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Lipid anomaly in a child with partial duplication 3p

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Abstract. – **The authors report a case regarding a 7-year-old girl affected by short height, bone growth delay, lipidic alterations (hypercholesterolemia, hypertriglyceridemia and high apolipoprotein B values) and by a partial duplication of the short arm of the third chromosome: 46,XX, dup(3)(p26-pter). This chromosomal alteration appears *"de novo"*, as the parent's karyotypes are normal and none of the patient's next of kin showed evidence of lipidic anomalies.**

The patient's short height and slight frontal bossing were the only features that could be described as typical of the dup3p syndrome.

Key-Words:

Dup (3p) syndrome, LC familial combined hyperlipidemia.

Intoduction

Partial duplication of the short arm of chromosome 3 is relatively rare and was first described by Rethoré et al[1]. To date 33 cases have been described[1-9]. In most of them, one out of parent showed a balanced translocation involving the short arm of chromosome 3. In spite of some cytogenetic differences, all patients showed a same characteristic dysmorphic pattern.

We report of a child in which duplication (dup) 3p arose "de novo", with few manifestations of this syndrome. Moreover, the child shows evidence of lipidic alterations, a feature previously unreported in this condition.

Case Report. A.S., a daughter born on 14 February 1987, is the second child of healthy, non consanguineous parents.

Her elder brother is in good state of health. Her father was aged 31 when A.S. was born while her mother was a year older. Term delivery and normal labour followed an uneventful pregnancy. A.S.'s weight at birth added up to 2.9 kg. A normal neonatal period followed. During her first year of life, the child lived with her mother in Buthan where she was fed rather incongruously, being breast-fed until 9 months, with the occasional administration of soup from the sixth month onwards. During this period she was frequently affected by diarrhoea.

At the age of 13 months, the child's weight was 7 Kg and her height 68 cm (lower than the third percentile). A vast range of tests was carried out in order to rule out a malabsorption syndrome (namely, screening for galactosemia and an antigliadin antibodies test were performed); all tests were negative. Once on a proper diet, the child's intestinal functions normalized.

The patient's psychosocial and neuromuscular development has always been regular; her weight and height measurements have always turned out to be lower than the third percentile. At the age of 4, her bone development was that of a child between 18-24 months.

Several other laboratory tests were performed in order to rule out the possibility of celiac disease (antigliadin and antiendomysial antibodies), parasites or endocrine disorders (measurements of thyroid hormones, TSH, GH both basal and following clonidine stimulation).

At each assessment of bone development (five, six and seven years), a constant delay of approximately three years with respect to age-appropriate development was reported. At six years and six months an increase of serum lipids was reported too: total cholesterol 259 mg/dL (nv <200), HDL cholesterol 27 mg/dL (nv 50-190), triglycerides 422 mg/dL (nv <160), apolipoprotein A 2.31 g/dL (nv

1.15-2.20), apolipoprotein B 2.52 g/dL (nv 0,06-1.5). Later, more tests reconfirmed these findings. When the child was aged 7, a karyotype was carried out using a high resolution banding techniques and fluorescence specific for chromosome 3, showing a duplication of the terminal segment of the short arm of the chromosome: 46,XX, dup(3)(p26-pter) in all metaphases observed.

The child came under our observation at the age of 7 years and four months. Her height and weight were respectively 108,5 cm and 18,9 Kg (lower than the third percentile, 1.9-2.5 SD).

The child's head showed prominent frontal bossing. Her psychosocial and neurological development was adequate for her age, enabling her to attend the second year of primary school, with rather good marks. Dysmorphic features were absent. A.S. is an attractive, smart child. Her only pathological characteristics are: the three years growth delay (-2.5 SD) and the altered lipidic profile. The values of total and HDL cholesterol, triglycerides and apolipoprotein B indicate a type II B variant of familial combined hyperlipidemia[10]. This condition is inherited as a dominant trait, however, none of her relatives, among those we examined (parents, brother, paternal grandparents), shows any evidence of altered lipidic values.

Unfortunately, the child's mother refuses her daughter to undergo any further medical intervention.

Discussion

The chromosomal alteration found in this child, a partial duplication of the short arm of chromosome 3, is relatively rare. Medical literature offers 33 published cases[2-9] (Table I); most of them are due to the defective segregation of a balanced translocation in one of the parents, involving chromosome 3 and an additional autosome. In one case only, reported by Cabral de Almeida[2], the translocation involved the X chromosome.

