

SHORT COMMUNICATION

Report of a diploid:tetraploid live-born infant*

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ABSTRACT

The present paper reports on a Brazilian child with tetraploid mosaicism and multiple malformations, who lived till eight months. Mental and developmental retardation, hypotony, protruding forehead, anomalous fontanelles, deformed ears, depressed nasal bridge, micrognathia, congenital cardiopathy and transverse palmar crease are clinical findings common to this child and the other cases reported in the literature.

INTRODUCTION

Polyploidy in humans is rare and usually incompatible with postnatal life. However, true triploids and tetraploids are not uncommon in spontaneous abortions; about 12% and 1.3% of all abortions occurring in the first three months of gestation are triploids and tetraploids, respectively (Hamerton, 1971; Boué *et al.*, 1975). Congenital malformations of differing types and severity have been described in both completed tetraploids (nine cases: Golbus *et al.*, 1976; Pitt *et al.*, 1981; Scarbrough *et al.*, 1984; Lafer and Neu, 1988; Shiono *et al.*, 1988; Pajares *et al.*, 1990; Coe *et al.*, 1993) and tetraploid mosaicism (12 cases: Kohn *et al.*, 1967; Kelly and Rary, 1974; Reddy *et al.*, 1977; Veenema *et al.*, 1982; Quiroz *et al.*, 1985; Wittwer and Wittwer, 1985; Aughton *et al.*, 1988; Wilson *et al.*, 1988; Urioste *et al.*, 1990; Wullich *et al.*, 1991; Edwards *et al.*, 1994). The

few cases so far reported in the literature demonstrates the rarity of tetraploid births.

CLINICAL REPORT

F.F.S. (Figure 1), born in 1987, male, third child of a non-consanguineous young couple. Pregnancy was normal except for a little vaginal bleeding in the sixth month. There was no history of intake of medicines during gestation and there was no family history of congenital defects. The delivery was by cesarian section due to an ultrasound diagnosis of macrocephaly. The newborn child cried shortly after birth, weighed 4.2 kg, was 47 cm in length and had head and chest circumferences of 39 and 37 cm, respectively. Because of convulsions and dyspnea the child was kept in the hospital for 10 days after birth. At the eighth month death occurred due to cardiac and pulmonary insufficiency.

At physical exam the following abnormalities were seen: macrocephaly, peculiar head shape (square), wide anterior fontanelle and wide interfrontal suture, flat occiput, short and folded helix on the left ear and protruding antihelix on both ears, narrow auditive duct, short and webbed neck with surplus skin. The chest was

* Before this manuscript was written, M.G.F. Sousa, who had made the first examination of the child, passed away, and this paper pays homage to her special devotion to clinical genetics.

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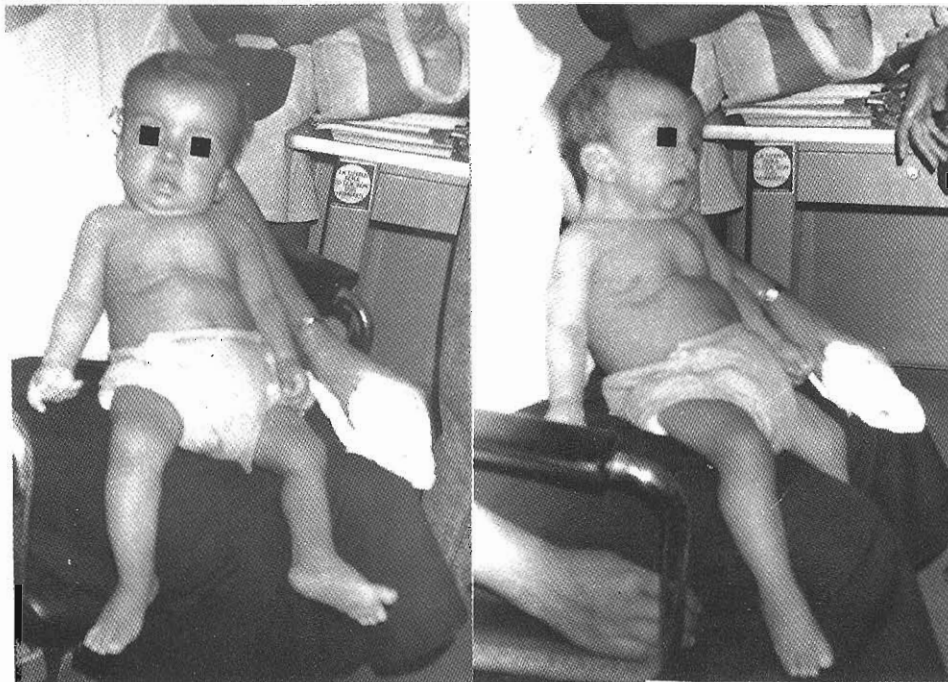


Figure 1 - F.F.S. aged six months.

wide with wide-spaced nipples. The left testicle did not descend. There was also a dimple in the sacral region and atypical bilateral simian creases.

