Partial trisomy 7 (q32→qter) syndrome in two children

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SUMMARY Two unrelated children are described with a partial trisomy 7 (q32→qter). Their phenotypes are compared with other reported cases with both this trisomy and others of the 7q arm. Several apparently useful pathognomonic features are distinguished. The phenotypic variability between trisomic persons within and between families is discussed. It is suggested that the disparate monosomies always associated with these trisomies may not make a major contribution to this variability. The importance for genetic counselling of reporting in detail the clinical appearance and development of all children with this rare trisomy is emphasised.

With the advent of chromosome banding techniques the description of hitherto unrecognised syndromes associated with partial trisomy and monosomy became possible. Unlike the 'classical' chromosome disorders, these new syndromes occur very infrequently and are noted for their phenotypic variability. This variability may be due to the occurrence of different concomitant partial monosomies. Consequently, it is of some importance that the clinical features of each person with a partial trisomy syndrome is described in full and compared with other published cases, so that common characteristic features can be delineated. Only in this way can the clear, unbiased characteristics of each such syndrome be determined.

Three syndromes have been described which are associated with the partial trisomy of different regions of the long arm of chromosome 7.¹ We describe here two cases. The first is a 14 year old girl with trisomy 7 (q32→qter), whose initial chromosome analysis in 1970, using orcein, was reported as 46,XX. She was thought to have been damaged during a difficult delivery. The second is a baby with the same partial trisomy who died in the first year of life.

Case reports

CASE 1 (FIG 1)

The patient was the second child of non-consanguineous, phenotypically normal parents. The first child was a phenotypically normal boy. The

pregnancy was normal and the delivery, though long, resulted in the spontaneous delivery of the child, Apgar score 9 at one minute, weighing 3232 g.

At the age of 7 months, the child was noted to have retarded development, a head circumference of 46.5 cm (at the upper limit of normal), normal fontanelles, and a grade 2 systolic murmur at the lower end of the left sternal border. X-ray of the chest showed a markedly enlarged heart with left ventricular predominance and marked pulmonary plethora.

FIG 1 Lateral appearance of case 1.

At 12 months the child was sitting with little support, rolling from back to front, eating ordinary food, and attempting to feed herself. Visual impairment and a coarse nystagmus were noticed at this time, together with a left convergent strabismus and fairly heavy pigmentation of both fundi.

At the age of 8 years, she was noticed to suffer from periods of absence. By this stage, a marked kyphoscoliosis with spastic tetraplegia and some athetoid movements had developed. Hypermobility of all joints was present with a very marked valgus position of the feet and externally rotated position of the legs.

Now, at the age of 14 years, the child is severely retarded with a hypotonic palsy. While she can feed herself, she is doubly incontinent and totally dependent for all other needs. She does not respond to her name and has no speech.

Her head circumference is now 56 cm (within 2 SD of the mean), her upper face is narrow with deep set eyes, small epicanthic folds, a left strabismus, and pendular nystagmus on fixed gaze. She has a high arched palate and irregular dentition. Both ears are low set and abnormally folded. She has a severe kyphoscoliosis, a very short sternum (13.5 cm), and long fingers with 'finger-like' thumbs. The metacarpophalangeal joints are hyperextensible and the fingernails are hyperconvex. On both feet, the big toe and fifth toe are longer than the other toes. Lymphoedema is present on the dorsum of both feet.

FIG 2 Frontal appearance of case 2.

CASE 2 (FIG 2)

This patient was the fifth child of unrelated parents with a normal delivery at 41 weeks' gestation. The father and mother are phenotypically normal as are his two sisters and two brothers. His father was 35 years old and his mother 30 years old at the time of his birth.

The patient was admitted to hospital at the age of 12 weeks for diagnosis because of his odd appearance. At this time the baby was hirsute, had antimongoloid slanting eyes, a broad nasal bridge, and low set, simple ears with a dimple on the left pinna. He had flexion deformities of the third fingers of both hands, micrognathia, a large fontanelle, and an umbilical hernia. He also had a systolic murmur due to a small atrial septal defect. An abnormal ultrasonic scan suggested that the liver had a cystic structure and that splenomegaly was present. The child subsequently died at home before the age of 1 year.

Cytogenetic studies

Chromosome preparations were made from peripheral blood by PHA stimulation in the usual manner. The chromosomes were then C and G banded for karyotype analysis.

CASE 1

G banding of the proband's chromosomes revealed a female karyotype with a large piece of extra chromosomal material translocated onto the short arm of chromosome 12 (46,XX,12p+). The mother (II.2, fig 3) was found to have a normal female

FIG 3 Pedigree of case 1.

karyotype while the father (II.1) and both brothers (III.1, III.3) of the proband were found to have a balanced translocation between the long arm of chromosome 7 and the short arm of chromosome 12 (46,XY,t(7;12)(q32;p13)) (fig 4). Consequently the karyotype of the proband is considered to be 46,XX,-12,+der(12),t(7;12)(q32;p13) pat resulting in partial trisomy for chromosome 7 (q32→qter) and concomitant monosomy for at least part of band 12p13.

On a further cytogenetic investigation of this family the proband's paternal grandmother (I.2) was found to have a normal female karyotype.

CASE 2

G banding revealed a male karyotype with a large piece of additional material on the long arm of

FIG 4 Partial karyotype of chromosomes 7 and 12 from the family of case 1. The derived chromosomes are to the left in each pair.

FIG 5 Pedigree of case 2.

