Two cases of interstitial deletion 1p

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Abstract

We report two cases of interstitial deletion of the short arm of chromosome 1. The first was a 10 year old boy whose karyotype was 46,XY,del(1)(p22.1p31.2); the second was a 6 month old boy with a chromosome complement of 46,XY,del(1)(p22.3p31.3). A number of the malformations observed were common to both cases. There has been one previously reported case with the same breakpoints as our case 1 and a phenotype that was strikingly similar.

Interstitial deletion of the short arm of chromosome 1 is very rare. To our knowledge, only five cases have been reported previously.¹⁻⁵ The locus for the enzyme phosphoglucomutase 1 (PGM1) has been suggested to be on band 1p22.1.⁶ In this paper we report two cases of interstitial deletion of the short arm of chromosome 1, in one of whom tests on PGM1 were carried out.

Case reports

CASE 1

The patient (fig 1), a 10 year old boy, was the third child of unrelated parents, born after an unremarkable pregnancy. Birth weight was 2700 g. The mother was 22 years old and the father 26 years old at the time of his birth. The family lived in an isolated island community and he was initially diagnosed as having Down's syndrome, but no chromosomal studies were performed.

Clinical features noted at that time included congenital absence of the left lens and a pupil abnormality with microphthalmia, hypertelorism, and a mongoloid slant to his eyes. The patient showed developmental delay and did not start to walk until 3 years of age. Examination at the age of 10 years

Figure 1 Case 1.

showed a head circumference that was on the 3rd centile, while height was below the 3rd centile and weight on the 10th centile.

He had a long, narrow, freckled face, fair hair, blue eyes, and a half opened mouth. The ears were rounded with thick, rolled over helices, the palate was high, and he had poor teeth. The hair line was low anteriorly and posteriorly. He had a marked thoracic kyphosis, marked clinodactyly of the little fingers, bilateral single palmar creases, and short, proximally implanted thumbs. The feet had prominent calcanei, mild talipes, and bilateral hallux valgus.

At a subsequent examination he was found to have quite severe joint laxity with dislocating patellae and rather tight hamstrings, suggesting a mild cerebral palsy.

He is mentally retarded and attends a school for children with severe educational difficulties (ESN(S)).

Cytogenetic findings

Cytogenetic studies were carried out on chromosome spreads prepared from cultured lymphocytes and

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Figure 2 Partial karyotype of case 1 showing $\text{del}(1)(\text{p}22.1\text{p}31.2)$.

fibroblasts, after staining with the trypsin-Giemsa banding technique. These showed an interstitial deletion of the short arm of one chromosome 1: $46,\text{XY},\text{del}(1)(\text{pter}\rightarrow\text{p}31.2::\text{p}22.1\rightarrow\text{qter})$ (fig 2). The parents were shown to have normal karyotypes, and the heterochromatic variants were uninformative as to the origin of the deleted chromosome 1.

Enzymatic findings

The PGM1 phenotype determined on red blood cells by isoelectric focusing was $\text{PGM}1^+$. The parents' phenotypes were $\text{PGM}1^+$ and $\text{PGM}1^+/1^-$. Unfortunately, the combination of parental phenotypes was not completely informative so that we were not able to know whether the patient was homozygous or hemizygous for PGM1.

CASE 2

This boy was the result of a normal pregnancy and delivery and the second child of unrelated parents. The mother was 39 and the father 44 years old at the time of his birth. He weighed 3400 g at term. His head circumference was just above the 50th centile.

On the third day of life he had a major apnoeic attack requiring hospital admission and was treated as

a 'near miss cot death'. At 6 weeks a further attack caused a 48 hour hospital admission. By the age of 2 months he showed developmental delay and was thought to be having seizures. An EEG showed a discharging focus in the left temporal region.

At physical examination, he had a narrow face and his head circumference was below the 50th centile. He had a prominent nose and a retracted lower jaw. His fingers were long with rather lax joints and his right thumb was adducted across the palm. It appeared that he might have been developing a spastic quadriplegia since, despite having lax joints, he was somewhat hypertonic.

He was developmentally delayed, but a full assessment was not performed. He died suddenly at home aged 7 months after a 48 hour mild upper respiratory tract infection. Necropsy showed no abnormality apart from congested lungs.

Cytogenetic findings

Cytogenetic studies were carried out on chromosome

Figure 3 Partial karyotype of case 2 showing $\text{del}(1)(\text{p}22.3\text{p}31.3)$.

spreads prepared from cultured lymphocytes, after staining with the trypsin-Giemsa banding technique. These showed an interstitial deletion of the short arm of one chromosome 1: 46,XY,del(1)(pter→p31.3::p22.3→qter) (fig 3).

Parental chromosomes were normal and, unfortunately, examination of the heterochromatic regions of chromosome 1 was not informative as to the origin of the deleted chromosome 1.

Discussion

The two probands have very similar short arm deletions of a chromosome 1, the first involving the segment between bands p22.1 and p31.2, and the second the region between bands p22.3 and p31.3. Both are therefore monosomic for band p31.1.

The finding of normal parental karyotypes indicates that the deletions arose de novo in both patients. Clinically, they have a number of features in common, such as a narrow face, lax joints, mild hypertonia, and developmental delay.

At least five other cases of interstitial deletion of the short arm of chromosome 1 have been previously reported. Ikeuchi *et al*¹ described a de novo deletion involving the region between bands p22.1 and p32.1. This includes the deleted segment observed in the two cases presented here. The case reported by Hertz and Jensen² was described as having del(1)(p21→p22.2) arising from a de novo translocation between chromosomes 1 and 2: (t(1;2)(1pter→1p22.2::2p25→2qter; 2pter→2p2.5::1p21→1qter). This has only two bands (p22.1, p22.2) in common with our deletions. This case is therefore monosomic for only p22.1 and does not include the regions deleted in our own cases. Bene *et al*³ described a case of de novo deletion of chromosome 1 involving the bands between p21 and p32. This is again larger than either of our deletions, both of which fall within this region. The phenotype described for this latter chromosome deletion shows some features in common with our two cases, including mental retardation, large, half opened mouth, rolled over helices, convex thorax,

long, thin fingers, and clinodactyly. Howard and Porteous⁴ reported a case of deletion of chromosome 1 involving the segment between bands p34.1 and p36.1, which does not include the regions deleted in our cases. The most relevant previous report was by Petersen and Warburg⁵ who reported a case of deletion of chromosome 1 in a 30 year old woman who carried a del(1)(p22.1p31.2) identical to that which we found in our first case. The clinical features were also very similar, including mental retardation, freckled face, half opened mouth, low hairline, microphthalmia, coloboma, tooth abnormalities, proximal implantations of the thumbs, valgus deformities of the big toes, clinodactyly, signs of joint laxity, and minor spasticity.

Although these features are often encountered in chromosomal disorders, the striking resemblance between our first case and the one described by Petersen and Warburg⁵ suggests that their association might be regarded as a recognisable pattern related to an interstitial deletion of the specific segment of the short arm of chromosome 1 lying between bands p31.3 and p22.1. Of particular interest is the presence in our second proband of some clinical features found in the two cytogenetically identical cases that we have just discussed, for example, narrow face, lax joints, hypertonia, and abnormality of the thumb, thus suggesting a possible relationship between these phenotypic signs and the loss of a wider chromosome segment between bands p31.3 and p22.1.

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