

Antenatally detected holoprosencephaly-polydactyly (pseudotrisomy 13) syndrome

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Introduction

Pseudotrisomy 13 syndrome was first suggested in 1989 by Hewitt BG, *et al*¹. It was identified in patients with holoprosencephaly and clinical features suggestive of trisomy 13, such as microcephaly, hypotelorism, cleft palate, and anophthalmia in the presence of a normal karyotype^{2,3}. Holoprosencephaly and polydactyly are the hallmarks in this anomaly⁴. We present a patient with phenotypic features of trisomy 13 with a normal karyotype.

Case report

A baby girl, weighing 2300g (-2SD to -3SD), was delivered at term by normal vaginal delivery to healthy non-consanguineous elderly parents (37-year-old mother and 43-year-old father) with two healthy children. This was the third pregnancy and there was no previous history of miscarriages or early neonatal deaths. Mother has taken pre-conceptional folic acid and the pregnancy was not complicated with any medical illness. The antenatal ultrasound scan (USS) done at 26 weeks of gestation revealed holoprosencephaly, ventricular septal defect (VSD) and midline facial cleft, suggestive of Patau syndrome (Trisomy 13) as shown in Table 1.

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The baby was born with Apgar scores of 8, 9 and 10 at 1, 5 and 10 minutes of age respectively. She was noted to have microcephaly (occipito-frontal circumference 28cm, <5th centile), short birth length (length 44cm, on -3SD), hypertelorism, bilateral cleft lip with midline cleft palate, postaxial polydactyly, long systolic murmur in left sternal edge suggestive of VSD, and epicanthic folds (Figure 1).

A clinical diagnosis of Trisomy 13 was made and karyotyping was arranged.

USS of the brain confirmed features of semi-lobar holoprosencephaly without hydrocephalus (Figure 2).

USS of the abdomen revealed a right sided cystic kidney (Figure 3).

2D echocardiogram revealed tetralogy of Fallot with pulmonary atresia and duct dependent pulmonary circulation. Spinal x-rays did not reveal any structural anomalies.

The baby was given multidisciplinary care with orthodontist, in view of repairing facial and palatal clefts, plastic surgeon, for removal of additional finger, nephrologist, for possible chronic kidney disease in future, and speech therapist for assessment of swallowing. She was fed with expressed breast milk via nasogastric tube and was discharged on day 12 of life after parental counselling for Trisomy 13, the diagnosis at that moment of time.

Parents were informed in detail about multisystem involvement with possible future complications, short life span and genetic counselling arranged considering the recurrence in future pregnancies. The baby passed away on day 32 of life, possibly due to the closure of the patent ductus arteriosus. It was only later that her karyotype was reported as normal which led us to consider Pseudotrisomy 13 (Figure 4).

Table 1: Antenatal ultrasound scan summary

Gestational age: 26 weeks and 1 day Estimated fetal weight: 804g		
Fetal Biometry		Gestational age
Biparietal diameter (BPD):	6.30 cm	25 weeks 3 days \pm 1 day
Head circumference (HC):	22.11 cm	24 weeks 1 day \pm 1 day
Abdominal circumference (AC):	21.17 cm	25 weeks 4 days \pm 1 day
Femoral length (FL):	4.61 cm	25 weeks 2 days \pm 1 day
Conclusion: This fetus is complicated with holoprosencephaly, midline facial cleft and ventricular septal defect suggestive of Trisomy 13.		



Figure 1: showing microcephaly, hypertelorism, bilateral cleft lip with midline cleft palate, postaxial polydactyly and epicanthic folds.

*Permission given by parents to publish photograph



Figure 2: Ultrasound scan of brain showing posteriorly connected single ventricle (red arrows) and fused thalami (blue arrow) suggesting semi-lobar holoprosencephaly



Figure 3: *Ultrasound scan of right kidney showing small multiple cysts indicated by red arrows*

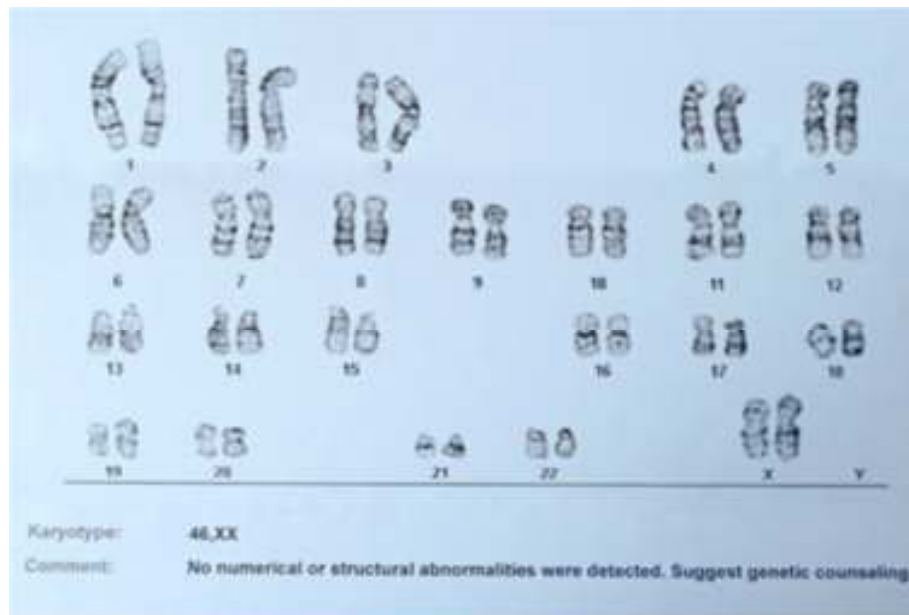


Figure 4: *Normal karyotype of baby*

Discussion

Pseudotrismy 13 is considered to have an autosomal recessive inheritance due to its occurrence in multiple children of normal parents and children born to consanguineous parents². However, a few sporadic cases have also been reported². Genes responsible for the disorder have not been confirmed yet. Some studies have indicated the gene FBXW11 of the long arm of chromosome 5 as responsible⁵. Recent evidence suggests it is not monogenic⁶.

