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Partial monosomy of 7q32 in a case of de novo rcp(7;15)(q32;q15)

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Abstract
A de novo apparently balanced translocation between chromosomes 7 and 15 with breakpoints in q32 and q15 respectively is reported in a female child. Clinical features included general growth and psychomotor retardation, feeding problems, microcephaly, low set ears, a short neck, and brachydactyly. These findings suggested possible physical or functional partial monosomy of the 7q32 or 15q15 segments. The phenotype of this case is similar to other cases of 7q deletion.

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Apparently balanced chromosomal rearrangements with often severe clinical abnormalities

pose problems in karyotype-phenotype correlation. Here we report an apparently balanced translocation involving chromosomes 7 and 15 in a girl with facial dysmorphism, developmental and growth retardation, and mental retardation. After a thorough review of published reports, we also relate the clinical features of our case to other cases of partial long arm monosomies of chromosomes 7 (table) and 15. The assignment of some of the dysmorphic findings to deletion of band 7q32 is also discussed.

Case report
The proband, a 4 year old girl, was the third child of non-consanguineous, healthy parents

Clinical features of patients with deletion of segments from 7q22 to 7qter

Deleted segments	q22-q32 (I)	q32-qter (II)	q33-qter (III)	q36-qter (IV)	q31-q34 (A)	q32-q34 (B) No 1	q32-q34 (B) No 2	q32-q34 (B) No 3	q32 Our case	q31-q34 (V)
References										
No of cases	9	14	15	6						5
Features										
Sex	4M/5F	7M/7F	5M/10F	2M/4F	F	F	F	M	F	1M/4F
Low birth weight	+++	+++	+++	+++	*				*	++
Growth retardation	+	+++	++	+++	*		*		*	+++
Developmental delay	++	+++	++	++	*	*	*	*	*	++++
Mental retardation	++	+++	++	++	*	*	*	*	*	++++
Microcephaly	+++	++	++	+++	*				*	++
Abnormal skull shape	++	+++	++	+++						
Prominent forehead		++	+							
Flat broad nasal bridge		++	++	++	*	*	*	*	*	++++
Bulbous nasal tip		++	++	++	*	*	*	*	*	++++
Bulbous/thickened nose		+	+	+	*	*	*	*	*	++++
Nose malformations		++	++	+++						
Ocular malformations		+	++	+						
Ocular abnormalities	++	+	+	+			*			+
Palpebral fissure slant	++	+	+	++						
Hypertelorism	++	++	++	Hypo +++		*	*	*		+++
Epicanthus	+		++		*				*	++
Micrognathia	+++	+	++			*			*	++
Ear malformations	+++	+++	+++	+++	*		*		*	++
Low set ears	++	++	++	++	*	*			*	+++
Cleft lip/palate		++	++	++						
Large mouth	+++	++	+			*	*	*	*	+++
Short neck	++		++						*	++
Brachydactyly	+	+	+						*	+
Other hand malformations	++	+	+	++	*					+
Foot malformations	++	++	++	+	*		*			++
Abnormal muscle tone	+++	++	++	++	*					+
Nervous system abnormalities	+	+	+					*		+
Seizures/abnormal EEG	+++	++	+			*	*	*		+++
Malformations of bone	++	+	++		*					+
Pulmonary abnormalities	++		+							
Coronary heart disease	+++		+	+						
Genital abnormalities	+	++	+	++						
Abnormal cry	+++		+		*					+
Poor suck	++	+	+							
Feeding problems	+++	+	+		*		*	*(c)	*(c)	+++
Frequent infections	+	+	+		*	*		*	*	++
Angioma		+	++						*	+

+ <25% positive/informative; ++ 25-45% positive/informative; +++ 45-65% positive/informative; ++++ 65-85% positive/informative.
(c) Allergy to cow's milk.
*Presence of the symptom.
(I) Abuelo et al,¹ Fagan et al² (case 3), Franceschini et al,³ Higginson et al,⁴ Martin-Pont B et al,⁵ Morey et al,⁶ Serup et al,⁷ Young et al⁸ (cases 4 and 5).
(II) Bernstein et al⁹ (cases 1 and 2), Bogart et al¹⁰ (cases 2, 3, 4 and 5), Friedrich et al,¹¹ Harris et al,¹² (cases 1, 2, 3 and 4), McMorow et al,¹³ Schwartz et al,¹⁴ Young et al⁸ (case 1).
(III) Baeteman et al¹⁵ (cases 1 and 2), Bogart et al¹⁰ (case 1), Fryns et al,¹⁶ Schinzel¹⁷ (cases 1 and 2), Schinzel,¹⁸ Smart et al,¹⁹ Taysi et al,²⁰ Tiller et al,²¹ Turleau et al,²² Verma et al²³ Vianello et al²⁴ (cases 1 and 2), Young et al⁸ (case 2).
(IV) Burrig et al²⁵ Kleczkowska et al²⁶ Krauss et al²⁷ (cases 2, 3, 4, and 5).
(A) Stallard and Jüberg.²⁸
(B) Nielsen et al.²⁹
(V) A+B+our case.

