



Dextroposition of the Heart Reflected Mosaic Fetal Trisomy 18

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Abstract

Introduction: Trisomy 18 in every cell is associated with multiple congenital anomalies.

Case: Anatomy scan of a 22 year old prima gravida at 19w4d showed a viable IUP with unilateral choroid plexus cyst and dextroposition of the heart without any other observed structural malformation. Amniocentesis revealed a normal male pattern for chromosomes 13, 18, 21, X and Y by fluorescence in situ hybridization (FISH). However, chromosomal microarray analysis (CMA) for circulating fetal DNA in maternal blood was consistent with mosaic Trisomy 18. The karyotype of cultured dividing cells confirmed 47, XY, +18/46, XY mosaicism.

Conclusion: Dextroposition of the heart (dextrocardia) identified by ultrasound prompted fetal DNA screening plus subsequent amniocyte analysis that together confirmed mosaic fetal aneuploidy.

Many studies show that 80%-100% of patients with trisomy 18 have congenital structural heart defects. In these fetuses, the common heart defects detected by prenatal ultrasonography are ventricular septal defect, patent ductus arteriosus, atrial septal defect and complex congenital heart defects [12-15]. The most common brain lesions observed by prenatal ultrasound are cerebellar hypoplasia, mega cisterna magna and choroid plexus cysts [12].

Cardiac malposition is a rare but important finding when detected on fetal ultrasound. Dextroposition of the heart is a congenital anomaly in which the heart is positioned in the right chest but normally oriented, with the cardiac apex pointing to the left. Dextroposition of the heart is almost always associated with intrathoracic malformations. The most common malformations are: left congenital diaphragmatic hernia (75%), cystic adenomatoid malformations located in the left chest (19%), and other pulmonary malformations (6%) [16].

Introduction

Trisomy 18 or Edwards's syndrome is a rare chromosomal anomaly due to the presence of an extra chromosome 18 defining full or mosaic trisomy 18 [1]. The first reported infants were described in 1960 by Edwards et al. and Smith et al. [2,3] resulting in 1 in 5500 live births [4,5] with a 3:1 female to male ratio. The abnormality results from meiotic nondisjunction that is enhanced in frequency by advanced maternal age. The ~10% of trisomy 18 fetuses that survive to birth have substantially reduced survival with a median survival range of 3 to 14.5 days [1,6,7].

Trisomy 18 is typically associated with multiple congenital anomalies. Currently in the North America and Europe most cases of trisomy 18 are prenatally diagnosed, based on screening by maternal age, maternal serum marker screening, or detection of sonographic abnormalities during the second and third trimester [8,9]. The prenatal sonographic pattern of trisomy 18 is characterized by growth restriction, polyhydramnios, "strawberry-shaped" cranium (brachycephaly and narrow frontal cranium), choroid plexus cysts, overlapping of hands fingers (second and fifth on third and fourth respectively), congenital heart defects, omphalocele, and single umbilical artery [9-11].

Case

A 22 year old prima gravida patient received a viability ultrasound in the Obstetrics and Gynecology Department at 13 weeks 4 days to test for any obvious phenotypic abnormalities. Simultaneously she declined any aneuploidy screening. Subsequently she was completed regular prenatal visits in the antenatal care clinic. She had her next ultrasound at 19 weeks 4 days at which time she also had a mid-trimester anatomy scan. The viable intrauterine pregnancy was noted to be accompanied by a unilateral choroid plexus cyst (Figure 1) along with dextroposition of the heart (Figure 2). The fetal heart was in the right hemithorax without discrete mass lesions in the left hemithorax while the stomach was appropriately positioned in the left upper quadrant and the diaphragm appeared intact. No complex cardiac defects or other structural malformations were identified (Figure 3 and Figure 4). Estimated fetal weight was appropriate for gestational age (Figure 5). These findings were discussed and all prenatal testing options were reviewed with the patient and her spouse. At 20 weeks 4 days a repeated ultrasound showed isolated dextroposition of the heart with the choroid plexus cyst no longer being evident. At that time the patient requested and completed amniocentesis. Amniotic fluid alpha fetoprotein levels were also

