COMMENT

The clinical and histopathological findings in this case are those of both granular and lattice dystrophy. The differences between these two dystrophies are summarised in Table 1. Amyloidosis is a localised or systemic disorder in which there is abnormal extracellular deposition of protein fibrils associated with sulphated glycosaminoglycans and serum amyloid P. The fibrils may be formed from a variety of precursor proteins including immunoglobulin light chains and keratin. The nature of corneal amyloid is currently unknown.[8] Our studies confirm that immunoglobulin light chains and keratin are not present in corneal amyloid.

Rodrigues et al [9] have demonstrated microfibrillar proteins in deposits of granular dystrophy. The protein gelsolin has been found by immunohistochemistry in both granular dystrophy and lattice dystrophy, type 1.[10] It is possible that some cases of lattice dystrophy and granular dystrophy may share another as yet unidentified microfibrillar protein. There have been reports of patients with lattice-like changes in otherwise typical granular dystrophy and reports of granular deposits in families with clinically typical lattice dystrophy.[7] Recently, amyloid deposition has been documented in association with granular dystrophy in families with ancestral origin from the Italian province of Avellino.[1-6] It has been suggested that this combined dystrophy is due to a variation of granular dystrophy involving deposition of lattice-like amyloid deposits.[5] These cases have been termed granular lattice (Avellino) corneal dystrophy.

Genetic linkage studies have found that Avellino type combined dystrophy, lattice type 1 dystrophy, and granular dystrophy share the same locus on the long arm of chromosome 5.[6] One of the families with Avellino type dystrophy, which had no Italian heritage, did not have the same alleles as the Italian families at the chromosome 5 locus. This suggests that a different mutation has given rise to the dystrophy in that family.[5] The patient reported here has no history of Italian heritage. Presumably, an independent mutation has caused her dystrophy. This case lends further weight to the emerging genetic and clinical information that granular and lattice type 1 dystrophies may represent differing phenotypic expressions of the same disease and that combined cases may be more frequent than has been generally appreciated.

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Accepted for publication 19 January 1996

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A new oculorenal syndrome: retinal dystrophy and tubulointerstitial nephropathy in cranioectodermal dysplasia

EDITOR,—Cranioectodermal dysplasia (CED) is a rare autosomal recessive condition with characteristic craniofacial, skeletal, and ectodermal abnormalities.[1-3] These include dolichocephaly (long skull), which is usually associated with sagittal suture synostosis, frontal bossing with hypotelorism, high arched palate, short narrow thorax, short limbs, and short stubby digits. Ectodermal manifestations include short nails, fine sparse slow growing hair, and small widely spaced teeth. Less frequent associations are cardiac valvular abnormalities, recurrent chest infections, and apparent hepatosplenomegaly as a result of the small thorax. Intelligence is normal.

Ophthalmic features which have been noted previously include hypotelorism, marked epicanthic folds, hyperopia, myopia, and nystagmus.[1] We now provide further details of two previously described siblings[2] both of whom have developed a symptomatic photoreceptor dystrophy and chronic renal failure.

CASE REPORTS

Case 1

The index case, a girl, was the second child of healthy unrelated parents. She was noted at birth to have dolichocephaly, clinodactyly of the fifth fingers, and apparent hepatosplenomegaly. Subsequently she was noted to develop the classic features of CED, including sagittal suture synostosis, short narrow thorax secondary to rib abnormalities, short limbs, short digits, single palmar creases, short thin hair, small teeth, and short nails[3] (Fig 1).

As an infant, she suffered recurrent chest infections and bronchospasm, at one stage requiring ventilation. She developed fits at age 3 years which were satisfactorily controlled with sodium valproate. Elevated serum creatinine was noted when she was aged 4 years: chronic renal failure due to tubulointerstitial nephropathy was to reach fatal end stage shortly before her sixth birthday.[4]

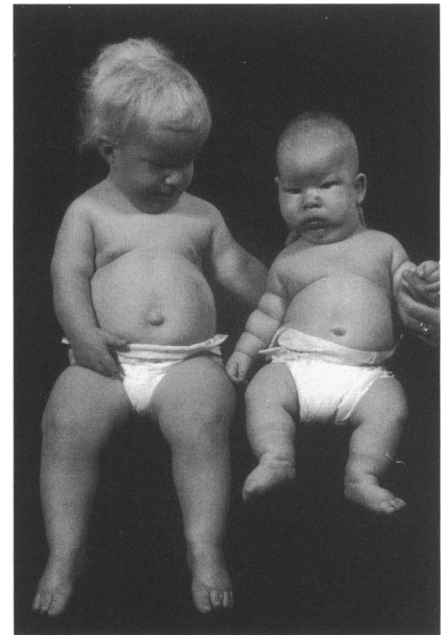From the age of 18 months her mother noticed that she had difficulty with distance

