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# A Case of 48, XYY, +21

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## ABSTRACT

A 3 month-old boy with a karyotype of 48, XYY, +21 is reported. The patient had the typical features of Down syndrome and normal male genitalia.

Analysis of Q- and R-banded chromosome heteromorphisms of the patient and the parents showed that two of the three chromosomes 21 in the patient originated as a result of failure of the paternal second meiotic division. Therefore both additional chromosomes in the patient resulted from nondisjunction at paternal meiosis II.

Double aneuploidy involving trisomy 21 is rare among live births, comprising less than 1% of all Down syndrome patients. The first report of a double trisomy with chromosome 21 and the Y was made by Hall[2] in 1963 who described two such patients and at least 13 other cases of 48, XYY, +21 individuals have subsequently been reported[1,4-11].

The recent development of chromosome heteromorphic analyses has made it possible to identify the parental origin of the additional chromosome(s) in some aneuploid patients including many with Down syndrome. However, there is only a single report of the origin of the additional chromosome 21 in a 48, XYY, +21 patient[8]. We report here a second 48, XYY, +21 patient in which the origin of the additional chromosome 21 was determined.

## CASE REPORT

The patient was the first child of unrelated parents, a 19 year-old mother and a 25 year-old father, born at 39 weeks of gestation after an uneventful pregnancy. The mother had previously had an induced abortion. There was no family history of chromosome abnormality or recurrent abortions. The birth weight of the patient was 3778 g and length was 50.5 cm. The main clinical findings at one month of age were: muscular hypotonia, dry skin, joint hyperflexibility, oblique eye fissures, epicanthic eye folds, flatness of the nasal bridge, left ear deformity, protruding tongue, short neck, loose skin of the neck, funnel chest, broad and stumpy hands and feet, short and incurved 5th fingers, and single creases on the 5th fingers. In X-ray examinations, hypoplastic 5th phalangeal bones were observed and iliac index was measured to be 71.5. The dermal configurations on the palms and soles showed distal triradii, 68° of right atd angle and 65° of left atd, single crease on both 5th fingers and tibial arch in hallucal area of the soles. There was no brachycephaly, simian line or heart murmur and the external genitalia appeared normal (Fig. 1). Serum hormone levels at 31 days were normal; testosterone 3.5 ng/ml, GH 3.0 ng/ml, LH 19 mIU/ml, and FSH 15 mIU/ml.

G- and Q-banded karyotypic analysis of the patient's cultured lymphocytes showed a 48, XYY, +21 constitution (Fig. 2) in 93 of 100 cells analyzed, the remaining seven cells being hypoploid as a result of random loss of chromosomes. Both parents had normal karyotypes. In Q- and R-banded hetermorphic analyses of the chromosomes 21 of the patient and parents, two

of the three chromosomes 21 of the patient showed a homozygous pattern which originated from one of the two homologous chromosomes of the father (Fig. 3).

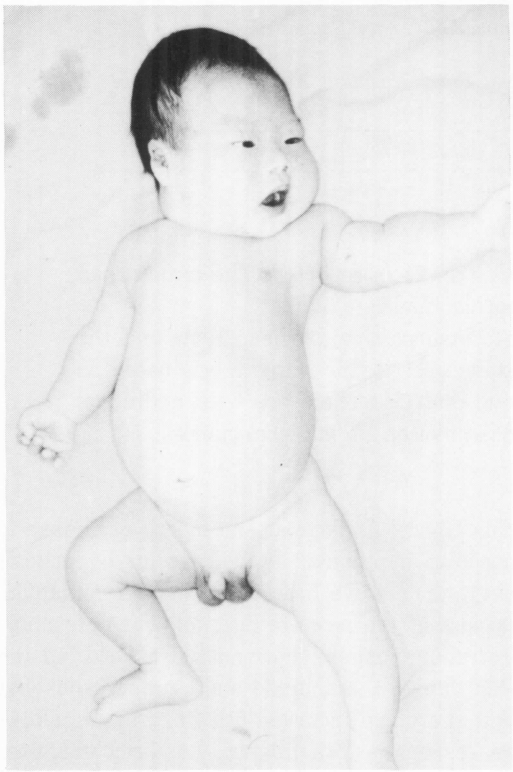

**Fig. 1.** Out-looking of the patient at 3 months of age. Note oblique eye fissures, flatness of the nasal bridge, short neck, funnel chest, broad and stumpy hands and feet, and normal external genitalia.

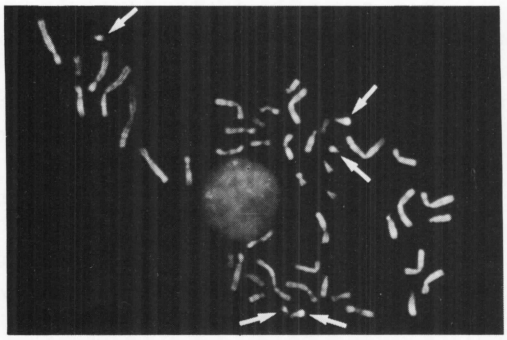

**Fig. 2.** Q-banded chromosomes of the patient. Arrows show three chromosome 21's and two Y's.

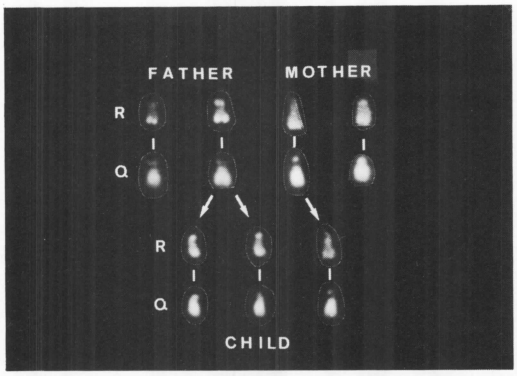


**Fig. 3.** R- and Q-banded hetermorphic patterns of chromosome 21 of the patient and the parents. One of two paternal chromosome 21's were transmitted in duplicate to the patient.

## DISCUSSION

The patient with a karyotype of 48, XYY, +21 described here had the typical features of Down syndrome, with no features associated with the additional Y chromosome. This is as expected as infants and most children with a XYY constitution are physically unremarkable.

Karyotypic screening of newborn infants shows both XYY and trisomy 21 to have a frequency of about 1 in 1000 births[3]. If nondisjunction of chromosome 21 and the Y occur independently, the frequency of 48, XYY, +21 individuals would be about 1 in 1,000,000 male births.

Analysis of chromosome heteromorphisms of the present case showed that the additional chromosome 21 resulted either from nondisjunction at paternal meiosis II or at the first mitotic division of the zygote with subsequent loss of the cell line monosomic for 21. Similarly, the additional y chromosome must also have resulted either from nondisjunction at paternal meiosis II or at the first mitotic division. According to our investigation of the literature, the only case of 48, XYY, +21 in which the additional chromosomes were analyzed for their parental origin was determined to have resulted from nondisjunction at paternal meiosis II[8]. Although a very small number of cases have been studied, these observations may indicate that a 48, XYY, +21 preferably results from nondisjunction at paternal meiosis II.

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