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Simultaneous de novo interstitial deletion of 16q21 and intercalary duplication of 19q in a retarded infant with minor dysmorphic features

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Abstract

We report on a retarded infant with minor dysmorphic features in whom deletion 16 and duplication 19q were discovered. The karyotype is 46,XX,del(16)(q13.08–21.05),dup(19)(q13.13–13.2). The origin and significance of the aberrant chromosomes are unknown.

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We report two rare unrelated chromosomal aberrations which were discovered in a young baby with minor dysmorphic features admitted to hospital for failure to thrive. Neither the origin of the aberrations nor their phenotypic significance can be explained at present.

Case report

The patient was the first child of healthy, unrelated parents. At birth paternal age was 25 and maternal age 21 years. During the pregnancy, which was uneventful, the mother was treated with Lithium because of depression. Delivery was by caesarean section at 42 weeks. Weight was 2570 g, length was 47 cm, and head circumference was 33 cm. Apgar score was 8.

The female newborn was admitted to hospital because of respiratory distress probably related to aspiration. There was some facial dysmorphism. Apart from bilateral dislocation of the hips and bilateral inguinal herniae no morphological or biochemical abnormalities were detected on extensive clinical examination. CT scan of the brain showed no gross abnormalities.

She has been failing to thrive since birth and psychomotor development has been retarded. All body parameters are below the 3rd centile but growth of the skull has been particularly slow.

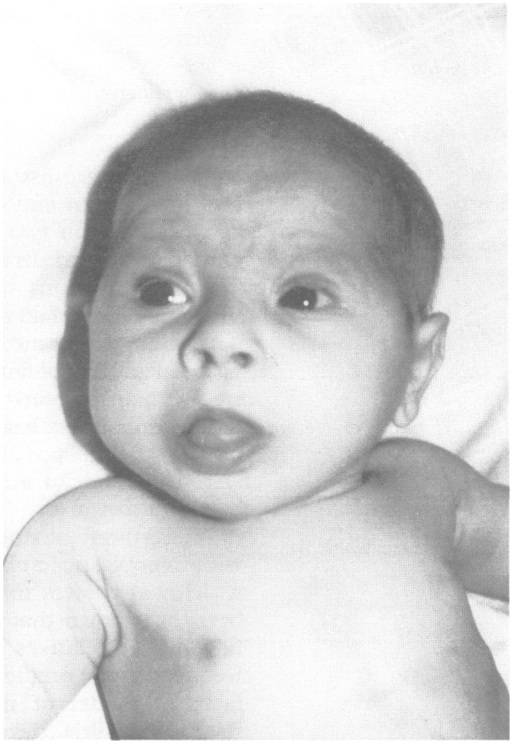

Figure 1 Facies of the patient at the age of 4 months.

CYTOGENETIC STUDIES

Metaphase spreads were prepared from lymphocytes after addition of ethidium bromide (5 µg/ml) and colcemid (0·1 µg/ml) for the last two hours of culture. GTG banding was performed at a level of approximately 550 bands and single chromosomes even more. Two different abnormalities were discovered: an interstitial deletion of 16q and an intercalary duplication of 19q. CISS hybridisation using the DNA libraries LA16NS03 and LL19NS01 (ATCC) confirmed this finding since no additional signals on any other chromosome were seen and the long arm of chromosome 19 was completely labelled. Therefore the elongation of 19 must be the result of additional material from chromosome 19.

The banding pattern of 19q could be pronounced in metaphases which had been exposed to higher concentrations of dye solution. Using the idiograms prepared at an 850 band stage (ISCN 1985)[1] as a scale, three bands instead of two can be seen between the tiny band 13.32, which is noticeable in the best preparations (fig 2B,C), and 13.12 which is consistently found. This increase may be the result of a tandem duplication of adjacent parts of 13.13 and 13.2. Moreover a tiny band was discovered close to the centromere (q12) which has been described only by Yunis *et al.*[2]

The karyotype therefore is provisionally described as 46,XX,del(16)(q13.08–21.05),dup(19)(q13.13–13.2) (fig 2).

The parental karyotypes were normal. Heteromorphism of the paracentromeric C band of chromosome 16 and of the centromeric G band of chromosome 19 was minor.

A lymphoblastoid cell line from this patient is banked in the Department of Human Genetics (F.S.29/92).

