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On a Case of Rare Chromosomal Aberration[1]

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Introduction

Translocations are chromosomal aberrations, consisting in the fusion of two chromosomes of the same group — or even of different ones — thus making the karyotype of the affected subject appear deficitary for a chromosome, while another anomalous chromosome is present, frequently showing different traits, as compared to those defining the various groups, according to the Denver classification.

The translocations more frequently described concern the groups of acrocentric chromosomes (D and G), and it is generally thought that the morphology of such chromosomes may make the phenomenon more easily take place.

More particularly, the translocation 21/21 consists in the centromeric fusion of the two little acrocentric chromosomes, resulting in one single chromosome — almost double in volume, and mesocentric in structure.

Among the first cases described in the literature (Turpin *et al.*, 1959; Polani *et al.*, 1960), particularly interesting was the case described by Polani, concerning a mongoloid subject with 46 chromosomes, due to the presence of a translocation 13/21.

The translocation 21/21 has been for the first time described by Fraccaro *et al.* (1960) in a mongoloid child with 46 chromosomes: one single chromosome 21 was present, as well as a little mesocentric one — similar to a 19-20 — which could be interpreted as the result of the fusion of two 21.

The same aberration has been subsequently described by other Authors (Penrose *et al.*, 1960; Hamerton *et al.*, 1961; Muckherjee *et al.*, 1962; Dallaire *et al.*, 1962; Shaw *et al.*, 1962; Zellweger *et al.*, 1962; Forssman and Lehman, 1962; Pfeiffer, 1963), who studied the karyotypes of the families of mongoloid children.

[1] Paper read at the VI International Congress of Pathology (Rome, October 3-8, 1966).

In the families studied by the above Authors, it was noted that the possible offspring of carriers of translocation 21/21 generally result in miscarriages or mongoloid children. The diagnosis of translocation 21/21 thus appears very important for eugenic purposes.

Particularly suggestive appears the case described by Forssmann & Lehman, concerning a carrier of the translocation married to a healthy woman, with no chromosomal abnormalities: of 8 pregnancies, 5 resulted in miscarriages and 3 in mongoloid children.

We have observed a case of translocation 21/21 in a woman who, after two miscarriages, gave birth to a mongoloid daughter. No alteration was found in the father's karyotype. The mother's karyotype — besides the fundamental aberration, shown by 100% of the examined plates — occasionally showed other alterations, which might be responsible of a number of light phenotypic alterations.

Personal observation

The patient — A.P., aged 39, married since 5 years with a man of 47, nonconsanguineous — applied to our Eugenic Counseling Service, because, after two miscarriages at the third month (the second one with vescicular mole), she had given birth to a mongoloid daughter. The latter, weighing 3030 gm at birth, died a few days later for cardio-circulatory insufficiency.

Direct examination of the child at birth indicated: poor general conditions, icterus of cutis and sclerae, cutis anelastica, limited subcutaneous tissue, hypotonic muscular masses; mesaticephalic skull, trident-shaped fingers, mongoloid palpebral fissures, flat nose, protrusive tongue, scarse and dry hair.

History and Direct Examination of the Patient

Common diseases of childhood. Completely recovered from post-partum thromboflebitis.

Negative general examination. Brachycephalia, mongoloid palpebral fissures, simian line in the right hand.

Negative skeleton's X-ray examinations and routine analyses. Blood groups: B MN Rh_1 Rh_1.

Family Examination

The patient's family tree shows two cases of sterility (a sister and a mother's brother). A sister, after a miscarriage at the fifth month, had no children. A paternal cousin is oligophrenic.

The husband does not show any noteworthy personal pathology, nor chromosomal alteration. Blood groups: B MN Rh_1 Rh_1. Among the five members of the sibship, two were still-born. Two sisters affected by congenital hip-joint malformation. A sterile maternal aunt (Fig. 1).

