

LETTER TO THE EDITOR

A MOSAIC EXTRA RING CHROMOSOME 4 IN A FEMALE PATIENT WITH POSTNATAL OVERGROWTH

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In this journal, Fryns *et al.* (4) reported on a 4-year old girl showing a non-specific dysmorphic syndrome and mild mental retardation. A 'de novo' mosaic small extra marker chromosome was seen in 16% of her lymphocytes. The authors concluded to the presence of a ring element because the extra small chromosome stained positive with C-banding but negative with Ag-NOR banding. However, its precise origin could not be determined by G- and R banding techniques. At birth, the length of the child was 51 cm. At the age of 4, speech disability was present and fine motor coordination was poor; her length was 122 cm (P97 is 114.7 cm), weight 21 kg (P90) and head circumference 49 cm (P25). At the age of 10, her length was 166.5 cm (P97 is 149 cm) with normal bone age. At the age of 11, she underwent a scoliosis fusion level D5-L1 due to dextro-convex thoracal scoliosis. Now, at the age of 22 years, her length is 183 cm (P97), weight 65 kg (P90) and head circumference 57 cm (P90). Her IQ was 80 at age 10. Later on, she could follow normal school education.

Using spectral karyotyping (5), also termed SKY-FISH, we tentatively identified the marker chromosome as being derived from chromosome 4. This assignment was confirmed by performing a FISH analysis using a paint of chromosome 4 (see Fig. 1a). The paint hybridized to both normal chromosomes 4 as well as to the marker chromosome. Since no telomeres could be detected on the marker chromosome using a telomeric peptide nucleic acid as a probe, the supernumerary chromosome is a ring chromosome without intrachromosomal telomeres (Fig. 1b) (2, 6). At least two other cases with a ring chromosome derived from chromosome 4 have been described before. A male fetus without mosaicism for extra element was prenatally diagnosed because of advanced maternal age and presented with alobar holoprosencephaly after termination (1). A second observation has been reported by Callen *et al.* (3) in a 36 years old man with moderate mental retardation and minor anomalies. In our patient, follow up revealed a developmentally and phenotypically normal female except for macrosomia. Thus, the observed pheno-

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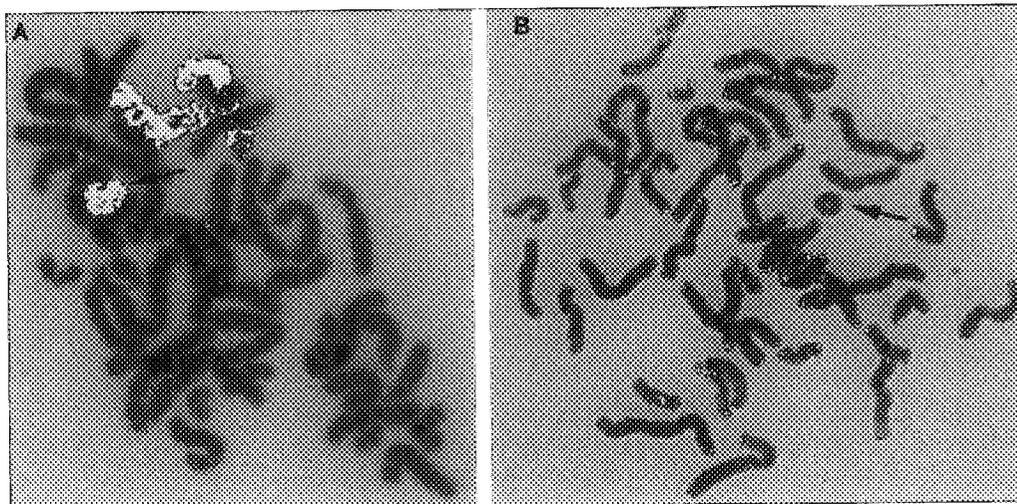


Figure 1: Metaphase spreads from the patient probed with (a) a chromosome 4 paint showing the marker chromosome is derived from chromosome 4 and (b) telomeric probe demonstrating telomeric sequences are absent on the marker. The arrow indicates the marker chromosome.

types in these three patients are different, despite the fact that these extra autosomal small ring marker chromosomes are derived from the same chromosome. Different phenotypes resulting from the presence of small autosomal ring chromosomes derived from a same chromosome are common and complicate diagnosis and genetic counseling (1-3). However, the identification of the supernumerary chromosome may aid the future diagnosis and may help to identify the molecular basis of severe postnatal overgrowth syndrome within the pericentromeric region of chromosome 4.

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