De Novo 13q Paracentric Inversion in a Boy with Cleft Palate and Mental Retardation

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Summary. A paracentric inversion in chromosome 13, inv(13)(q12q22), is described in a boy with mild mental retardation and multiple minor anomalies. Bromodeoxyuridine-late replication studies showed no changes in the replication pattern of bands in the abnormal chromosome 13. The relation between the proband's phenotype and his inv(13) is unclear.

Introduction

Paracentric inversions are well-known in the chromosomes of many plants and animals, especially Drosophila (Lindsley and Grell, 1967). To date, however, there are only two reports of such an occurrence in man: In one case, it was not associated with either mental retardation or physical anomalies (Shimba et al., 1976) and in the other case the inversion was coincidental to another chromosome anomaly (Bass et al., 1978). We present here a child with mild mental retardation and minor congenital anomalies who has a paracentric inversion of 13q, without detectable loss of chromatin or apparent change in its replication pattern. Although a causal relationship between unbalanced chromosome aberrations and mental retardation–multiple anomaly syndromes is well established, and a number of balanced translocations have been associated with mental retardation–multiple anomaly disorders (Therapel et al., 1977; Bell and Warburton, 1977; Fried et al., 1977; Knuutila et al., 1977) there are few useful data relating balanced intrachromosomal rearrangements, as seen here, with such a phenotype.

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Materials and Methods

Peripheral blood specimens were cultured using phytohemagglutinin stimulation and standard techniques for metaphase spreads or amethopterin synchronization techniques for prometaphase and prophase spreads (Yunis, 1976). In both cases G-bands were elicited by standard trypsin digestion and Giemsa staining. Peripheral blood specimens were also cultured to differentiate early and late replicating chromosomal segments: Bromodeoxyuridine (BrdUrd, $10^{-6} \text{M}$) along with 5-fluorodeoxyuridine ($4 \times 10^{-7} \text{M}$), uridine ($6 \times 10^{-6} \text{M}$) and deoxycytidine ($1 \times 10^{-4} \text{M}$), was added 4h before an unsynchronized harvest or used in place of thymidine to release leukocytes from the amethopterin block. The BrdUrd-substituted cells were harvested, and either stained with acridine orange (Dutrillaux et al., 1973) for R-banding or aged, trypsinized and stained with Giemsa for G-banding.

Case Report

LL was a 4$\frac{1}{2}$ year old white boy referred for evaluation of developmental delay. He was the second of two children, the product of an uncomplicated 37-week pregnancy and delivery. There were no teratogenic exposures, neither parent had excessive or unusual exposure to radiation or other environmental hazards, and the family history was negative for other instances of mental retardation, facial/palatal clefting or other anomalies. His mother and father were 27 and 28 years old, respectively, when he was born; they were nonconsanguineous. At birth he was noted to have a cleft palate and in infancy he demonstrated mild, nonspecific feeding difficulties. All developmental milestones were achieved significantly later than by his older sister—he sat alone at 7 months, walked alone at 17 months, was toilet trained at 36 months, used only two-word phrases at 2$\frac{1}{2}$ years and began to use sentences only at 4$\frac{1}{2}$ years. At 4 years of age his IQ was measured at 70 on the Stanford-Benet scale and 79 on the Leiter scale. Bilateral conductive hearing loss was noted at that time. He suffered frequent bouts of bilateral otitis media until surgical repair of his cleft palate at age 16 months.

On physical examination his weight was 114 cm, weight 21.1 kg and head circumference 55.5 cm all at or above the 97th percentiles. His overall appearance (Fig. 1) was unremarkable except for mild telecanthus: interpupillary distance 49.8 mm, inner canthal distance 30.0 mm and palpebral fissure length of 26.4 mm, right and left. Extraocular movements and the findings from ophthalmologic microscopic examinations were normal. The pinnae were normal, but the

Fig. 1. Proband's face: note its normal appearance except for the telecanthus