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SYNDROME OF CATARACT, MILD MICROCEPHALY, MENTAL RETARDATION AND PERTHES-LIKE CHANGES IN SIBS

A. CZEIZEL and R.B. LOWRY[1]

Department of Human Genetics and Teratology, WHO Collaborating Centre for the Community Control of Hereditary Diseases, National Institute of Hygiene, Budapest, Hungary and Alberta Hereditary Diseases Program, Alberta Children's Hospital, Calgary, Canada[1]

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Cataract, microcephaly, mental retardation and Perthes-like changes in hips were found in two sibs. This combination of congenital anomalies may be a syndrome of autosomal recessive origin.

INTRODUCTION

We report a brother and sister with cataracts, microcephaly, mental retardation and Perthes-like changes in the hips. They are the only children of a healthy, unrelated Hungarian couple whose family history is negative for any similar disorders. At the time of the elder child's birth the father was 27 years and the mother 26 years of age. In each instance the pregnancy went full-term and was unremarkable (no abnormal drug or teratogen exposures including alcohol). Each child weighed 2800 gms at birth. The children have almost identical phenotypes and the major features are listed in the Table. A cesarean section was performed in the first pregnancy because of breech presentation and a possible short cord and a cesarean section was repeated for the 2nd child.

Akadémiai Kiadó, Budapest

TABLE

Clinical Findings

	Case 1	Case 2
SEX	M	F
Bil. nuclear cataract	+	+
Mental retardation	+	+
Growth retardation (height and weight)	$< 3^0$	$< 3^0$
Microcephaly	+	+
Abn. CT scan of skull	+	-
Pes calcaneovalgus	+	+
Perthes-like changes	+	+
Gal-1-PO_4 activity	N	N
Galactokinase activity	N	N
Hearing	N	N

+ = present
- = absent
N = normal

PATIENTS AND METHODS

Case 1. Anemia was present at birth (Hgb 12.5 mg %) and treated by blood transfusion. Her cataracts developed at 31 months, each requiring surgery within a year. Her mental and growth retardation became evident at the age of 3. At the age of 6 her OFC was 46 cm ($< 3^0$) and her full scale intelligence quotient 36. A CT examination of the brain showed bilateral symmetric hypodens regions in the anterior pallidum and the head of the caudate nucleus indicative of a lesion in the corpus striatum. Her upper lip looks slightly thinned out for lack of philtrum. Left ear is somewhat lower. She had a derotation osteotomy for left sided Perthes disease at age 5. Additional laboratory tests included amino acid and carbohydrate screening, tests for toxoplasmosis, listeriosis and rubella serology, finally karyotype which were all normal.

Case 2. was born 2 years later and his neonatal jaundice was treated by phototherapy. Diagnosed mild anemia did not require any treatment. His cataracts were diagnosed at 24 months, he underwent surgery the same year. Mental and growth retardation were noted at 18 months. At two years his I.Q. was 36, at 4 years his height and weight were less than the 3rd centile and the OFC was 49 cm ($< 10^{O}$). A CT examination of the skull was normal. His palpebral fissures suggest a slight downward sloping. Left ear is somewhat lower. Bilateral simian creases are obvious. Perthes-like changes were observed in the left hip and he underwent surgery. Genital examination was normal. He had the same laboratory investigations performed as those on his sister and they were all normal.

DISCUSSION

These patients show a similar pattern of anomalies to the sibs described by Lowry et al /1/and listed by McKusick /2/ catalog under Item 21253 entitled "Cataract, microcephaly, arthrogryposis, kyphosis syndrome (Camak syndrome)". The disorder of these patients was much more severe than that of the present sibs and had low birth weight, much earlier onset of cataracts (3 weeks) and progressive limitation of joint movements including subluxation of the hips in the affected girl. Additional features were deep-set eyes, narrow palpebral fissures, sparse hair growth, extreme failure to thrive and the mental retardation was much more profound. The affected boy had cryptorchidism and a small penis. Dolman and Wright /3/ published the necropsy findings in the first patient of Lowry et al /1/ and an extensive calcification was found in the cerebellum and cerebrum as well as terminal obesity.

