

Partial trisomy 14q— and parental translocation of No. 14 chromosome

Report of a case and review of the literature

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SUMMARY A case of partial trisomy 14 (47,+14q—) is presented. The proband's mother had a balanced translocation of 14q with the long arm of a No. 3 chromosome. Clinical and cytogenetic findings of this case are compared with 5 other cases of 47,+14q—, in which one parent had a balanced translocation of the distal part of the No. 14 long arm to another chromosome. It appears that this chromosomal aneuploidy produces a fairly typical clinical picture.

Several cases of partial trisomy 14q— have been reported which have been confirmed by cytogenetic studies. Five of them (Fryns *et al.*, 1974; Raoul *et al.*, 1975; Reiss *et al.*, 1972; Short *et al.*, 1972; Turleau *et al.*, 1975), showed karyotype abnormalities comparable to a case which was studied in our centre and which will be presented in this paper. In all 6 cases, the partial trisomy 14q— derives from a parental balanced translocation. The reports of partial trisomy 14 of Allderdice *et al.* (1971), Laurent *et al.* (1973), and Muldal *et al.* (1973) were excluded because the karyotypic alterations were not fully comparable to the other cases.

Case report

A white baby girl was referred to the University Hospitals at the age of 8 months because of failure to grow. She was the full-term product of the second pregnancy of a 24-year-old mother and a 41-year-old father. Both parents and a 3-year-old sister are phenotypically normal.

Birthweight was 2730 g, body length 49 cm, and head circumference 32 cm. She was described as a good baby who did not cry much, but smiled and babbled. Her psychomotor development was very slow. She rolled over at the age of 6 months, yet did not reach for toys, and made no effort to crawl or sit up at the age of 8 months. At that time, her weight was 5.7 kg, her height was 63 cm, and her head

circumference was 42 cm. All measurements were below the third centile for her age.

Physical examination revealed epicanthal folds (Fig. 1), antimongoloid slant, ptosis, slight hypertelorism, slight asymmetry of the head, ears normal in shape but low-set, triangular shaped mouth, very high and narrow palate; and bifid uvula. The muscle tone of the upper extremities was increased. Her lower extremities were hypotonic. Plantar reflexes were exaggerated in the uppers and active in the lowers. Heart, lungs, abdomen, and external genitalia were unremarkable.

Dermatoglyphs showed proximal palmar triradii with an *atd* angle of 37° and 47°, respectively. The fingertip pattern revealed 8 arches, 1 ulnar loop and 1 radial loop.

At the age of 14 months, her developmental quotient was below 50. She could roll over and reach for objects, but was not able to sit.

Blood count, urinalysis including ferric chloride test, serum protein, serum albumin, calcium, cholesterol, glucose, urea nitrogen, uric acid, alkaline phosphatase, bilirubin, serum aspartate aminotransferase, blood electrolytes, thyroid studies, venereal disease reaction, and toxoplasma, rubella, and cytomegalovirus titres were normal. Radiological studies showed normal skull, chest, and intravenous pyelogram. Serum inorganic phosphorus was 6.6 and 7.2, and lactic dehydrogenases were 221 and 286 (normal range 100-225). A barium swallow gave evidence suggestive of tracheomalacia.

No other cases of congenital anomalies or mental retardation are known in this family (Fig. 2). Two



Fig. 1 Proband at age 14 months. Note microcephaly, slight asymmetry of head, epicanthal folds, antimongoloid slant, ptosis, triangular shaped mouth.

distant relatives of the mother have each had several spontaneous abortions. Cytogenetic studies on these 2 subjects have not yet been performed.

Cytogenetic studies

Chromosomal analysis of the proband's leucocytes showed 47 chromosomes, including a supernumerary,

small, acrocentric, satellited chromosome, comparable in size to a number 22 chromosome which, after Giemsa banding, was suggestive of a partially deleted number 14 chromosome (Fig. 3B). The proband's father had a normal karyotype. The mother showed only one number 14 chromosome and, in lieu of the second number 14 chromosome, the same small acrocentric chromosome which was found as an extra chromosome in the proband's karyotype; moreover, one of her number 3 chromosomes had an elongated long arm. By Giemsa banding, the mother's karyotype was identified as a balanced translocation: t(3;14) (q29;q21) (Fig. 3A). The same balanced translocation was found in the proband's sister, in 5 of 6 sibs of the mother and in 2 children of one of them. The maternal grandmother had a normal karyotype. It can be assumed that the translocation had been inherited from the maternal grandfather who was not available for chromosomal analysis. Chromosome analyses of his sibs are not yet available.

