CASE REPORT

Mosaic trisomy 13 and a sacral appendage

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SUMMARY

Mosaic trisomy 13 occurs when there is a percentage of trisomic cells for an entire chromosome 13, while the remaining percentage of cells is euploid. The prevalence of this syndrome ranges from 1 in 10 000 to 1 in 20 000 births. Complete, partial or mosaic forms of this disorder can occur. The phenotype of mosaic trisomy 13 patients varies widely. Patients with mosaic trisomy 13 usually have a longer survival and a less severe phenotype compared to patients with complete trisomy 13. Genetic counselling is difficult due to the wide variation among the clinical manifestations of these patients. There have been 49 cases of mosaic trisomy 13 reported in the literature. We report the case of a patient with mosaic trisomy 13, a sacral appendage and a cleft lip and palate.

counselling is extremely important for the parents and for the patients.

CASE PRESENTATION

The patient is a 2.5-month-old girl born to a 28-year-old G2P1C1 mother at 36 weeks gestation through a caesarean section due to an abnormal antepartum non-stress test showing late decelerations and bradycardia and a biophysical profile score of 4. The parents were healthy and non-consanguineous. Apgar scores were 9 at 1 min and 10 at 5 mins. There was no family history of any other genetic condition. The mother denied any exposure to medications or teratogens during pregnancy. Birth weight was 2.4 kg (2nd–5th centile) and length 48 cm (25th–50th centile). On physical examination, weight was 3.4 kg (<2nd centile), length 53 cm (<5th centile), head circumference 35.5 cm (<2nd centile), external intercanthal distance 7.2 cm (75th–97th centile), internal intercanthal distance 1.6 cm (<5th centile) and interpupillary distance 4 cm (<5th centile). She had bilateral cleft lip and palate (figure 1), a left preauricular tag, a haemangioma in the occipital region and a sacral appendage (figure 2).

Transfontanelar ultrasound, abdominal ultrasound and echocardiogram were normal. The lumbosacral ultrasound showed a small thickening and an increased echogenicity of the filum terminale,

BACKGROUND

Physicians should be aware of the different presentations of trisomy 13 such as mosaic trisomy 13. Trisomy 13 has a broad range of clinical manifestations and the mosaic form could be misdiagnosed or unnoticed. Prenatal diagnosis should be carried out to identify devastating cases. The mosaic form of this condition is usually less severe than the complete form of trisomy 13. The percentage of mosaic cells in a karyotype does not correlate with the severity of the clinical manifestations. Genetic

Figure 1 The facial alterations of the patient.

Figure 2 The sacral appendage of the patient.

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which could correspond to a lipoma. Chromosome analysis from peripheral blood leucocytes using giemsa banding technique at 100 metaphase demonstrated trisomy 13 mosaicism; 46 XX [80]/47, XX, +13 [20]. Both parents had normal karyotypes.

OUTCOME AND FOLLOW-UP

The patient is still alive and at 6 months shows cephalic dominance.

DISCUSSION

In 1960, Patau *et al*^{1 2} identified for the first time the trisomy 13 syndrome in the laboratory, although it was already described by Bartholin. The prevalence of this syndrome ranges from 1 in 10 000 to 1 in 20 000 births. There is no sex predominance and complete, partial or mosaic forms of this disorder can occur.²

Complete trisomy 13 occurs when three copies of chromosome 13 are present in every cell. It is responsible for almost 80% of all trisomy 13 cases. This syndrome is associated with characteristic physical anomalies such as microcephaly, scalp defects, holoprosencephaly, microphthalmia, orofacial clefting, congenital heart defects, polydactyly, profound mental retardation, early death and is present in 1% of spontaneous abortions (100-fold greater than in live births).^{2 3} Death occurs within the first days to weeks of life. The most common causes of death are cardiopulmonary arrest (69%), congenital heart defects (13%) and pneumonia (4%).⁴

Partial trisomy 13 occurs when a portion of chromosome 13 is present in every cell. Approximately 20% result from chromosomal translocations. The most common is the t (13q14q). A majority (95%) of these translocations arise de novo, while 5% are transmitted by one of the parents.²

