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Macular coloboma and skeletal abnormality

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The purpose of this communication is to describe a brother and sister who have bilateral macular coloboma, cleft palate, hallux valgus, and various other abnormalities. Only one other family with a similar, but not identical, syndrome seems to have been described in the literature (Sorsby, 1935).

Material

The propositus (Case 1) was a boy aged 14 years at the time of examination; his sister (Case 2) was 2 years older. The results of examination and investigations are listed in the Table. Fig. 1 shows the fundi of Case 1 and Fig. 2 (overleaf) her extraordinarily small feet. These two affected children have two unaffected siblings.

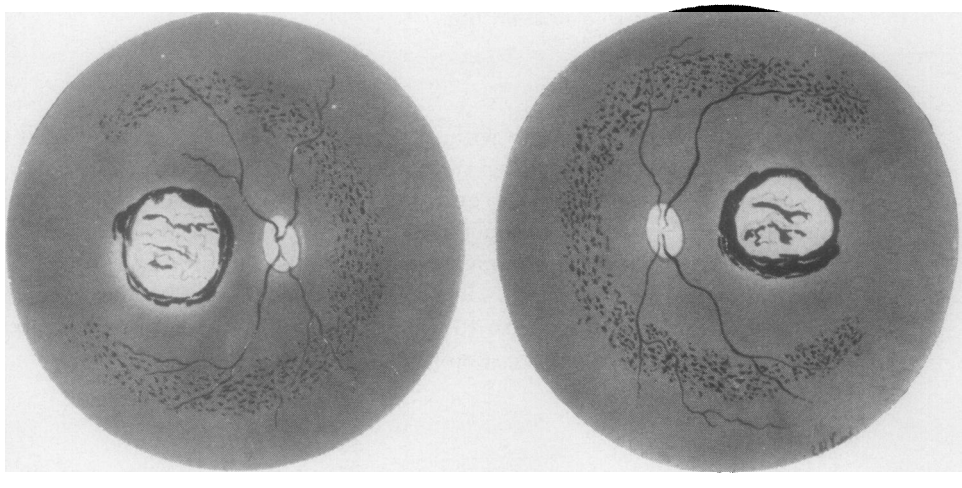

FIG. 1 *Fundi of girl aged* 16 *(Case* 2*) showing bilateral macular colobomata and almost complete rings of lesions resembling those of primary pigmentary degeneration of the retina. Examination was difficult because of nystagmus. As in her brother's case, the macular lesions were markedly "punched out", probably indicating ectasia of the sclera in that area*

Of the other members of the family only the patients' mother was examined clinically by us and no abnormality was found. She gave a clear account of the large family on her own and her husband's side and mentioned only one individual with an abnormality: this was the blind child of a paternal aunt of the propositi who married a full cousin. However, the findings of his ophthalmologist (corneal scarring, anterior polar cataract, and nystagmus with a normal fundus in his right eye and phthisis bulbi in the left eye) suggest no relationship with the present cases.

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Table *Clinical findings in two cases*

Case No.	1	2
Sex	*Male*	*Female*
Date of birth	May 17, 1951	August 8, 1949
Birth weight	6 lb.	3 lb. ¾ oz.
Age when examined (yrs)	14	16
Mental state	Normal	Retarded (? by 4 years)
Height	5′ 3¼″ (aged 15)	4′ 5¾″ (aged 16)
Physical Development	Normal Red hair Secondary sex characteristics normal	Retarded Red hair No menstruation
Skull	Cleft palate (surgically repaired) Sloping forehead Platybasia without basilar invagination	Cleft palate (surgically repaired) Small canines and upper lateral incisors
Fingers	? Long middle phalanges with spindling at proximal i.p. joints Hyperextensible middle two fingers of both hands Flexion deformity of distal i.p. joints of both little fingers	? Proximal phalanges abnormally long Flexion deformity etc., as brother
Lower limbs	Normal	Aged 12 recurrent left dislocation of patella (tibial tubercle transplanted) Aged 14 bilateral genu valgum appeared (– tibial osteotomy) Bilateral coxa valga with increased external rotation of hips
Feet	Length: normal for age Severe bilateral hallux valgus ? Abnormally short second metatarsal	Length: 6 inches Bilateral hallux valgus Short 2nd digit and long 4th digits
Blood pressure	135/75	95/60
Central nervous system	Normal	Normal
Urine (including chromatogram)	Normal	Normal
Other blood tests	Normal serum proteins, cholesterol, calcium, acid phosphatase, blood urea, haemoglobin, and blood sugar	Normal calcium, phosphorus
Chromosomes	Normal male karyotype 44A; XY	Normal female karyotype 44A; XX
Eyes	Bilateral macular coloboma with low visual acuity Nystagmus Hypermetropia	Bilateral macular coloboma with "primary pigmentary degeneration" of retina and low visual acuity Nystagmus Hypermetropia
Visual Acuity	*Right:* 4/60 *Left:* 3/60	*Right:* 3/60 *Left:* 3/60
Refraction	*Right:* +4 D sph., +1·5 D cyl., axis 15° *Left:* 5 D sph., +1 D cyl., axis 150°	*Right:* +4·75 D sph., +0·75 D cyl., axis 105° *Left:* +3·75 D sph., +0·5 D cyl., axis 75°

