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Partial deletion of short arm of chromosome 18

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Three cases of partial deletion of the short arm of chromosome 18 (pll-pter) are presented. The cytogenetic and clinical features of the patients observed are compared to cases found in the literature. 18p-aberration produces a fairly unique phenotypic alteration, but on the sole basis of the clinical manifestation, without cytogenetic analysis, correct diagnosis cannot be established.

The most frequent autosomal deletion syndromes, the 4p, 5 and 18— aberrations, are featuring unique phenotypic alterations.

Partial deletion of the short arm of chromosome 18 is a fairly frequent chromosomal disorder, the number of hitherto published cases is near to 100. Based on the clinical findings, characteristic phenotypic and dysmorphic changes may be delineated.

Recently three cases of partial 18p deletion have been discovered in our laboratories. Cytogenetic investigations were carried out from peripheral lymphocyte cultures using C, G and GAG banding techniques. Our purpose is to present the clinical findings and to compare them to the corresponding chromosomal alteration.

Case Reports

Patient No. 1: 7 years old boy.

Family history: The patient was born from the 6th uneventful pregnancy. From the 1st and 3rd pregnancies healthy boys were born, the 2nd ended with spontaneous, the 4th and 5th with artificial abortion. The healthy father was 32 and the mother 28 years of age at the time of birth of the index patient.

History: Birth weight 2000 g, uneventful perinatal period. Strabism was corrected at 3 years of age. Delayed somatic and psychomotor development was observed.

Status: Height 107 cm, weight 19 kg (both values below the 3rd percentile), head circumference 51 cm. The boy is attending special school for mentally handicapped children.

Dysmorphic signs: High protruding forehead, round skull, narrow face, protruding ears, wide spaced nipples (Figs 1*a* and *b*).

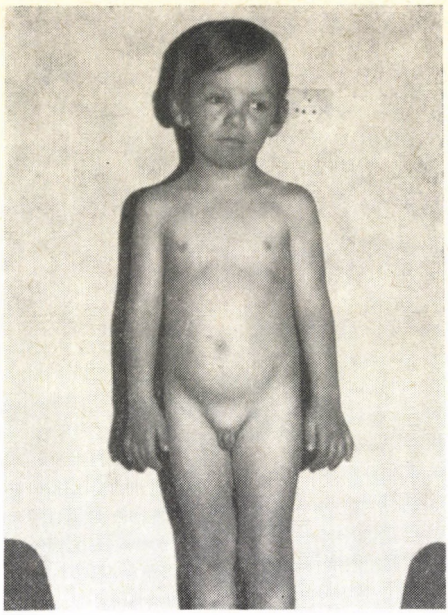
Neurologic signs: Muscle tonicity is normal, motor coordination and development are retarded. EEG revealed bradyarrhythmia, without any specific signs.

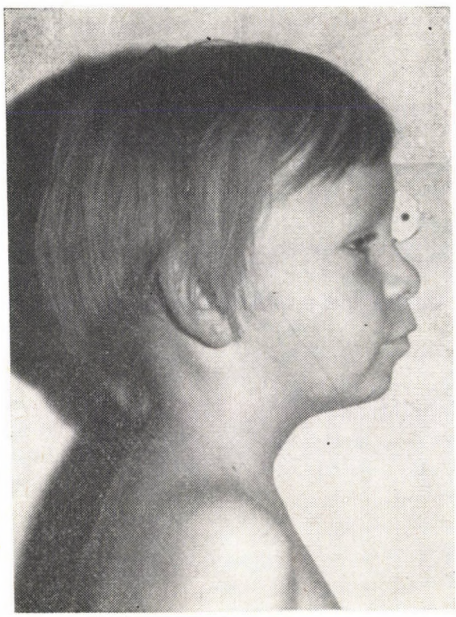
Cytogenetic investigation revealed in all mitoses 46 chromosomes, with partial deletion of the terminal segment of chromosome 18. The karyotype was 46, XY, del [18] (pll-pter) (Fig. 2). The karyotypes of all family members were normal.

Patient No. 2: 8 years old boy.

Family history: The patient was born from the 3rd uneventful pregnancy. The parents were 38 and 32 years old. From the mother's first pregnancy a healthy girl was born, the second was terminated by artificial abortion.

