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A case of recurrent anterior abdominal wall defects and other congenital anomalies and autosomal recessive genetic disorder

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Objective

Recurrence of anterior abdominal wall defects in multiple pregnancies is rare. Familial chromosomal aberrations and Beckwith-Wiedemann syndrome have previously been reported with recurrent ventral abdominal wall defects. This case report demonstrates the probability of a rare gene mutations involved in causation on anterior abdominal wall defects.

Methods

A consanguineous (first-cousin) healthy, Indian couple presented in their fourth pregnancy. The first pregnancy was diagnosed with a large omphalocoele at 16 weeks and a medical termination of pregnancy was performed. The third pregnancy resulted in the birth of a healthy daughter. The second and fourth were diagnosed antenatally with identical multiple anomalies including increased nuchal translucency (first trimester), micrognathia, omphalocoele/ umbilical hernia, IUGR and bilateral choroid plexus cysts (second trimester). Genetic counselling and DNA storage from antenatal CVS sampling was done before the couple opted to discontinue the fourth pregnancy. Postnatal examination of the fetus confirmed the antenatal findings. Whole exome sequencing of stored fetal DNA revealed bi-allelic pathogenic nonsense variations in FTO gene (c.964C>T variant in exon 5 of fat mass and obesity-associated gene (FTO, OMIM 610966). Carrier status in both parents was confirmed by Sanger sequencing. Genetic counselling regarding 1 in 4 recurrence risks in a future pregnancy and availability of definitive prenatal diagnosis and/or pre-implantation genetic diagnosis was discussed with the family.

Results

Pathogenic variations in both copies of the FTO gene causes an autosomal recessive multiple congenital anomaly syndrome characterized by severe growth retardation, developmental delay, facial dysmorphism (GDFD) with anterior abdominal wall and congenital heart defects (OMIM 612938). Homozygous or compound heterozygous mutations in FTO gene, which encodes for an iron and 2-oxoglutarate-dependent oxygenase, have been identified in only two previous families till date. It is characterized by various multisystem congenital anomalies which includes severe antenatal growth restriction, facial dysmorphism, cardiac, CNS anomalies and anterior abdominal wall defects, also seen in our case.

Conclusion

This report highlights another cause for recurrent abdominal wall defects as a part of a multiple congenital anomaly syndrome inherited in autosomal recessive pattern.