Partial Deletion of a Group-F (19-20) Chromosome in a Physically Handicapped Psychiatric Male Patient*

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Among autosome abnormalities, those involving group-F (19-20) chromosomes are seldom encountered. Even in abortuses where chromosome defects, namely trisomies, are more frequent than in live births, Carr (1969) stated that group-F chromosomes anomalies are relatively rare.

The previous cytogenetic studies involving group-F autosomes concerned only patients with haematological diseases. Borges, Wald, and Hoffman (1964) while studying a large family harboring the gene for congenital nonspherocytic haemolytic anaemia of the glucose-6-phosphate dehydrogenase variety (CNSHA) noted that two boys and their maternal grandfather, all with CNSHA, showed mosaicism with the minor (10 to 15%) cell population lacking one F group chromosome. The boys' parents and one normal brother showed no mosaicism. Kiosoglou, Mitus, and Dameshek (1965) reported a deleted group-F chromosome present in 6 of 7 cells karyotyped in a patient with acute granulocytic leukaemia. Kay, Lawler, and Millard (1966) described 4 cases of polycythaemia vera treated by radio-phosphorus in whom a small F chromosome was found in the bone marrow. Millard *et al* (1968) made further observations of a similar finding in three more patients with polycythaemia vera, two of them had received ³²P and one busulphan only. Group-F chromosome anomalies were found also in 5 out of 6 patients with idiopathic sideroblastic anaemia (de Grouchy *et al*, 1966), 2 of whom had a partially deleted group-F chromosome and the 3 others a probable pericentric inversion of the same autosome. Goodman *et al* (1968) noted a small group-F chromosome in conjunction with a ring chromosome in a 79-year-old female patient who had myelofibrosis secondary to polycythaemia vera. Following a pretreatment cytogenetic study of a 25-year-old male with chronic myeloid leukaemia

and localized lymphadenopathy, de Nava *et al* (1969) observed the presence of the Ph¹ chromosome, the loss of an F and the acquisition of an extra 16 chromosome in bone marrow cultures.

The present paper describes a partially deleted group-F chromosome found in a malformed male patient with severe mental retardation.

Case History

R.B., a 22-year-old male, has been hospitalized since 15 September 1953, at the age of 4, because of mental retardation and behavioural troubles. He is of French-Canadian descent, born to a 29-year-old mother and a 25-year-old father, both healthy and nonconsanguineous. He has 7 brothers and sisters, none of whom has congenital abnormalities nor mental deficiency. One paternal uncle, however, was admitted at the age of 17 to a psychiatric institution where he died at 43. A maternal aunt spent 3 years in another mental hospital.

The patient's birth was uneventful, but a striking retardation in mental development became apparent when he was one year old. At 4, he was unable to walk, could not talk nor eat unaided, was incontinent and agitated, and has remained in this state.

On examination no intellectual development was evident and the patient had a dull appearance and was unable to utter a word. Though of normal stature, he presented a microcephaly, a general muscular hypotonia and diffuse adiposity with striations of pregnancy type in the superior thigh regions. Walking was difficult due to ankylosis of both knees (Fig. 1). He was blond, with a clear skin, and scanty pilosity. Bilateral cataracts with a posterior luxation of the right eye lens and iris atrophy in both eyes explained the patient's apparent total blindness.

All laboratory examinations, including blood and urine hepatic function analyses, were within normal range. A dermatoglyphic study could not be performed because of the patient's non-cooperation.

Cytogenetic Studies. Three chromosome analyses were performed between 1966 and 1969, by short-term cultures of heparinized whole blood. Metaphases were photographed and examined, and 22 cells were selected for karyotypes.

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FIG. 1. The patient at age 20 years.

Autoradiography was carried out after labelling some peripheral blood cultures for the last 5 hours of the culture with $1.0 \mu\text{C}/\text{ml}$ of $(6\text{-}^3\text{H})$ thymidine. Chromosome preparations were dipped in Ilford L-4 photographic emulsion and developed 4 to 5 days later.

Results

Most of the cells had a normal number of chromosomes with an XY complement. Few were hypodiploid but the absent chromosomes were variable, indicating a random loss. However, in all the metaphases examined, a group-F chromosome was lacking and a small acrocentric chromosome supernumerary. The extra chromosome had no satellites. Its short arm was more distinct than that of the Y chromosome and it had no secondary constriction. It was obviously a group-F autosome partially deleted (Fig. 2).

Measurements of the 3 normal group-F chromosomes revealed that one was slightly longer than the two others and that, consequently, the missing one was a No. 19 (Fig. 3).

Autoradiographic study showed that the presumed deleted F chromosome replicated early and had the same labelling characteristics as No. 19.

Discussion

In the very few instances where anomalies of group-F chromosomes were reported, the chromosomal disorders resulted seemingly from clonal evolution. Millard *et al* (1968) noted one of their cases, who had a normal karyotype following the first cytogenetic analysis, later on showed the F-deleted chromosome. Their hypothesis was that in polycythaemia vera the chromosome defect probably arises during the course of the disease. De Nava *et al* (1969) observed a Ph^1 , F-, 16+ cell line in a case of chronic myeloid leukaemia that produced a high frequency of polyploid cells, and they believed that the event was post-zygotic and evolved from an haploid set only, but independently of therapy. The clonal evolution hypothesis is strengthened by the fact that the cytogenetic study revealed the presence of group-F chromosome anomalies in less than 100% of the cells examined in the majority of the cases reported.

Furthermore, the influence of the chromosome defects has been considered in the aetiology of the haematological disorders. De Grouchy *et al* (1966) suggested that, in sideroblastic anaemia, the chromosome anomaly either would be directly

FIG. 2. Metaphase with presumed deleted autosome 19 (arrow) from lymphocyte of the propositus.

responsible for the disturbances of the intracellular iron metabolism or for a differentiation and maturation defects of the erythroblastic stem line. Millard *et al* (1968) stated that in both sideroblastic anaemia and polycythaemia vera the increased erythroid cell turnover may be a favourable condition of stress for the appearance of an abnormality such as the F deletion.

The index case with his group-F autosome deletion is different from those reported with a similar chromosome defect. His mental and physical state is greatly altered but laboratory analyses did not reveal any haematological disturbance. Further, the F chromosome deletion was present in the totality of the cells analysed. The chromosome anomaly originated probably during gametogenesis. Although parents and sibs could not be examined because of remoteness, it is hypothesized that the patient's phenotypic alterations are related to his chromosome abnormality.

Summary

A deleted group-F chromosome was found in

leucocyte cultures from a 22-year-old malformed and mentally retarded male patient. Although previously reported F chromosome defects were observed in haematological disorders only, the patient's blood cells were normal. Measurements and autoradiographic study indicated the abnormal chromosome was a No. 19 with partial deletion of its short arm. Parents and sibs could not be examined.

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FIG. 3. Partial karyotypes of the F, G, and Y chromosomes from lymphocytes of the propositus. The abnormal group F autosome, which was paired with a 19, has a deletion that presumably affects its short arm.

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