Rethoré[1] describes three sibling carriers of dup(3)(p21-p26), whose mother was a carrier of inv (?) ins (7;3)(q31;p21;p26). Actually, in

Table I. Clinical characteristic of partial 3p trisomy.

	3p21->pter	*3p21->p26*	*3p22->pter*	*3p23->pter*	*3p24->pter*	*3p25->pter*	*3p26->pter*
N. cases reported	15	3	1	7	2	4	our case
Sex ratio m/f	8/7	3/0	1/0	6/1	1/1	4/0	0/1
Prenatal growth retardation	1/11	0/3	–	1/6	0/2	1/4	+
Postnatal growth retardation	6/10	1/3	–	1/4	2/2	2/3	+
Neuromotors retardation	9/ 9	1/3	1/1	2/4	2/2	3/3	–
Micro/brachycefafaly	10/14	2/3	1/1	5/7	0/2	1/4	–
Frontal bossing	10/14	3/3	1/1	2/6	2/2	3/4	+
Depressed temporal regions	10/14	2/3	1/1	2/6	0/2	2/4	–
Square face	10/14	3/3	1/1	2/6	2/2	1/4	?
Epicanthus	12/14	3/3	1/1	2/7	1/2	1/4	–
Hypertelorism	10/14	3/3	0/1	4/6	2/2	3/4	–
Cleft palate	5/14	1/3	0/1	3/6	0/2	0/4	–
Prominent philtrurn	5/14	2/3	0/1	2/6	0/2	1/4	–
Micro-retrognathia	9/14	2/3	1/1	2/6	2/2	1/4	–
Short nose, large nasal tip	7/14	0/3	0/1	2/6	0/2	3/4	–
Short neck	9/14	3/2	1/1	3/6	1/2	1/4	–
Congenital heart disease	14/14	2/3	1/1	4/7	1/2	2/4	–
Urogenital anomalies	7/13	3/3	1/1	5/7	1/2	3/4	–
Dermatoglyphics	13/15	3/3	1/1	3/6	2/2	1/4	–
Anomalies CNS	3/15	0/3	0/1	1/6	1/2	1/4	–
Cryptorchidism	3/13	0/3	0/1	3/6	0/1	2/4	–
Short stature	1/ 1	0/3	?	0/1	0/1	1/2	+

these three cases only, in addition to the one reported by the authors, a "pure" trisomy was present. In the present case only, however, did the duplication take place "de novo".

All patients, apart from the duplicated 3p portion and the presence or absence of monosomic segments, show the following symptoms: a form of cranio-facial dysmorphism characterized by a square face, prominent frontal bossing and depressed temporal regions, rounded cheeks, hypertelorism, rounded nasal tip, short upper lip with prominent philtrum and large mouth with down- turned corners. Among the most commonly occuring organic anomalies are cardiac (24/32) and genitourinary (20/31) malformations; mental retardation (18/23) and growth delay (13/23) are also common, and a short adult height was ascertained in 3 out of 6 cases. The high forehead with prominent frontal bossing, the depressed temporal regions and full cheeks are typical childhood features which tend to disappear in time, due to normal growth and development.

Sixteen out of 34 patients died before the age of 2, congenital cardiopathy being reported as the most common cause of death. According to several authors, such uniformity of clinical presentation can be a syndrome, and seems to be due to the duplication of segment 3p25-pter[5,7].

Of 6 adult patients described in our case-study, 3 were of rather short height. No given values are reported for hyperlipemia or any other ematochemical indicators.

In fact, even if the 3p trisomy can involve wider or narrower portions of the short arm of chromosome 3, and the second chromosome involved in the translocation can vary, however, the main phenotype stays essentially the same.

In our patient, only her frontal bossing and remarkable growth delay can be considered as apparent characteristics of partial dup 3. As far as the altered lipidic profile is concerned, it is undoubtedly to be considered as idiopathic and not due to other morbid conditions. We cannot yet establish whether this might be a casual association or rather a consequence of the chromosomal anomaly. In the short arm of the chromosome 3 there are no genes involved in determining the lipidic profile, so we can rule out any form of expression in triple dose of gene products. Apo B genes have been localized in 2p24, and the hyperlipoproteinemia type I B in 19q13.3. However, there might be more unknown genes involved in the process[11].

Up to date, such a lipidic profile has gone unreported in literature. When dealing with chromosomal alterations, it would be very helpful to report the largest number of biohumoral parameters, so as to provide valid criteria for treatment and prognosis, especially when indications favour the possibility of a longer life expectancy for the patient.

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