13-15 Trisomy Mosaicism in a Normal-looking 14-year-old Retarded Girl*

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A syndrome involving 13-15 trisomy first described by Patau, Smith, Therman, Inhorn, and Wagner in 1960, has since been reported by other investigators (Atkins and Rosenthal, 1961; Carr, 1963; Ellis and Marwood, 1961; Ferguson-Smith, 1962; Gustavson, Ivemark, Zetterqvist, and Böök, 1962; Lubs, Koenig, and Brandt, 1961; Northcutt, 1962; Patau, Therman, Smith, and Inhorn, 1961; Smith, Patau, and Therman, 1961; Smith, Patau, Therman, Inhorn, and DeMars, 1963; Therman, Patau, Smith, and DeMars, 1961; Townes, DeHart, Hecht, and Manning, 1962; Yunis, Hook, and Mayer, 1964). The cases displayed basically the same syndrome, and Therman *et al.* (1961) suggested that the extra chromosome was always the same one, and called the syndrome D_1 trisomy: this has been substantiated by Yunis and his associates (1964) using tritiated thymidine to compare the pattern of desoxyribonucleic acid replication in the trisomic group. In 1963 an analysis of the reported cases (14 in all) was made by Smith *et al.* (1963) and established as a well-defined clinical entity involving mental retardation and a wide variety of clinical disorders. D_1 trisomy is not compatible with a long life, and it has been suggested that it might be a cause of spontaneous abortion (Carr, 1963). Most of the patients reported died within the first few months of their lives, though some did survive a few years.

In 1962 two reports appeared on 13-15 trisomy mosaicism, one by Uchida, Patau, and Smith, in which no clinical detail was presented, and one by Warkany, Rubinstein, Soukup, and Curless, in which the patient was described in some detail. The latter paper involved a 6½-year-old, mildly retarded boy, having clinical symptoms less severe than

those seen in complete D_1 trisomy, but including a communicative disorder, motor incoordination, absent patellae, camptodactyly, mild hydronephrosis, submucous cleft of the posterior hard palate, and other minor anomalies. Cytological examination revealed that 70% of his leucocytes contained 47 chromosomes, the extra one being large acrocentric of the 13-15 (D) group. More recently, a similar case of 13-15 trisomy mosaicism with an incomplete clinical syndrome has been reported by Forteza, Baguena, Amat, Barcia, and Juan (1964).

The present report describes a further case of this type of chromosome mosaicism.

Case Report

Clinical History. The propositus was a retarded normal-looking 14-year-old girl, who appeared to have grown and developed in a clinically normal manner. She was born at full-term after an apparently normal pregnancy and delivery. At the time of birth the mother was 31 and the father 30 years of age. Birth weight was 5½ lb. (2494 g.), teeth erupted at 5 months, she sat at 6 months, stood at 7-8 months, and walked at 9-10 months. There was no history of head injuries, convulsions, or prolonged high fever. Retardation was suspected because she could speak only a few words at the age of 3 years.

On admission to the Wrentham State School at the age of 7, her IQ was 63. Height was 48.25 in. (123 cm.) and head circumference was within normal limits (19.5 in. (49 cm.)). Apart from a slight deformity of the maxilla and some speech difficulty, no other abnormal findings were recorded. Recent and extensive clinical examinations at the age of 14 showed, in addition to some asymmetry of the maxilla and a difficulty in the articulation of certain consonants, a slight impairment of hearing on the right side, a slight deviation of the sacrum toward the left side, and a mild systolic murmur. Height 60.25 in. (153 cm.), and weight 106 lb. (48 kg.); cranial circumference 21.1 (53 cm.) (width 5.12 in. (13 cm.)) length 7.1 in. (18 cm.)).

Received November 9, 1965.

* This work has been supported by grants (Nos. HD-00349-02 and FR-05528-04) from the National Institutes of Health.