Computerized axial tomography of the skull showed slight enlargement of the supratentorial ventricular system, wide Silvius cisterns and interhemispherical fissures, obliterated front-parietal grooves and extensive frontal hygroma (Figure 2). In the skull, X-rays showed narrowing of parietal bones with protrusion of brain tissue (Figure 3). Accentuated hypoplasia of the right ventricle, resulting in an apparent single ventricle was disclosed by an ecocardiogram.

Chromosome analysis was made of the patient (328 cells) and his parents (30 cells), with metaphases obtained from conventional cultured lymphocytes, using GAG banding. The parents chromosomes were normal, but the propositus had 10 tetraploid cells,

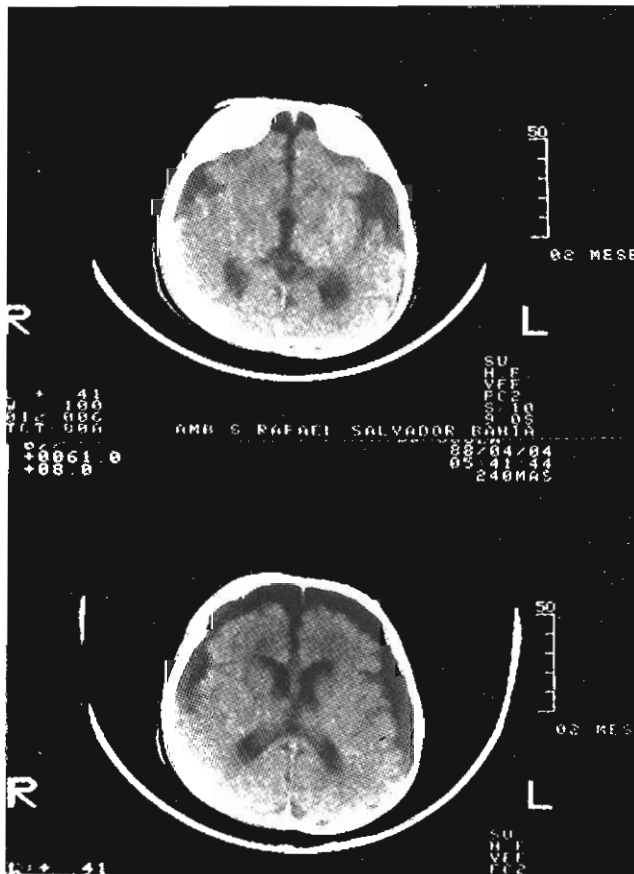


Figure 2 - Computerized axial tomography taken at two months, suggesting hygroma in the front convex of the brain.

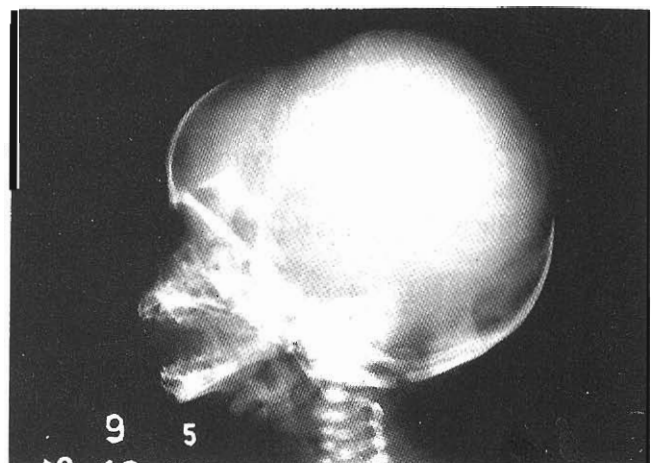


Figure 3 - X-ray of the skull showing the narrowing of the bones with protrusion of brain tissue.

