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Tandem duplication of the terminal band of the long arm of chromosome 7 (dir dup (7) (q36→qter))

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Abstract

We report on a new case of a single band duplication of the long arm of chromosome 7, dir dup (7)(q36→qter). The major manifestations are developmental delay (particularly speech), frontal bossing, macrocrania, and constant drooling. When compared with other cases involving a 7q duplication of various segments, our patient has a few minor anomalies. This case illustrates the genotype/phenotype correlation in a child with a single band duplication which has resulted in duplication of 7q36→qter. A tabulation of reported cases with duplication of various segments of 7q is provided, which may serve as an aid for clinicians.

In recent years, numerous attempts have been made to correlate syndrome manifestation with specific chromosome segments. Delineation of a distinct syndrome resulting from duplication of 7q was first reported by Vogel.[1] During the past few decades, several reports have appeared describing the clinical consequences associated with duplications of various segments of 7q.[2] The longest reported duplicated segment is 7q21→qter, while the smallest is 7q33→qter. It has been suggested that at least three possible distinct clinical syndromes can be established, based on three segments corresponding to regions q21 or 22→q31, q31→qter, and q32→qter.[3] Patients with duplication of 7q21 or 22→q31 are more severely abnormal than those with duplications of the other two segments. We present a case where the smallest portion of the long arm of chromosome 7 (q36→qter) is tandemly duplicated with a few clinical manifestations. We suggest that these manifestations are associated with this region. A table listing the anomalies associated with duplications of various regions of 7q is also provided.

Case report

A 3½ year old boy was referred for developmental delay, particularly speech. He was delivered at term to a 41 year old mother with no prenatal or postnatal complications. His mother gave a history of mild delay in gross motor development and of ADL skills with significant delay in speech and language.

On physical examination he had frontal bossing and macrocrania. Neurologically, he had a short attention span, poor socialisation, and unintelligible speech with delayed graphomotor skills. Constant drooling was noted. There were no cranial nerve abnormalities. Tone was slightly increased in the left Achilles tendon with a few beats of ankle clonus. However, deep tendon reflexes were normal and there were no cerebellar abnormalities or sensory deficits.

He was first referred to rule out fragile X in his peripheral blood and was found to be negative. However, additional genetic material on the long arm of chromosome 7 was noted. The aberration occurred de novo as the parents are cytogenetically normal. A tandem duplication seems the most likely explanation and is compatible with the banding pattern of band 7q36→qter (figure). The cytogenetic findings of this patient can be described as 46,XY,dir dup(7)(q36→qter). The parents refused photographic documentation, and the patient has been impossible to trace for dermatoglyphic evaluation. A cell line is not available from this patient.

Discussion

A number of reports describing duplication of the long arm of chromosome 7 (7q) have appeared since 1972. These reports suggested that the duplication of various segments can be classified into at least three distinct syndromes relating to q21 or q22→q31, q31→qter, and q32→qter. The most frequent type of aberration resulting in duplication is 7q32→qter.[4] The clinical findings observed in previous cases are summarised in the table. Obviously, the severity of the clinical manifestations is related to the size of the chromosomal segment involved. However, a few exceptions have been observed. For example, cleft palate was reported in a case of dup 7q22 to q31→qter[2] and renal microcysts and retardation were seen in most cases.[5] All patients with duplication of 7q31→qter died soon after birth, while those with other types of aberration lived over one year.[3]

Various attempts have been made to describe a so called 'dup 7q syndrome'. It is debatable whether it can be identified as a distinct syndrome before cytogenetic evaluation because of the highly variable physical characteristics. The present case was referred to rule out fragile X syndrome. Recently, Bartsch *et al*[5] suggested that "a recognizable phenotype may result in some patients with partial duplication (7q), even if the duplication is small". However, this is not the case in our patient, who has minimal clinical features and

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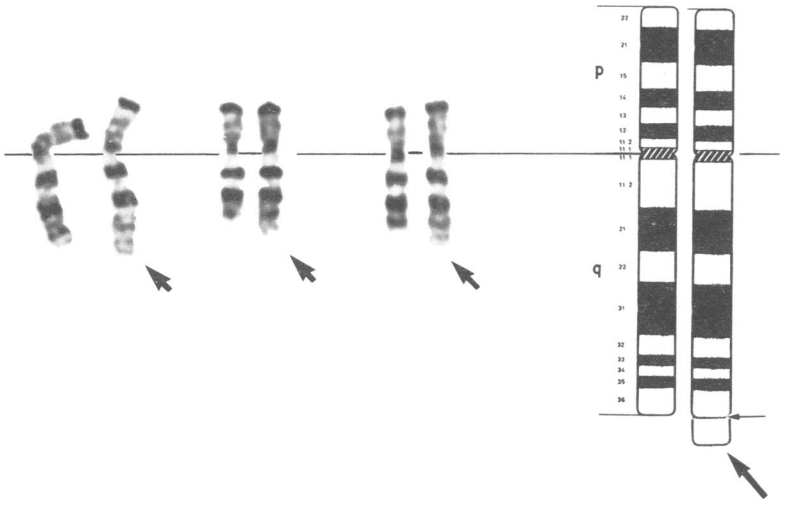
*Clinical manifestations associated with various segments of chromosome 7q.**

