Night blindness, characteristic facies, and skeletal abnormalities in two brothers

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SUMMARY Two brothers are described with a similar physical appearance characterised by minor periorbital anomalies, malar flatness, a maxillary overbite, retrognathia, sloping shoulders, joint hyperextensibility, and minor radiological anomalies. In addition, they had a slowly progressing night blindness, myopia, and extinguished electroretinograms. The mother had mild expression of some of the physical anomalies and a decreased electroretinogram response to red light. We have been unable to find any report of similarly affected children. The possible modes of inheritance are discussed.

This paper describes two brothers with progressive night blindness and a facies characterised by downward slanting palpebral fissures, mild synophrys, epicanthus, ptosis, malar flatness, a maxillary overbite, and retrognathia. Additional findings included: gliotic fundi, myopia, sloping shoulders, joint hyperextensibility, and minor radiological abnormalities. Expression of the syndrome was more severe in the elder boy and the mother showed some of the physical anomalies. Both boys had an extinguished electroretinogram, while the mother showed a diminished response to red light. X-linked recessive inheritance with partial expression in the mother, or autosomal dominant inheritance with marked variability in expression, are possible modes of inheritance.

Family history

The pedigree of the H family is shown in Fig. 1. The parents were unrelated and of French-Irish and Belgian origin. There was no previous family history of short stature, skeletal or visual problems.

Case reports

PATIENT II.3

This boy weighed 4152 g at birth after a normal term pregnancy and delivery. Early motor milestones were slightly delayed, he did not speak any words until he

Fig. 1 Pedigree of H. family.

was more than 2 years of age, and he is considered to be of borderline normal intelligence. He is employed as a night janitor.

When first seen at the age of 21 years he complained of slowly progressive night blindness, which had first been noted shortly after he began school. He was 155 cm tall (<3rd centile), of normal weight for his size, and had a head circumference of 55.2 cm (Fig. 2a). His hair was of normal texture with a midline parietal whorl, slight widow's peak, a normal posterior hairline, and moderate synophrys. There was slight epicanthus, mild ptosis, and fullness of the upper eyelids; the palpebral fissures were downward slanting. The inner and outer canthal distances were at the 50th centile; corneae measured 8.5 × 9.5 mm (<3rd centile), and there was a striking heterochromia irides. He was mildly myopic with a

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Fig. 2(a) Full frontal photograph of II.3 showing relative short stature, downward slanting palpebral fissures, small mandible, narrow sloping shoulders, and subluxated position of the left thumb. (b) Lateral view of II.3 showing maxillary overbite, marked retrognathia, and low, posteriorly rotated ears with increased space between the helix and antihelix. (c) Lateral view of II.6 showing facial resemblance to II.3 in addition to sloping shoulders and upper sternal deformity. (d) Lateral view of mother of II.3 and II.6, showing maxillary overbite, retrognathia, and minor ear anomaly.

corrected visual acuity of 20/30 OD and 20/40 OS with mild loss of peripheral vision. The fundi showed waxy pale discs with some attenuation of the retinal vessels. A retinal hole with a floating operculum was seen superotemporally in the right eye. This was sealed after treatment with laser beam photocoagulation. There was only one clump of irregular pigmentation on the inferonasal quadrant of the left eye. There were no typical bony corpuscles in this pigment clump. Dispersed peripherally in both retinæ were pale, colloidal like, yellowish, opalescent corpuscles, somewhat reminiscent of fundus albipunctatus. There was significant maxillary

hypoplasia and the mandible was retrognathic (Fig. 2b). The mouth was 4.5 cm wide, the palate was high and narrow, and the maxillary central incisors were very prominent. Four teeth had been removed because of extreme dental crowding with eruption in parallel rows. Both ears measured 4 cm in length (<3rd centile), were posteriorly rotated, and inserted at a level 0.5 cm below a line through the inner canthi. The helix and antihelix were widely separated with the former ceasing halfway down the ear (Fig. 2b). His neck measured 30 cm in circumference and sloped anteriorly. His span was 156 cm, his upper segment/lower segment ratio 1.06 (normal), chest circumference 77 cm, and internipple distance 20 cm. The shoulders were narrow and drooping.

All joints were hyperextensible, but this was most marked at the fingers and the first metacarpophalangeal joint could easily be subluxated. The fingertips were bulbous. The middle finger measured 7.7 cm and the palm 11.3 cm in length; the middle phalanges of the fifth fingers were short. His kneecaps could be easily subluxated. The feet measured 21.5 cm in length and there was marked bilateral pes cavus with hammer toes. Dermatoglyphs were unremarkable. His reflexes were abnormally brisk; there was bilateral ankle clonus, a positive Hoffmann's sign, and poor fine motor co-ordination. There was no ataxia, and no focal neurological signs were noted.