History: Birth weight 3800 g, negative peri- and postnatal history. The clinical





FIGS. 1*a*, *b*. Patient No. 1, seven years old boy with 18p-aberration

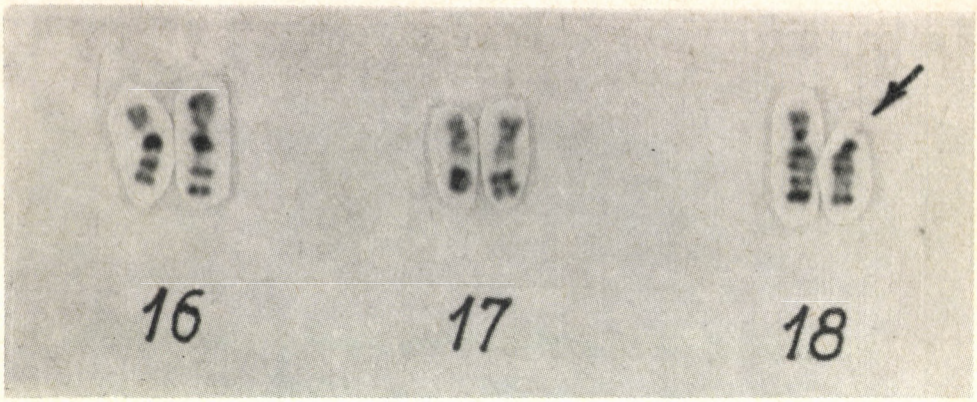


FIG. 2. Partial deletion of short arm of chromosome 18 with GAG banding

investigation was carried out on account on dysmorphic features and psychomotor retardation.

Status: Height 115 cm, weight 20 kg, head circumference 49.5 cm (all values below the 3rd percentile).

Dysmorphic signs: Microcephaly, protruding ears, broad nasal bridge (Figs 3*a* and *b*), short fingers and cryptorchidism on the right side could be observed.

Psychological examinations: expressive speech disorder, delay in fine motor development, uneven structure of intelligence and debility were present. IQ = 66.

Cytogenetic investigation showed in all mitoses 46 chromosomes, with partial deletion of the short arm of chromosome 18. The karyotype is 46, XY, del (18) (pll-pter). The karyotype of the parents proved to be normal.

Case No. 3: 1 1/2 years old girl.

Family history: 2nd pregnancy, the firstborn girl is healthy. The parents were 24 and 21 years old.

History: The patient was born in the 40th week of gestation, with a birthweight of 2850 g, length 45.5 cm, head circumference 32 cm (all values below the 10th percentile).

Status: Marked delay in somatic and psychomotor development was accompanied by severe muscular hypotonicity.

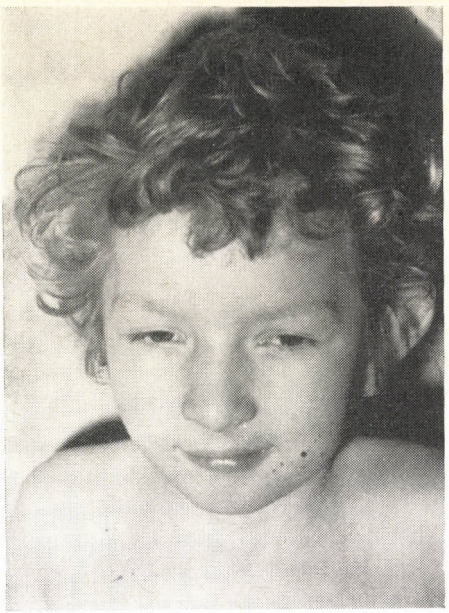
Dysmorphic signs: Microcephaly, flat, round face, flat occiput, short neck, hypertelorism, broad nasal bridge, anteverted nostrils, bilateral ptosis of eyelids, carp shaped mouth and bilateral talipes equinovarus (Figs 4*a* and *b*).

