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## Duplication-deletion with partial trisomy 1q and partial monosomy 3p resulting from a maternal reciprocal translocation rcp(1;3)(q32;p25)

**SUMMARY** A mother with a translocation rcp(1;3)(q32;p25) gave birth to a son with duplication of 1q32→qter and deletion of 3p25→pter.

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At 17½ years of age, the proband was severely mentally retarded and presented a pattern of multiple minor dysmorphic stigmata and anomalies, including hypertrichosis, synophrys, ocular hypertelorism, ptosis, convergent squint, cleft uvula and narrow palate, poorly modelled auricles, funnel chest, kyphoscoliosis, umbilical and inguinal hernias, and cubitus valgus. He had normal stature and did not have any apparent malformations.

Before chromosome banding techniques, duplication-deletions could usually only be assumed from the clinical picture when the deletion of a particular chromosome segment was known to cause specific clinical features. Banding techniques allowed the determination of a variety of duplication-deletions. The present report adds a further example to this list, a case of monosomy 3p25→pter and trisomy 1q32→qter following a maternal reciprocal translocation.

### Case report

The proband, a male, was the youngest of three children. The birthweights of his maternal half-brother and his sister were 3750 g and 4120 g, respectively. His father and mother were 35 and 36 years old at his birth. After an uneventful pregnancy, vertex delivery took place at 38 6/7 weeks of gestation. He had neither asphyxia nor cyanosis. Weight at birth was 2910 g (10th to 50th centile), length was 46 cm (15th centile), and head circumference was 33 cm (10th to 50th centile). The placenta weighed 620 g and was normal on inspection, the umbilical cord containing three vessels. His mother remembered him as "hairy, like a little animal," but no other abnormalities were noticed at birth. He fed poorly and regurgitated frequently during and after feeding. At the age of 4 months he was referred for paediatric evaluation because of suspicion of delayed motor development. Weight (6.15 kg) and head circumference (41 cm) were at the 25th centile while length (59 cm) was about the 3rd centile. He did not smile, or fix on objects with his eyes and only rarely followed objects, or lift his head from a prone position. Spontaneous movements were poor, and muscle tone was suspected to be increased. A pattern of minor dysmorphic stigmata was observed (fig 1a, b), notably synophrys and bushy eyebrows, intermittent convergent squint, recessed mandible, short neck with limited excursion, bilateral inguinal hernias and a small umbilical hernia, and short hands, feet, fingers, and toes. Inspiratory stridor and

