Syndrome of Pigmentary Retinal Degeneration, Cataract, Microcephaly, and Severe Mental Retardation*

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Two brothers with pigmentary retinal degeneration, cataracts, arachnodactyly, hyperextensible joints, mild scoliosis, microcephaly, and severe mental retardation have been studied. We know of no reports of a similar syndrome of abnormalities and consider these patients to have a previously undescribed and presumably hereditary disorder.

Case Histories

R.M. was born in 1943 and was the product of a full term pregnancy and a precipitous delivery. His birth weight was 2925 g. He was hypotonic at birth. Failure to thrive was evident in infancy. At 6 months of age he had spastic lower limbs and slow psychomotor development. When he was 2½ years old he was given braces to facilitate walking and glasses for myopia. At 6 years he understood many words and had no evidence of spasticity. At 13 years his vision had diminished markedly. At 21 years he was noted to have posterior polar lens opacities. His intelligence quotient was estimated to be 32.

When examined at age 28 years he was 177 cm tall, weighed 54½ kg and had a head circumference of 52 cm (less than 3rd centile) (Fig. 1).

Eye examination showed the following findings. Vision in the right eye was reduced to light perception with intact horizontal and vertical following movements. No following movements were noted in the left eye. Both pupils were briskly reactive to light. He had an extropia of approximately 15 prism dipters. There was no nystagmus. The corneas were of normal size and transparency. The lenses in both eyes showed anterior and posterior axial irregular white subcapsular opacities. Both fundi showed optic atrophy, attenuated retinal vessels and conspicuous equatorial bone spicule pigmentation. He had long slender fingers and toes (Figs. 2

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36 years old. Delivery was precipitous after 6 hours of intensive labour. His birth weight was 2080 g. During the neonatal period he had difficulty with feeding and received oxygen supplementation for 2 weeks. At 6 months he was unresponsive to people. At 26 months he was able to sit and crawl and his mental age was estimated to be 7 months. He walked with support at age 3½ years. At this time his height was 92 cm (below the 10th centile), weight 14 kg (10th centile), and head circumference 44 cm (below the 3rd centile). He walked without support at age 6½ years. At this time he was able to understand a few words.

He had a vitreous opacity in the right eye and a small opacity in the left eye. Both optic discs were yellowish and the retinal arteries extremely narrow. Retinitis pigmentosa was present. His vision progressively deteriorated and his mental status remained unchanged. At 17 years his intelligence quotient was estimated to be 10.

When examined at age 24 years, he was 164 cm tall and weighed 58-5 kg. His head circumference was 20 inches (below the 3rd centile). His head tapered toward the vertex and his mandible was small (Fig. 4).

On eye examination abnormalities similar to those of his brother were noted. There was no evidence of vision. An exotropia of 35 prism diopters was present. There was no nystagmus. The corneas were clear and of normal size. The irides were firmly attached to the anterior lenticular surfaces by synechial processes compatible with posterior irides. The pupils could not be dilated. Both lenses were totally cataractous (Fig. 5) and appeared shrunken in size. The fundi could not be examined. He had no pectus deformity or heart murmur.

He had long hands and fingers, but a negative thumb sign (Steinberg, 1966). He had striking hyperextensibility of all finger joints and long flat feet. His arm span was 163-5 cm. The upper to lower segment ratio was 81/82 cm or 1:0 (normal white adult mean value 0:93 [McKusick, 1966a]). His palmar dermatoglyphic patterns were within normal limits, except for a unilateral incomplete simian crease. He had no pectus deformity, no heart murmur, and normal secondary sexual characteristics (see Fig. 1). He did not have either hypertonia or hyperreflexia, as had been noted when he was younger. He spoke only a few words. There was no other neurological abnormality.

M.M. was the product of a 6-month pregnancy. He was born in 1946 when his mother and father were each

and 3), hyperextensible fingers, and a positive thumb sign (Steinberg, 1966). His arm span was 179 cm and his upper to lower segment ratio was 83/94 cm or 0:88 (normal white male adult mean value 0:93 [McKusick, 1966a]). His palmar dermatoglyphic patterns were within normal limits, except for a unilateral incomplete simian crease. He had no pectus deformity, no heart murmur, and normal secondary sexual characteristics (see Fig. 1). He did not have either hypertonia or hyperreflexia, as had been noted when he was younger. He spoke only a few words. There was no other neurological abnormality.

Laboratory Studies

A radiological survey of both brothers revealed microcephaly and a normal interorbital distance. Their arachnodactyly was reflected in an increased metacarpal index which is the ratio of length to width. R.M. had a metacarpal index of 10:0 by the measurement method of Sinclair, Kitchin, and Turner (1960) (upper limit of normal for adult male 8:4) and 10:8 by the method of Eldridge (1964) (upper limit of normal 9:4). M.M. had metacarpal

Fig. 2.