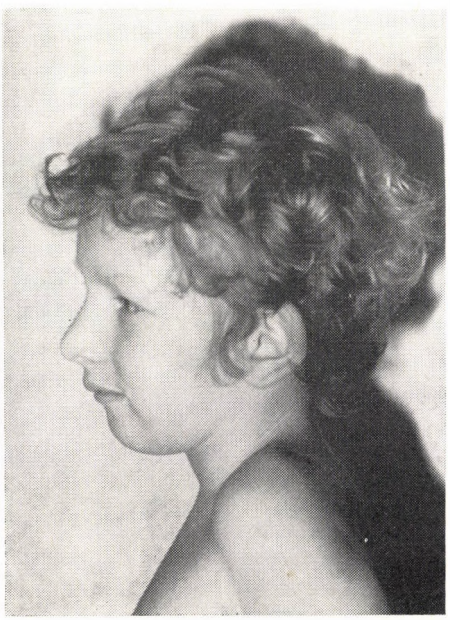
Cytogenetic investigation revealed in all mitoses 46 chromosomes with almost complete loss of the short arm of chromosome 18. The karyotype is 46, XX, del (18) (pll-pter). The karyotypes of the family members were normal.

DISCUSSION

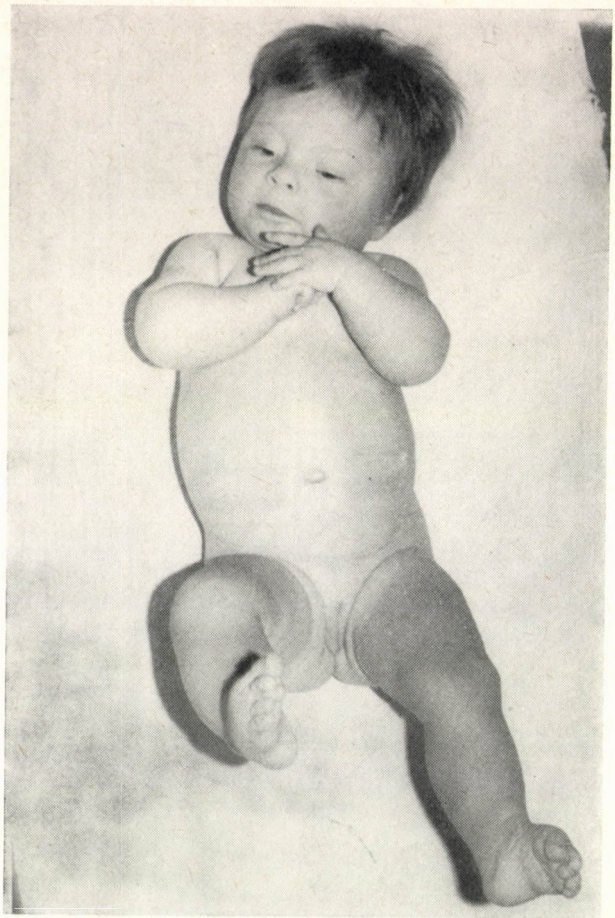
Since the first description of 18p- aberration by de Grouchy et al. [3] about 100 cases could be traced in the literature. Aksu et al. [1] based on data of 83 cases summarized the main clinical, somatic and dysmorphic signs of 18p- aberration, and a fairly unique phenotypic appearance may be delineated as a well-defined clinical syndrome.

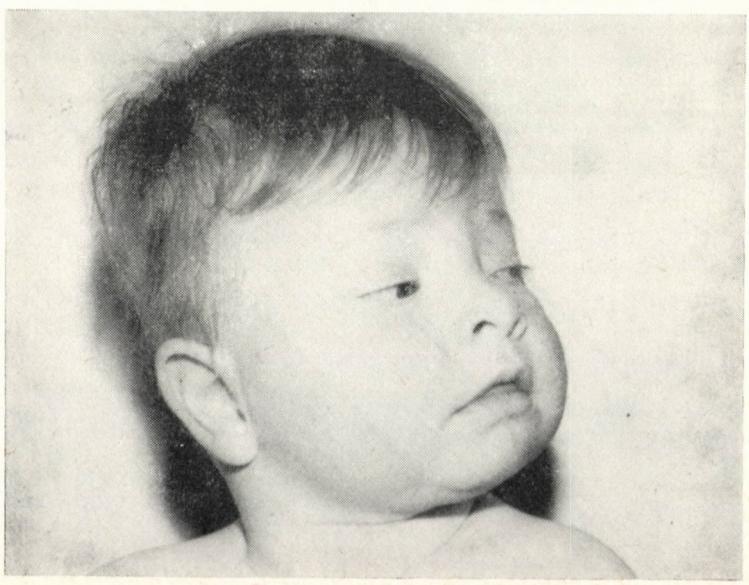
The most important clinical findings and dysmorphic signs of our three patients are summarized in Table I which comprises the data reported by Aksu et al [1] as well as those of other observations published recently [2, 7, 8].





