right or inverted into chromosome 2 at q21 (fig 6). The karyotype of the balanced carriers was 46,XX,inv(2;7)(q21;q32q34), or in more detailed form, 46,XX,inv(2;7)(2pter-→q21::7q32→q34::
4q21→2qter;7pter→q32::7q34→7qter). The proband’s karyotype was 46,XY,der(2)inv(2;7)
(q21;q32q34)mat, or in more detailed form, 46,XY,
der(2)inv(2;7)(2pter-→2q21::7q32→7q34::
4q21→2qter)mat.

The father (III:1) has a normal karyotype with an
enlarged satellite region on one chromosome 21 which has apparently been inherited by the index
case but not by his sister.

The genetical imbalance of the index case IV.2 is
therefore a duplication of the segment 7q32→q34.
In addition, there may be effects on control of
rearranged genes in the vicinity of the breakpoints.

Discussion

Absence of an external ocular muscle has not
previously been described in association with chromo-
somal abnormalities and there have been only a few
reports of absent eye muscles in association with a
syndrome. It has been reported with Axenfeld’s
anomaly1 and Apert’s syndrome.2 In Duane’s syn-
drome, in which there is little or no abduction
beyond the midline, the lateral rectus muscle is well
formed, but the sixth cranial nerve nucleus is absent
and the muscle is innervated from the third cranial
nerve nucleus.

We have not found any other record of duplica-
tion of the segment 7q32→q34. The numerous case
reports cited by Schinzel3 of dup(7)(q32→qter)
describe variable features which are not found in our
case. However, Nielsen et al4 reported one family
transmitting 46,XX,ins(13;7)(q32;q34): three chil-
dren had a deletion of 7q32→q34, all were retarded,
and one, a girl, had bilateral optic atrophy and
hypermetriopia. This family is obviously at risk of
segregating the duplication of this segment
7q32→q34 as in our case. The palatal ridging, skin
creases on the soles, absent eye muscle, and optic
nerve hypoplasia of our patient are unusual features
which may be characteristic of 7q32→q34 duplica-
tion.

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Concurrent de novo interstitial deletion of band 2p22 and reciprocal
translocation (3;7)(p21;q22)

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SUMMARY A child is described with a de novo interstitial deletion of band 2p22 and a reciprocal
translocation (3;7)(p21;q22). The child has mild developmental delay, coloboma of the right eye,
and Hirschsprung’s disease. The clinical and cytogenetic findings are described.

Case report

The proband, the second child of normal unrelated
parents aged 28 and 30, was born at term by elective
lower segment caesarian section. Birth weight was
3035 g and the Apgar scores were 8 at one minute
and 10 at five minutes. She was mildly jaundiced,
lethargic, and floppy at birth. The only dysmorphic
features noted were epicanthic folds and coloboma
of the right iris, which was atypical, being upwards
and medially located (fig 1). Shortly after birth she
developed respiratory distress, abdominal disten-
sion, and persistent vomiting. Abdominal x rays
revealed generalised bowel distension with multiple
fluid levels. A suction rectal biopsy showed an
absence of ganglion cells and was acetylcholinesterase
positive. A diagnosis of Hirschsprung’s disease was
made. A left iliac fossa loop colostomy was per-
formed on day 3. Seromuscular biopsy revealed ganglion cells at the low pelvic colon level. The colostomy was closed when the child was two years old after Duhamel's pull through procedure. The child achieved continence by four years of age. At three years of age Shepherd's tubes were fitted when the child developed conductive deafness associated with unresolving middle ear infections. There is no visual handicap associated with the coloboma.

Overall development has been delayed. Gross motor development has been affected by increased mobility of the hip and wrist joints. The child was walking at the age of two, but still unsteady at three years. When she was assessed at three years two months of age she was found to be functioning generally at around an 18 month level of development, though possibly lower in language skills. At four years of age, she was performing at a three to three and a half year level except for receptive language which was at a two year old level. She had regular speech therapy, has attended normal kindergarten, and has recently entered the regular school system.

**CYTOGENETIC FINDINGS**

Cytogenetic analysis of peripheral blood lymphocytes using GTL banding and prophasic technique revealed an interstitial deletion with breakpoints in 2p21 and 2p23-1. Both of these breakpoints were very close to the margins of 2p22 so the resulting deletion is primarily of the dark band, leaving the adjacent pale bands apparently intact (fig 2). As well as this deletion, all cells, in a total of 50 examined, had an apparently balanced translocation, t(3;7)(p21;q22-1). The imbalance of genetic material results from deletion of band 2p22. Parental chromosomes were normal with the father having a variant short arm of one chromosome 15 which was transmitted to the affected daughter.

The karyotype of the proband is 46,XX,del(2)
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(p21p23-1), t(3;7)(p21-3;q22-1). In the complete nomenclature it is 46,XX, der(2)(pter→p21::p23-1→qter), der(3)(q7pter→q22-1::3p21-3→3qter), der(7) (7pter→7q22-1::3p21-3→3qter). There have been only two reports of interstitial deletion of the short arm of chromosome 2 and neither involved band 2p22; similarly, t(3;7)(p21-3;q22-1) has not previously been reported.

Discussion

Specific phenotypic abnormalities associated with a small chromosome deletion provide some evidence that those abnormalities might map to that region of the karyotype. In the present case two specific abnormalities, atypical coloboma of the iris and Hirschsprung's disease, were seen in association with a small deletion of the band 2p22; however, only coloboma of the iris has been previously reported associated with a deletion of chromosome 2, but of a different region, 2p25-1→pter. The situation is complicated by both Hirschsprung's disease and coloboma of the iris being probably multifactorial in their causation.

Apart from the concordance of a small specific deletion with well defined physical features, the major interest in this case lies in the possible origin of two apparently independent chromosomal rearrangements. The simplest interpretation is the misrepair of four simultaneous breaks. This gains support from the many rearrangements which have been observed to occur after three or more breaks. In almost all of these, the rearranged chromosomes are such that it is necessary to postulate simultaneous breaks. Although it is possible that the deletion and translocation seen in the proband were successive events, there is no evidence to support this, such as mosaicism, or the presence of a balanced translocation in one parent.

Cases such as this support the hypothesis that at least in some cells breaks are being repaired. It is possible that multiple breaks occur frequently in all cells, but repair results in normal chromosomes, and it is only the occasional error of rejoining that permits observation of this activity.

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References


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