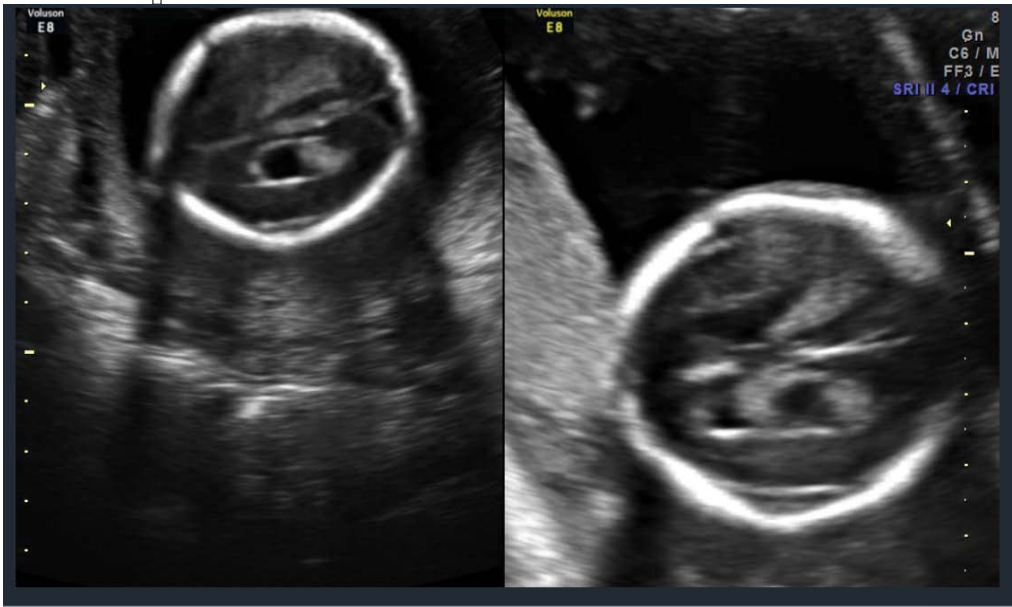


Figure 1: Pictures of choroid plexus cyst.