FIGS 3*a*, *b*. Patient No. 2, eight years old boy





FIGS 4*a*, *b*. Patient No. 3, 1 1/2 years old girl

TABLE I

Data of patients with partial deletion of short arm of chromosome 18

	Aksu et al. [1] n=83	Christensen, Nielsen [2]	Motegi et al. [7]	Stotter et al [8]	Present cases		
					1st	2nd	3rd
Mental retardation	76/76	+	+	+	+	+	+
Somatic retardation	52/65	+	+	+	+	+	+
Microcephaly	16/23	−	+	+	−	+	+
Micrognathia	34/40	+	+		−	−	−
Carp shaped mouth	41/45	+	+		−	−	+
Hypertelorism	32/53	−			−	−	+
Epicanthus	28/43			+	−	−	+
Ptosis	30/48	+	+	+	−	+	+
Low set large ears	55/59	+		+	+	+	+
Cryptorchidism			+		−	+	
Paternal age	35.3		29		32	38	24
Maternal age	31.2		28		28	32	21
Sex f/m	50/33	m	m	f	m	m	f

Evaluating the clinical findings and dysmorphic signs of our three patients it may be stated that only patient No. 3 displayed all the main characteristic patterns of the 18p-syndrome. In this case the craniofacial dysmorphism seemed typical. In case No. 1 the psychosomatic retardation as well as the dysmorphic features have prompted us to perform cytogenetic investigations. Case No. 2 showing almost identical dysmorphic signs and psychomotor delay as did patient No. 1, the suspicion of 18p deletion arose immediately after the physical examination.

In about one third of the patients with 18p deletion IgA deficiency and consequential immunologic disorders could be observed [1, 6]. IgA determination was not carried out in patients 1 and 2, since the history did not reveal any significant data indicative of deficient immunologic function. In patient No. 3, estimation of immunoglobulins in serum revealed IgG 100 mg/dl; IgA 16 mg/dl; and IgM 68 mg/dl. No further investigations could be carried out since the parents did not agree to further examinations and the patient was lost for follow-up.

From the differential diagnostic point of view, in male patients first of all fragile X mental retardation may be considered [9]. The craniofacial dysmorphism with protruding large ears and high forehead seems to be a common characteristic. Speech disorder is also common in both chromosome aberrations. It must, however, be emphasized that one of the most frequent and most important signs in almost every form of mental retardation are speech disorders; they cannot therefore be considered a significant part of each syndrome [5].

In the case published by Christensen and Nielsen [2] in certain aspects there was a similarity between the features of 18p deletion and the Silver—Russell syndrome. Since, however, hemihypertrophy is a basic symptom of the Silver—Russell syn-

drome, it was observed only in the case of the above mentioned authors. The cranio-facial dysmorphism may be somewhat similar, but it seems certain that this observation was only a coincidence.

A recent paper by Stotter et al [8] is noteworthy in that gonadal failure and hypothyroidism were developing in a 17 years old mentally retarded girl in whom 18p deletion was discovered. Further observations are needed to ascertain whether this condition occurred by chance or a general consequence in females with 18p deletion.

Thus, in 18p deletion syndrome, as well as in other structural chromosome aberrations, somato-mental retardation associated with cranio-facial dysmorphism are the most important symptoms which necessitate to perform cytogenetic analysis [4]. The partial deletion of the short arm of chromosome 18 produces fairly unique facial and ear anomalies, but based only upon the phenotypic alterations, without analysis of the karyotype, the diagnosis cannot be established realiably.

The prognosis of 18p deletion is generally favourable. Most of the published cases were children, but it seems that the life-span was not altered, since visceral or other major malformations are extremely rare with the condition.

Most cases of 18p deletion originated from fresh mutations, therefore in the forthcoming pregnancies no antenatal diagnosis is necessary.

Acknowledgement

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