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Dubowitz syndrome

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Four children including two siblings with Dubowitz syndrome are presented. All four were preterm or small-for-dates. On the basis of their symptoms, it is suggested that infantile eczema is not an essential sign of the disorder, whereas the high frequency of hernia, strabism and upward slant of the palpebral fissures is underestimated in the literature.

The congenital disorder characterized by peculiar face, growth deficiency with prenatal onset, infantile eczema and mild microcephaly was initially described by Dubowitz [2]. The syndrome is regarded as a rare autosomal recessive disorder; approximately 26 cases have been reported [12]. Recently we have observed four further children with this syndrome.

CASE REPORTS

The first two patients were siblings. Their parents were healthy; consanguinity, malformations, small stature and skin disease could not be detected in their families.

Case 1. S.C., a girl, was born on the 36th week of her mother's uneventful pregnancy. The placenta was considerably shrivelled. Birthweight was 1640 g, length 43 cm, head circumference 29 cm; each of these parameters were under the 10th percentile of the local growth chart. The ponderal index was 2.06. Because of feeding difficulties the infant failed to thrive. Retardation of psychomotor development was noticed at the age of 10 months, when detailed examinations revealed normal blood chemistry with normal 46,XX karyotype. At that time she had a convulsion without fever.

At the age of 5 years she weighed 11 kg, her height was 94 cm, her bone age 4.5 years. Physical examination showed microcephaly (head circumference, 45 cm), small facies, high sloping forehead, shallow supraorbital ridges, sparsity of hair and eyebrows, hypertelorism, epicanthic folds, broad nasal bridge, hypoplastic alae nasi, low-set ears, small mandible (Fig. 1 A,B). In addition, bifid uvula, bilateral simian crease, 2 whorle (W) 8 ulnar loop (Lu), clinodactyly, wide distance between toes I and II, pes planus, umbilical hernia were noted. Blood and urine chemistry was normal.

The Denver Developmental Screening Test revealed significant delay in each component (gross motor 28

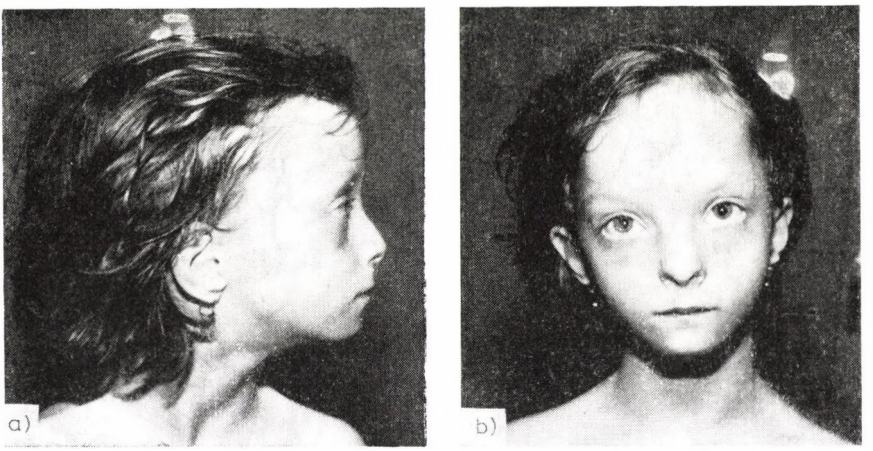


FIG. 1/A—B Case 1 at 7 years of age

months, fine motoradaptive 22 months, language 38 months, personal-social 28 months).

At the age of 7 6/12 years she weighed 13.2 kg, her height was 109 cm, head circumference 46 cm.

Case 2. H.C. was the brother of Case 1. He was born in the 40th gestational week with signs of severe intrauterine growth retardation. The placenta was unusually small, birthweight was 2180 g, length 47 cm, head circumference 32 cm, ponderal index 2.11. His appearance was very similar to that of his sister. In addition he had a cleft palate which caused accessory difficulties in oral feeding and an inguinal hernia.

At the age of 8 months he was examined because of somatic and psychomotor retardation; the most frequent inborn errors of metabolism could be excluded, the karyotype was 46,XY.

At 12 months age his weight was 5.7 kg and he was 64 cm tall. He had microcephaly (head circumference 42 cm), sparse hair and eyebrows, high sloping forehead, flat supraorbital ridges, pseudohypertelorism, epicanthic fold on the left eye, mild ptosis, strabismus, mild facial asymmetry. Dental eruption was delayed. He had a complete simian crease on the right and a Sydney line on the left palm with bilateral clinodactyly, 3 W, 7 Lu. According to the Denver test, his performance corresponded to the 7 month level. At that time he had seizures connected with fever.