Features	7q21 →qter	7q21+q22 →qter	7q22 →q31	7q22 →qter	7q31 →qter	7q32 →qter	7q33+q34 +q35→qter	7q34 →qter	7q35 →qter	Present case
Microcephaly	2/2	3/5	2/3	1/1	4/6	7/16	1/3	0/1	1/1	+
Wide open fontanelles	1/2	2/5	0/3	1/1	4/6	7/13	1/2	0/1	1/1	−
Frontal bossing	0/2	2/5	2/3	1/1	4/6	7/16	1/3	0/1	1/1	+
Prominent occipital bones	1/2	3/5	0/3	1/1	3/6	1/16	1/3	0/1	0/1	−
Small palpebral fissures	2/2	3/5	2/3	0/1	2/6	3/16	1/3	0/1	1/1	−
Hypertelorism	2/2	4/5	2/3	1/1	2/6	4/16	0/3	0/1	0/1	−
Epicanthic folds	0/2	0/5	2/3	0/1	1/6	8/16	1/3	0/1	1/1	−
Downward slanting eyes	2/2	3/5	0/3	1/1	2/6	5/16	2/4	1/1	0/1	−
Strabismus	NR	0/5	3/3	NR	1/6	4/16	1/3	NR	NR	−
Small nose	2/2	3/5	1/3	1/1	2/6	6/16	1/3	0/1	1/1	−
Depressed nasal bridge	2/2	4/5	2/3	1/1	2/6	5/16	1/3	0/1	1/1	−
Macroglossia	1/2	3/5	0/3	1/1	2/6	3/16	1/3	0/1	1/1	−
Microretrognathia	2/2	5/5	0/3	1/1	5/6	4/16	0/3	0/1	0/1	−
Low set ears	2/2	5/5	2/3	1/1	4/6	10/16	1/3	0/1	0/1	−
Large ears	0/2	1/5	3/3	1/1	0/6	1/16	2/3	1/1	1/1	−
Malformed ears	2/2	5/5	1/3	1/1	5/6	7/16	3/3	1/1	1/1	−
Short neck	2/2	4/5	1/3	1/1	3/6	3/16	1/3	0/1	1/1	−
Single crease	0/2	2/5	1/3	0/1	3/6	7/16	2/4	0/1	1/1	−
Kyphoscoliosis	0/2	1/5	0/3	1/1	1/6	6/16	0/3	0/1	0/1	−
Skeletal anomalies	0/2	1/5	0/3	1/1	5/6	13/16	0/3	0/1	0/1	−
Hip dislocation	0/2	2/5	0/3	1/1	1/6	5/16	0/3	0/1	0/1	−
Cleft palate	1/2	3/5	0/3	0/1	6/6	1/16	0/4	0/1	0/1	−
Congenital heart defects	0/2	1/5	0/3	0/1	3/6	4/16	3/4	1/1	1/1	−
Cerebral malformations	1/2	1/5	2/3	0/1	3/6	3/16	1/4	0/1	1/1	−
Visceral malformations	NR	0/5	0/3	NR	3/6	4/16	0/4	NR	NR	−
Genital malformations	NR	1/5	0/3	NR	2/6	1/16	1/4	NR	NR	−
Cases	2	5	3	1	6	16	4	1	1	1

* Modified from Forabosco *et al.*[2]



GTG banded partial karyotype of the proband. The abnormal chromosome 7 is marked by arrows and in addition a diagrammatic representation of dir dup 7q36→qter is shown (see text).

the smallest duplication observed. The dysmorphic features observed in the present case may be correlated with a single band duplication. However, this should not imply that future cases with similar chromosomal abnormalities will have identical clinical consequences.

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2 Forabosco A, Baroncini A, Dalpra L, *et al*. The phenotype of partial dup (7q) reconsidered: a report of five new cases. *Clin Genet* 1988;**34**:48–59.
3 Novales MA, Fernandez-Novoa C, Hevia A, San Martin V, Galera H. Partial trisomy for the long arm of chromosome 7. Case report and review. *Hum Genet* 1982;**62**:378–81.
4 Yunis E, Ramirez E, Uribe JG. Full trisomy 7 and Potter syndrome. *Hum Genet* 1980;**54**:13–8.
5 Bartsch O, Kalbe U, Ngo TKN, Lettau R, Schwinger E. Clinical diagnosis of partial duplication of 7q. *Am J Med Genet* 1990;**37**:254–7.