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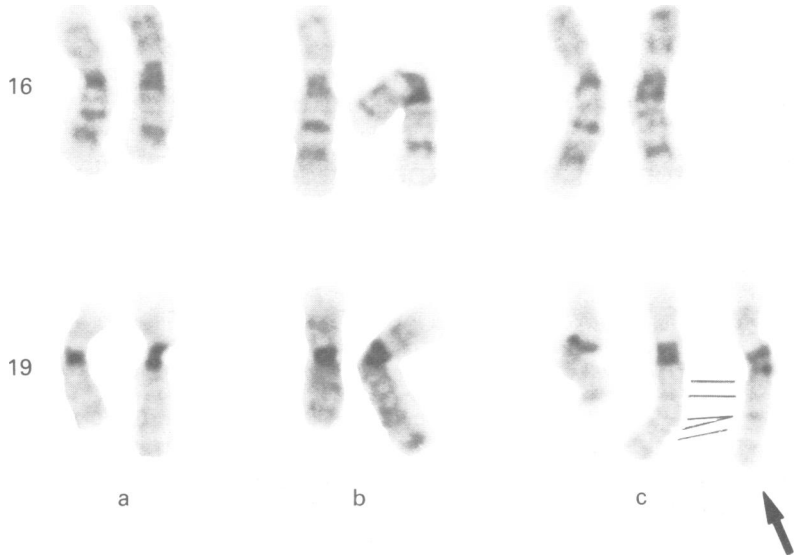

Figure 2 Chromosome pairs 16 and 19 from three selected metaphases. One normal chromosome 19 at the same stage of resolution (arrow) has been added in order to show the proposed location of the duplication.

Discussion

While the deletion of chromosome 16 was related to breakpoints at q13 and q21 the duplication of 19q cannot be delineated precisely. From the findings described we concluded that the elongation of the long arm was the result of a tandem duplication of 13.13 and a portion of 13.2. Although there is a remarkable polymorphism of paracentromeric heterochromatin of chromosome 16 and of the centromeric G band of chromosome 19 we were unable to trace the origin of either aberration.

At least 12 patients with an interstitial deletion of 16q have been reported.[3,4] All are single cases except for two families with two affected sibs each. Edelhoff *et al*[4] reported the first observation of an inherited deletion. From the correlation of clinical and cytogenetic findings a specific syndrome was delineated,[5–7] but the critical region is uncertain. While Edelhoff *et al*[4] proposed q21, Fujiwara *et al*[3] suggested q22, and the deleted segments are clustered between q13 and q22 with the exception of one observation.[5]

Despite the precise location of the breakpoints leaving a distal portion of q21, the observation reported here does not contribute further to the identification of the critical region but some similarities with previous cases and the lack of gross anomalies lend support to the significance of a segment which includes adjacent parts of q21 and q22.

A recent summary of published duplications of 19q lists 11 cases,[8] most of them familial and resulting from a parental balanced translocation. In all cases the duplications are in the distal region and of different sizes. As the patients with the largest duplication (q13→ter) were the most severely affected,[9] it has been hypothesised that the extent of duplication is correlated with the phenotype.[8] This conclusion must be questioned not only because of the low banding level of the original report but because of the lack of support from patients with trisomy 19 mosaicism. The comparison of our observation with the findings in two sibs[10] would rather suggest that duplication of segments proximal to q13 might cause major anomalies. From the present data, however, the delineation of one or more recognisable syndrome(s) of partial trisomy 19q is premature.

There is an obvious lack of concordance of band description in 19q. Two diagrams published in ISCN[1] and one by Yunis[2] show various sizes of 13.2 and 13.12. While in this case one more band is clearly present its relation to the normal pattern is not quite clear (fig 2C). Moreover we do not know why the banding pattern in the aberrant homologue is more pronounced.

Whether there is some variation of q12 also remains uncertain. Being located close to the centromere any answer to this question is related to the location, size, and variation of the centromeric C heterochromatin and the centromeric G band. It is noteworthy that the two phenomena were not distinguished explicitly in two frequently quoted papers. Crossen,[11] who proposed a classification of centromeric dark staining band polymorphism, used a C banding-like technique, and Friedrich,[12] emphasising the variability of the centromeric region, did not mention the method she had used. Therefore studies are needed in order to show the differences and to understand the morphological relationship of C heterochromatin and G bands.

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