At the age of 4 years, the growth retardation was conspicuous. He weighed only 9.2 kg, his height was 86 cm, the head circumference 46 cm. He had a high-pitched hoarse voice. No epiphyseal ossification centres were seen on the wrist roentgenogram. The dysmorphic signs were the same as recorded earlier (Fig. 2 A,B). The Denver test revealed a perfor-

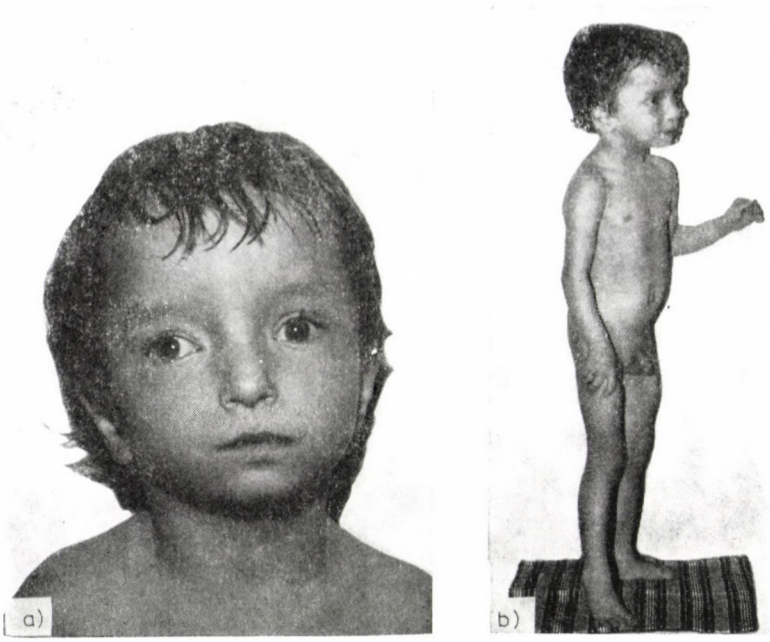


FIG 2/A—B Case 2 at 4 years of age

mance corresponding to 20 to 22 months.

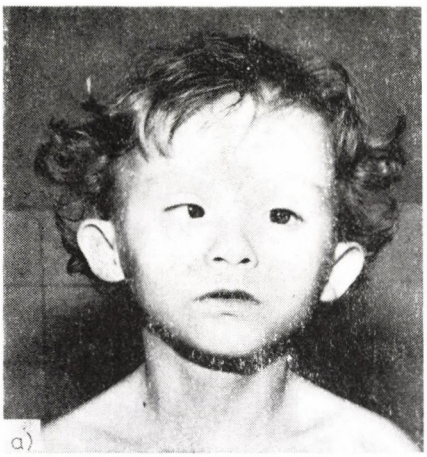
Case 3. Z.L. was a small-for-gestational age newborn boy. The mother was 36 years of age and had already had two healthy twins in her first marriage. As the present husband reported, she had often consumed alcohol during her pregnancy with the proband. No consanguinity, malformation, or short stature were present in the relatives.

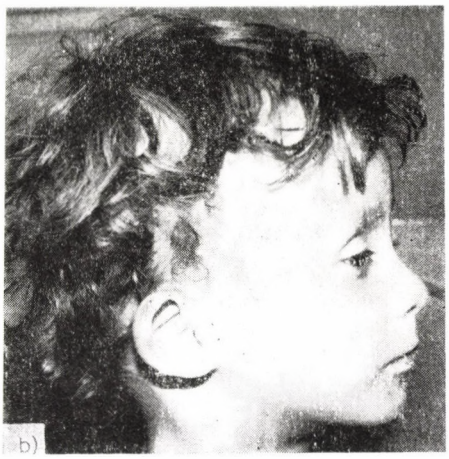
The baby was born in the 36th week of gestation, with 1500 g weight, 39 cm length, and 29 cm head circumference. His cry was high-pitched, oral feeding was extremely difficult.

At 3 years of age he weighed 8.25 kg and was 80 cm tall. At 7 years of age his weight was still only 14 kg, his height was only 111 cm. He had microcephaly (head circumference 47.5 cm), flat occiput, high sloping forehead, sparse hair, flat supraorbital ridges, ptosis with short palpebral fissures, strabism, protruding ears with lack of anthelix and with hypoplastic tragus, pilonidal dimple (Fig. 3 A,B,C). Bone age was 5.5 years. The karyotype was 46,XY; no increase in sister chromatid exchange frequency could be recorded (mean SCE per mitosis = 5.09).

