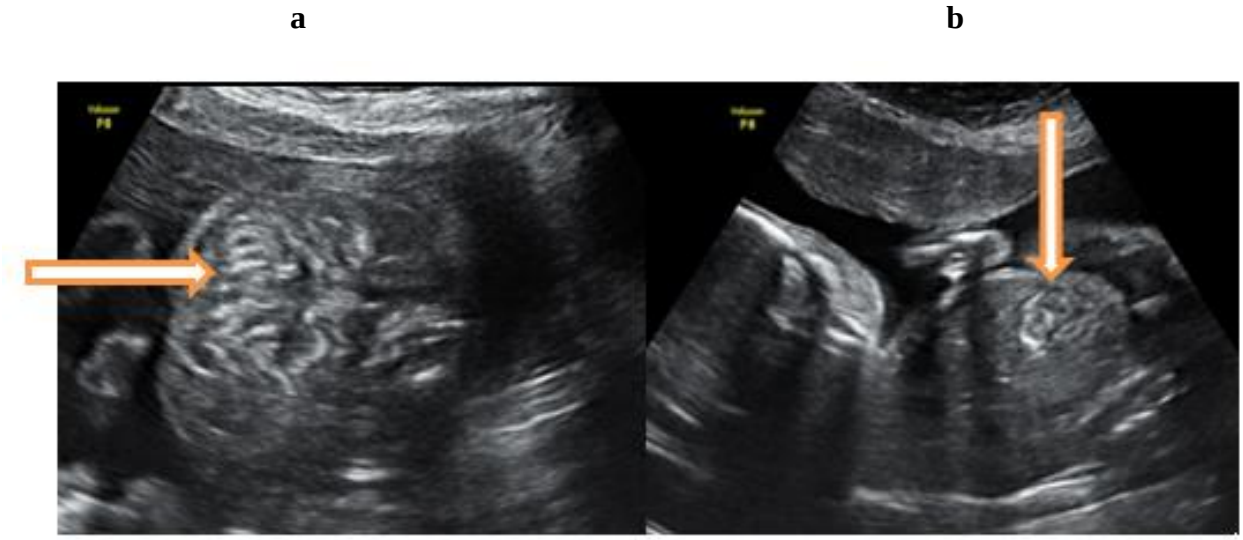

Figure 2: Transabdominal Ultrasound of the abdomen of the fetus at 24 weeks GA (a)transverse and (b) sagittal views showing the echogenic bowel (arrows)

DISCUSSION

Trisomy 18, also known as Edwards syndrome, is a common chromosomal disorder due to the presence of an extra chromosome 18, either full, mosaic trisomy, or partial trisomy 18q. [4] It is the second most common autosomal trisomy syndrome after trisomy 21. The prevalence is estimated as 1/6,000-1/8,000/live births, but the overall prevalence is higher (1/2500-1/2600) due to a high frequency of early fetal loss and pregnancy termination after prenatal diagnosis. [4,5]

The risk factors for having a child with trisomy 18 include increasing maternal age and history of a child with full trisomy 18. [5] The mother in the presented case was 35 years but there was no history of a previous child with aneuploidy.

Currently, most cases of trisomy 18 are diagnosed prenatally either by maternal serum marker screening or detection of ultrasonographic abnormalities.[4,5] However, ultrasound scan for fetal anomalies has been found to be the most effective screening test for trisomy 18 during which two types of markers are detected. These are soft markers for aneuploidy and major structural abnormalities. [5] The soft markers include increased nuchal translucency thickness, choroid plexus cysts, single umbilical artery and rarely echogenic bowel. While the major structural abnormalities include overlapping of fingers, congenital heart defects, clenched fists, brachycephaly, low set ears and rock bottom feet. [5,6] Choroid plexus cyst and echogenic bowel were the soft markers detected in the index case, while the only major anomaly detected prenatally was a major cardiac anomaly- ventricular septal disease. Some other major anomalies (clenched fist and low set ears) were detected after delivery.

The presence of a choroid plexus cyst has been associated with increased risk of trisomy 18, and studies have shown that up to 70% of trisomy 18 fetuses have CPC.[5.6] The CPC are fluid

accumulation seen within the substance of the choroid plexus. They can be single or multiple, unilateral or bilateral. They could be small or large. When very large it could be misdiagnosed as ventriculomegaly. [6] The presented case was referred on account of suspected ventriculomegaly which was later confirmed to be CPC. CPC can even be the only abnormality detected at ultrasound screening, which is termed isolated CPC but most cases are usually associated with additional sonographic abnormalities as in the patient presented. [7]

The diagnosis of echogenic bowel is made when the echogenicity of the fetal bowel is equal to or greater than the echogenicity of the surrounding bone. Its presence has been associated with trisomy 21 but rarely with trisomy 18. Very few studies have however reported its association with trisomy 18. [7,9] It was one of the soft markers detected in the index case.

Intrauterine growth retardation is one of the most frequent prenatal findings in trisomy 18 with a mean birth weight of 1700-1800 g at a mean gestational age of 37 weeks. Also, there could be preterm delivery, 35% higher compared to the general population.[4,7] The case presented had intrauterine fetal growth retardation and subsequent preterm delivery because mother developed preeclampsia. Baby weighed 1200g at 34weeks GA which was below the 10th percentile.

About 50% of trisomy 18 infants die within the first week of life while the majority of the remaining ones die in the next 12 months. Only 5-10% of the affected children will survive beyond the first year[8]. Seldom has an affected individual survived for ten or more years.[10] The early neonatal death is attributed to central apnea, upper airway obstruction, respiratory insufficiency, aspiration, cardiac failure, or a combination of these and other factors [10,11. However, those who survive end up having marked psychomotor and cognitive developmental delay. [9] In our case, as of the time of writing this case report, the baby is still alive at 3 years of age but yet to achieve any significant developmental milestone.

The diagnosis of trisomy 18 is usually done prenatally with amniocentesis in the developed countries. [5,12] This is not readily available in our environment; in our patient the diagnosis was made outside the country when the baby went for cardiac surgery.

CONCLUSION

We have presented a case of a fetus with prenatal suspicion of a chromosomal disorder because of the presence of sonographic soft markers- choroid plexus cysts and echogenic bowel, as well as ventricular septal defect. The diagnosis of Edwards syndrome was made after delivery because karyotyping is not readily available in the country.

RECOMMENDATION

In a resource poor country, like ours, where karyotyping for the diagnosis of chromosomal disorders is not readily available, the presence of soft markers with additional major congenital anomalies should make the managing team to suspect a chromosomal disorder, which should be explained to the parents to help them in making an informed decision on the pregnancy.

Conflict of interest: The authors declare no conflict of interest.

Authors' Contributions: Both authors were involved in the design of the study and drafting of the manuscript. Both authors approved the final version of the manuscript.

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