A Fetus with Trisomy 12p: Prenatal and Postnatal Presentation

Seema Thakur[1], Chanchal Singh[2], Manju Gupta[3]

[1]Genetic Medicine Unit, Fortis Hospital, Delhi- NCR, India

[2]Fetal Medicine Unit, Madhukar Rainbow Children Hospital, Delhi, India

[3]Department of Obstetrics & Gynaecology, Jaypee Hospital, Noida, India

Correspondence to: Dr Seema Thakur *Email:* seematranjan@gmail.com

Abstract

Trisomy of the short arm of chromosome 12 is a rare chromosomal abnormality. We have compared the ultrasound features and autopsy features of a fetus with trisomy 12p with a previous reported antenatal case and Pallister Killian syndrome. Ours is the second case report on fetal features of trisomy 12p.

Introduction

Trisomy of the short arm of chromosome 12 is a rare chromosomal abnormality with an estimated incidence of 1 per 50,000 births and only over 30 cases reported worldwide (Segel et al.,2006).The first case with trisomy 12p was reported by Uchida and Lin (1973) due to a malsegregation of a balanced parental chromosome rearrangement (Uchida &Lin, 1973). Trisomy 12p syndrome is associated with moderate to severe psychomotor retardation, generalized hypotonia and facial dysmorphism characterized by a round face with prominent cheeks, prominent forehead, broad nasal bridge, short upturned nose, long philtrum, thin upper lip, broad everted lower lip, and abnormal ears (Rauch et al.,1996; Tekin et al.,2001; Tsai et al., 2005).

We report here a 23-24 weeks fetus with trisomy 12p and compare the antenatal and postnatal features with the previous reported fetus with 12p trisomy and Pallister Killian syndrome.

Case Report

A 34-year-old primigravida was referred to our fetal medicine centre in view of lower limb abnormality detected in the anomaly scan. She had no history of fever with rash, diabetes, drug intake or radiation exposure. Nuchal translucency was within normal range in the first trimester ultrasound. First trimester biochemistry showed low risk for Down syndrome (PAPPA 2.27 MoM and beta hCG 0.46 MoM). Ultrasound was done using a Voluson E10 scanner (GE Healthcare, Milwaukee, WI) equipped with a convex 4–8 MHz abdominal transducer and a 6–12 MHz endovaginal probe. Two-dimensional ultrasound showed a single live intrauterine fetus with overall fetal growth corresponding to 20 weeks gestation. However all long bones were below the 5th centile for gestation. There was lower limb length discrepancy. The left femur was below the 1st centile for gestation and showed bowing. The left lower limb showed a curved tibia and very short segment of fibula. The left foot showed valgus deformity with overcrowding of toes (Figure 1c). There was no polydactyly. Clavicle and scapula were seen. Fetal spine appeared normal. Fetal head showed brachycephaly. There was no other structural abnormality nor any other marker for chromosomal abnormalities. The couple was offered amniocentesis for microarray and advised consultation with paediatric orthopaedician. However, they opted for termination of pregnancy and consented for a complete postnatal evaluation.

On postnatal external examination, foot length was 3.5 cm corresponding to 21 weeks, crown heel length was 30 cm, consistent with 24 weeks and crown rump length was 20.3 cm, consistent with 24 weeks and HC was 20 cm, consistent with 23 weeks gestation. There was brachycephaly, short nose, depressed nasal bridge and long philtrum (Figure 1a). There was no cleft lip or cleft palate. Ears were low set. Neck was short. Anus was anteriorly placed. In left lower limb there was bowing of tibia (Fig 1b). Histopathology of internal organs like liver, spleen, kidneys and lungs was normal. Placental histopathology was normal.