LABORATORY STUDIES

An electroretinogram (Grass photostimulator) showed no evoked response (Fig. 3a). Colour vision testing with HRR plates showed achromatopsia. Routine biochemical studies, including serum cholesterol and triglycerides, were normal as was Q-banded karyotype. An audiogram was borderline normal in high frequencies and impedance showed slightly hyperactive tympanic membranes.

X-rays showed the hypoplastic mandible with increased antegonial notching (Fig. 4a), abnormally shaped clavicles, a mild thoracic scoliosis, and slightly high vertebral bodies, most marked in the lumbar region. There were multiple Schmorl's nodes (Fig. 4b), particularly in the thoracic region and the bodies of the lumbar vertebrae had mild posterior scalloping. The acetabular roofs were slightly steeper than normal. The shafts of the long bones were constricted, so that the ends of these bones appeared prominent and there was bilateral subluxation of the first metacarpal-carpal joint (Fig. 4c). Metacarpal and phalangeal measurement showed the middle phalanges were all at least 3 SD below the mean, and the first and second distal phalanges were 4 and 2.5 SD below the mean respectively (Poznanski, 1974).

Fig. 3 Electroretinograms of II.3 (a) and II.6 (b) (intensity $\times 16$) showing no evoked response to white light, and of the mother (c) showing normal response to white light (intensity $\times 1$) and (d) diminished response to red light (intensity $\times 16$).

Fig. 4 (a) Lateral view of skull of patient II.3 showing increased antegonial notch of the mandible indicating mandibular hypoplasia. (b) Lateral view of thoracic spine of II.3 showing slightly increased height of vertebral bodies and narrowing of some of the disc spaces, with Schmorl's nodes in adjacent end plates. (c) Hands of II.3 showing subluxation of the first metacarpophalangeal joints and visible hypoplasia of distal phalanges of thumbs. The middle, first, and fifth distal phalanges are short on measurement.

PATIENT II.6.

This boy was born at term weighing 3950g after an uncomplicated pregnancy and delivery. His early development and schooling have been entirely normal. At the time of examination his only complaint was that of poor physical co-ordination and diminished night vision.

At the age of 10 years, he was 138 cm (50th centile) tall, weighed 27.25 kg (25th centile), and had a head

circumference of 53.5 cm (50th centile). His hair was of normal texture with a single anticlockwise, right-sided, parietal whorl, a slight widow's peak, a normal posterior hairline, and mild synophrys. The palpebral fissures were horizontal and there was slight ptosis and epicanthus of the upper eyelids. The inner canthal distance was 2.9 cm (50th centile), the outer canthal distance 8.3 cm (<50th centile), and both corneae were 10 mm in diameter (lower limit of

normal). He was myopic and astigmatic, and had a maximally corrected visual acuity of 20/40 in both eyes. The fundi were normal except, perhaps, for some pallor of the optic discs and slight narrowing of blood vessels. The nasal bridge was slightly low, the malar region was flat, and there was significant retrognathia (Fig. 2c). The mouth measured 4.6 cm in width, and the palate was high with prominent palatal shelves. The maxillary central incisors were protruding and there was severe dental crowding and malocclusion. Both ears had a simple, thick helix, with a large space between the helix and the prominent antihelix. The right ear was 5.5 cm in length (25th centile) and inserted on the inner canthal plane; the left ear measured 5.25 cm (15th centile) and was inserted 0.5 cm above the inner canthal plane (<10th centile). His neck was 27.6 cm in circumference and sloped anteriorly; his shoulders were narrow and sloping. His span was 131 cm (7.7 < height, <3rd centile), his chest circumference 61 cm (<10th centile), and internipple distance 17.4 cm (80th centile). There was marked outbowing of the upper sternum. He had a grade 2/6 ejection systolic murmur over the left lower sternal border which was considered to be functional. All joints were hyperextensible, particularly the elbows, thumbs, and distal interphalangeal joints, which could be readily subluxated. There was mild clinodactyly of the fifth fingers. The middle fingers measured 6.5 cm (50th centile), the palms 9 cm (50th centile), and the feet 21 cm in length. The toes were bulbous with a wide space between the first and second, and the second toe appeared large and deviated medially. Reflexes were brisk and symmetrical. He showed poor co-ordination and poor fine motor movement with some mirror movements.

LABORATORY STUDIES

An electroretinogram showed almost non-existent response (Fig. 3b). Examination of visual fields was considered to be unreliable, but was probably normal. There was a mild red-green colour defect on HRR plates. Routine laboratory studies, including cholesterol, triglycerides, and an electrocardiogram, were normal.

