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Partial deletion of short arm of chromosome 8

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46, XY, del(8) (p21-pter) aberration was found in a 5 years old boy with moderate craniofacial dysmorphia, mental and somatic retardation. The cytogenetic and clinical features of the patient were compared to 11 cases found in the literature. Partial 8p monosomy does not produce a unique phenotypic alteration. Postnatal growth deficiency, craniofacial dysmorphia and mental retardation are the main and common characteristics of many structural autosomal aberrations. The importance of cytogenetic analysis in such cases is stressed.

Partial monosomy of the short arm of chromosome 8 is a rare condition. According to the latest reviews [3, 4], altogether 11 cases have been reported in which the 8p- aberration occurred as a fresh mutation. In two further cases the 8p monosomy originated as the consequence of balanced parental translocation [5, 8].

Report of a Case

The 5 years old boy was referred to us for clinical evaluation on account of moderate mental retardation, small stature and dysmorphic signs.

History The boy was born from the 4th pregnancy. The pre- and postnatal events were unremarkable. At the time of birth the father was 37, the mother 30 years old. The first two pregnancies of the healthy couple ended with miscarriage, and from the third pregnancy a healthy boy was born.

The proband was born in the 42nd gestational week with 3100 g birthweight. The weight gain and motor development was markedly delayed in the first 12 months of life. He began to speak at 2 1/2 years of age and started to walk at 27 months of age. Regular nocturnal bedwetting existed at the time of examination.

Status at 5 years of age Height 99 cm, weight 13.5 kg (both values below the 3rd percentile), head circumference 49 cm (25 percentile). Horizontal nystagmus and moderate muscular hypotonicity were present but otherwise the neurological examination revealed no pathologic symptoms. Heart, renal or other visceral malformations could not be detected, the genitals were normal.

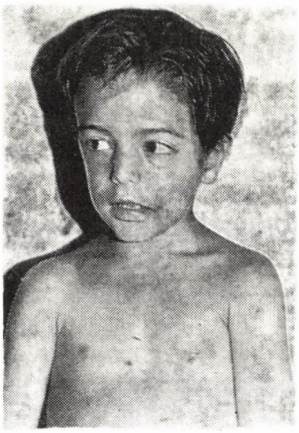
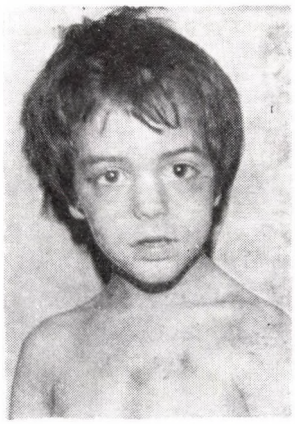
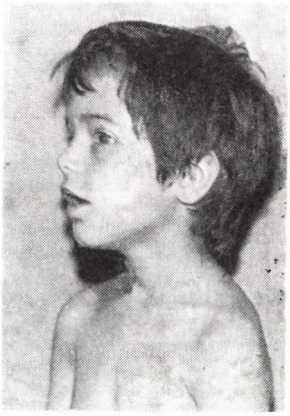


FIG. 1. 5 years old boy with partial 8p monosomy





FIGS 2 and 3. The same patient at 8 years of age

Dysmorphia Dolichocephaly, high, broad forehead; dense eyebrows, large ears, low posterior hairline, wide spaced nipples (Fig. 1), mild pectus excavatum and simian crease on the left palm.

Status at 8 years of age Height 113 cm, weight 15 kg (values below the 3rd percentile), head circumference 49.5 cm (25 percentile). He is attending a special school for the handicapped. The facial appearance did not change in the meantime (Figs 2 and 3). The parents seem to be satisfied with his school performance. Nocturnal bed-wetting still occurs.

Cytogenetic investigation This was carried out from peripheral lymphocyte cultures using GAG, G and C banding techniques. In every mitosis

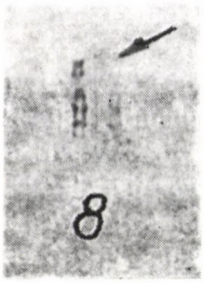


FIG. 4. Partial deletion of short arm of chromosome 8 with GAG banding

46 chromosomes were present and partial deletion of chromosome 8 was revealed. The karyotype was defined as 46, XY, del(8)(p21-pter) (Fig. 4). The karyotype of the parents and of the healthy brother was normal.