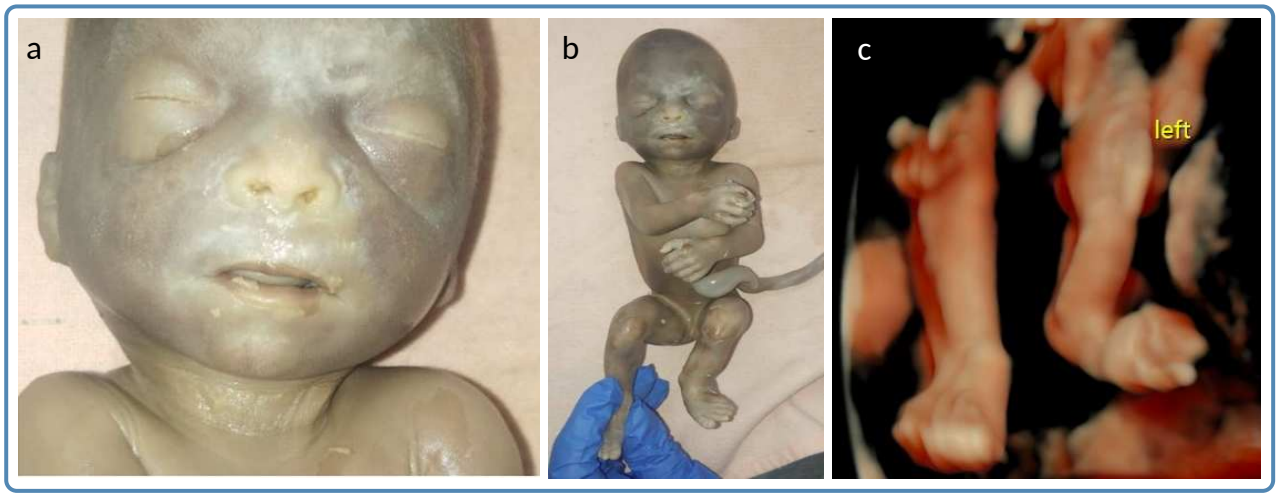

Figure 1 a) Fetal autopsy evaluation showing facial dysmorphism. b) Valgus deformity and bowing of tibia noted in the fetus. c) Antenatal ultrasound showing bowing of tibia on the left.

Histopathology of left leg showed disorganised cartilaginous tissue.

Chromosomal microarray from fetal DNA showed a female karyotype with duplication of 18.1 MB at cytoband 12p13.33p12.1 [arr 12p13.33p12.1(803488-24653237) x 3]. This duplication has 182 genes.

Discussion

Phenotypic similarity between trisomy 12p and tetrasomy 12p has been described in the literature. We have compared ultrasound features of one antenatal case described previously and Pallister Killian syndrome fetus with our case in Table 1. However, it has to be kept in mind that mosaic tetrasomy 12p can have a similar pattern in chromosomal microarray as trisomy 12p. As conventional karyotyping was not done in this case, the possibility of mosaic tetrasomy 12p could not be entirely ruled out.

Hung et al. reported a fetus with trisomy 12p at 30 weeks in a primigravida (Hung et al.,2012). Ultrasonography features included polyhydramnios, short lone bones and abnormal spine curvature. Fetal facial dysmorphism included hypertelorism, marked prenasal thickness, broad and flat nasal bridge, cleft palate, large philtrum with thickened everted upper lip, and micrognathia.

Doray et al. stated that the three most frequent ultrasound indicators were polyhydramnios (84%), congenital diaphragmatic hernia (CDH) (16%) and micromelia of predominantly rhizomelic type (10%) (Doray et al., 2002).

The fetus we described also had short long bones but there was no polyhydramnios probably because of the early gestation at detection. Left tibia was small and deformed. Histopathology of bone showed localized dysostosis. Oligonucleotide-based aCGH showed a 35.4 MB duplication of 12p [arr 12p13.33p11.1 (0–35,400,000) × 3] in the case reported by Hung et al. Our case had duplication of 18.1 MB at cytoband 12p13.33p12.1. Izumi et al. described a minimal critical region for Pallister Killian Syndrome phenotype in a case with duplication of 26 genes (Izumi et al.,2014). Three genes, *ING4, CHD4*, and *MAGP2* represent strong candidate genes for minimal critical region of this phenotype. *ING4* gene plays important role in transcriptional regulation and *CHD4* gene is involved in chromatin remodelling, DNA damage response and cell cycle control.

This case highlights the importance of a well-performed antenatal ultrasound. Down syndrome may be the commonest chromosomal abnormality but a low risk on the combined first trimester screening does not exclude other abnormalities. Another point to be emphasized is that any structural abnormality warrants microarray over conventional karyotyping. A complete postnatal evaluation including infantogram and fetal autopsy is essential to confirm ultrasound findings and to establish the diagnosis, which is instrumental in assigning appropriate recurrence risk.

Table 1 Comparison of antenatal features of trisomy 12p and tetrasomy 12p.

Antenatal ultrasonography features	Huang et al., 2012	Pallister Killian Syndrome	Fetus described in our study
Polyhydramnios	+	+	-
Short long bones	+	+	+
Increased nuchal translucency	+	+	-
Congenital diaphragmatic hernia	-	+	-
Cardiac anomaly	-	+	-
Polydactyly	-	+	-
Fetal growth restriction			-

Table 2 Comparison of facial features of Pallister Killian syndrome and trisomy 12p.

Features	Pallister Killian syndrome	Huang et al., 2012	Fetus reported in our study
Brachycephaly	+	+	+
Round face	-	+	
Coarse facies	+	-	+, mild
Flat facial profile	+	+	+
Broad nasal bridge	+	+	+
Anteverted nostril	+	+	+
Long Philtrum	+	+	+
Upper Lips	Thin	Thick	Thin
Short Neck	+	+	+

Conclusion

Our report further expands the spectrum of antenatal and postnatal phenotype of trisomy 12p.

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