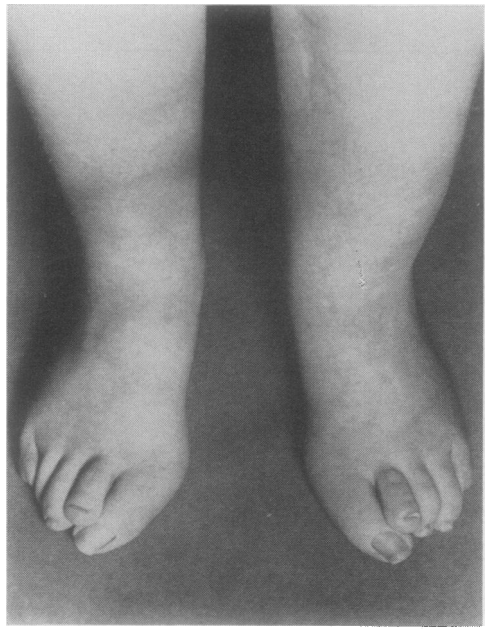

FIG. 2 *Feet of Case 2, showing bilateral hallux valgus and short second and long fourth digits. The feet were only 6 inches long. A scar can be seen over the left tibia in the upper third of which a wedge osteotomy had been done to correct genu valgum*

Discussion

Many cases of bilateral and unilateral macular coloboma have been recorded in the literature (Sorsby, 1935; Waardenburg, Franceschetti, and Klein, 1961), but there have been few reported instances of their association with other congenital abnormalities: Car (1925) mentioned microcephaly, large ears, thick wrists, "pearl-string" fingers, and abnormally short little fingers; Clark (1927) undescended testis and "bad development of most of the facial bones"; Feilchenfeld (1911) abnormally prominent ears; and Sorsby (1935) a series of malformations.

In our patients there were some findings similar to those described by Sorsby, but nothing to suggest any consanguinity between the two families. Abnormalities of the skeleton of the hands and feet are present in both groups. Hallux valgus is present in the radiograph of Mrs. S. (Sorsby's Fig. 12) and was noted in both our cases. Otherwise our cases do NOT share the details of the other abnormalities noted by Sorsby, *viz.* a tendency to atrophy of the terminal phalanges of both hands and feet with rudimentary nails on the index fingers and large toes, a tendency to bifurcation of the terminal phalanx of the thumb, a tendency to diminution or suppression of the second phalanx of the little finger, and bifurcation (in all but one case) of the terminal phalanx of the big toe. In Sorsby's family, a mother and five of seven children were affected, which suggests an autosomal dominant mode of inheritance. In the present study, two out of four siblings were affected, their parents being normal, which suggests an autosomal recessive mode of inheritance: the parents, however, were not blood relatives.

The mechanism of production of the coloboma is difficult to explain on embryological grounds, unless intrauterine inflammation be postulated (Mann, 1957). We consider inflammation to be unlikely here because a brother and sister are affected and there are other bizarre abnormalities: some defect in the development of the cone-bearing area of the retina and/or the related choroid or sclera is more probable.

At first, a high level of serum alkaline phosphatase was found (60 King Armstrong units for the boy aged 14 and 42 KA for the girl aged 16), but later more detailed analyses in the children and parents failed to confirm this except for a rather high bone alkaline phosphatase in the physically retarded girl at the chronological age of 18 years.

Summary

A brother and sister of a sibship of four, with normal parents, have macular colobomata, cleft palate, flexion deformity of the distal interphalangeal joints of the little fingers of the hand, and hallux valgus; the girl had additional abnormalities (retarded growth and delayed sexual maturity, recurrent dislocation of left patella, bilateral coxa valga and genu valgum, and very short feet). A recessive gene is considered to be the cause. Although macular colobomata have been frequently described in the literature, few instances have been mentioned of an association with non-ophthalmological abnormalities; only one family with skeletal abnormalities similar to those reported in this sibship has been described.

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