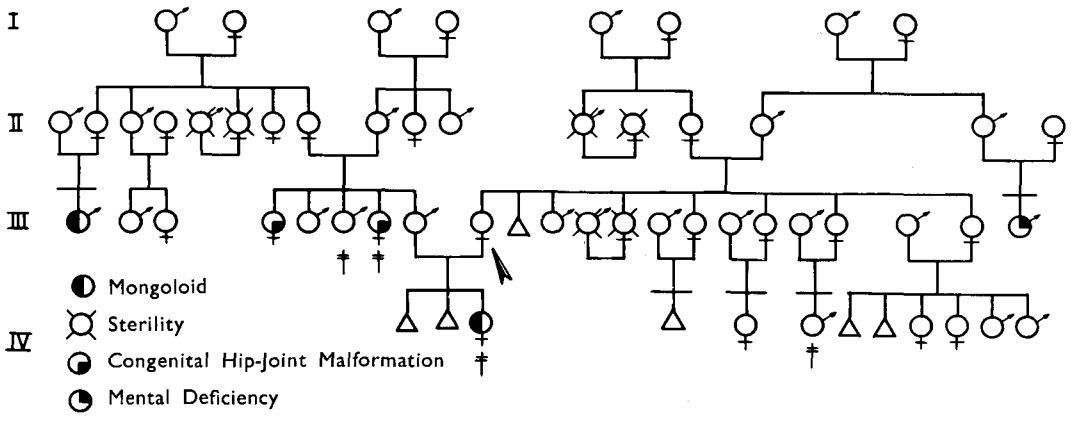

Fig. 1

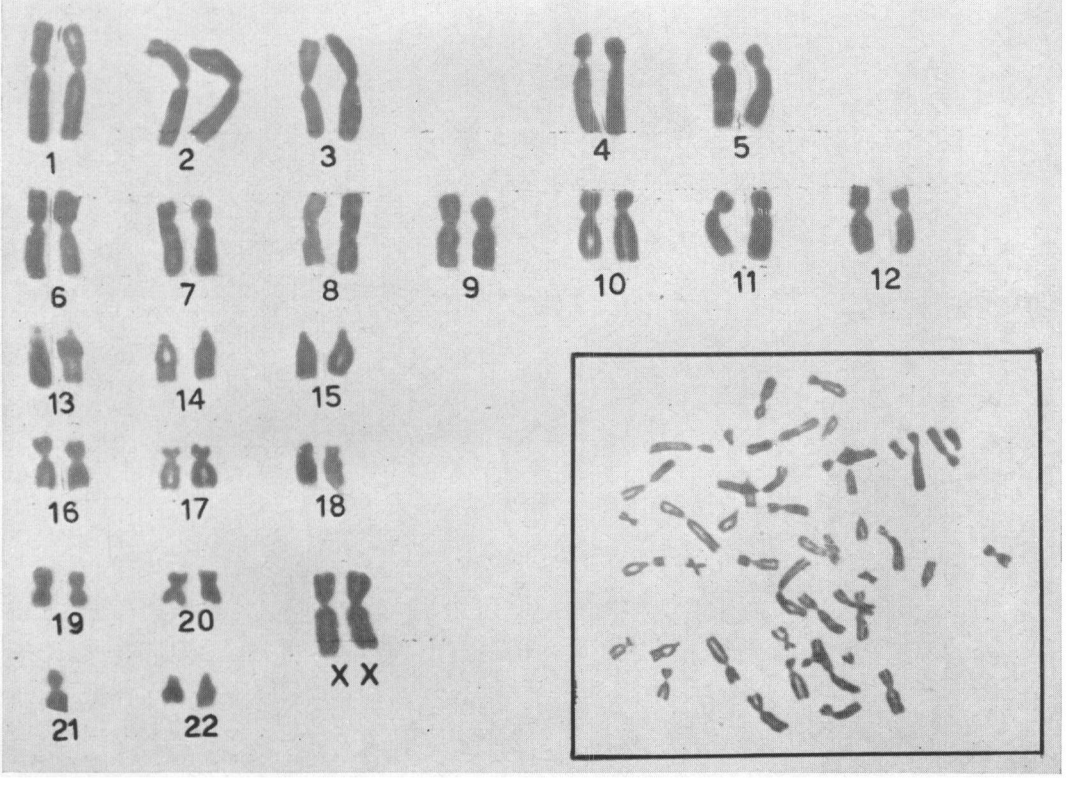

Fig. 2

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Chromosomes

The patient's chromosomes have been examined twice, in different times, on heparinized circulating blood. Both times, the results were concordant. The plates have been studied by means of direct examination and microphotography. The data reported in the following are those obtained on photographic magnifications.

54 plates have been examined. The modal distribution curve shows that 75% of them have 45 chromosomes. In all plates examined, the translocation 21/21 is present (Fig. 2). In a number of plates, aberrant chromatine fragments may be observed, and a long arm of a 6-12 chromosome appears shorter than the other. In five plates, an acrocentric chromosome in position 22 is absent and substituted by a small sub-mesocentric one (Fig. 3).