Figure 1 Front and side view of the proband aged 4 years.

and was born at term after an uncomplicated pregnancy and a normal delivery, weighing 2100 g and measuring 46 cm. Apgar scores were 8 at one minute and 10 at five minutes. She was bottle fed from birth and proved to have cow's milk intolerance. She was weaned at 5 months, spoke her first words at 9 months, and walked at 19 months. At the age of 4 years, body measurements were: weight 10.5 kg (<3th centile), height 88.4 cm (−2.5 SD), and head circumference 46 cm (<3th centile). The bone age was advanced compared to her stature. Physical examination showed a dysmorphic face with a planoangioma on the mid-forehead, a wide, flat nasal bridge, a bulbous nose with thickened alae, epicanthus, a large mouth, a small receding chin, normal but low set and slightly anteverted ears, a short neck (fig 1), brachydactyly, and genu valgum. Neuropsychological examination showed normal tone and reflexes, but mild psychomotor retardation. Respiratory, cardiovascular, renal, and gastrointestinal systems, genitalia, liver, and spleen were apparently normal.

CYTOGENETIC STUDIES

Cytogenetic studies were performed on peripheral blood lymphocytes using standard techniques and GTG-CBG banding. Chromosome

Figure 2 Partial karyotype of the proband.

analysis showed an apparently balanced reciprocal translocation: 46,XX,t(7;15)(q32;q15) (fig 2). Unfortunately, a cell line is not available from this patient, but frozen lymphocytes could be made available. The karyotypes of the parents were normal.

Discussion

Our case with an apparently balanced translocation showed some clinical features characteristic of chromosome anomalies, suggesting an intrachromosomal imbalance in chromosomes 7 and 15. An extensive review of published reports led us to conclude that the clinical features of this case were the expression of physical or functional loss of part of band 7q32.

Cases of partial monosomy 7q are roughly classified as proximal, interstitial, and terminal, and only the terminal deletion of 7q32-pter is thought to comprise a distinct syndrome. Therefore, in order to gain better knowledge of 7q monosomies, and in particular to identify some clinical characteristics connected with the 7q32 region, we reviewed cases which include this band in their deletions. Furthermore, as we could not find any other report of the deletion of this single band, we have included cases with monosomy from 7q22 to 7qter. Particular attention was paid to cases described by Stallard and Juberg²⁸ and Nielsen *et al*²⁹ showing smaller deletions, 7q31-34 and 7q32-34 respectively, around the band involved in our patient.

General opinion is that it is very difficult to characterise one or more definite phenotypes (distinct syndromes) resulting from deletions, as many cases are monosomic for different sizes of chromosomal segments, and also because cases which share common deletions do not exhibit uniform clinical features. Moreover, the severity of the clinical findings does not often seem proportionally related to the size of chromosomal segment loss. However, the clinical manifestations of the present case and of patients with 7q interstitial deletions from bands q31 to q34 are quite similar and generally less severe than other 7q distal monosomies. In all these cases a term pregnancy and delayed development are found. Mental retardation is also a constant finding and can be mild when the chromosomal region is limited to around the q32 segment. Common facial dysmorphism includes a large, wide mouth, low set ears, small receding chin, and an identical bulbous nose shape with thickened alae and broad, flat, depressed bridge. Low birth weight, growth retardation, and microcephaly, present in our case and that of Stallard and Juberg,²⁸ are frequent symptoms in 7q22-q32 and 7q32-qter monosomies. Feeding problems mainly of unspecified cause are constant findings in monosomies involving band q32. With reference to this, we would like to underline the intolerance to cow's milk found in the third case of Nielsen *et al*²⁹ and in our patient as a possible trait to consider in future studies. The neurological abnormalities like seizures, slight spasticity, ear malformations, susceptibility to infections, and hypertelorism found by Nielsen *et al*,²⁹ Stallard and Juberg,²⁸ and other authors (table), in various segment losses, were absent in our case. To summarise the above, we think that our case is a monosomy 7q32 which suggests that the above mentioned mild dysmorphism that produces a slightly peculiar facies and other non-specific features characterise band q32 involvement.

In conclusion we generally agree with Verma *et al*²³ that it is very difficult to diagnose a 7q- syndrome clinically because pathognomonic features are absent. However, if one considers the different bands separately and the possibility of gene deregulation for position effects, a more distinct pattern could emerge.

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