He showed no mental retardation, but had behavioural problems with hyperactivity and short attention span.

Case 4. P.K., a boy, was born after





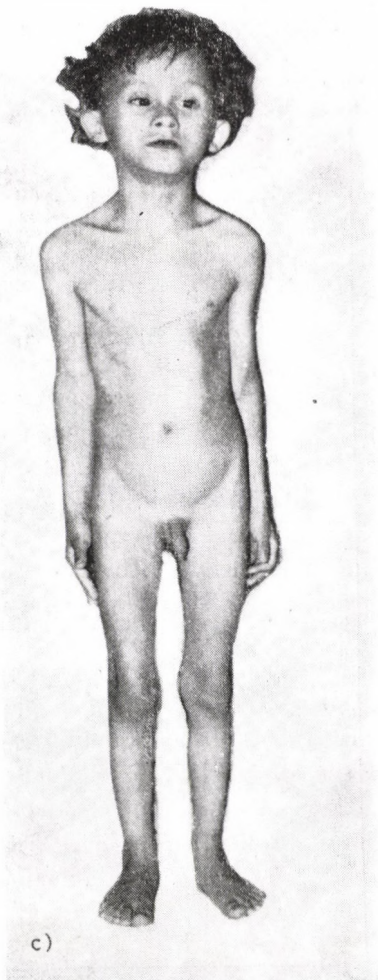


FIG. 3/A—C Case 3 at 7 years of age

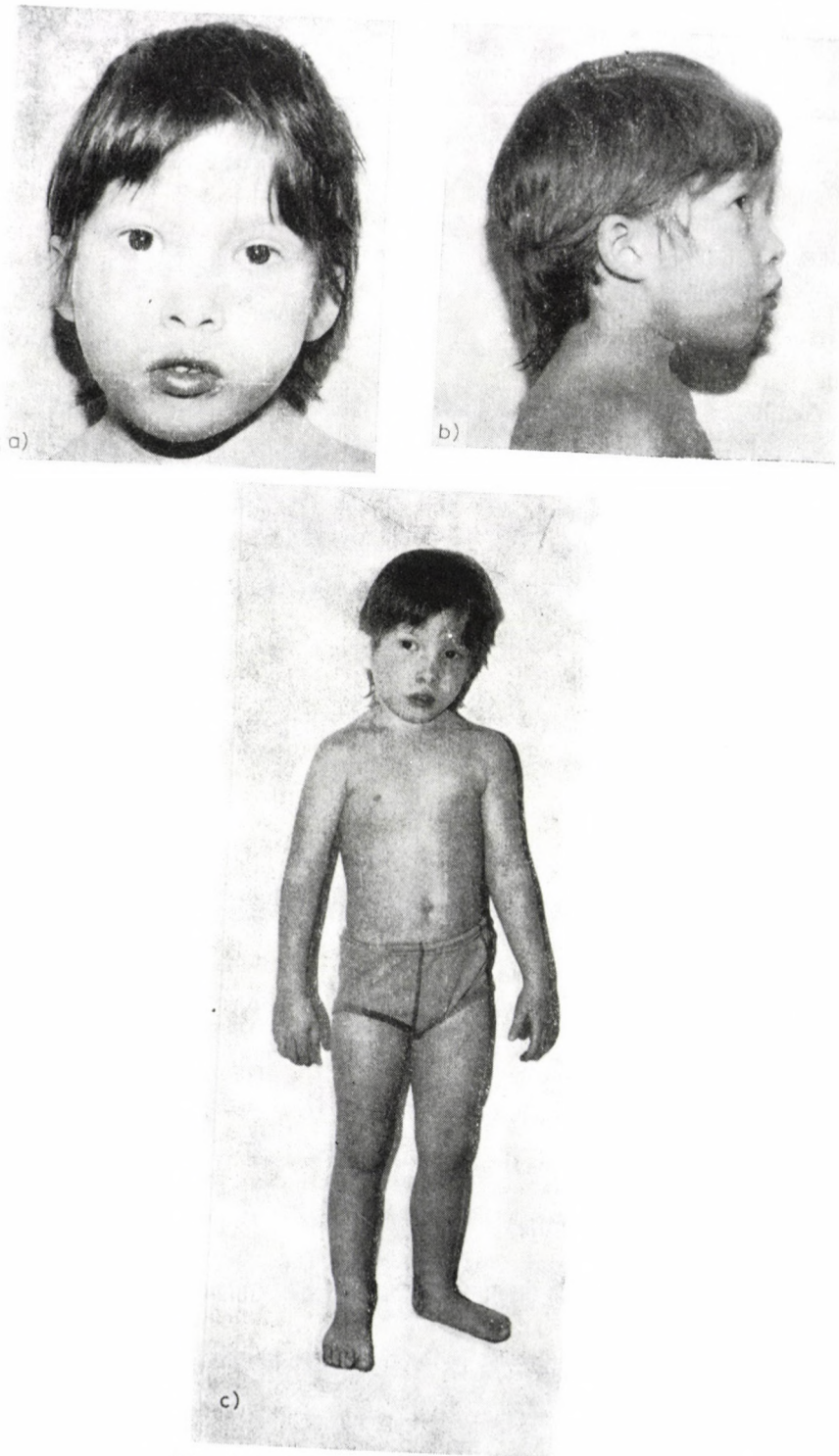


FIG. 4/A—C Case 4 at 5 years of age

TABLE I

Main symptoms of Dubowitz syndrome

Symptoms	Cases in the literature [2, 4, 5, 6, 7, 12]	Present cases			
		S.C.	H.C.	Z.L.	P.M.
		sibs			
Data of delivery					
Placental problems	1/26	+	+	?	?
Preterm birth	5/26	+	−	+	+
Prenatal growth failure	20/26	+	+	+	+
Growth					
Dwarfism	19/26	+	+	+	+
Delayed postnatal weight gain	24/26	+	+	+	+
Microcephaly	25/26	+	+	+	+
Face					
Sloping forehead	21/26	+	+	+	+
Narrow face	9/26	+	+	−	+
Shallow supraorbital ridge	10/26	+	+	+	+
Broad nose	13/26	+	+	+	+
Micrognathia	19/26	+	+	−	−
Eye and periorbital area					
Strabism	4/26	−	+	+	−
Ptosis	16/26	−	−	+	−
Epicanthus	11/26	+	+	−	+
Telecanthus/Hypertelorism	15/26	−	+	−	−
Short palpebral fissures	5/26	−	−	+	+
Slanting palpebral fissures	12/26	+	+	+	+
Incomplete morphogenesis					
Ear	20/26	+	+	+	+
Cleft palate	7/26	+	+	+	−
Gothic palate	7/26	−	−	+	−
Hernia		+	+	−	+
Sacral dimple	5/26	−	−	+	−
Cryptorchidism	5/11		−	−	−
Syndactyly	9/26	−	−	−	−
Clinodactyly	11/26	+	+	−	+
Foot deformity	8/26	+	+	−	−
Retarded bone age	11/26	+	+	+	+
Ectodermal hypoplasia					
Teeth problems (delayed eruption, decay, etc.).	11/26	−	+	+	+
Hair, eyebrow: sparse, thin	18/26	+	+	+	+
Eczema	11/26	−	−	−	−
Dermatoglypha: L_u dominant	11/26	+	+	+	+
Neuro-psychologic signs					
Behavioural problems/Hyperactivity	10/26	+	+	+	+
Mental retardation	9/26	+	+	−	+
Eating and swallowing problems	16/26	+	+	+	+
