

# FURTHER STUDIES OF A KINDRED HAVING AN ABERRANT AUTOSOME (13-15) WITHOUT APPARENT PHENOTYPIC EFFECT

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## INTRODUCTION

In an earlier paper (Chandra and Hungerford, 1963), we described the presence of an unusual satellited submetacentric chromosome, detected during a survey of randomly selected apparently normal subjects, in a healthy 21-year-old girl. The chromosome was subsequently found in her father. Since then, four additional members of the kindred have been studied cytologically, and the proposita herself has undergone a number of clinical studies aimed at revealing possible latent effects of her karyotypic anomaly; this report summarizes these clinical and cytological findings.

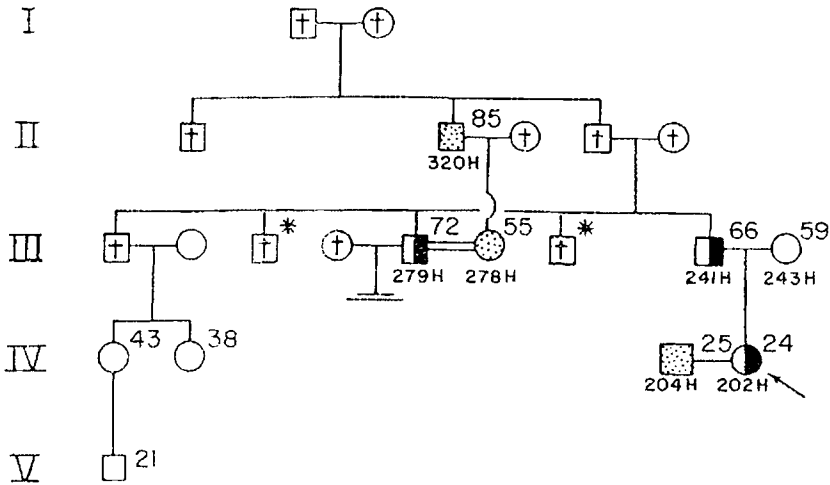


Fig. 1. The Pedigree. Open symbols indicate members whose chromosomes have not been examined. Half-open symbols are individuals who are heterozygous for the aberrant chromosome; shaded ones are those in whom the chromosome was not found. The numbers to the upper right of symbols refer to respective ages. Those immediately below are our case numbers. The proposita is indicated by an arrow. III-3 and III-7 (indicated by asterisks) died in World War I, when they were 24 and 19 years old respectively.

## THE KINDRED

Fig. 1 illustrates the pedigree. Questioning of the proposita's parents did not disclose any history of significant patterns of disease or of fertility problems which might be

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related to the chromosome change. There is no obvious phenotypic effect in the carrier individuals whom we have seen, nor is any reported in the additional carrier (III-5) living abroad.

#### CHROMOSOME ANALYSES

Chromosome preparations were made, according to the methods described by Moorhead et al. (1960), from cultured leukocytes of the proposita (202H), her father (241 H), and her husband (204 H). In addition the chromosomes of the proposita were studied in skin cultures, according to the methods described by Hayflick and Moorhead (1961) as were those of her father, her mother (243 H), uncle (279 H), aunt (278 H), and great uncle (320 H).

As described in our earlier paper, all suitable metaphases of the proposita and her father exhibited the marker chromosome. It has subsequently been found also in her paternal uncle (279 H, Fig. 2) and is morphologically identical to that observed in the proposita and her father (Chandra and Hungerford, 1963). Her paternal aunt (who is also a paternal cousin), and paternal great uncle did not have the chromosome. The chromosomes of the mother and of the husband of the proposita were likewise morphologically completely normal.

In the three carriers, only five normal representatives of the 13-15 group were present in addition to the marker, which is presumed to be a derivative of the remaining member of the group. No other abnormality was detected in their karyotypes.

#### CLINICAL STUDIES

A clinical evaluation of the proposita elicited the following information. Results of physical and hematological examinations were normal. The height was 64 inches (162.6 cm.) with an upper/lower ratio of 27/37. Dentition was normal and the extremities revealed no anomalies. Examination of the eyes, including slit lamp examination, produced normal findings. Electrocardiogram and electroencephalogram were both within normal limits. A 24-hour urine specimen was analyzed chromatographically for amino acids and indoles, all of which were normal. No gynecological abnormalities were found. Cephalometry (Sassouni analysis) was performed at the Growth Study Center, University of Pennsylvania, and no abnormalities were detected.

The results of blood group and serum protein examinations were as follows. Red cell phenotypes: A<sub>1</sub>, CCDee, NNss, U+, kk, Fy<sup>a</sup>+ and Le<sup>a+b-</sup>; haptoglobin type 2-2, transferrin type CC. She was tested with five different antilipoprotein (Ag) antisera and reacted as follows: C.de B.-; N.Y.+; J.B.+; S.L.+; A.DiB.-.