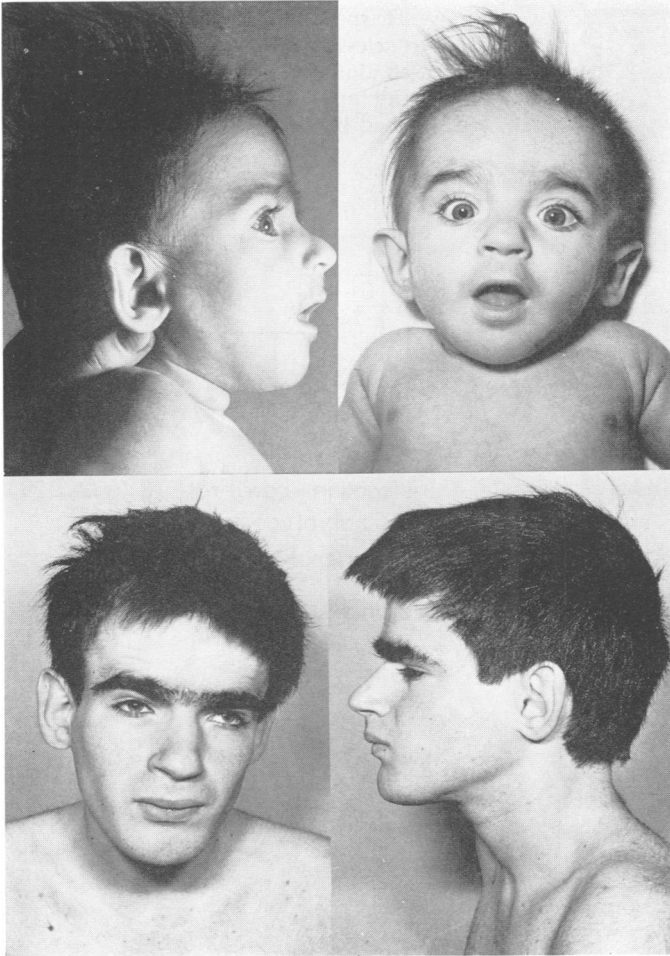


FIG 1 *Head of the proband at 5½ months and 17½ years. Note hypertrichosis, synophrys, hypertelorism, short upper lip, and misshapen ears.*

a 2/6 systolic murmur were also noted. The texture of the skin was fine and bluish with marked venous patterning, especially over the temporal regions. An oesophagogram showed torsion of the stomach and excluded a tracheo-oesophageal fistula. Radiographs of the skull, chest, spine, pelvis, right forearm, and both hands were normal as was an EKG. Direct laryngoscopy showed a "long and thick epiglottis."

Motor and mental development were delayed: he sat up without help at 18 months, walked at 4 years, and used single words at 5 years of age. At 7 years he was transferred to a school for mentally retarded children. At that age, he fed and undressed himself and formed short sentences, but he was still incontinent of urine. Muscular tone was now decreased, his gait was broad based and clumsy, and fine motor function and co-ordination were poor.

During the following years, his height, weight, and head circumference were mostly along the 10th, 75th, and 95th centile, respectively. Pubic hair growth started when he was 10 years old, but other pubertal signs did not appear before the age of 14. He suffered from recurrent otitis and upper respiratory tract infections.

At clinical examination at 17 7/12 years of age (figs 1c, d, and 2) he presented as a distinctly mentally retarded, overweight, and microcephalic boy, with a height of 161 cm, a weight of 56 kg, and a head circumference of 59 cm. There was hypertrichosis, especially over the shoulders, arms, the gluteal regions, and the legs, and the hair line was low both frontally and nuchally. The occiput was prominent. Facial characteristics included confluent bushy eyebrows, long lashes, orbital hypertelorism (inner

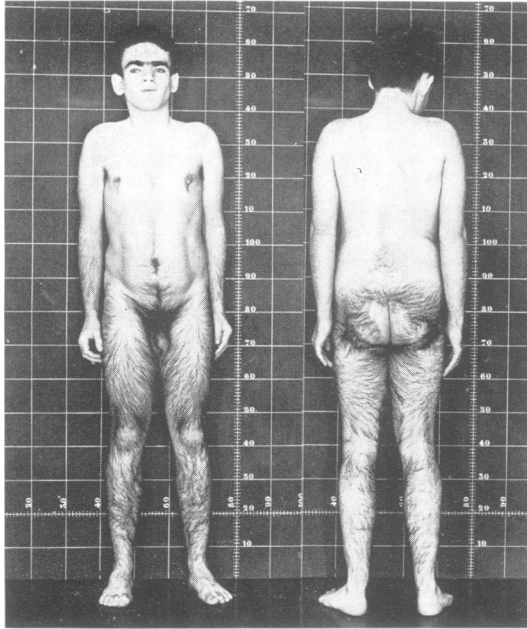


FIG 2 Proband at 17½ years. Note hypertrichosis, especially over shoulders, arms, gluteal regions, and legs.

canthal, interpupillary, and outer canthal distances all about the 85th centile), horizontal position of the eye axes, ptosis of the upper lids, normal size and shape of the nose, short distance between the nasal alae and upper lip and poorly designed philtrum, narrow and high palate with bifid uvula, a normal sized mandible, irregular position of the incisors, normal sized, protruding, and poorly formed auricles with folded helices, prominent antitragi, and hypoplastic lobules. There was no nystagmus or epicanthus, the pupils reacted symmetrically to light, and the fundi were normal.