FIG 6 Partial karyotype of chromosomes 7 and 18 from the family of case 2. The derived chromosomes are to the left in each pair.

chromosome 18 (46,XY,18q+). The father (II.4, fig 5) has a normal male karyotype while the mother (II.5), a sister (III.1), and two brothers (III.3, III.4) of the proband all carry a reciprocal translocation between the long arm of chromosome 7 and the long arm of chromosome 18 (46,XY or XX, t(7;18)(q32;q23)) (fig 6). The proband was thus also considered to have partial trisomy for chromosome 7 (q32→qter) and presumed also to have monosomy for band 18q23 (46,XY,-18,+der(18),t(7;18)(q32;q23)mat).

Discussion

We are aware of 15 cases of partial trisomy for chromosome 7 (q32→qter) reported to date, including a single case reported as trisomy for q33→qter. There have also been many reports of two other

TABLE Clinical features of partial trisomy 7q syndromes.

Reported features	Partial trisomy regions			Case 1	Case 2
	q22→q31	q31→qter (incl q22→qter)	q32→qter (incl q33→qter and case 1 and 2)		
Low birth weight	1/3	4/5	8/17	-	-
Retardation of development	3/3	2/2	16/16	+	
Wide open fontanelle	0/3	3/3	3/11	-	+
Hypertelorism	2/3	3/4	4/14	-	
Epicanthus	2/3	0/3	8/12	+	
*Strabismus	3/3	1/5	4/12	+	
Small palpebral fissures	0/1	3/4	0/9	-	
Low set ears	2/3	4/4	11/16	+	+
Ear anomalies	0/3	3/4	8/17	+	+
Small nose	2/3	2/4	8/14	+	+
*Cleft palate	0/3	5/5	1/17	-	-
Large tongue	0/3	1/1	3/8	-	
*Microretrognathia	0/3	5/5	4/16	-	+
Frontal bossing	2/3	2/4	4/13	+	+
*Skeletal anomalies	0/3	3/4	12/14	+	+
*Kyphoscoliosis	0/3	0/5	7/14	+	-
Dislocation of the hips	0/3	0/5	4/14	-	-
Hypotonia	2/3	1/1	10/14	+	+
Hypertonia	1/3	1/2	2/14	-	-
*Early postnatal death (<1 year)	0/3	4/4	2/17	-	+

The features marked by an asterisk are those considered to be most useful in distinguishing the three syndromes.

partial trisomies relating to different regions of the long arm of chromosome 7. These are trisomies of the interstitial region q22→q31 (three cases) and of the larger distal region q31→qter (five cases including a single case reported as trisomy for q22→qter).^{1,2}

From their statistical analysis of the presence or absence of pathogenic features, Novales *et al*¹ suggest that these trisomies represent three distinct syndromes. This can now be updated by the two cases of Klasen *et al*² and the two cases of Bass *et al*³ together with the two cases reported here (table).

There appear to be six features which are most useful in distinguishing these three syndromes (table). Early postnatal death has occurred in all four cases of trisomy q31→qter while the other two trisomies appear to be relatively viable. The single early death previously reported with trisomy q32→qter was in a child with apparent additional symptoms of cri-du-chat syndrome where a 5p arm was involved.⁴ Trisomy q31→qter is also strongly associated with cleft palate, which has only once been reported in a case of trisomy q32→qter where there was a family history of this defect, and with microretrognathia, which otherwise has previously only been reported in three of 14 cases of trisomy q32→qter.

On the other hand, kyphoscoliosis has only been reported in trisomy q32→qter where half the patients have been affected. Its reported absence in all subjects with the larger trisomy 7 (q31→qter) is

particularly surprising. Skeletal anomalies are commonly present except for the interstitial trisomy where it was not recorded in the three cases reported. Finally, strabismus has been found in all cases with the interstitial trisomy.

One point of importance is the large sampling errors associated with these syndromes due to the small populations involved. It underlines the need for the publication of the major clinical features of all such patients encountered.

Another complication is the obvious variation in the stigmata present between subjects with apparently the same partial trisomy imbalance. It may be that this is mainly due to the different monosomies present in each case. It is well recognised that chromosomal deletions have a much greater clinical effect than similar sized trisomies. However, even when the partially trisomic subjects are of the same family^{2,3} and consequently have identical monosomies, noticeable phenotypic differences exist. Variation in the phenotype may also be due to small interfamilial variability in the size of the partial trisomy. Therefore, the effect of monosomy on the phenotypic variability of partially trisomic subjects is uncertain and may in fact be small.

All the monosomies associated with the trisomy 7q syndromes only involve the terminal pale band, and since all such bands are early replicating they may be considered to be gene rich. However, they differ from interstitial pale bands by containing the telomere which may render these regions relatively

deficient in major genes, at least at the most distal parts. The actual amount of the terminal band which is absent in a partially trisomic subject is also usually difficult to estimate and is often not apparent.

Case 2 died within the first year of life and, like the case of Turleau *et al.*,⁴ had partial monosomy of a chromosome which is associated with a viable syndrome, the 18q- (de Grouchy) syndrome. However, it has been reported that band 18q21 is always involved in the phenotypic expression of this syndrome⁵ and apart from a slightly retracted mid-face this patient had none of the stigmata of the 18q- syndrome. This band was not involved in the translocation. It appears possible therefore that this is the first case of partial trisomy of 7q32→qter without a clinically significant monosomy to die soon after birth.

Case 1 illustrates the problem of bias in reporting cases. The proband was born after a long labour and her obvious mental retardation and physical deformities were considered to be due to this. When chromosome analysis was done in 1970 using solid staining it was thought that she had a normal karyotype.

It seems likely that those cases with the most

distinct dysmorphic features and malformations will stand a relatively higher chance of being reported. This emphasises the importance of analysing the chromosomes of all children who have multiple physical deformities in addition to mental retardation.

References

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