Case reports

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Interstitial deletion of the long arm of chromosome 2 with normal levels of isocitrate dehydrogenase

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SUMMARY We report a 16 year old boy with the abnormal karyotype 46,XY,del(2)(q32.2q33.1) who has mental retardation, microcephaly, epilepsy, craniofacial dysmorphism, distinctive scalloped skin pigmentation, and normal levels of isocitrate dehydrogenase.

Over 20 persons with interstitial deletions of the long arm of chromosome 2 have been described.[1–3]

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We report a further patient with an interstitial deletion with breakpoints del(2)(q32.2q33.1) which have not previously been reported, who has distinctive clinical features including an unusual pattern of skin pigmentation. We compare his cytogenetic and clinical findings with those of eight previously reported cases in the largest subgroup of 2q deletions: del(2)(q31q33).[2–8]

Case report

The proband is the third child of healthy, unrelated parents, the mother being 23 years at delivery. The pregnancy was normal until 32 weeks of gestation

FIG 1 *The proband aged 16 years.*

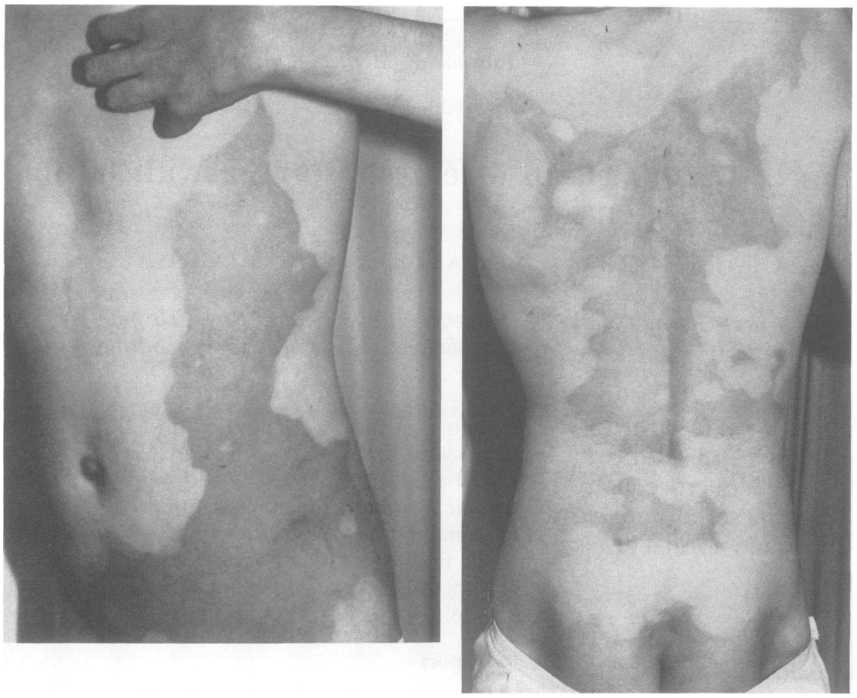

FIG 2 *The proband's distinctive skin pigmentation.*

when premature delivery occurred following an antepartum haemorrhage. The birth weight was 2070 g. Global developmental retardation and epilepsy were apparent from early childhood and ultimately resulted in his admission to an institution for the mentally handicapped. Evaluation at 16 years showed mental retardation with no comprehensible speech and total dependency, microcephaly (OFC 47 cm, −5·3 SD), short stature (149·5 cm, −3·2 SD), a large beaked nose, bilateral corneal ectasia, divergent strabismus, bilateral ptosis, and a cleft palate (fig 1). He has a striking pattern of scalloped skin pigmentation, present from birth, which is approximately symmetrical on the trunk and proximal limbs and clearly demarcated from the normal skin (fig 2). His gait was slow and jerky but there were no other neurological signs.

An EEG showed diffuse abnormalities on an irregular polyrhythmic background.

A G banded karyotype of peripheral lymphocytes showed an interstitial deletion of the long arm of chromosome 2: del(2)(q32.2q33.1) (fig 3). Skin fibroblasts from both normal skin and pigmented skin showed the same karotype: 46,XY del(2)(q32.2q33.1). The parents were unavailable for study.

Assay of the activity of the soluble form of isocitrate dehydrogenase (ICD-S, E.C.1.42) activity in red cells from the index case gave normal activity (1·13 IU/g Hb, mean of 18 controls 0·93 IU/g Hb, SD 0·28).