Among the clinical features of Pseudotrismy 13 described in the literature, cerebellar hypoplasia, cleft palate, cryptorchidism, holoprosencephaly, thyroid hypoplasia, hydrocephalus, hypoplasia of the penis, hypoplasia of the premaxilla, hypospadias, hypertelorism, low-set, posteriorly rotated ears, microcephaly, microphthalmia, muscular hypotonia, oral cleft, postaxial hand polydactyly, are considered to be common manifestations^{2,7}.

The Meckel syndrome, Pallister-Hall syndrome, trisomy 13, Hydrolethrus syndrome and Smith-

Lemli-Opitz syndrome must be excluded using characteristic findings. *Hydrolethalus syndrome* is characterized by the absence of midline cerebral structures, hydramnios, external hydrocephalus, preaxial polydactyly of the feet, postaxial polydactyly of the hands, congenital heart defects, and micrognathia^{4,8}. Our patient did not have polyhydramnios, pre-axial polydactyly of the feet and hydrocephalus to suggest Hydrolethalus syndrome. *Meckel syndrome* occurs with polycystic kidneys, occipital encephalocele and polydactyly, and *Pallister-Hall syndrome* may be associated with post-axial polydactyly, syndactyly, hypothalamic hamartoblastoma, hypopituitarism, imperforate anus and, occasionally, with holoprosencephaly^{4,8}. *Smith-Lemli-Opitz syndrome* has characteristic facial features including anteverted nostrils, ptosis of eye lids, syndactyly of second and third toes, polydactyly and microcephaly. Our patient did not have occipital encephalocele to suggest Meckel syndrome and hypothalamic hamartoblastoma, syndactyly and evidence of pituitary insufficiency to suggest Pallister-Hall syndrome and facial features were not in favor of Smith-Lemli-Opitz syndrome.

Antenatal diagnosis of Pseudotrisomy 13 is possible with the use of ultrasound imaging and karyotyping of samples from amniocentesis. Antenatal diagnosis is very important for genetic counselling and prognostication.

References

1. Hewitt BG, Seller MJ, Bennett CP, Maxwell DM. Holoprosencephaly, polydactyly and normal chromosomes: pseudo-trisomy 13? *Clinical Genetics* 1989; **36**: 141-3.
<https://doi.org/10.1111/j.13990004.1989.tb03177.x>
PMid: 2766571
2. Cohen M, Gorlin R. Pseudo-trisomy 13 syndrome. *American Journal of Medical Genetics* 1991; **39**(3): 332-5.
<https://doi.org/10.1002/ajmg.1320390316>
PMid: 1867286
3. Bachman H, Clark R, Salahi W. Holoprosencephaly and polydactyly: a possible expression of the Hydrolethalus syndrome. *Journal of Medical Genetics* 1990; **27**(1): 50-2.
<https://doi.org/10.1136/jmg.27.1.50>
PMid: 2407847 PMCID: PMC1016881
4. Verloes A, Ayme S, Gambarelli D, Gonzales M, Le Merrer M, Mulliez N *et al*. Holoprosencephaly-polydactyly (pseudotrisomy 13) syndrome: a syndrome with features of Hydrolethalus and Smith-Lemli-Opitz syndromes. A collaborative multicentre study. *Journal of Medical Genetics* 1991; **28**(5): 297-303.
<https://doi.org/10.1136/jmg.28.5.297>
PMid: 1865466 PMCID: PMC1016846
5. Koolen D, Herbergs J, Veltman J, Pfundt R, van Bokhoven H, Stroink H *et al*. Holoprosencephaly and preaxial polydactyly associated with a 1.24 Mb duplication encompassing FBXW11 at 5q35.1. *Journal of Human Genetics* 2006; **51**(8): 721-6.
<https://doi.org/10.1007/s10038-0060010-8>
PMid: 16865294
6. Marquis-Nicholson R, Aftimos S, Ashton F, Love J, Stone P, McFarlane J *et al*. Pseudotrisomy 13 syndrome: Use of homozygosity mapping to target candidate genes. *Gene* 2011; **486**(1-2): 37-40.
<https://doi.org/10.1016/j.gene.2011.06.028>
PMid: 21756987
7. Pseudotrisomy 13 syndrome. Available from:
<https://rarediseases.info.nih.gov/diseases/344/pseudotrisomy-13-syndrome> [cited 28 July 2022].
8. Dincsoy M, Salih M, Al-Jurayyan N, Al Saadi M, Patel P. Multiple congenital malformations in two sibs reminiscent of Hydrolethalus and pseudotrisomy 13 syndromes. *American Journal of Medical Genetics* 1995; **56**(3): 317-21.
<https://doi.org/10.1002/ajmg.1320560321>
PMid: 7778599