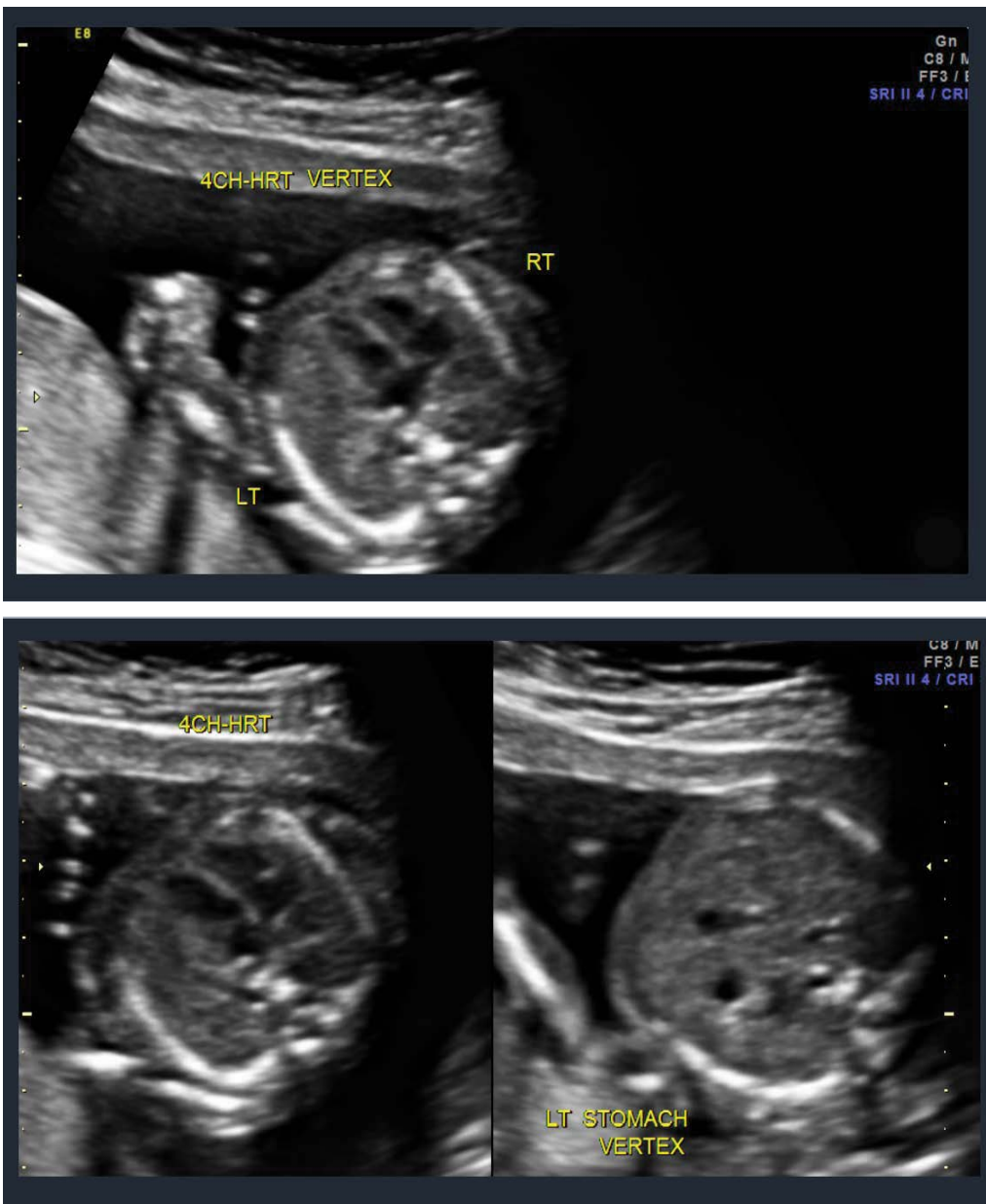


Figure 2: Pictures of the dextroposition of the heart.

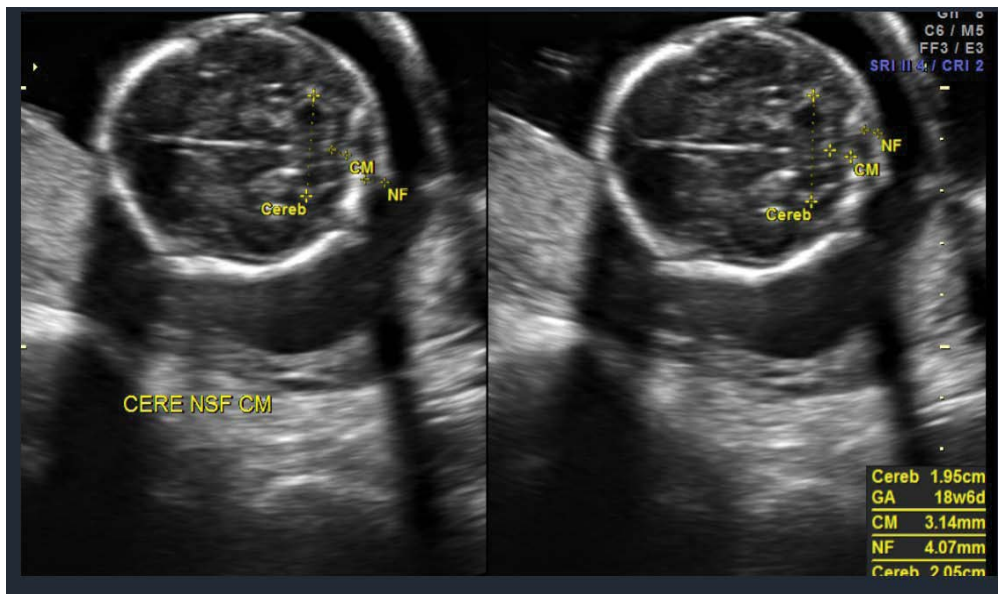


Figure 3: Pictures of normal calvarial counter without strawberry shaped skull.

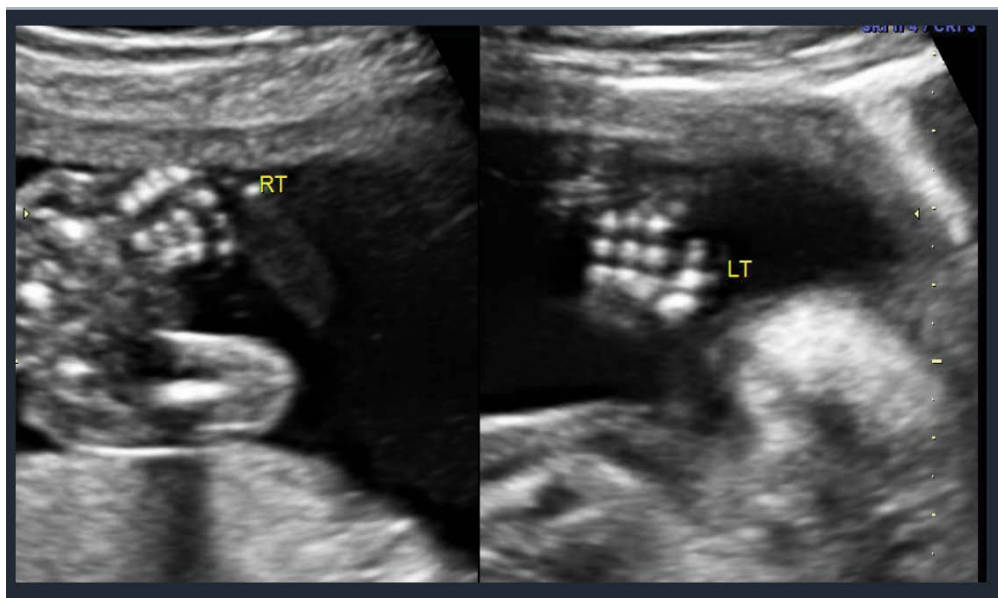


Figure 4: Pictures of normal hands without overlapping digits.