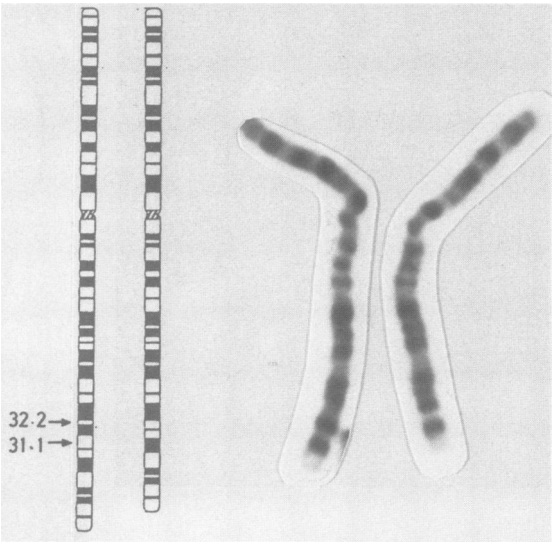

FIG 3 *Idiogram and G banded chromosome 2 of the proband indicating the breakpoints of the deletion.*

TABLE *Clinical features in cases of interstitial deletion of 2q31–q33.*

	Present case	*Benson et al*[2]	*Young et al*[3]	*Buchanan et al*[4]	*Al-Awadi et al*[5]	*Franceschini et al*[6]	*Taysi et al*[7]	*Pai et al*[8]
Deletion	2q32·2–q33·1	2q31–q33	2q31–q33	2q31–q33	2q31–q33	2q31–q33	2q31–q33	2q32
Sex	M	F	M	F	F	M	F	F (2 sibs)
Mental retardation	+			+	+	+	+	+
Prenatal growth failure	–	+	+	+	+	+	–	
Postnatal growth failure	+		–	+	+	+	+	+
Microcephaly	+	–		+	+	–	+	–
Prominent forehead	–	–	–	+	+	–	–	+
Seizures or abnormal EEG	+	–	–	+	+	–	–	+
Microphthalmia	–	+	+	+	–	+	–	–
Corneal abnormality	+ (Bilateral ectasia)	–	+ (L opacity)	+ (L clouding)	–	–	–	
Ptosis	+	–	–	–	–	+	+	–
Beaked nose	+	–	+	+	–	+	+	+
Large or low set ears	+	+	+	–	+	–	+	+
Micrognathia	–	–	+	+	+	+	–	+
Cleft palate	+	+	–	+ (Bifid uvula)	+	+	–	–
Clinodactyly of 5th fingers	–	–	–	–	+	–	+	+
Camptodactyly of fingers	–	+	–	+	+	+	–	–
Syndactyly of toes	–	+	+	–	–	+	–	
Congenital heart defect	–	+	–	+	–	–	+	–
Other features	Strabismus, skin pigmentation	Tapering and overlapping digits, renal hypoplasia, abnormal temporal gyral pattern, ectrodactyly of both feet	Bilateral iris colobomata		Macrostomia, joint laxity	Joint laxity		Father shown to have balanced intrachromosomal translocation 46,XY, t(2q32→2p13)

Discussion

The most frequently reported interstitial deletion of 2q involves the segments del(2)(q31q33) and the clinical features of the other eight reported cases are outlined in the table. It is apparent that in addition to the general features shared with other 2q deletions (mental retardation, microcephaly, growth failure, and congenital heart defects),[1-3] more specific features of del(2)(q31q33) deletions, as suggested by Schinzel,[9] include microphthalmia, corneal anomalies, ptosis, a beaked nose, micrognathia, cleft palate, large or low set ears, clinodactyly of the fifth finger, camptodactyly of the fingers, and syndactyly of the toes.

The present case shares some of the features of this subgroup of 2q deletions but he also shows distinctive skin pigmentation. The distribution of the skin abnormality did not follow Blaschko's lines and we found no evidence of chromosomal mosaicism by demonstrating the identical karyotypes in the fibroblasts derived from the pigmented and non-pigmented skin. The skin pigmentation may be related to the breakpoints of this deletion allowing expression of an otherwise suppressed gene, or it may represent a coincidental abnormality; further assignment of gene loci to 2q31–q33 may resolve this question.

The structural gene for the soluble form of isocitrate dehydrogenase (ICD–S, E.C.1.42) has been previously mapped to 2q33.3 by somatic cell hybridisation and gene dosage studies.[10] The presence of normal levels of ICD-S in the proband suggested that the deletion breakpoint in band q33 lies proximal to the ICD-S locus.

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A terminal deletion (14)(q31.1) in a child with microcephaly, narrow palate, gingival hypertrophy, protuberant ears, and mild mental retardation

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SUMMARY A female child with a terminal deletion on the long arm of chromosome 14, 46,XX,del(14)(q31.1), presented with microcephaly, narrow palate, gingival hypertrophy, protuberant ears, and a small haemangioma on the back. She was mildly mentally retarded. Only a few patients with a partial deletion of 14q (14q−) have been reported without consistent clinical findings. Although a clinical syndrome associated with ring chromosome 14, r(14), has been established, no distinct pattern has been so far reported in 14q−.

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Five patients with 14q− have been reported.[1-4] Three patients had interstitial deletions (fig 1, cases 1, 2, and 3). One patient had a terminal deletion (fig