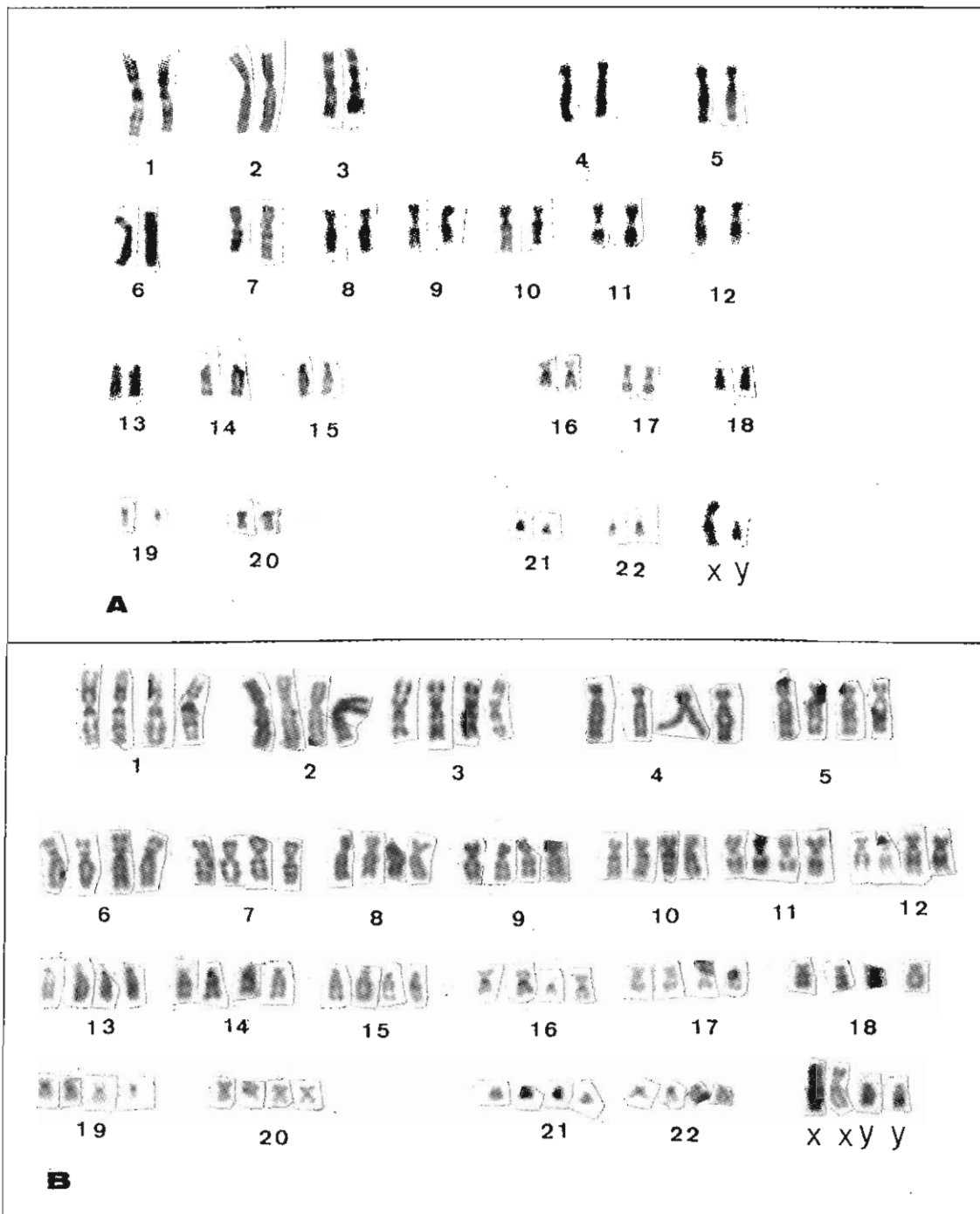


Figure 4 - Karyotype of the diploid/tetraploid. A. 46,XY Cell. B. 92,XXYY Cell.

characterizing a diploid/tetraploid mosaicism (Figure 4).

DISCUSSION

Reports of tetraploid generally refer to spontaneous abortions or liveborn infants, with a wide variation of congenital anomalies, growth and mental retardation. The significance of this chromosomal disturbance and its relationship to malformations is poorly understood. Survival of the patients has been

from a few minutes after birth to 21 years (Edwards *et al.*, 1994). The few reported cases of diploid-tetraploid mosaicism in association with minimal anomalies (Scarborough *et al.*, 1984) and polycystic ovaries (Rojanasakul *et al.*, 1985) likely resulted from later errors in cell division.

In complete tetraploidy, the most common clinical findings are craniofacial abnormalities and limb defects (Pajares *et al.*, 1990; Wullich *et al.*, 1991). The known manifestations of mosaic tetraploidy are shown in Table I. The clinical signs affect multiple organ

Table I - Clinical features of diploid/tetraploid mosaicism.