High pitched cry/Speed defect, delay	12/26	+	+	+	+
Seizures	1/26	+	+	−	−

36 weeks of gestation, with 2420 g birthweight, 44 cm length, 32 cm head circumference, 2.84 ponderal index. He had to be treated repeatedly for loss of appetite and failure to thrive. At 10 months of age he weighed only 7.7 kg, with a length of 66 cm and a head circumference of 45 cm.

At 5 years of age his weight was 15 kg, height 100 cm, and head circumference 49 cm. At this time the following characteristic features were observed: dolichomicrocephaly, sparse hair, hypoplastic lateral part of the eyebrows, upward slant of the somewhat short palpebral fissures, flat supraorbital ridges, epicanthic folds, broad nasal bridge, low-set ears (Fig. 4 A,B). His teeth grew irregularly, exhibited caries and enamel hypoplasia. He had a short neck, mamillary hypotelorism, bilateral inguinal hernia, mild scoliosis, bilateral clinodactyly, simian crease on the right palm (Fig. 4 C). Bone age was 4 years. Serum and urine amino acid chromatography was normal, the karyotype proved to be 46,XY. The Denver test referred to a performance of about 3 years of age. The child had serious behavioural problems including high-grade hyperactivity and speech disorders.

The most important data and symptoms of the patients are summarized in Table I.

Discussion

In accordance with previous observations, intrauterine and postnatal growth retardation were obligate symptoms in our patients. As shown in Fig 5, each of the parameters measured were significantly smaller than expected according to chronological age. The delayed growth of the head circumference seemed to be the most conspicuous sign, while the delay in ossification was less striking.