Discussion

Diversified cases of the possible partial trisomy D had been reported before banding techniques became available. Whether or not the extra chromosome in each case was in fact a partially deleted D chromosome or, rather, a number 22 chromosome, or a fragment of some other larger chromosome remains an open question. For the case reported from our laboratory in 1962 (Zellweger *et al.*, 1962) it was possible on clinical grounds to change the diagnosis from partial trisomy D to trisomy 22 (Zellweger *et al.*, 1975).

Now autoradiography and banding techniques allow an accurate differentiation of the individual

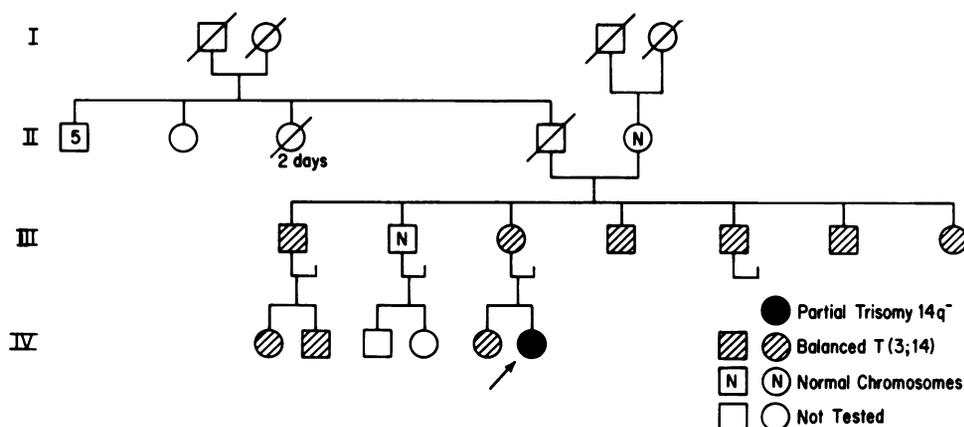


Fig. 2 Family pedigree.

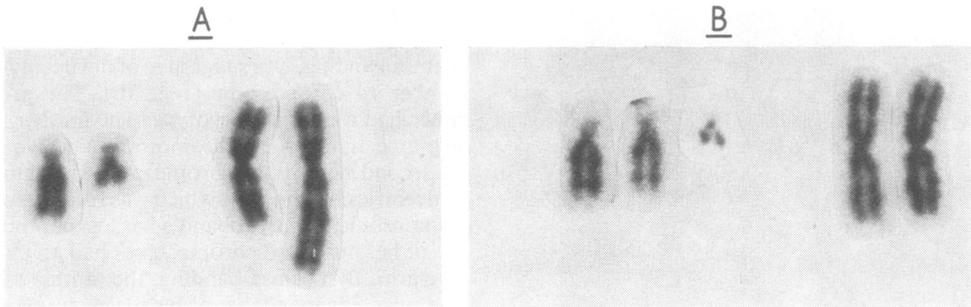


Fig. 3 (A) No. 3 and No. 14 chromosomes of mother. (B) No. 3 and No. 14 chromosomes of proband.

chromosomes. The chromosomes 13, 14, and 15 are easily distinguishable if present in full size, yet not if partially deleted. In the case of a simple deletion, the deleted chromosome can be identified through the process of elimination, by identifying the other D group chromosomes. In case of a partial supernumerary chromosome, this process would not be effective. However, it again becomes possible to identify a partially deleted D chromosome if, as in the case presented here, a balanced translocation is found in the proband's family. The mother of our

proband, as well as several relatives, has a balanced 3;14 translocation.

It is interesting to note that all cases of definitely identified partial trisomy 14q— reported to date derived from a parental translocation of a number 14 chromosome with another chromosome. In each of the 6 cases listed in the Table, the number 14 chromosome was translocated to a different chromosome.

