A Case of 48,XYY,21+ in an Infant with Down's Syndrome*

RICHARD L. NEU, ALFRED Q. SCHEUER, and LYTT I. GARDNER

From the Genetic and Endocrine Unit, Department of Pediatrics, State University of New York, Upstate Medical Center, Syracuse, New York, USA

Three cases with 48,XYY,21+ karyotype have been reported (B. R. Migeon, personal communication; Verresen and van den Berghe, 1965; Uchida, Ray, and Duncan, 1966) and the patients in these cases have presented with the classical features of Down's syndrome.

The purpose of this communication is to report another such case discovered as the result of the evaluation of an infant for possible Down's syndrome. Further verification of the presence of two Y chromosomes was obtained by staining of the preparations with quinacrine mustard dihydrochloride; the two Y chromosomes showed bright fluorescence at the distal ends of the long arms. In addition, many interphase nuclei showed two fluorescing bodies.

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Case Report

A 6-week old white male (Fig. 1) examined in December 1970, was the first offspring of a 20-year-old mother and a 24-year-old father. The pregnancy terminated spontaneously two weeks after the calculated date and the delivery was uncomplicated. The mother had experienced an upper respiratory infection during the fourth month of gestation and had had one dental x-ray one month later. The infant's birth weight was 2.95 kg (6 lb 6 oz) and the child's postnatal course was unremarkable except for a mild upper respiratory infection.

The patient presented as a pale infant with a weak cry. Weight was 3.7 kg (<3rd centile), length 51 cm (<3rd centile), and head circumference 36.75 cm (within 2 SD of the mean). Anterior and posterior fontanelles were patent and cranial sutures slightly separated. Epicanthal folds and Brushfield spots were evident bilaterally, but the typical mongoloid slant of the eyes was not observed. The ears were slightly low-set and flattened against the head, and the tongue protruded

FIG. 1. Front and side view of patient; note epicanthal folds and flat nasal bridge.

minimally. Examination of the heart revealed a harsh systolic murmur along the lower left sternal border. The second pulmonic sound was pure and accentuated. The genitalia were those of a normal, immature male. Generalized hypotonia was noted, and bilateral simian creases and short incurved fifth digits were present on both hands.

Cardiac catheterization confirmed an endocardial cushion defect of the AV canal type with large atrial and ventricular septal defects.

Cytogenetic Studies. Examination of metaphases from both peripheral blood and skin cultures revealed a complement of 48 chromosomes with two extra chromosomes in the G group. The karyotype was designated as 48,XYY,21+ (Fig. 2). Two Y chromosomes were readily recognized on morphological criteria, and the other extra G group chromosomes was presumed to be a 21.

Fluorescent staining (quinacrine mustard dihydrochloride) of preparations from both cultures was per-

formed following the technique described by Caspersson *et al* (1970). The two Y chromosomes were immediately identifiable because of their bright fluorescence at the distal ends of the long arms (Fig. 3). Two, small brightly fluorescing bodies (presumably Y chromosomal material: Pearson, Bobrow, and Vosa, 1970) were also observed in a number of the interphase nuclei from both cultures (Fig. 4).

Discussion

The clinical appearance of the present case and the three previous cases of 48,XYY,21+ individuals was that of Down's syndrome. The genitalia were normal for their ages, except in one case (Uchida *et al*, 1966), where the genitalia were described as rudimentary with undescended testes situated at the internal inguinal rings. Uchida's case may represent the XYY-testicular agenesis entity described by Carakushansky, Neu, and Gardner (1969).

FIG. 2. Karyotype from blood culture, 48,XYY,21+ showing F and G groups.

FIG. 3. A metaphase figure showing the characteristic fluorescence of the Y chromosomes after staining with quinacrine mustard.

FIG. 4. An interphase nucleus showing two fluorescing chromatin bodies which indicate the presence of two Y chromosomes.

The range of maternal ages at birth of the 4 patients was from 20 to 35 years (average 26); the paternal ages ranged from 24 to 44 years (average 32). The karyotypes of the parents in all cases were normal; one father was unavailable for karyotyping (Uchida *et al*, 1966). Sibs, when present, were clinically normal.

The aneuploidy found in the 48,XYY,21+ patients must have originated from meiotic and/or mitotic non-disjunction. Double non-disjunction could have occurred during spermatogenesis or

during the first division of the zygote. A combination of single non-disjunctional events upon fertilization could also be responsible for the aneuploidy. These could have occurred during oogenesis, spermatogenesis, or at the first zygotic division.

Summary

A 6-week-old male with Down's syndrome and a 48,XYY,21+ chromosome complement is described. The two Y chromosomes were readily identified by fluorescent staining with quinacrine mustard dihydrochloride. Three earlier cases of 48,XYY,21+ individuals are briefly reviewed.

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