incidental finding. It is anticipated that accumulation of data from newly reported cases will help determine whether a possible association between joint contractures and partial 3p trisomy syndrome exists, or whether these clinical manifestations may, in part, be the result of the presence of additional 15 material.

We wish to thank Drs Allan Bloom, Nuhad Dinno, Bernard Weisskopf, and Frank Yen for their helpful comments.

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De novo duplication 1q32-q42: variability of phenotypic features in partial 1q trisomies

SUMMARY A de novo tandem duplication 1q32-q42 was observed in a 7-month-old mentally retarded and malformed male infant.

Karyotype-phenotype correlation in other similar unbalanced trisomies has shown psychomotor retardation, micro- or retrognathia of both, and low set or malpositioned ears to be the most common features associated with this newly recognised syndrome. However, after reviewing patients with duplication of regions 1q2, 3, and 4 and 1q2 and 3, it was concluded that similar non-specific clinical features are also present in these 1q imbalances.

On the whole, a rather wide range in phenotypic expression has been observed in different cases. Thus it is concluded that, at present, it is impossible to delineate the profile of the syndromes resulting from partial 1q trisomies.

A number of structural variations and anomalies of chromosome 1 have been reported.¹ Among duplications of the long arm (1q+), the 1qh variant is the most common.²⁻³ The enlargement of chromosome 1 is in these instances the result of an elongation of the heterochromatic secondary constriction (h).

Acquired anomalies of chromosome 1 are found in 16.2% of malignant disorders, most of which are full or partial trisomies.⁴⁻⁵

Among congenital anomalies of the long arm of chromosome 1, 25 partial 1q trisomies have been reported, most of which were segregating from parents heterozygous for balanced reciprocal translocations involving the long arm of chromosome 1 (Vianello, 1979, personal communication).⁶⁻¹⁸ In six patients, partial duplication 1q occurred as a de novo mutation.¹⁹⁻²⁴ The clinical picture in these patients is variable.

We report a 7-month-old infant who came to our attention. Karyotype-phenotype correlations are attempted on data derived from 16 cases of partial 1q imbalances.

Case report

The proband was the product of the second pregnancy of a 20-year-old mother and a 25-year-old father. The parents were healthy and unrelated. A

Received for publication 10 December 1979

previous pregnancy terminated in spontaneous abortion in the third month. The family history was unremarkable.

The gestation was 35 weeks and was complicated by threatened abortion during the first trimester. Delivery was uncomplicated and birthweight was 2250 g.

Soon after birth the baby was admitted to hospital with jaundice. At 15 days of life he suffered generalised tonic-clonic seizures which occurred repeatedly. An EEG performed in this period showed slow activity and focal lesion in the right hemisphere. Repeated routine haematological analyses gave normal values.

At the age of 7 months, when referred to us for clinical evaluation and cytogenetic studies, he had a length of 62.5 cm (<3rd centile), a weight of 4450 g (<3rd centile), and a head circumference of 40 cm (<3rd centile). Craniofacial abnormalities

were microcephaly with asymmetrical wide fontanelles, triangular face with flat profile, shallow orbits, horizontal palpebral fissures, small nose with rounded tip, long philtrum, carp-shaped mouth, high arched palate, and dysmorphic ears with a poorly modelled helix, deep conchae, and hypoplastic lobes (fig 1a). On the thorax widely spaced nipples and five café-au-lait spots were noted. First degree hypospadias was present. Hands showed bilateral simian lines and the dermatoglyphs were unremarkable. Toes 2 and 4 overrode toes 1 and 3, respectively (fig 1b). Psychomotor development was severely delayed and muscle tone was normal.

Extensive biochemical screening, including amino-acid chromatography of blood and urine and thyroid function, gave normal results. Ophthalmological evaluation was negative.

CYTOGENETIC STUDIES

Chromosome preparations were obtained from short term lymphocyte cultures. All cells, after conventional Giemsa staining, showed 46 chromosomes and a structural anomaly of chromosome 1.

QFQ, GTG, and RBA banding showed an additional segment resulting from direct duplication of region 1q32-q43.²⁵

Thus the karyotype was 46,XY,dir dup(1)(pter → q43::q31 → q43::q43 → qter) (fig 2).

The karyotypes of the parents were normal.

Discussion

Our case represents the seventh de novo partial trisomy for the long arm of chromosome 1. Six previous patients have been reported.¹⁹⁻²⁴

On the basis of cytogenetic and clinical data available in published reports, Taysi and Sekhon¹⁷ and Forabosco and Dallapiccola²⁶ have tentatively divided the subjects into three distinct groups.

The first group (duplication of two-thirds of the long arm: regions 2, 3, 4) is characterised by intra-uterine growth retardation, cleft lip and palate, cardiac defects, thymic hypoplasia or aplasia, absence of the gallbladder, and short survival varying between 5 and 48 hours. Hypertelorism, micrognathia, undescended testes, and long fingers are generally also found.

The second group (duplication of the distal third of the long arm: regions 3, 4), to which our case belongs, is characterised by low set ears, micrognathia, narrow craniofacial features, long fingers, and longer survival. Growth and mental retardation are always found.