There was moderate thoracolumbar kyphoscoliosis and the nipples were inverted, but of normal size and location. Genitalia were normal and postpubertal, the testes measuring 6 and 8 ml, respectively. He shaved daily. There was cubitus valgus and reduced flexion in both wrists. Hands and fingers were of normal size, and the distal interphalangeal joints showed reduced flexion with almost invisible flexion creases. Dermatoglyphs included bilateral bridged transverse palmar creases, *t* position of the palmar axial triradii, proximal loops on the thenar and whorls on the hypothenar eminences, and on the fingertips there were six whorls and four ulnar loops.

The patient's muscular tone was normal, but strength was poor. His gait and fine motor functions

were clumsy. He spoke in short defective sentences in a deep and toneless voice. He ate, dressed, and undressed himself alone and helped in the kitchen and household. Full urine continence has never been achieved. He had little contact with children of his

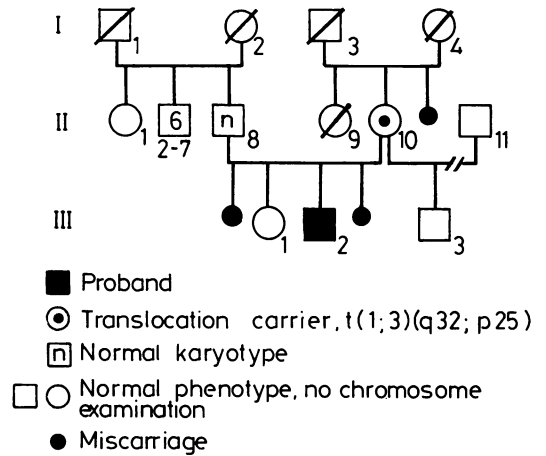


FIG 3 Pedigree of family.

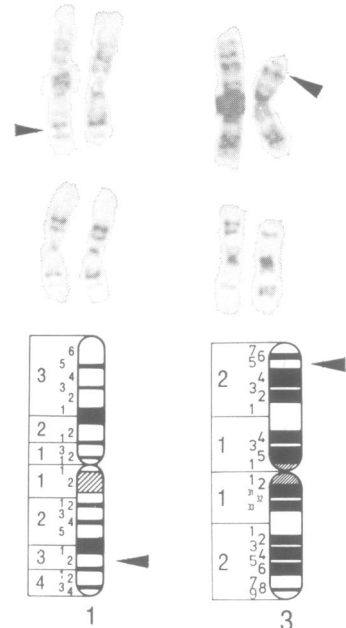


FIG 4 Chromosome pairs 1 and 3 from a karyotype of the mother (upper row) and proband (middle row), using G banding, and diagram (lower row). Note 1;3 translocation in the mother and rearranged No 3, but two normal chromosomes 1 in the son. Arrows on normal homologues indicate breakpoints.

age and preferred adults around him. He was easily distracted, often agitated, and rarely aggressive, but, if so, always towards younger children. For years he used to drink whatever was available; for example, he drank the water from any flower vase available.

Radiographs of the chest, pelvis, and right forearm were normal. An *x*-ray of the right hand at 7 years showed pseudoepiphyses on metacarpals 2 and 5, a dicentric ossification centre of the triquetral, and no ossification centre of the lunate. Skull *x*-rays showed orbital hypertelorism, small orbitae, and sclerosis of the calvarian bones. An EKG was normal.

The patient's mother (fig 3, II.10) has had five pregnancies. Two resulted in the birth of the patient's healthy sister (III.1) and half-brother (III.3), and two ended in spontaneous abortion in the fourth month. The mother's older sister (II.9) died at the age of one year for unknown reasons, and her mother's last pregnancy had ended in a spontaneous abortion.