Fig. 2 and 3. The long slender fingers and toes of R.M.
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Fig. 4. M.M. at 24 years showing microcephaly, no evidence sexual maturation, and long slender fingers and toes.

indices of 9·4 and 10·0 by the same methods. Both also had small left dorsal scoliosis. M.M. had a retarded bone age (14–15 years) and unfused epiphyses in the vertebral bodies and upper humerus. R.M. had a urinary 17-ketosteroid excretion of 8·8 mg/24 hr at age 6 years. M.M. had a 17-ketosteroid excretion of 3·2 mg/24 hr at 24 years (normal adult male more than 3 mg/24 hr [Vestergaard, 1951]). R.M. had a plasma follicle stimulating hormone level of 13·8 MIU/ml and M.M. had a level of 8·7 MIU/ml (normal adult male 3·9–42 MIU/ml). Their plasma leutinizing hormone levels were 5·6 MU for R.M. and 8·0 and 7·2 MU for M.M. (normal adult male 2·5–31 MU [Saxena et al, 1968]). Their plasma testosterone levels were 0·50 µg and 0·01 µg/100 ml respectively at ages 28 and 24 years (normal adult male more than 0·3 µg/}

100 ml [Weinstein, Kliman, and Scully, 1969]). Because of his low plasma testosterone level, M.M. received 20,000 units of human chorionic gonadotropin intramuscularly in 4 successive days. On the 5th day his plasma testosterone level was 0·25 µg/100 ml (in normal adult males the minimal rise is 0·26 µg/100 ml [Weinstein et al, 1969]). His testes did not increase in size during this period. This subnormal fasting level and minimal response to chorionic gonadotropin suggests that M.M. had testicular dysfunction.

Urinary nitroprusside tests and amino-acid chromatography were normal. Both had a normal male 46,XY chromosome karyotype. R.M. had a normal electromyogram.

Family History

There is no known consanguinity. The father of R.M. and M.M. died at age 40 from a collagen disease, possibly periarteritis nodosa. He was 186·5 cm tall. He had normal intelligence. Photographs show that he did not look like either of his two sons. The mother was evaluated at age 60. She was 183 cm tall and had an arm span of 178 cm. Her upper to lower segment ratio was 82/103 cm or 0·8 (normal adult female mean 0·92 [McKusick, 1966a]). Her metacarpal index was 8·3 by the method of Sinclair et al (1966) (upper limit normal for adult female 8·4) and 8·8 by the method of Eldridge (1964) (upper limit normal 9·6). She had no chest or spine deformity and no heart murmur. Her head circumference was 60 cm. Ophthalmologic examination showed no evidence of retinal degeneration, cataracts or any other significant ocular abnormality. The 29-year-old sister of R.M. and M.M. was 186 cm tall with an arm span of 189 cm and upper and lower segment ratio of 86/102 cm or 0·83. Her metacarpal indices were 8·8 and 9·4 by the same 2 methods of measurement (normal female 8·4 and 9·6 respectively). Her head circumference was 59 cm. She had no ocular abnormalities, no pectus deformity, or heart murmur. She had normal intelligence.
Discussion

The abnormal physical features of these 2 brothers, namely pigmentedary retinal degeneration, cataracts, microcephaly, hyperextensible joints, mild scoliosis, and severe mental retardation, seem to constitute a unique, possibly hereditary, clinical syndrome. Arachnodactyly is another possible feature of this syndrome. Both boys have elongated fingers and toes and abnormally high metacarpal indices. The relevance of the arachnodactyly is made less certain by the fact that their mother and sister had metacarpal length to width ratios that were at the upper limit of normal. Furthermore, both women had abnormally long lower limbs as reflected in their abnormally low upper to lower segment ratios. This latter feature was present in R.M. but not in M.M. who was hypogonadal. One might interpret the presence of the arachnodactyly in two otherwise normal family members in 3 ways. (1) It is a coincidental finding in these 2 women. (2) It is a mild expression of the same syndrome of pigmentedary retinal degeneration, cataracts, microcephaly, mental retardation, and arachnodactyly as the brothers have to a more severe degree. (3) The arachnodactyly in the mother and sister is the heterozygous expression of the syndrome for which the brothers are homozygous. While we favour the first possibility, it is obvious that the appropriate interpretation will be more apparent once additional affected individuals with this syndrome have been reported.

While the particular combination of physical abnormalities in these brothers seems to be unique, some of these features have been reported in other hereditary disorders. For example, Duke-Elder (1938) described 2 sibs with cataracts, retinal pigment degeneration, myopia, and mental retardation. Hallgren (1959) reported sibs with retinitis pigmentosa and mental retardation, one of whom also had a cataract. However, these patients also had congenital deafness and ataxia. Kjellin (1959) described two brothers with retinal degeneration and mental retardation, but they also had spastic paraplegia with amyotrophy.

The association of arachnodactyly and mental retardation has been reported by McKusick (1966a) who briefly described 2 brothers who also had muscle hypotonia and hyperactive deep tendon reflexes. Cerebellar atrophy was present in the only one in whom pneumoencephalography was performed. Quaasroopem (1970) reported a man with pigmentedary retinal dystrophy, hypogenitalism, arachnodactyly, and mental retardation. Unlike our 2 patients, he had ataxia, nystagmus, and pes cavus and did not have cataracts.

Individuals with microcephaly and retinal abnormalities have also been reported. McKusick et al. (1966b) described 8 sibs with microcephaly, retinal degeneration, hypertonia, and other ocular anomalies, such as hypermetropia and microcornea. Kujath (1937) described a severely retarded 43-year-old girl with microcephaly, retinal degeneration, and hyperextensible joints. She did not have cataracts. The association in our 2 patients of retinal pigmentedary degeneration, hypogonadism, and mental retardation brings to mind the Laurence–Moon syndrome (Bisland, 1951; Ciccarelli and Vesell, 1961). However, individuals with this autosomal recessive disorder typically have postaxial polydactyly and do not have either cataracts or arachnodactyly.

Summary

Two brothers with a clinical syndrome of pigmentedary retinal degeneration, cataracts, microcephaly, kyphosis, arachnodactyly, and severe mental retardation have been studied. One of them also has hypogonadism. These brothers appear to have a previously unreported disorder, which is presumably hereditary.

References


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