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Tetraploidy in a liveborn infant

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Abstract

We report a 3 month old boy with tetraploidy, found in peripheral blood and skin fibroblast cultures, with severely delayed growth and neurodevelopment, and with a cleft lip; these findings have not been described before. This report brings to seven the total number of liveborn infants with a 92,XXYY karyotype.

Tetraploidy, the existence of four complete sets of chromosomes, has been reported infrequently in liveborn infants. To date, there have been six cases of full tetraploidy published. All these cases have been associated with multiple congenital defects and survival varies from hours to 22 months. We present a 3 month old infant with multiple congenital anomalies and tetraploidy.

Case report

The proband (figure) was the first child of a 19 year old mother and 25 year old father. There was no family history of consanguinity, multiple abortions, congenital malformations, or mental retardation. The mother took medication for headaches during early pregnancy. The patient was delivered vaginally at 37 weeks of gestation, weighing 1900 g.

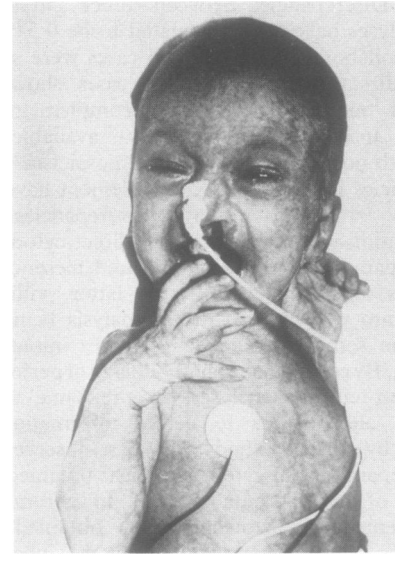
Physical examination showed a small for dates male infant with a flat occiput and short palpebral fissures. The ears were low set and had a rudimentary preauricular appendage on the right. Bilateral coloboma and left cleft lip with complete cleft palate were also evident. There was arachnodactyly of the hands (with low set thumbs) and feet and cutis marmorata of all the skin. He had normal male genitalia.

Ultrasound examination showed a normal abdomen with kidneys of normal shape and size, although serum creatinine was raised (around 88 μmol/l).

EEG at 19 days was normal. Cerebral ultrasound showed a hypoplastic vermis cerebelli and few fissures. A systolic murmur was present from the early perinatal period, with moderate cyanosis that worsened with crying, but without signs of cardiac insufficiency. Echocardiography confirmed the presence of severe tetralogy of Fallot. With the results of the chromosome studies and with parental consent, we adopted a conservative approach to the cardiopathy. He is growing poorly.

CYTOGENETIC STUDIES

The patient's chromosomes were studied in peripheral blood lymphocytes. All of the 200 metaphases



Patient at 2 months of age. Note the cleft lip and the arachnodactyly.

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Clinical manifestations in tetraploid patients.

	Golbus *et al*[1]	Pitt *et al*[2]	Scarbrough *et al*[3]			Lafer and Neu[4]	Our case
			1	2	3		
Maternal/paternal age	26/30		22/?	19/?	23/?	25/?	19/25
Sex	M	M	M	F	M	F	M
Gestation (wk)	Term	36–38	41–42	36	37	41	37
Birth weight (g)	2150	2650	2460	1560	2120		1900
Hypotonia	+			+	+	+	
Fetal distress			+		+		
Craniofacial							
Microcephaly	+		+	+	+		
Prominent, narrow forehead	+	+		+		+	
Micrognathia		+		+		+	
High arched/cleft palate			+	+	+	+	+
Cleft lip							+
Ocular hypertelorism		+		+			
Short palpebral fissures	+		+		+	+	+
Microphthalmia	+		+	+	+		
Coloboma				+		+	+
Low set ears	+		+		+	+	+
Preauricular tags	+						+
Dysplastic ear cartilage	+	+		+	+	+	
Limbs							
Positional limb defects	+	+	+	+	+	+	+
Structural limb defects					+	+	+
Congenital heart disease					+		+
Urinary tract							
Hypoplastic kidneys					+		
Urethral stenosis	+		+				
CNS abnormalities							
Delayed development	+					+	+
Death	51wk	15d	11h	2d	9wk	Alive 22mth	Alive 3mth

analysed had 92 chromosomes. GTL banded metaphases showed a 92,XXYY karyotype A fibroblast culture was established from a skin biopsy; 100 metaphases were analysed and all of them had 92 chromosomes. The patient's parents have not been studied.

Discussion

Tetraploidy has been reported infrequently in liveborn infants. Most of these patients have been mosaics with a tetraploid and a normal cell line. This patient is the seventh case of full tetraploidy to be reported so far. The six other patients with 'pure' tetraploidy have been reported by Golbus *et al*,[1] Pitt *et al*,[2] Scarbrough *et al*[3] (three patients), and Lafer and Neu.[4]

Our patient is compared with these other cases in the table. The most common manifestations are microcephaly, prominent, narrow forehead, high arched/cleft palate, short palpebral fissures, microphthalmia, low set and dysplastic ears, and positional and structural limbs defects. Our patient had a cleft lip and cutis marmorata, which have not been described before.

It is interesting to note the survival of these patients, from a few hours to 22 months. Our patient is alive at 3 months.

As observed by Golbus *et al*,[1] these patients with 46 extra chromosomes had abnormalities comparable to those seen in patients with a single extra chromosome, such as trisomy 13 or trisomy 18. They suggested that the balance between chromosomes and the ratio between different portions of the chromatin is more important than the absolute number of chromosomes present, but they did not deny the fact that even 'balanced' polyploidy is developmentally deleterious.

1 Golbus MS, Bachman R, Wiltse S, Hall BD. Tetraploidy in a liveborn infant. *J Med Genet* 1976;13:329–32.
2 Pitt D, Leversha M, Sinfield C, *et al*. Tetraploidy in a liveborn infant with spina bifida and other anomalies. *J Med Genet* 1981;18:309–11.
3 Scarbrough PR, Hersh J, Kukolich MK, *et al*. Tetraploidy: a report of three liveborn infants. *Am J Med Genet* 1984;19: 29–37.
4 Lafer CZ, Neu RL. A liveborn infant with tetraploidy. *Am J Med Genet* 1988;31:375–8.