A radiographic survey showed hypoplasia of the mandible with increased antegonial notching, fewer Schmorl's nodes than in his brother, mild hypoplasia of the iliae, and slight lateral subluxation of the first metacarpal-carpal joint. The spine, clavicle, and long bones were otherwise normal. Measurement of the metacarpal and phalangeal bones showed that the middle third and middle fourth phalanges were 3 and 4 SD below the mean, respectively. The remaining measurements were within normal limits.

OTHER FAMILY MEMBERS

The mother (I.2) of the two affected boys was 48 years old at the time of this study, was of normal intelligence, and had always enjoyed good health. She was 155 cm tall, had a span of 154 cm, weighed 57.5 kg, and had an OFC of 55.3 cm. Her skull was of normal shape, her hair of normal texture and distribution. There was a slight medial flare of her eyebrow on the left. Her palpebral fissures were downward slanting and there was a fullness of the lateral portion of the upper eyelids. Her inner and outer canthal distances and her fundal examination were normal. She had a normal nasal bridge and no significant malar flatness. Her mouth measured 5 cm in width, her palate was normal, there was moderate retrognathia, prominent maxillary central incisors with a severe outbite, and mild dental crowding. Her ears were normal in position, shape, and size. Her neck was 33.3 cm in circumference and did not slope anteriorly. She had a normal chest and shoulders. Her hands and feet were of normal size and shape, and there was no significant joint laxity. An electroretinogram showed a diminished response to red light (that is, cone area), but a normal response to white light (Fig. 3c, d). A skeletal survey, including metacarpal and phalangeal measurements, showed none of the abnormalities seen in the boys.

The father (I.1) was 49 years old at the time of this study and was of normal intelligence. All measurements were within normal limits and physical examination did not show any of the abnormalities seen in the two affected boys. He had suffered a severe coronary thrombosis at the age of 47 years and had severe limiting angina. Radiological studies did not show any of the abnormalities seen in the boys and his electroretinogram was entirely normal.

The remaining three boys in the family were all of normal intelligence and in good health. None of them resembled their mother and affected brothers in physical appearance. They all had normal electroretinograms.

Discussion

We have been unable to find previous reports of patients similar to the two boys in this family, who presented with nyctalopia, minor skeletal anomalies, and an unusual facies. Their physical appearance probably constitutes part of the syndrome, as it was distinctive from that seen in their three other unaffected brothers, but bore some resemblance to the mother, who also had an abnormal electroretinogram.

The mode of inheritance of this condition cannot be determined with certainty from this single family. We believe that the physical resemblance of the

mother to the two affected boys is evidence of mild expression of the syndrome, because the three unaffected boys bear no physical resemblance to her. This is supported by her diminished electroretinographic response to red light. The findings in this family are compatible with X-linked recessive inheritance with partial expression in the female, though autosomal dominant inheritance with variable expressivity cannot be ruled out.

The electroretinographic studies in both boys were compatible with retinitis pigmentosa, and yet neither boy showed evidence of significant pigment dystrophy despite clinical symptoms of night blindness, dating back at least 13 years in the older boy. It is unusual to have this duration of symptomatic retinitis pigmentosa in the absence of significant retinal pigment (Pearlman *et al.*, 1976). The association of myopia and choreoretinal degeneration with night blindness is well known and may occur in a sex linked recessive pattern of inheritance (François and De Rouck, 1965). Both our patients and their mother had myopia, but the significance of this association in our family is questionable, since one of the normal brothers was also myopic. Night blindness or diminished night vision may be seen as a component of a large number of syndromes including the Hallgren, Biemond, Frolich, Refsum, and A- β -lipoproteinaemia syndromes, but these can be ruled out on clinical and biochemical grounds (Geeraets, 1976).

The skeletal changes seen in our patients are relatively non-specific and do not appear characteristic of any of the established skeletal dysplasias. The elder boy had a brachydactyly which involved all the middle phalanges and the distal fifth and first phalanges. This does not exactly fit any of the defined brachydactylies, but is most like a combination of A1 and D brachydactyly (Temtam and McKusick, 1978). An excess of type D brachydactyly has been reported among retarded patients (Villevre and Da Silva, 1975). The brachydactyly in the younger boy was confined to the middle third and fourth phalanges. Previous reports of retinitis pigmentosa associated with skeletal abnormalities include a father and son with bony sclerosis reported by Antoine *et al.* (1963), and the syndrome of familial nephropathy associated with retinitis pigmentosa, cerebellar ataxia, and skeletal anomalies reported by Mainzer *et al.* (1970) and Popović-Rolović *et al.* (1976). Though there is some parallel between the

phalangeal changes seen in our older patient and the latter syndrome, our patients can be clearly distinguished by the absence of ataxia or renal pathology. Schmorl's nodes, overtubulation of the long bones, and myopia are seen in Stickler's syndrome, but the other features are sufficiently distinctive to separate the two conditions (Herrmann *et al.*, 1975).

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