#### CYTOGENETIC EXAMINATION

Unbanded karyotypes examined in 1969 were interpreted as normal 46,XY. G banding of a blood

culture from the patient performed in 1979 showed a 46,XY karyotype with a chromosome 3 with extra material on its short arm. Examination of the mother's chromosomes clarified the origin of the patient's rearrangement: her karyotype showed a reciprocal translocation between 1q and 3p. The segment distal to 1q32 was translocated on to 3p while the segment distal to 3p25 was attached to 1q32 (fig 4). The patient, who had normal homologues No 1, was therefore trisomic for segment 1q32→qter and monosomic for 3p25→pter, his karyotype being 46,XY,der(3),rcp(1;3)(q32;p25) mat. The father had normal chromosomes and the two sibs were not available for chromosome examination.

#### Discussion

The proband is trisomic for the segment 1q32→qter and monosomic for 3p25→pter as a result of a maternal reciprocal translocation, rcp(1;3)(q32;p25). These two aberrations have already been reported: deletion of 3p25→pter was observed in a 1½-year-old

TABLE Comparison of some findings in the proband with findings in a non-familial case of the same chromosome aberration,<sup>9</sup> cases with only deletion of 3p25 → pter, and familial cases with only duplication of 1q32 → qter. Left, newborns and young children; right, adults

|                                       | Newborns and young children |                          |                            |                      | Adults  |                            |                               |
|---------------------------------------|-----------------------------|--------------------------|----------------------------|----------------------|---------|----------------------------|-------------------------------|
|                                       | Proband                     | Yunis et al <sup>9</sup> | Verjaal et al <sup>1</sup> | n = 3 <sup>3-5</sup> | Proband | Fineman et al <sup>2</sup> | Taysi and Sekhon <sup>6</sup> |
| Duplication of 1q32→qter              | +                           | +                        | -                          | +                    | +       | -                          | +                             |
| Deletion of 3q25→pter                 | +                           | +                        | +                          | -                    | +       | +                          | -                             |
| Birthweight <2800 g                   | -                           | +                        | +                          | 1/2                  | -       | +                          | 1/2                           |
| Height <3rd centile                   | -                           | -                        | +                          | 0                    | -       | +                          | 2/2                           |
| Microcephaly                          | -                           | -                        | +                          | nm                   | -       | +                          | 0/2                           |
| Severe mental retardation             | +                           | nm                       | +                          | 0                    | +       | +                          | 2/2                           |
| Brachycephaly                         | -                           | +                        | nm                         | nm                   | -       | +                          | 2/2                           |
| Low frontal hairline                  | +                           | +                        | +                          | 0/1                  | +       | -                          | 0/2                           |
| Hypertelorism                         | +                           | +                        | -                          | 1/2                  | +       | nm                         | 1/2                           |
| Synophrys                             | +                           | -                        | -                          | nm                   | +       | +                          | 2/2                           |
| Ptosis                                | +                           | +                        | +                          | 0                    | +       | +                          | ?1/2                          |
| Upward slanting palpebral fissures    | -                           | -                        | -                          | 0/1                  | -       | +                          | 0/2                           |
| Esophoria                             | +                           | -                        | +                          | 0/3                  | +       | -                          | 0/2                           |
| Narrow palate                         | +                           | nm                       | nm                         | nm                   | +       | nm                         | 2/2                           |
| Cleft palate and/or uvula             | +                           | -                        | -                          | 1/3                  | +       | -                          | 0/2                           |
| Irregular position of teeth           | 0                           | 0                        | 0                          | 0                    | -       | -                          | 2/2                           |
| Short mandible                        | +                           | -                        | nm                         | nm                   | -       | -                          | 2/2                           |
| Poorly modelled auricles              | +                           | nm                       | +                          | 3/3                  | +       | nm                         | 2/2                           |
| Preauricular pit                      | -                           | -                        | r                          | 0/3                  | -       | -                          | 0/2                           |
| Short neck                            | -                           | +                        | nm                         | nm                   | -       | nm                         | nm                            |
| Pectus excavatum                      | -                           | nm                       | nm                         | nm                   | +       | +                          | nm                            |
| (Kypho-)scoliosis                     | -                           | nm                       | nm                         | nm                   | +       | +                          | 1/2                           |
| Umbilical hernia                      | +                           | +                        | nm                         | nm                   | -       | -                          | 1/2                           |
| Inguinal hernia(s)                    | +                           | -                        | nm                         | nm                   | -       | -                          | 1/2                           |
| Cryptorchidism                        | -                           | 0                        | +                          | 0/1                  | -       | 0                          | 0/2                           |
| Hypertrichosis                        | +                           | nm                       | +                          | nm                   | +       | nm                         | nm                            |
| Cubitus valgus                        | +                           | nm                       | nm                         | nm                   | +       | nm                         | 2/2                           |
| Clinodactyly of little fingers        | -                           | +                        | +                          | nm                   | +       | +                          | nm                            |
| Postaxial hexadactyly of fingers/toes | -                           | -                        | +                          | 0/3                  | -       | +                          | 0/2                           |
| Congenital heart defect               | ?                           | -                        | ?                          | 2/2                  | -       | -                          | ?1/2                          |