Mosaic trisomy 13 occurs when a percentage of cells are trisomic for an entire chromosome 13, while the remainder percentage is typically euploid. A recent article about the epidemiological characteristics of the trisomies 13, 18 and 21 describes the cytological and epidemiological findings in 985 trisomy 13 diagnoses between 2004 and 2009 included in the National Down Syndrome Cytogenetic Register of England and Wales. Of the 985 diagnoses, 12.6% were live births, 75.5% were terminated, 3.2% were late fetal deaths and 8.7% were waiting for an outcome. There were only 11 diagnoses of mosaic trisomy 13 compared to 892 diagnoses of complete trisomy 13. The maternal age was raised in mosaic trisomy 13 diagnoses compared to the normal population and there was a high proportion of males among the diagnoses. No recurrences of mosaic trisomy 13 were seen.⁵ The phenotype of mosaic trisomy 13 varies widely; some patients may have the typical phenotype of trisomy 13 with neonatal death, while others may have few dysmorphic features and prolonged survival. The reason for this variation is that the phenotype changes according to the distribution of the abnormal cells in specific tissues.⁶ Therefore, the phenotype and natural history of the patients with mosaic trisomy 13 has not been well characterised. Griffith *et al*⁷ summarised the most frequently featured in 48 mosaic trisomy 13 cases. Of note, the characteristic findings seen in complete trisomy 13 were rarely seen in the mosaic cases. Birth weight and head circumference <5th centile was reported in less than 40% of patients. Haemangiomas are a common clinical finding being reported in two of every three patients. Cleft lip and cleft palate were also common findings. Cleft lip has been

Table 1 Features reported in patients with mosaic trisomy 13 compared with features of our patient

Physical findings	Frequency	Percentage of cases	Our patient
Broad nasal bridge	7 of 7	100	(+)
Short nose	4 of 4	100	(+)
Sloping forehead	6 of 7	86	(-)
Telangiectatic nevus	4 of 5	80	(-)
Upturned nares	4 of 5	80	(-)
Uterine anomalies	3 of 4	75	(-)
Depressed nasal bridge	8 of 9	89	(+)
Cryptorchidism	6 of 7	86	(-)*
Upslanting palpebral fissures	6 of 8	75	(-)
Low-set ears	17 of 21	81	(-)
Epicanthal folds	5 of 7	71	(-)
Microtia	5 of 7	71	(-)
Skin redundancy	6 of 7	86	(+)
Apnea	4 of 6		(-)
Finger clinodactyly	8 of 11	73	(-)
Frequent respiratory infections	5 of 6	83	(+)
Low posterior hairline	4 of 6	67	(-)
Pigmentary abnormalities	5 of 6	83	(+)
Short neck	9 of 10	90	(+)
Small forehead	4 of 6	67	(-)
Tapered fingers	4 of 6	67	(-)
Patent ductus arteriosus	7 of 10	70	(-)
Cleft palate	18 of 22	82	(+)
Facial asymmetry	3 of 5	60	(-)
Flat occiput	4 of 5	80	(+)
Hearing loss	6 of 9	67	(-)
High forehead	4 of 5	80	(+)
Poor suck/swallow	3 of 5	60	(-)
Malformed ears	12 of 17	71	(-)
Seizures	14 of 20	70	(-)
Hypotelorism	6 of 8	75	(+)
Joint contractures	5 of 8	63	(-)
Vertebral anomalies	5 of 8	63	(-)
Widely spaced nipples	5 of 8	63	(-)
Ventricular septal defect	7 of 10	70	(-)
Micrognathia	9 of 14	64	(-)
Clenched hands	6 of 10	60	(-)
Finger camptodactyly	7 of 12	58	(-)
High palate	8 of 12	67	(+)
Umbilical hernia	5 of 9	56	(-)
Cleft lip	9 of 13	69	(+)
Downslanting palpebral fissures	4 of 6	67	(+)
Hypoplastic nose	4 of 6	67	(+)
Pterygium	3 of 6	50	(-)
Two-vessel umbilical cord	3 of 6	50	(-)
Atrial septal defect	5 of 10	50	(-)
Rib anomalies	4 of 8	50	(-)
Cognitive/developmental findings			
Speech delay	3 of 3	100	Unknown
Intellectual disability	17 of 21	81	Unknown
Global developmental delay	15 of 22	68	(-)

The table was adapted from Griffith *et al*⁷.

*Our patient is a girl.

already described in eight patients, and in this case, cleft palate is present as well.⁷ Hypotelorism and sacral appendages are the two findings of the patient we described that have not been reported in the research. Sacral appendage has been associated with Pallister-Killian syndrome, a dysmorphic condition caused by mosaicism for tetrasomy of chromosome 12p.⁸ Dao and Netsky⁹ classified sacral (caudal) appendages into true tails and pseudotails. True tails are the remnant of a structure found in embryonic life, defined as a vertebrate, caudal, midline protrusion capable of spontaneous or reflex motion composed of skin covering muscle, adipose and connective tissue. It is due to a lack of regression of the vertebrated portions during the seventh to eighth week of gestation. A pseudotail was defined as a caudal protrusion composed of different types of tissue not capable to move.⁹ The tissue identified in pseudotails include teratomatous components of the embryonal kidney type, adipose tissue in lipomas and cartilage in the case of hyperplastic chondrodysplasia.^{10 11} In 49% of human tail cases, spinal dysraphism such as meningocele and spina bifida have been found. Lipoma has been reported to appear in 28% of cases.¹⁰ There are no reports of mosaic trisomy 13 and sacral appendages.