Features	Reported cases of tetraploid mosaicism													Total
	1	2	3	4	5	6	7	8	9	10	11	12	13	
General														
Sex	M	F	M	M	M	M	F	F	M	M	F	F	M	8M/5F
Gestation (weeks)	42	40	40	32	34		32	38		41	43		40	38.2
Abnormal placenta/ oligohydramnio	-	-		+	-				+	+				3/6
Low birth weight	+	+	-	+	-		+				+	+	-	6/9
Hypotonia	-	+	+			+	-	-		+	+		+	6/9
Failure to thrive	+	+	+		+	+		-			+	+	+	8/9
Cranio-facial anomalies														
Anomalous fontanelles	+	+		+			+		+	+			+	7/7
Abnormal head shape/ craciosynostose	+	+	-	+	-	-	+	-					+	5/9
Prominent forehead	-	+		+	-	-		+					+	4/7
Microcephaly	+	+		+	-		+	-	+		+		-	6/9
Corneal anomaly	+	-		-	-	-	-	-					-	1/8
Microphthalmia/ anophthalmia	-	-		-	-	-		+					-	1/7
Coloboma	-	-	-	-	-	+							-	1/7
Broad nasal root/ prominent nose	+	+			+	+	+	-			+	-	+	7/9
Small mouth	+	+					-			+			+	4/5
Malformed ears	-	+		-	+		+	+		+	+	+	+	8/10
Low set ears	-	-			+		+					+	+	4/6
Cleft palate/bifid uvula	-	-		-	-		+	-					-	1/7
Micrognathia	+	+		-	+		+	-		+	+	+	+	8/10
Internal anomalies														
Cardiac	+	-	-	-	-		+	+		+		-	+	5/10
Renal/urinary tract	-	-		-			-	-	+	+	+	-		3/9
Cryptorchidism	-	-		-	-				+				+	2/6
Adrenal	-			+									-	1/3
Cerebral or spinal deformities	-	-		-			+				+	+	+	4/7
External anomalies														
Short and winged neck	-			-	-		-	+					+	2/6
Positional/structural limb defects	+	-				+		-			+	+	+	5/7
Deformities of the feet	+	+	-	+	-	-		-	+	+	+	+		7/11
Simian crease/abnormal dermatoglyphics	+	+	+		-		+	-					+	5/7
Percent of tetraploid cells in various tissues														
Lymphocytes	69	3.9	21.4	16	40	11	0	72		21.5	0	0	3.0	
Skin							0	29	49	43.8	62	33		
Bone marrow	1	2.7						95						
Others	0							1						
Survival														
	Died (36 weeks)	2 years	10 1/2 year	Died (after birth)	2 years	6 years	Died (2 days)	3 months	Still born	Died (9 weeks)	21 years	11 years	Died (8 months)	

Mosaic tetraploidy cases: 1 (Kohn *et al.*, 1967); 2 (Kelly and Rary, 1974); 3 (Reddy *et al.*, 1977); 4 (Veenema *et al.*, 1982); 5 (Quiroz *et al.*, 1985); 6 (Wittwer and Wittwer, 1985); 7 (Aughton *et al.*, 1988); 8 (Wilson *et al.*, 1988); 9 (Urioste *et al.*, 1990); 10 (Wullich *et al.*, 1991); 11 and 12 (Edwards *et al.*, 1994); 13 (Present case).

Clinical features are presents (+), absent (-), or not specified in the report (blank).

systems and there is no relationship between percent of tetraploid cells and severity of malformations. Aughton *et al.* (1988) observed that tetraploid cell lines could be present in several tissues and more extensive cytogenetic studies could show how specific tetraploidies affect the complex process of hematopoiesis. Quiroz *et al.* (1985) found reduction of the tetraploid cell population in cultures at different times, and suggested selection against the abnormal cell population.

The present case had several dysmorphic signs also found in other cases of tetraploidy: failure to thrive, hypotony, cranio-facial anomalies (abnormal fontanelles, protruding forehead, deformed ears, depressed nasal bridge, micrognathia), cardiac anomalies, abnormal flexion creases and limb defects. Other anomalies such as the short and winged neck have already been registered in other carriers of diploid/tetraploid mosaicism (Wilson *et al.*, 1988). The paucity of reports does not permit a conclusion about whether polyploidy is the cause of the congenital defects observed or merely a secondary phenomenon.

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RESUMO

Este trabalho apresenta um novo caso de mosaicismo diplóide/tetraplóide em criança brasileira do sexo masculino com malformações congênicas múltiplas que sobreviveu até os 8 meses. Achados clínicos comuns a esta criança e outros casos relatados na literatura incluem: retardamento mental e do desenvolvimento, hipotonia, frontal saliente, fontanelas anômalas, orelhas malformadas, ponte nasal larga, micrognatia, cardiopatia congênita e prega simiesca.

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