Scott-Emuakpor et al /4/ published details of a similar family in which three girls and one boy, of a sibship of seven, with similar findings which McKusick lists under a separate category (21254) as CAMFAK with the F standing for failure-to-thrive. We think that CAMAK and CAMFAK syndromes are one in the same. Sugarman /5/ suggested that the syndrome described by Lowry et al /1/ was a severe allelic form of Cockayne syndrome (CS), however, Lowry and Tischler /6/, Dolman and Wright /3/ and Scott-Emuakpor et al /4/ did not agree. The issue was further

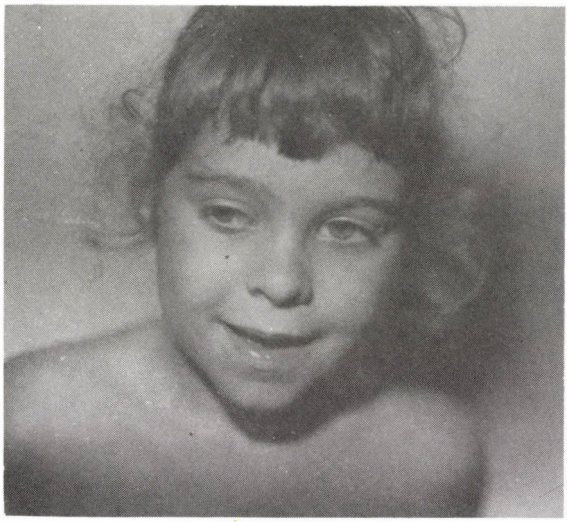

Fig.1. A. Frontal facial view of Case 1.

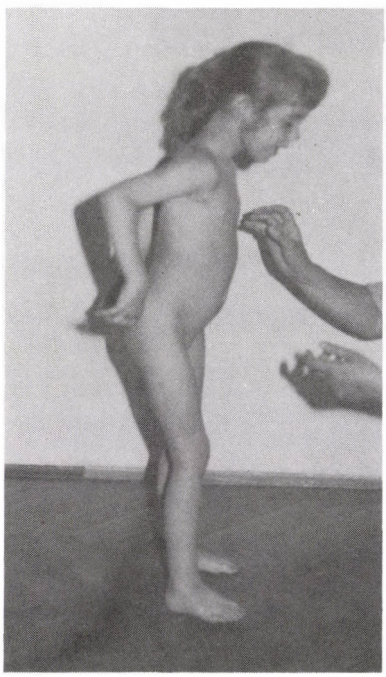

Fig. 1. B. Her full length

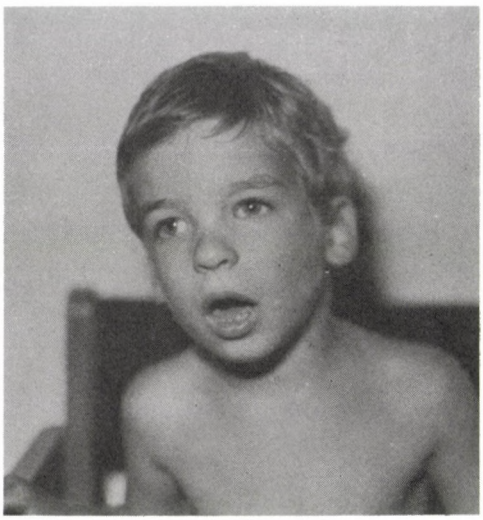

Fig. 2. A. Frontal facial view of Case 2.

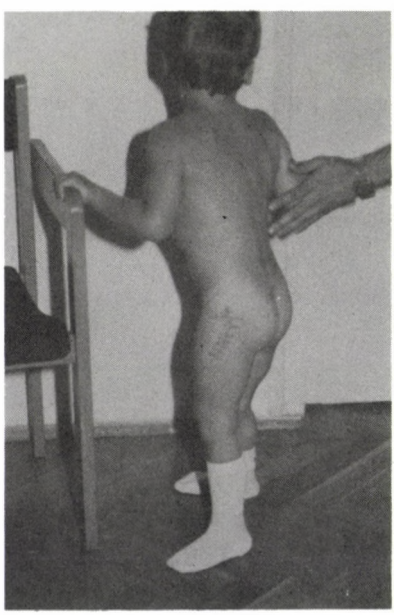

Fig. 2. B. His full length

confused when Pena and Shokeir described the syndrome named COFS (cerebro-oculo-facio-skeletal) and now named Pena-Shokier Type II syndrome /7/ and in a later report Pena, Evans and Hunter /8/ suggested that COFS might be an early infantile form of CS. Later these issues were summarized by Lowry /9/.

Cataract, mental retardation and hypogonadism were described by Martsolf et al /10/ in two brothers who were the offspring of a consanguineous Jewish couple and recently the literature on Martsolf syndrome was summarized by Strisciuglio et al /11/ who reported a non-Jewish boy with the Martsolf syndrome.

Nuclear cataracts are usually inherited in a dominant fashion, however, pedigrees consistent with recessive inheritance have certainly been reported previously. Our two patients have some similarities with the CAMAK or CAMFAK syndrome, however, there are other dissimilarities including the lack of kyphosis, spasticity and bird-like facial appearance. There may be a milder variant with the same condition or a new syndrome. However, from the pedigree it is certainly strongly suggestive of autosomal recessive origin.

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A. CZEIZEL, MD
Gyáli út 2-4.
1966 Budapest
Hungary