Delatycki and Gardner⁶ concluded that the percentage of trisomic cells in lymphocytes is a poor predictor of intellectual outcome. We gathered data from the 48 patients described in Griffith's article and agreed to his presumption that it is very complicated to establish a relationship between the percentage of affected cells on the karyotype and the patient's clinical outcome. First of all, there is no specific data about the mental retardation of these patients regarding severity, tools used to measure it, age of measurement and specific deficiencies. Second, the percentage of mosaicism on the karyotype changes with time. The decrease in the percentage of cells with time implies that some 'natural selection' exists against the abnormal cells.¹² The majority of the cases with mosaic trisomy 13 do not report the time when the karyotype was carried out, so the percentages are not comparable. Third, the percentage of mosaic cells varies at the same moment according to where the sample is taken. This is explained by the different embryonic origins of each tissue, so that in any instance, a specific embryonic line could have different percentage of trisomic cells than another line.¹³

Genetic counselling is difficult due to the variation among the clinical manifestations of these patients. Patients with mosaic trisomy 13 usually have a longer survival and a less severe phenotype compared to complete trisomy 13 (table 1). These patients may be fertile and should be aware of the theoretical risk of gonadal mosaicism and the production of offspring with mosaic or complete trisomy 13.¹⁴

Learning points

- ▶ Mosaicism exists in about 5% of all trisomy 13 cases.
- ▶ The phenotype and natural history of the patients with mosaicism trisomy 13 have not been well characterised.
- ▶ It is very complicated to establish a relationship between the percentage of affected cells on the karyotype and the patient's clinical outcome.
- ▶ Genetic counselling is difficult due to the wide variation among the clinical manifestations of these patients. These patients may be fertile and should be aware of the theoretical risk of gonadal mosaicism and the production of offspring with non-mosaic trisomy 13.

Contributors HP and LME participated in the data research for the case report, designed the figures and drafted the manuscript. HP had the idea for this case report, was involved in the analysis of the data and revised the manuscript. HP and LME read and approved the final manuscript.

Competing interests None.

Patient consent Obtained.

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REFERENCES

- 1 Patau K, Smith DW, Therman E, *et al*. Multiple congenital anomaly caused by an extra autosome. *Lancet* 1960;1:790–3.
- 2 Hennekam RCM, Krantz ID, Allanson JE, *et al*. *Gorlin's syndromes of the head and neck*. 5th edn. Oxford; New York: Oxford University Press, 2010.
- 3 Hook EB. Rates of 47, +13 and 46 translocation D/13 Patau syndrome in live births and comparison with rates in fetal deaths and at amniocentesis. *Am J Hum Genet* 1980;32:849–58.
- 4 Brewer CM, Holloway SH, Stone DH, *et al*. Survival in trisomy 13 and trisomy 18 cases ascertained from population based registers. *J Med Genet* 2002;39:e54.
- 5 Alberman E, Mutton D, Morris JK. Cytological and epidemiological findings in trisomies 13, 18, and 21: England and Wales 2004–2009. *Am J Med Genet A* 2012;158A:1145–50.
- 6 Delatycki M, Gardner RJ. Three cases of trisomy 13 mosaicism and a review of the literature. *Clin Genet* 1997;51:403–7.
- 7 Griffith CB, Vance GH, Weaver DD. Phenotypic variability in trisomy 13 mosaicism: two new patients and literature review. *Am J Med Genet A* 2009;149A:1346–58.
- 8 Chaouachi S, Ben Hamida E, Ennine I, *et al*. Pallister-Killian syndrome with additional manifestations of cleft palate and sacral appendage. *Tunis Med* 2010;88:614–16.
- 9 Dao AH, Netsky MG. Human tails and pseudotails. *Hum Pathol* 1984;15:449–53.
- 10 Salunke P, Sura S, Tripathi M, *et al*. Human tail continuing as transitional lipoma. *Neurol India* 2011;59:637–8.
- 11 Lu FL, Wang PJ, Teng RJ, *et al*. The human tail. *Pediatr Neurol* 1998;19:230–3.
- 12 Chen M, Yeh GP, Shih JC, *et al*. Trisomy 13 mosaicism: study of serial cytogenetic changes in a case from early pregnancy to infancy. *Prenat Diagn* 2004;24:137–43.
- 13 Di Giacomo MC, Susca FC, Resta N, *et al*. Trisomy 13 mosaicism in a phenotypically normal child: description of cytogenetic and clinical findings from early pregnancy beyond 2 years of age. *Am J Med Genet A* 2007;143:518–20.
- 14 Chen CP. Prenatal diagnosis and genetic counseling for mosaic trisomy 13. *Taiwan J Obstet Gynecol* 2010;49:13–22.

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