The clinical findings described in our case and in the 5 reported cases with chromosomal abnormalities

Table Summary of findings in partial trisomy 14q— from 5 reported cases and present case

Cases	Raoul <i>et al.</i> (1975)	Turleau <i>et al.</i> (1975)	Short <i>et al.</i> (1972)	Reiss <i>et al.</i> (1972)	Fryns <i>et al.</i> (1974)	Present case
Mother's age	41	26	22	21	18	24
Gestation	7 mth	39 wk	N	40 wk	40 wk	40 wk
Birthweight (g)	1800	2650	2910	2400	2200	2730
Birth length (cm)	?	?	42	46	?	49
Head circumference at birth (cm)	32	?	32	33	?	32
Small stature	+	+	+	+	+	+
Severe mental retardation	+	+	?	+	+	+
Microcephaly (cm below means)	-5	-2	-2	-5	-4	-4
Large mouth	+	+	+	+	?	-
Blepharophimosis	+	?	+	+	-	-
			(microphththalmus)			
Antimongoloid slant	+	-	-	?	-	+
Large nose	+	+	+	Uprturned	+	-
Palate	Cleft	Cleft	Cleft*	Cleft	High arched	High arched, bifid uvula
Deep-seated ears	-	?	+	Receded	-	+
Dysmorphic ears	-	?	+	-	-	-
Short neck	+	+	+	Nuchal skin fold	+	+
Undescended testes	-/-	?	+/-	+/-	F	F
Pes equinovarus	+	?	+	-	-	Metatarsus adductus
Palmar crease	Sydney	-	Simian	-	-	-
Arches on fingertips	5	N	?	6	?	8
Karyotypes:						
Proband	47, +14q-	47, +14q-	47, +14q-	47, +14q-	47, +14q-	47, +14q-
Missing portion	14q (23→ter)	14q (22→ter)	14q distal	14q distal	14q distal	14q (22→ter)
Mother	46, t(10p+; 14q-)	46, t(12q+; 14q-)	46, t(9p+; 14q-)	N	46, t(14q-; 19q+)	46, t(3q+; 14q-)
Father	N	N	N	46, t(2q+; 14q-)	N	N

N = normal.

* Cleft of alveolar process only.

† Moderate.

comparable to this case are listed in the Table. Consistent findings are: prenatal and postnatal growth failure, delay in psychomotor development which was severe to profound in 4 cases and mild to moderate in the case reported by Fryns *et al.* (1974), head circumference 2 to 5 cm below the mean for age. Three cases had a cleft palate; one child had a median cleft of the alveolar process; and in our case, the cleft was limited to the uvula; a high and narrow palate was found in our case and in the one reported by Fryns *et al.* (1974). Two other frequent findings were large mouth and large nose, which may be beaked or upturned in some instances. Other, less consistent, findings were: blepharophimosis and/or microphthalmia; hyper- or hypotelorism; anti-mongoloid slant; deep-seated, in one case (Reiss *et al.*, 1972) receded ears; and pes equinovarus. In 3 of 4 cases, digital arches prevailed. The cases listed in the Table had a number of clinical features in common which, if confirmed in future observations, may allow the description of a clinical syndrome attributable to the presence of a supernumerary, partially deleted number 14 chromosome which is clearly distinct from the clinically well-delineated trisomy 13 or Patau syndrome.

Minor phenotypic differences between the cases of partial trisomy 14 may originate from two sources:

(1) The length of the deleted segment of the long arm of chromosome number 14 varied from case to case.

(2) The distal segment of the number 14 chromosome long arm is translocated in each case to a different chromosome and, in consequence, in each case the terminal segment of a different chromosome is reciprocally translocated to the partially deleted number 14 chromosome and, hence, present in triplicate. This may account for some phenotypic differences, even if it represents a very small segment of the other chromosome. It should be emphasized, however, that a reciprocal translocation cannot always be found (Zellweger *et al.*, 1975) or may, at least, escape certain staining procedures as Ferguson-Smith and Page (1973) showed for a translocation involving two C chromosomes (10;11). Attempts in our case to show a terminal segment of a number 3 chromosome on the partially deleted number 14 chromosome by G, Q, and R banding yielded inconclusive results (Francke, 1972).

An interesting point to consider is the mechanism which leads to the partial trisomy in the child whose one parent has a balanced translocation.

Various possible karyotypes of offspring have been discussed by Short *et al.* (1972): normal, balanced translocation, partial trisomy of the distal portion of

the number 14 long arm with 46 chromosomes (Pfeiffer *et al.*, 1973), and partial 14q— monosomy. The latter may account for some of the abortions noted in several families. The occurrence of a partial trisomy 14 with 47 chromosomes, including the short arm, centromere, and the proximal part of the long arm deserves a special explanation. Since chiasma formation in the centromeric regions is often suppressed, an unstable bivalent between the complete and the partially deleted number 14 chromosome could be assumed, leading to premature desynapsis or even asynapsis and subsequent segregation of the two number 14 chromosomes to the same spindle pole (Cohen *et al.*, 1975).

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