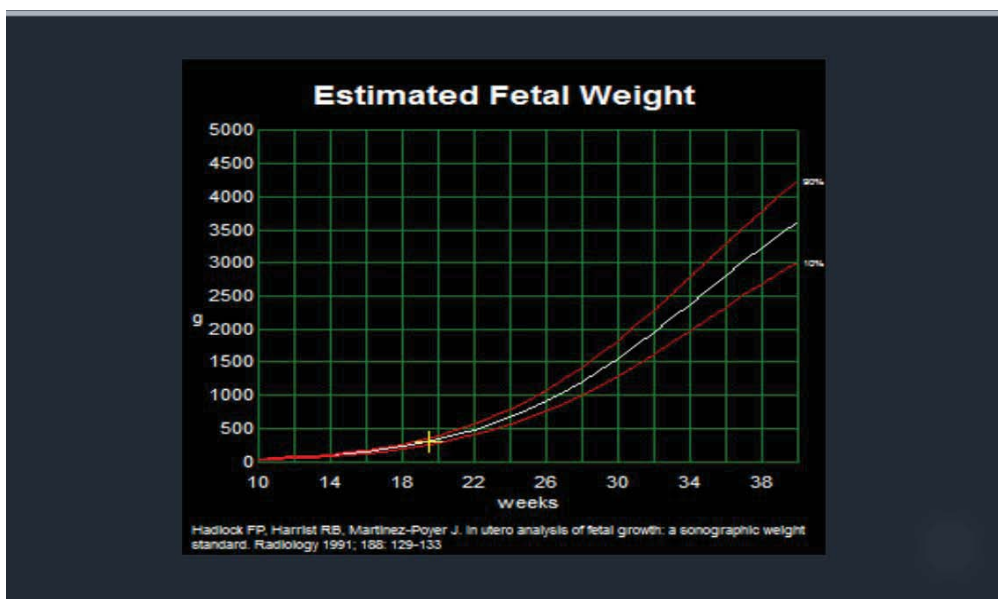


Figure 5: Picture of normal growth chart.

normal. Initial cytogenetic analysis for common chromosome aneuploidy revealed a normal male pattern for chromosomes 13, 18, 21, X and Y by fluorescence in situ hybridization (FISH). However, the chromosomal microarray analysis (CMA) suggested mosaic Trisomy 18. An abbreviated karyotype subsequently confirmed three copies of chromosome 18 in three out of four metaphase cells confirming 47,XY,+18/46,XY mosaicism. The patient elected to terminate the pregnancy based upon these results, Dilution and evacuation (D&E) was completed at 22 weeks and 4 days. The autopsy revealed: Normal heart in shape and size. Left pulmonary artery, aortic trunk with valve and atrial septum are disrupted. The right pulmonary artery is intact and normal. The left atrial appendages are normal in shape and consistent with normal isomerism. The mitral, pulmonic and tricuspid valves are normal. There is no ventricular septal defect. Heart anomalies are not identified. However, the examination was suboptimal due to fetal disruption secondary to the (D&E) procedure.

Conclusion

Mosaicism reported in ~2% of all CVS biopsies is confined to the placenta in ~4 of 5 cases and modifies fetal cells in the remaining ~1 in 5 cases [17]. Mosaicism can involve all chromosome abnormalities from whole chromosome aneuploidy to aneuploidy gene on chromosome regions. Chromosome karyotypes most reliably illustrate visible chromosome abnormalities in the clearly banded proportion of mosaic cells in the sampled dividing cellular tissue. In contrast, fluorescence in situ hybridization may not detect a very low proportion of mosaicism in poor quality interphase nuclei. The proportion of mosaicism in each result depends upon sample quality and available time to isolate mitotic cells.

The trisomy 18 amniocyte karyotypes confirm the fetus has true trisomy 18 mosaicism. A wide diversity of sonographic abnormalities has been reported for Trisomy 18 during positive mid-trimester anatomic surveys. However, no known case had been reported for heart dextroposition reflecting mosaic trisomy 18. Our future identification of heart dextroposition will include consideration of testing for fetal gene aneuploidy.

Conflicts of Interest

None of the authors have any conflicts of interest.

Precise

This article demonstrates true trisomy 18 fetal mosaicism with an abnormal cardiac phenotype.

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