Figure 1 The siblings, cases 1 and 2, at ages 2½ years and 3 months, respectively. (Photograph reproduced with permission of the children's mother.)

vision. Ocular examination at age 2 years demonstrated −4·50 DS myopia for which spectacles were prescribed, but no other abnormality was found. In her third year of life she began to have difficulty navigating in dim illumination, walking with arms outstretched to avoid unseen obstacles. When examined at age 4 years the visual acuity was 6/36 with an unchanged myopic correction, and fundus examination was normal. However, electroretinography using skin electrodes demonstrated a grossly reduced scotopic response ('b' wave amplitude 8 μV both eyes: normal minimum 20 μV), and a moderately reduced photopic response ('b' wave amplitude 3·2 μV right, 5·6 μV left: normal minimum 5 μV) with critical flicker fusion reduced at 20 Hz for both eyes. Flash visual evoked response showed normal latency from each eye but reduced amplitude on the right. A year later she was symptomatically stable, and visual acuity and electrodiagnostic findings showed no significant change.

Case 2

The younger brother of case 1 exhibited clinical findings very similar of those of his sister (Fig 1). In addition to the features of CED, he too had multiple chest infections and evidence of renal failure. At 18 months he was found to have vertical pendular nystagmus and moderate hypermetropic astigmatism (+2·00 DC both eyes). Funduscopy showed normal discs, vessels, and retina. Despite corrective spectacles, Snellen acuity remained poor at 6/18 and the child complained that he could not see in dim lighting conditions. When aged 4 years, skin electrode electroretinography showed grossly reduced amplitude of both photopic and scotopic 'a' and 'b' waves, with no consistent flicker response. When last reviewed at age 5 years, visual acuity was unchanged, and funduscopy showed normal discs and vessels with a slightly granular appearance of the mid-peripheral retina.

COMMENT

The cranioskeletal and ectodermal findings in these siblings are typical of those

Table 1 Differential diagnosis of oculorenal syndrome in cranioectodermal dysplasia

System involvement	EEM[5]	Senior-Loken[6]	Mainzer-Saldino[7]	Jeune[8]	CED[1-4]
Retina	Macular dystrophy	Tapetoretinal degeneration	Tapetoretinal degeneration	Occasional retinal pigmentation	Nyctalopia, retinal dystrophy
Kidneys	–	Juvenile nephronophthisis	Juvenile nephronophthisis	Tubulointerstitial nephropathy	Tubulointerstitial nephropathy
Skeleton	Ectrodactyly	–	Cone-shaped epiphyses	Small chest and short limbs	Short small chest and short limbs
Ectodermal	Hypodontic and sparse hair	–	–	–	Small teeth and nails. Sparse fine hair
Other	–	Deafness	Cerellar ataxia	Polydactyly	Craniosynostosis
Inheritance	Autosomal recessive	Autosomal recessive (?mitochondrial)	Autosomal recessive	Autosomal recessive	Autosomal recessive

EEM=ectodermal dysplasia, ectrodactyly, macular dystrophy; CED=cranioectodermal dysplasia.

described in cranioectodermal dysplasia. This is an extremely rare disorder with fewer than 12 cases having been reported. Information about its natural history is limited and these are the first reported cases with a photoreceptor dystrophy or kidney problems. We are aware of a further pair of monozygous twins with CED and what is probably the same oculorenal syndrome, and the renal aspects of these four cases are more fully described elsewhere.[4] Our observations show that progressive retinal involvement is a feature of CED and indicate that the underlying genetic defect involves not only morphogenesis but also subsequent maturation of organs as diverse as the kidney and the retina.

These findings also indicate that CED falls within the spectrum of a family of disorders which show variable involvement of the kidneys, eyes, skeleton, and ectodermal structures. In particular, the differential diagnosis includes the EEM,[5] Senior-Loken,[6] Mainzer-Saldino,[7] and Jeune[8] syndromes (see Table 1). The EEM syndrome can be distinguished by the finding of ectrodactyly ('lobster claw deformity') in the hands or feet. Ectodermal and skeletal abnormalities, other than cone-shaped epiphyses, are not found in the Senior-Loken and Mainzer-Saldino syndromes. Jeune's syndrome shares many features in common with CED, but lacks the characteristic ectodermal changes. Whether these autosomal recessive disorders are aetiologically related will only become clear when their causative genes have been identified and characterised. Until then, doctors caring for these children should be alerted to the possibility of both progressive renal and retinal involvement.

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