Another plate shows tetraploidy: 90 chromosomes are present with a double translocation 21/21 (Fig. 4).

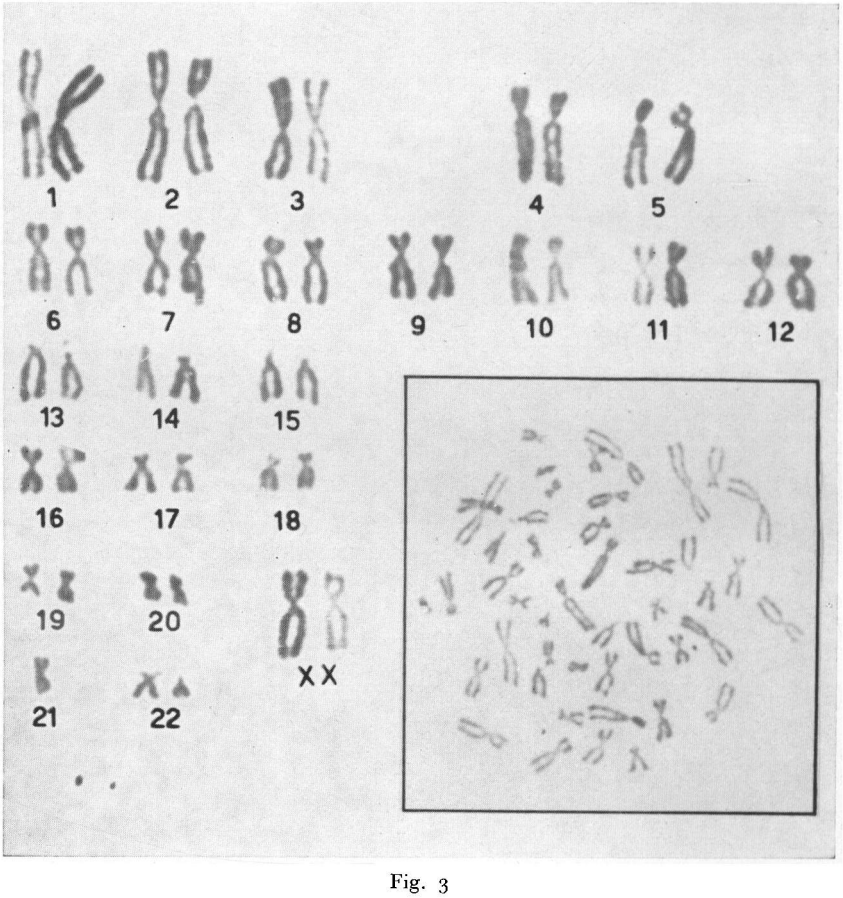

Fig. 3

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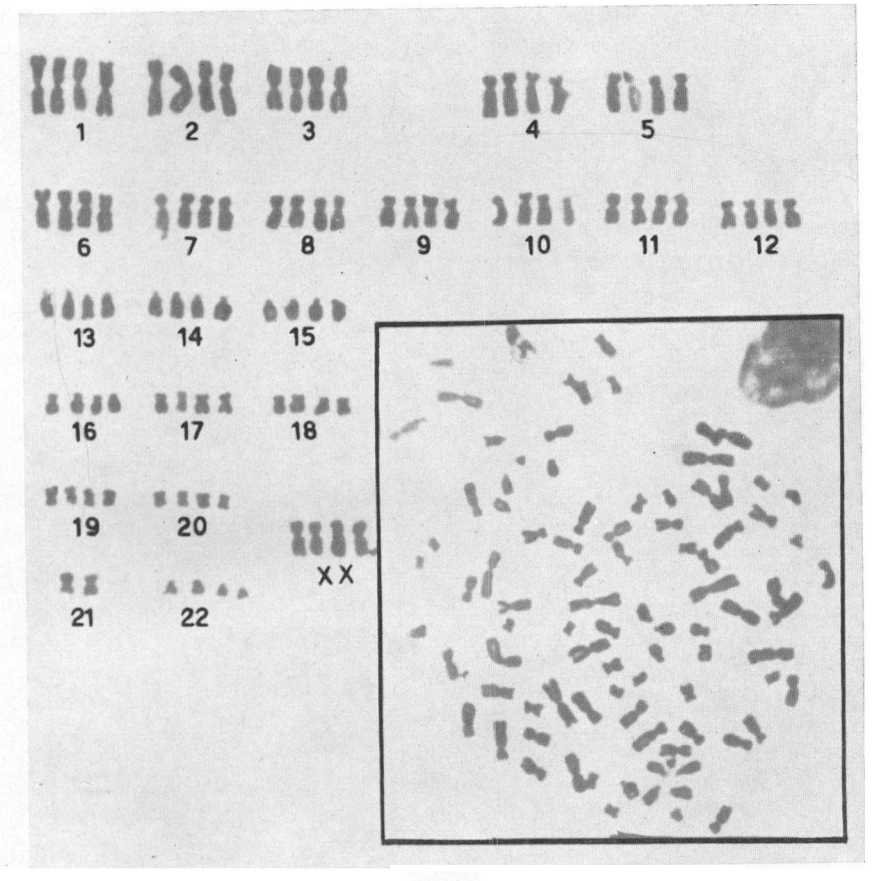