The third group (duplication of the interstitial segment: regions 2, 3) shows variability ranging from a mildly abnormal phenotype and normal growth^{10 14}

FIG 1 (a) Face of the patient at the age of 2 months; (b) the feet of the patient.

FIG 2 (a) Karyotype of the patient (GTG bands); (b) chromosome 1 pair from selected metaphase plates (RBA bands).

to gross phenotypical anomalies.^{13 14} This phenotypical variation cannot be simply because of involvement of different segments of chromosome 1, since in two of the patients of Pan *et al*¹⁴ a different clinical picture was observed in the presence of the same chromosomal rearrangement.

These observations underline the difficulties in giving a correct prognosis for affected subjects.

Our case displays many of the features of the second group and his phenotype is very similar to

that of the patient reported by Steffensen *et al*.²² Discrepancies between our patient's phenotype and other cases belonging to this group might be the result of either the coexistent partial monosomy for another autosome involved in the translocation or of a position effect, which can be different in different types of rearrangement.

In the table clinical data of 18 patients with trisomies of different 1q regions are shown.

The patients described by Sanger *et al*¹⁵ were not

Case reports

TABLE Clinical features and relative frequencies in patients carrying different partial 1q trisomies.

Clinical features	Trisomic regions		
	1q2-1q4	1q3-1q4	1q2-1q3
Mean birthweight (g)	2156	2660	3103
M/F ratio	3/1	5/3	0/6
Growth retardation	—	5/8	2/6
Psychomotor retardation	3/4	6/8	4/6
Normal or macrocephalic skull	—	5/8	5/6
Wide fontanelles	—	6/8	3/6
Frontal bossing	2/4	5/8	3/6
Large auricles	—	3/8	1/6
Low set or malpositioned ears	2/4	4/8	4/6
Microphthalmia	—	3/8	2/6
Downward slanting palpebral fissures	2/4	4/8	—
Long nose	2/4	3/8	—
Broad and prominent nasal bridge	2/4	—	—
Cleft lip and/or palate	2/4	—	—
Micro- and/or retrognathia	3/4	6/8	5/6
Dysplastic teeth enamel	—	—	2/6
Short neck	—	4/8	2/6
Redundant skin of neck	—	3/8	—
Widely spaced nipples	—	5/8	4/6
Malformed chest	2/4	4/8	4/6
Long and tapering fingers	2/4	6/8	1/6
Anomalous implantation of the toes	—	5/8	4/6
Cerebral malformations	2/4	2/8	—
Cardiac malformations	4/4	6/8	2/6
Renal malformations	2/4	3/8	—
Intestinal malformations	1/4	3/8	—
Ocular malformations	—	1/8	—
Thymic hypo- or aplasia	3/4	1/8	—
Cryptorchidism	3/3	3/5	—
Short chorda penis	—	4/5	—

Data were derived from the following sources: Bonfante *et al.*,⁶ Dagna Bricarelli *et al.*,⁷ Flatz and Fonatsch,¹⁹ Garrett and Finley,⁹ Garver *et al.*,¹⁰ Neu and Gardner,¹¹ Norwood and Hoehn,¹² Palmer *et al.*,¹³ Pan *et al.*,¹⁴ Rehder and Friedrich,²⁰ Schinzel,²¹ Steffensen *et al.*,²² Van den Berghe *et al.*,¹⁸ Vianello, 1979, personal communication, Yunis *et al.*,²³ and our case.

included in the review as they were not described fully; the two patients of Taysi and Sekhon¹⁷ were also omitted because the advanced age precludes adequate clinical comparison with the other cases. The patient of Zuffardi *et al.*²⁴ was not considered either, since the phenotypic features could be reduced by the spreading effect of the X inactivation to chromosome 1 carrying the duplicated 1q segment.

None of the features reported in the table seems to be characteristic of a specific imbalance. Furthermore, because of the overlap of features in the three groups, it seems impossible at present to delineate the clinical profile of these chromosomal syndromes.

Nevertheless, the following points can be made. Psychomotor retardation, micro- or retrognathia or both, and low set or malpositioned ears are the most common features in 1q trisomies. Cranial anomalies are mostly present in insertions and trisomies of the distal third while in trisomies of the distal two-thirds anomalies of the face, including cleft lip or palate or both, are more evident. Long and tapering fingers

are observed in all three groups with different incidences. Cardiac malformations are common to the three syndromes while anomalies of the kidney, gastrointestinal tract, brain, thymus, and genitalia seem mostly to affect patients trisomic for the distal third of the long arm of chromosome 1.

The breakpoint located on band q32 in 16 of the 26 cases reported confirms earlier findings, suggesting an increased vulnerability of this band which has been considered a breakage 'hot-spot'.^{17 22 27}

In the presence of a normal karyotype in the parents, the origin of the duplicated segment in our case can be interpreted in one of the following ways: unequal sister chromatid exchange during meiosis or mitosis, leading to the formation of a duplicated and deficient chromosome 1; or unequal exchange or crossing over during meiosis; or reciprocal translocation between the long arms of the two chromosome 1 homologues. None of these hypotheses can be confirmed or excluded in any way.

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