Pathogenic Variants Detected by Chromosomal Microarray in Variety of Abnormal Fetal Ultrasound Findings

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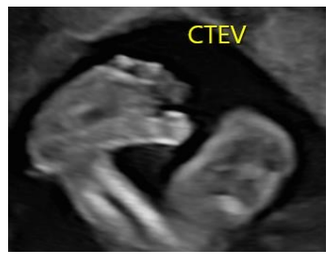
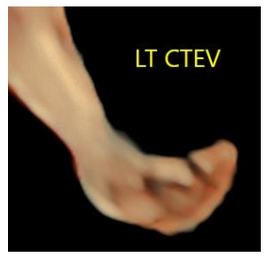
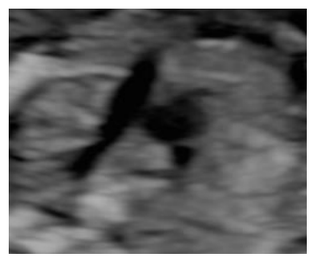
Introduction: In prenatal diagnostic samples with a **normal karyotype**, chromosomal microarray will diagnose a clinically significant sub-microscopic chromosomal deletion or duplication in approximately **1% of structurally normal pregnancies and 6% with structural anomaly**. It is capable of detecting copy number variations (CNVs) with much higher resolution compared to Karyotype.

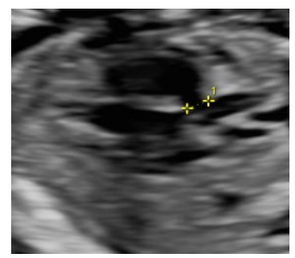
Patient Details	Ultrasound Findings	Chromosomal Microarray Report	Phenotypic Features associated with Pathogenic Variant
Primigravida, Thalassemia Carrier Couple for Prenatal Diagnosis	Single live fetus of 12 weeks Ductus Venosus a-wave reversal	**Microdeletion in chr 15q11.1-q11.2 (deletion of BP1- BP2 chr 15 region) of size 3.026 Mb. This region contains four highly conserved and non-imprinted genes, TUBGCP5, CYFIP1, NIPA2, and NIPA1**	**Prader-Willi / Angelman Syndrome** associated with congenital heart disease, developmental delay, learning disabilities, cognitive impairment, impaired social interactions, intellectual disability, and behavioural abnormality
G2A1, FTS Low Risk for Routine Anomaly Scan	Single live fetus of 18 weeks with Unilateral CTEV	**Duplication of 3q29 of size 2Mb**	**Chromosome 3q29 microduplication syndrome,** a rare chromosome abnormality characterized by developmental delay, speech delay, intellectual disability (ID), ocular and cardiac anomalies, microcephaly,dental anomalies, obesity, and seizures.
Primi, 18 weeks for Routine Anomaly Scan	2.2mm perimembranous VSD, normal outflow tracts, Aorta prominent than PA	• **Copy number variation in chromosome 15 (q13.2-q13.2) and** • **Partial trisomy of sex chromosome**	• **15q13.3 microduplication** is a rare syndrome associated with a developmental delay (DD), intellectual disability (ID), epilepsy, hypotonia, autism spectrum disorders (ASD), attention-deficit hyperactivity disorder, schizophrenia, feeding problems, difficulty sleeping (insomnia), low muscular tone (hypotonia) and seizures. • **Sex chromosome aberrations** includes eunuchoid body habitus, feminine distribution of body fat and hair, gynecomastia, and micropenis; cardiovascular abnormalities
Primi gravida **II opinion of Binder facies**	Single live fetus of 20 weeks with Depressed nasal bridge	**Gain of a 3.7 Mb on long arm (q) of chr 15 encompassing UBE3A, ATP10A, GABRB3, GABRA5, GABRG3, OCA2, HERC2 and APBA2 genes**	Neurodevelopment disorder that frequently include **autism spectrum**
12 weeks 3 days, G3P0 Came for IInd opinion of NT scan showing absent/ hypoplastic nasal bone	NT 2.4mm at 66mm CRL (>95th %ile) Unossified Nasal Bone Scan based risk high for T21 (1:26) and T13 (1:42)	**15 Mb duplication on q arm of chromosome 3**	Feeding difficulties, short stature, anteverted nares, downturned mouth corners, short nose, frontal bossing, hypotonia, microcephaly, brain neoplasm, delayed speech and language development and intellectual disability.

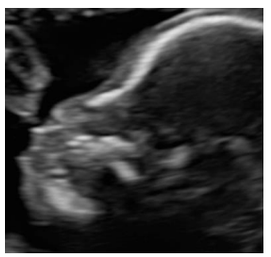
Objective: Retrospective analysis of 5 cases with abnormal fetal ultrasound, normal karyotype & pathogenic variant detected in Chromosomal Microarray.

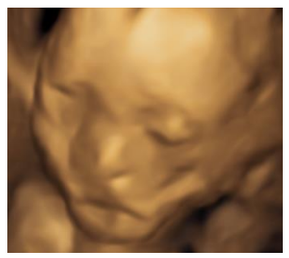












Conclusion: Above cases signify importance of invasive testing in fetal structural anomaly and role of Chromosomal Microarray in detection of submicroscopic imbalances. ACOG/SMFM recommends that CMA replace or supplement karyotype for prenatal evaluation of fetuses with major structural anomalies. We are now transitioning towards prenatal precision medicine and can readily use these tools for the benefit of our patients and their families.