Fig. 1 Karyotype of propositus, showing trisomy at 13-15

Dermatoglyphic examination showed an essentially normal pattern. There were no horizontal palmar creases, neither was there a distal mean axial triradius, a finding that appears to be consistently found in D_1 trisomics. In addition there were well-developed loops in the hallucal areas of the soles of the feet. The fifth digits showed two creases rather than one, as found in some trisomics (Uchida *et al.*, 1962), and there was only one simple arch on the second digit of each hand. Haemoglobin studies by starch gel electrophoresis revealed a normal pattern and the absence of foetal haemoglobin.* Nuclear sexing studies offered no evidence for the presence of an extra 'X' chromosome. Psychological examinations indicated an IQ of 37.

Both parents and a brother who was 4 years older were normal. Among 12 relatives of the father and 5 of the mother there was only one known mentally retarded individual (with hunch-back deformity): he was the son of a paternal aunt of the mother of the patient.

Chromosome Studies. Peripheral blood leucocytes were cultured according to the method of Moorhead, Nowell, Mellman, Battips, and Hungerford (1960), and stained by Giemsa stain. Three separate cultures were carried out at different times, and approximately 30 cells were studied in each culture. Out of a total of 92 cells counted and/or photographed, 14 (15%) had 47 chromosomes, the extra chromosome belonging to the 13-15 group (Fig.), whereas all cells with 46 chromosomes had a normal karyotype. The results were similar

in each of the three separate cultures, the percentage of trisomic cells being 19, 9, and 16, respectively.

Chromosome studies were carried out on both parents and a normal brother. In each of these 30-32 metaphase cells were studied, and all showed a normal karyotype.

Discussion

It appears that with the exception of 3 cases of mosaicism, the previously reported findings on D_1 trisomics indicate that all, or practically all, of the cells examined contain 47 chromosomes. The subjects are afflicted with a wide variety of clinical abnormalities, and death usually occurs within the first few months or years of life. In both the complete trisomics or the mosaics, retardation is a common factor.

In our patient the almost complete lack of the clinical signs that are usually associated with D_1 trisomy conforms to the fact that clinical features of trisomy become milder with mosaicism. This was reported by Lindsten, Alvin, Gustavson, and Fraccaro (1962) in patients with 21 trisomy mosaicism, who exhibited incomplete mongoloid features, and in similar cases with normal or almost normal phenotypes, which have been published by Blank, Gemmell, Casey, and Lord (1962), Smith, Therman, Patau, and Inhorn (1962), Weinstein and Warkany (1963), and Verresen, van den Berghe, and Creemers (1964), wherein a relatively low percentage of the cells showed 21 trisomy. Indeed,

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our patient (with only 15% 13-15 trisomy) had considerably fewer clinical irregularities than those reported by Warkany *et al.* (1962) for a mosaic containing 70% 13-15 trisomy in the leucocytes.

Complete D₁ trisomics do not appear to constitute an important group among the mentally retarded or normal populations, since they are either aborted or die at an early age. However, 13-15 trisomy mosaicism, by reason of a decrease in the harmful effects of the extra chromosome, may be significant in mental retardation, in view of the fact that though three previous cases have been reported, cytological identification of low percentage mosaicism can easily be missed, and our patient, while lacking the characteristic features of 13-15 trisomy, did show mental retardation as the major symptom. Indeed, preliminary observations being undertaken on a large population of retarded children at Wrentham State School indicate that 13-15 trisomy mosaicism occurs more frequently than has previously been considered.

Summary

A 14-year-old mentally retarded girl (IQ 37) is reported with presumptive 13-15 trisomy mosaicism without the clinical picture usually associated with this type of chromosomal abnormality.

It is hoped to employ radioautographic techniques in order to verify that the 13-15 trisomy we have seen is identical with the D₁ chromosome group.

We wish to thank Dr. E. M. Bixby for her help during this study, and Miss Jane Wolfe for technical assistance.

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