The only gene definitely assigned to this region is the 'oncogene' *c-myb* which is localised to 6q22→24,¹ but it would be premature to predict what clinical effect its loss might have.

No other child with this deletion has as yet been reported, but such familial deletions and insertions are becoming more readily recognised as cytogenetic definition improves.

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Interstitial deletion 1p in a 30 year old woman

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SUMMARY High resolution chromosome analysis showed the karyotype 46,XX,del(1)(p22.1 p31.2) in a 30 year old woman with psychomotor retardation and various malformations. Determination of the enzyme phosphoglucomutase 1 (PGM1) showed that she was a heterozygote. Three other cases of interstitial deletion 1p have been reported previously, and one of these cases had several features in common with our case, suggesting a distinct syndrome.

Short arm deletions of chromosome 1 are very rare. A large, presumably terminal, 1p deletion was described by Aarskog.¹ A few other cases of terminal deletion have been reported previously,²⁻⁶ but only three cases of interstitial deletion.⁷⁻⁹ The locus for the enzyme phosphoglucomutase 1 (PGM1) has been localised to band 1p22.1.¹⁰ We present a case of interstitial deletion 1p where the PGM1 phenotype was determined.

Case report

The proband (fig 1) was born at term to a 32 year old mother and a 36 year old father. An older brother was healthy and the parents were not consanguineous. The pregnancy was complicated by a febrile illness during the first and second months. The birth was uncomplicated, birth weight 3100 g, but at

FIG 1 The proband at 15 years of age.

three days of age she became cyanotic due to a throat infection which was successfully treated.

Development was severely retarded. She sat at 22 months of age, stood at three years five months, and walked at four years 11 months. Speech never developed. At 30 years of age her weight was 40 kg, height 128 cm, and head circumference 48 cm.

Puberty was delayed and menstruation began at the age of 20 years and was regular. The breasts were small and the pubic and axillary hair was sparse.

In childhood and throughout the time of observation she had microcephaly, a low hairline, and synophrys. The face was coarse and freckled, with a broad, flat root of the nose, small primitive ears, large, half open mouth, and micrognathia, but with broad jaws laterally, giving the face a round appearance. She had bilateral microphthalmia with colobomas of the iris and chorioid, but could fix and follow small objects. The external auditory canals were very narrow. Hearing tests showed perception of music at 20 dB at the age of 18 years. She had retention of seven teeth with microdontia of those present, chronic gingival inflammation, and a flat palate.

She had a short neck, clinodactyly of the left fifth finger, and proximal implantation of the thumbs. There was subluxation of the left hip joint with a steep acetabulum and mild dysplasia of the iliac bone on the left side. She had a mild spastic palsy, bilateral equinovarus with severe valgus deformities of the big toes, and a hypoplastic nail on the second left toe.

ECG, EEG, and x ray examination of the thorax and ossification centres of the hands during childhood were normal.

CYTOGENETIC FINDINGS

Unbanded chromosomes showed a 46,XX karyotype in 1963. Further chromosome analysis was carried out in 1982 at the age of 30 years (fig 2). QFQ banding of chromosomes from peripheral lymphocyte cultures showed a deletion of the short arm of one of the chromosomes 1. The exact breakpoints were determined by chromosome analysis of RBA banded prometaphases using methotrexate synchronised peripheral lymphocyte cultures. The karyotype was 46,XX,del(1)(p22·1p31·2) or 46,XX,del(1)(pter→p31·2::p22·1→qter). The parents refused to have their chromosomes analysed.

ENZYMATIC FINDINGS

The PGM1 phenotype was determined on red blood cells and showed heterozygosity: 1+1-.

Discussion

A large de novo deletion of chromosome 1 was described by Aarskog in 1968.¹ This was before the banding era, but it was noted that the deleted segment was a large part of the distal early replicating region, and therefore was most likely a terminal deletion of 1p. Hain *et al*² reported two unrelated children with terminal 1p deletion due to

FIG 2 Chromosomes 1 from the proband showing del(1)(p22·1p31·2). Banding methods indicated above. Arrows indicate the breakpoints.

unbalanced familial t(1;15)(p36;q11), where loss of material from 15q was present too. A de novo terminal rearrangement (1p;21p) was described by Yunis *et al*³ who thought that a minimal deletion of terminal 1p could account for the phenotype of the patient, although no chromosomal loss could be shown. Desangles *et al*⁴ reported a case of monosomy 1p36 and trisomy 9p12→pter resulting from a familial t(1;9)(p36;p12). Steele *et al*⁵ reported an unusual case of tdc(1;13)(1qter→1p36·2::13p11·2→13qter) with monosomy 1p36·2→pter, and Pálová *et al*⁶ reported a de novo deletion 1p34→pter. However, it is not yet possible to delineate a monosomy 1pter syndrome because of the paucity of reported cases, the difference in the segment deleted, and the overlapping of other chromosomal imbalances.

To our knowledge only three cases of interstitial deletion 1p have been published previously.⁷⁻⁹ In one case of de novo del(1)(p22·1p32·1), the phenotype of the patient was not described.⁸ Bene *et al*⁷ reported a de novo del(1)(p21p32) in a 14 year old girl with psychomotor retardation and various dysmorphic features. Common features with our case are severe psychomotor retardation, short stature, round face, large, half open mouth, small ears, micrognathia, short neck, and clinodactyly of the fifth finger. Bene *et al*⁷ found phenotypical similarities with a 'Schafsgesicht' syndrome described by Wiedemann and Tolksdorf¹¹ and again by Schöenberg and Habedank.¹² This might, however, be another distinct syndrome or the same syndrome with different aetiologies, as 1p deletion was not found in these patients, one having a 2q+ karyotype and three having normal karyotypes. High resolution karyotypes, however, were not described. Hertz and Jensen⁹ described a del(1)(p21p22·2) due to a de novo t(1;2)(1pter→1p22·2::2p25→2qter;2pter→2p25::1p21→1qter). Common features with our case are psychomotor retardation and bilateral coloboma of the iris. More cases are required to delineate a syndrome associated with interstitial deletion of 1p, although the resemblance between our case and the case reported by Bene *et al*⁷ is striking.

There are many reports on the regional assignment of the enzyme PGM1 to chromosome 1 and the shortest region of overlap (SRO) has been suggested

to be within p22·1.¹⁰ Our patient showed heterozygosity for this enzyme, as did the patient reported by Ikeuchi *et al*,⁸ so the breakpoint in these two cases must be distal to the locus for PGM1, if the suggested SRO is maintained.

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