The small placental weights observed in two cases seemed to be important, but are probably not specific to the Dubowitz syndrome.

As to symptoms, hernia, strabism and upward slant of the palpebral fissures showed a high frequency in our cases in spite of not being mentioned among the specific features of the syndrome [1, 3, 9, 11]. Feeding difficulties were also typical in our patients as well as an abnormal voice. In agreement with Opitz et al [6], we believe that eczema is not an essential sign of the disorder: none of our patients suffered from skin disease. However, the sparsity of hair and eyebrows, and the more or less expressed enamel hypoplasia reflected an ectodermal affection.

In spite of microcephaly the mental retardation of the patients was variable but their behavioural problems were serious in each case. The latter seem to be a remarkable characteristic of the syndrome [8].

From the differential diagnostic point of view, first of all the fetal alcohol syndrome should be considered. Although in our Case 3 the mother had consumed alcoholic drinks during pregnancy, the anomalies of the child differed from those seen in the fetal

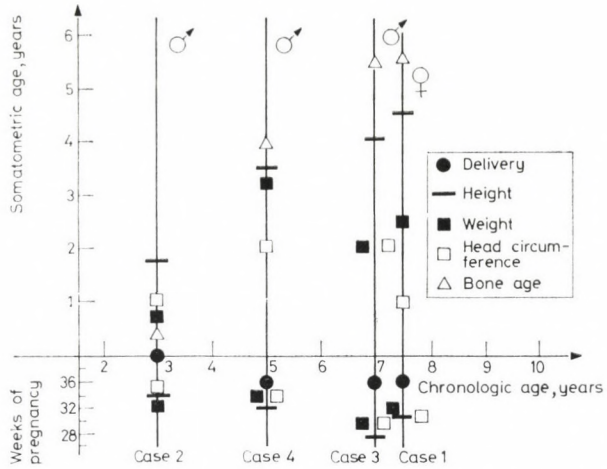


FIG. 5. Anthropometric proportions of our Dubowitz syndrome patients

alcohol syndrome, and just this child had a normal mental development.

All the other syndromes with primordial short stature and mental and behavioural problems could easily be distinguished on the basis of the typical combination of major and minor birth defects.

The present data strengthen the hypothesis of the Dubowitz syndrome being of autosomal recessive inheritance [1, 3, 4, 5, 6, 7, 9, 10, 12]. The parents were apparently healthy and of medium height in each of the families. Cases 1 and 2 were siblings and this too may correspond to an autosomal recessive trait.

Although our findings do not permit an epidemiologic estimation, the fact that 4 cases from 3 families were simultaneously discovered in a town of about 100 000 inhabitants, raises the possibility that the Dubowitz syndrome is not so rare as usually believed [5].

REFERENCES

1. Bergsma D: Birth Defects Compendium, 2nd ed, The National Foundation, March of Dimes, 1979, p 349
2. Dubowitz V: Familial low birthweight dwarfism with unusual facies and skin eruption. J Med Genet 2: 12, 1965
3. Goodman R, Gorlin R: The Face in Genetic Disorders 2nd ed C V Mosby, St Louis 1977. p 266
4. Grosse R, Gorlin J, Opitz JM: The Dubowitz syndrome. Z Kinderheilk 110: 175, 1971
5. Majewski F, Michaelis R, Moosman K, Bierich JR: A rare type of low birthweight dwarfism: the Dubowitz syndrome. Z Kinderheilk 120: 283, 1975
6. Opitz J, Pfeiffer RA, Hermann JPR, Kushnik T: Studies of malformation syndromes of man XXIV B: the Dubowitz syndrome, further observations. Z. Kinderheilk 115: 1, 1973
7. Orrison WW, Schnitzler ER, Chun RVM: The Dubowitz syndrome: further observations. Amer J Med Genet 7: 155, 1980
8. Parrish JM, Wilroy RS: The Dubowitz syndrome: the psychological status of ten cases at follow-up. Am J Med Genet 6: 3, 1980
9. Smith DW: Recognizable Patterns of Human Malformations. 3rd ed. V. B. Saunders, Philadelphia 1982, p 62
10. Taybi H: Radiology of Syndromes and Metabolic Disorders. 2nd ed Year Book Medical Publishers. 1983 p 102

11. Wiedemann HR, Grosse FR, Dibbern H: Das charakteristische Syndrom. 2 Auflage. FK Schattauer Verlag, Stuttgart—New York 1982, p 112

12. Wilroy RS, Tipton RE Jr, Summitt RL: The Dubowitz syndrome. Amer J Med Genet 2: 275, 1978

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