DISCUSSION

The main clinical and dysmorphic features of partial 8p monosomy based on the hitherto published cases are summarized in Table I. Only the cases of de novo originated 8p monosomies are included since the phenotypic expression may be influenced in patients in whom the monosomy is due to unbalanced translocation.

No specific dysmorphia could be delineated which would or might be characteristic of partial 8p monosomy. Somato-mental retardation, short stature, small head circumference are present in almost all cases. The craniofacial dysmorphia observed in our patient, namely the diminished fronto-occipital diameter, high forehead, large ears, furthermore the wide spaced nipples and pectus excavatum as

TABLE I

Main clinical and dysmorphic features of patients with partial 8p monosomy. Based on 11 published cases (1–4, 7, 9–13)

	Reported cases	Present case
Male/female	6/5	male
Prenatal growth deficiency	6/11	–
Postnatal growth deficiency	9/11*	+
Dysmorphia		
Microcephaly	10/11	±
Narrow skull	6/11	–
High forehead	5/11	±
Epicanthal fold	5/11	–
Low set or malformed ears	7/11	+
Wide spaced nipples	5/11	+
Malformations		
Complex heart defect	7/11	–
Cryptorchidism	5/6	–
Inguinal hernia	4/11	–
Hypogonadism (female)	1/5	
Mental retardation	9/11*	+
Died in infancy or childhood	3/11	
Karyotype:		
p21-pter: 8		p21-pter
p22-pter: 1		
p23-pter: 1		
p21–p22 1		

* death in early infancy

compared to the pictures and descriptions of the published cases are showing some similarity. These patterns are, however, unspecific and are resembling the well known variabilities of almost every structural autosomal chromosome aberration.

Heart malformations were detected by several authors [3, 4, 7, 11, 12]. These malformations, if present, are usually severe and led to early death in 3 patients [3, 4]. Complete atrioventricular canal with monoatrium combined with various anomalies of the great vessels occurred in 3 cases [3, 4, 11], pulmonary stenosis with ASD and VSD in 2 further cases [12, 13], and tetralogy of Fallot and complex malformation was reported in 1 case [3, 7]. A relationship between the missing chromosome segment and the presence of dysmorphia and/or heart malformation could not be established. In the 7 cases showing severe cor triloculare type malformations usually combined with transposition of the great vessels, the distribution of karyotypes was p21: 5, p22: 1, p?: 1. The remaining 5 cases, including our patient, p21 occurred 3 times, and p23 and p21–22 each once [1, 2, 9, 10].

Genital malformations, first of all cryptorchidism and less frequently hypospadias may occur in males. One 18 year old female patient [1] showed hypogonadotropic hypogonadism. Inguinal hernias are fairly common in boys.

In the present case no cardiac, visceral or genital anomalies were present. The main concern of the parents was the stunted growth. Therefore, several unnecessary laboratory investigations had earlier been performed in other institutions, namely growth hormone detection, biopsy of small intestine, carbohydrate tolerance tests, to exclude growth hormone deficiency, coeliac syndrome or other chronic malabsorption syndromes. These investigations revealed normal results. Finally, the cytogenetic investigation discovered the structural aberration of chromosome 8, which led to correct diagnosis and ensured a satisfactory explanation for the entire clinical picture.

From the point of view of differential diagnosis in our patient, first of all the fragile X syndrome should be taken into consideration. The observed craniofacial dysmorphia, e.g. the high and broad forehead, large ears, normal birthweight, delay in somatic development as well as the mild mental retardation are the main characteristics of the fragile X syndrome in the younger age group [14]. On the other hand, earlier we observed 2 cases with partial 18p monosomy in which a somewhat similar craniofacial dysmorphia, stunted growth and mental retardation occurred [6].

Craniofacial dysmorphia in partial 8p monosomy is not characteristic, but postnatal growth deficiency and mental retardation in dysmorphic children stresses the indication of chromosome analysis. This ensures the correct and definitive diagnosis and helps to avoid unnecessary laboratory and other investigations.

In most cases partial 8p monosomy occurs as a de novo mutation. Still,

investigation of the family is recommended to exclude a translocational origin.

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