nm = not mentioned

male<sup>1</sup> and in a 24-year-old female.<sup>2</sup> In addition, many cases of duplication-deletion following pericentric inversions of chromosome 3, inv(3)(p25q21) or inv(3)(p25q25) have been reported,<sup>2</sup> all of whom had monosomy of 3p25→pter and trisomy of segments of 3q. Trisomy 1q32→qter because of a familial rearrangement was observed in three neonates who died in early infancy<sup>3-5</sup> and in two male adults.<sup>6</sup> Probable de novo direct duplication of a similar segment has also been reported in two newborns.<sup>7-8</sup> The combination of the two previously mentioned aberrations was assumed from G banded karyotypes of a 1-year-old girl with a de novo rearrangement of chromosome 3.<sup>9</sup>

The table lists major clinical features of the proband compared to the case of Yunis *et al*<sup>9</sup> and to cases with pure monosomy 3p25→pter<sup>1,2</sup> and to cases with familial trisomy 1q32→qter.<sup>3-6</sup> As many dysmorphic features are age dependent or even age specific, and as some of the patients were observed in adulthood and others in early infancy, young infants and adults are compared separately. The proband, who is the only patient who was followed clinically from early infancy to adulthood, is included in both age groups.

As seen in the table, it is at present not possible to define a characteristic pattern of abnormalities for any of the three aberrations because of the small numbers of cases with duplications of 1q32→qter, deletion of 3p25→pter, and a combination of the two aberrations. Both the more uncharacteristic findings in the proband (hypertelorism, short mandible, malformed auricles) and the more specific findings (hypertrichosis, ptosis, synophrys) were found in a proportion of cases who had only the 1q32→qter duplication or only the 3p25→pter deletion. We expect that further reports will show which aberrations are particularly characteristic of trisomy 1q32→qter, monosomy 3p25→pter, and of the combination of the two.

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## Trisomy 14 mosaicism in a translocation 14q15q carrier: probable dissociation and isochromosome formation

**SUMMARY** A case of trisomy 14q mosaicism is described and compared with three other similar reported cases. The clinical picture is characterised by severe developmental retardation, failure to thrive, and somatic abnormalities including skeletal asymmetry, high arched or cleft palate, and low set dysplastic ears. The present chromosome imbalance probably resulted from dissociation of a balanced 14q15q translocation with subsequent formation of a 14q isochromosome.

Chromosome 14 trisomy appears to be exceedingly rare in newborns. Trisomy 14 mosaicism and partial trisomy 14 have also been very infrequently reported; a survey of published reports reveals three cases of trisomy 14 mosaicism.<sup>1-3</sup> We report an infant with trisomy 14 mosaicism probably caused by an unstable 14q15q translocation with the resulting formation of an isochromosome 14q.

#### Case report

The proband was born after a term pregnancy to a gravida 4, para 3, 30-year-old mother. Pregnancy and Received for publication 2 April 1980