#### DISCUSSION

The nature and possible modes of origin of this aberrant chromosome have been discussed in our previous report. As mentioned there, the proposita was the first case showing an anomalous karyotype detected during a survey of karyotypes of 50 appa-

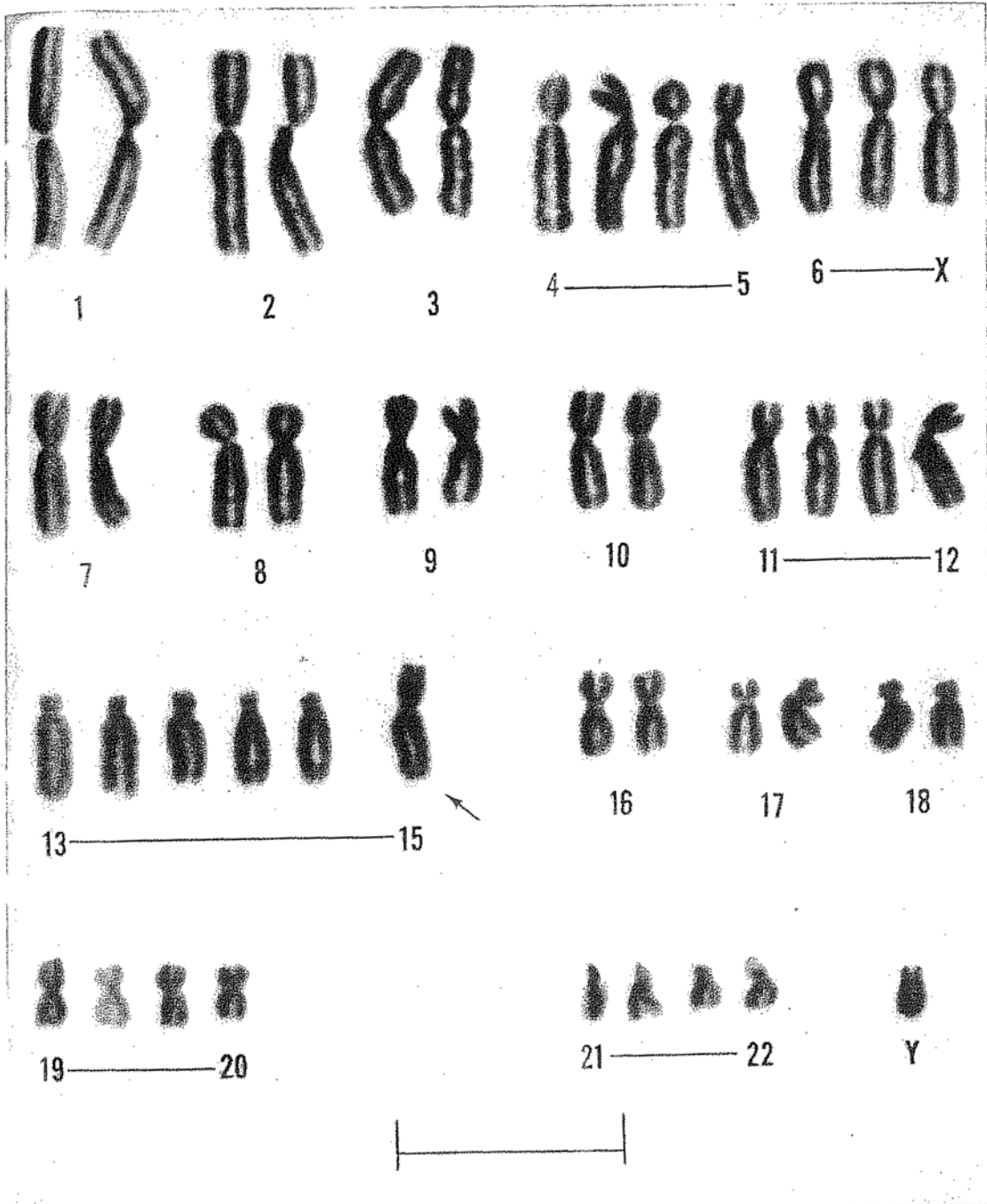


PLATE 18

Fig. 2. Karyotype analysis from skin culture of case 279H, paternal great uncle of the proposita. Note marker chromosome (arrow). Scale indicates 10 $\mu$ .

rently normal individuals. This survey has since been extended to include approximately 100 individuals, without further detection of abnormal chromosome constitution in any normal individuals. Our "normal" series comprises three types of donor: hospital patients from whom skin specimens are secured during surgical procedures, blood donors at local hospitals, and scientific coworkers. In the last category, either or both types of culture (blood or skin) may be represented.

Casual inquiry among other investigators had led us to the impression that such aberrations were probably very rare in most apparently normal human populations. However, Jacobs et al. (1964) have recently reported a high frequency (nine out of 189 individuals, or 4.2%) of individuals with karyotypes deviating from the normal, among subjects randomly selected from geriatric services in and outside Edinburgh. These authors have classified variant karyotypes which were characteristic of these individuals into two categories: (a) those which were definitely abnormal, and which involved prior chromosome breakage, and (b) those which could be either abnormal or extreme variations of normal; the cases in the latter category might or might not have involved prior chromosome breaks.

#### SUMMARY

A girl and her father, both apparently normal, had been reported earlier as carriers of a satellited submetacentric chromosome in place of a long acrocentric chromosome. A morphologically identical chromosome has now been found in the proposita's paternal uncle, but in neither a paternal cousin nor a paternal great uncle. Clinical studies of the proposita did not reveal any deviations from normality.

#### ACKNOWLEDGEMENTS

It is a pleasure to acknowledge the generous cooperation of members of this family during the course of the study.

We are indebted to Doz. Dr. H. G. Schwarzacher of the University of Vienna, who was of great help to one of us (H.S.C.) in collecting biopsy specimens from 278H and 279H, and who later collected and sent to us biopsy specimens from 320H. In addition, he independently established cultures from 320H and reached the same conclusions as we concerning the chromosome constitution of this individual.

The majority of the clinical studies of the proposita were carried out by members of the staff of the Hospital of the University of Pennsylvania, to whom we are grateful. Our appreciation is also extended to Dr. Fred H. Allen of the New York Blood Center and to Dr. B. S. Blumberg of this Institute for the blood group and serum protein determinations.

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