Fig. 4

Discussion

In our case, the diagnosis of translocation 21/21 was made both on account of morphology (in all plates, two small acrocentric chromosomes being lacking) and of the constant presence of a mesocentric chromosome, probably originated by fusion of the two lacking acrocentric ones.

The anamnestic finding concerning the patient's offspring — consisting of two miscarriages and a mongoloid child — is in favour of a translocation 21/21. In fact, the offspring of a carrier of translocation 21/21 and of a normal individual may only be mongoloid (trisomy 21) or nonvital (monosomy 21).

In the patient, on the other hand, a translocation 21/22 should be excluded. In this case, in fact, 50% of the offspring should be healthy. It could be inferred, however, that this 50% be not yet expressed in our case.

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A translocation 22/22 should, finally, be excluded. This situation, in fact, does generally not give rise to mongoloid children. These considerations are naturally based on the current assumption that Down syndrome be caused by trisomy 21, rather than by a G group aberration, as claimed by a few Authors.

It should also be noted that light phenotypic alterations are present in our patient (simian line, mongoloid palpebral fissure). Such alterations may not be related to the translocation 21/21, which — according to bibliographical data — should not produce phenotypic alterations in the carrier. They might, perhaps, be referred to the small chromosomal alterations present in only a number of plates, as reported in the patient's chromosome examination.

Summary

The Authors report a case of translocation 21/21 in a woman who, after two miscarriages, gave birth to a mongoloid daughter — dead a few days after birth. The chromosomal aberration was present in 100% of the plates examined.

Occasional chromosomal alterations, found in the patient's karyotype, might be held responsible of small phenotypic alterations. No alteration was found in the husband's karyotype.

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RIASSUNTO

Gli AA. descrivono il caso di una traslocazione 21/21 in una donna che ha avuto due aborti ed una bambina mongoloide venuta a morte dopo pochi giorni dalla nascita. L'aberrazione cromosomica è stata rilevata nel 100% delle piastre esaminate con lo studio cariologico sul sangue periferico. Sono state rilevate altre malformazioni cromosomiche meno costanti nel cariotipo della candidata che secondo gli AA. potrebbero spiegare alcune alterazioni rilevate nel fenotipo. Nessuna alterazione è stata rilevata nel cariotipo del marito.

RÉSUMÉ

Les Auteurs décrivent un cas de translocation 21/21 chez une femme qui, après deux avortements, accoucha une fille mongoloïde — qui mourut quelques jours après sa naissance. L'aberration chromosomique était présente en 100% des plaques examinées. D'autres altérations chromosomiques, occasionnellement trouvées dans le caryotype de la probande, pourraient être responsables de quelques légères altérations phénotypiques. Le caryotype du mari ne montre pas d'altérations.

ZUSAMMENFASSUNG

Verf. beschreiben den Fall einer Translokation 21/21 bei einer Frau, die bereits zwei Fehlgeburten sowie ein mongoloides Mädchen geboren hatte, das wenige Tage nach Geburt starb. Die Chromosomenaberration wurde bei 100% der bei karyologischer Untersuchung auf peripherem Blut kontrollierten Blutplättchen festgestellt. Es wurden noch andere weniger konstante Chromosomenmissbildungen im Karyotyp der Probandin beobachtet, welche den Verf. gemäss einige im Phänotyp bemerkten Alterationen erklären könnten.

Im Karyotyp des Ehemannes war keine Alteration festzustellen.

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