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A familial translocation 4/11 : t(4;11) (q22;q24) identified by means of G-bands

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SEZIONE III

(Botanica, zoologia, fisiologia e patologia)

Citogenetica. — *A familial translocation* 4/11 : *t* (4 ; 11) (*q*22 ; *q*24) *identified by means of* G–*bands*. Nota (*) di NICOLETTA ARCHIDIACONO, ADRIANA DE CAPOA, MARINA FERRARO, ANGELA ROCCHI e ANTONELLA SCAPELLATI, presentata dal Socio G. MONTALENTI.

RIASSUNTO. — Viene descritta una traslocazione familiare bilanciata $4q^-/11q^+$ identificata mediante G–bande, presente in due maschi di due generazioni. Uno dei portatori ha avuto un figlio con gravi malformazioni congenite, deceduto due giorni dopo la nascita, di cui non è stato possibile eseguire l'analisi del cariotipo.

INTRODUCTION

According to the latest data reported by Jacobs *et al.* [6], the incidence among the adult general population of balanced rearrangements involving the autosomes is 3.32 $^0/_{00}$. Among these the most common type is translocation. As for the rearrangements involving B group chromosomes, the cases reported in the literature are relatively few in number. In particular, with regard to the translocation in which chromosome no. 4 is involved, two cases of reciprocal translocation (4/5; and $4q^-/18q^+$) have been identified by Shaw [11] and by Surana and Conen [12] by means of autoradiography. De la Chapelle [1], Schrott [8], Francke [3], and Dutrillaux *et al.* [2] by using banding techniques, have given detailed descriptions of a case of partial monosomy and four cases of partial trisomy of the long arm of chromosome no. 4 in the offspring of carriers of balanced reciprocal translocation (4/21 ; $4q^-/13q^+$, $4q^-/20q^+$ and $4q^-/18q^+$, $4q^-/18q^+$, $4q^-/2q^+$). In addition, Ockey *et al.* [7] and Golbus *et al.* [4] have described two cases of deletion of the long arm of chromosome no. 4 and Dutrillaux *et al.* [2] a case of partial trisomy of the long arm of the same chromosome in children whose parents showed a normal karyotype. Two cases of presumably balanced translocation carriers ($4q^-/1q^+$, $1q^+/4q^-$) with abnormal phenotypes have been studied by means of R and Q–banding techniques by Skovby and Niebuhr [9].

The present work describes a case of a balanced translocation, involving the long arm of chromosome no. 4 and the long arm of chromosome no. 11, observed in the father and the grandfather of a child that died two days after birth.

FAMILY HISTORY

This family (fig. 1) was examined following the birth of a male child that died two days after birth, whose characteristics, taken from the medical card, were: congenital hydrocephalus (cranial circumference 40 cm) with dehiscent

(*) Pervenuta all'Accademia il 5 agosto 1975.

sutures and very thin bones of the theca, hexadactyly of the right hand, clinodactyly of the right thumb, subluxation of the distal phalanges of the fingers, rocker-bottom feet and muscular hypertonia. Death was caused by bilateral broncho-pneumonia, and the post mortem showed: renal hypoplasia, passive congestion of the liver and spleen, normal conformation of the heart. It was not possible to carry out a chromosome analysis, since the parents came to our observation after the child's death. The pregnancy, which ended with a full-term caesarean birth, had not followed a normal course: at the second month an internal abortion had been diagnosed and a curettage had been performed.

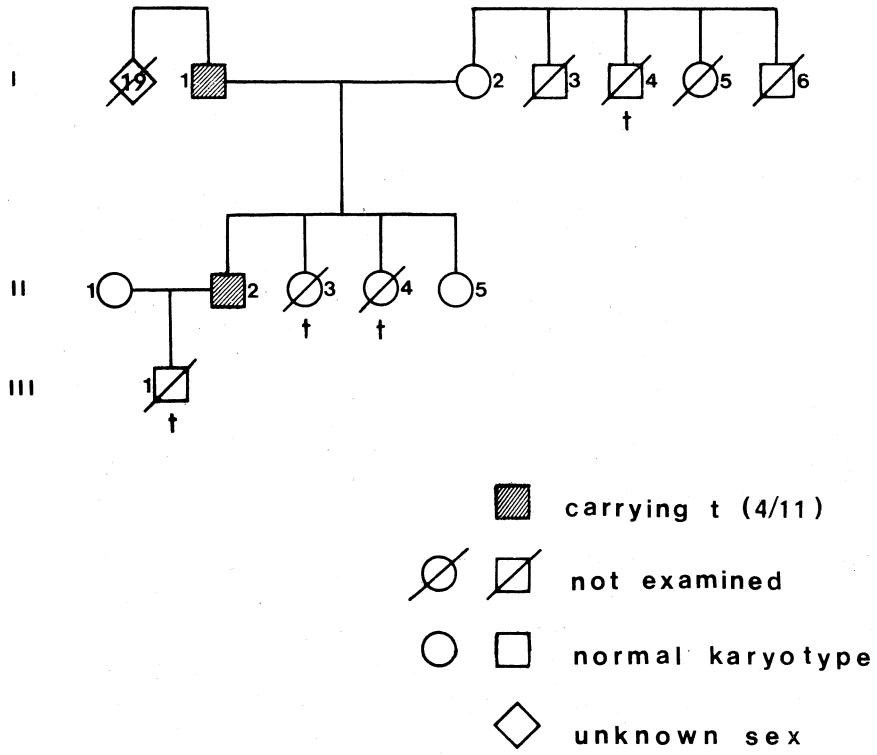

Fig. 1. – Pedigree of the family.

Two months later, on account of a suspected ovarian cyst, a laparatomy had been performed, which had revealed the presence of a uterus four months pregnant. Despite all this, the pregnancy had been brought to full term with the birth of the child described above. A karyotype analysis was carried out on the mother (II, 1) and on the father (II, 2), who were 25 and 29 years of age respectively at the birth of the child. Analysis of the pedigree on the father's side showed that the grandmother of the child had had—in addition to the father of the child and another living daughter (II, 5)—two other pregnancies, which terminated with the birth of: a female child born at the eighth month of pregnancy, which died after 40 days due to causes not stated, but

not from an infectious disease (II, 3) and a foetus, macerated and still-born at the seventh month of amenorrhoea (II, 4). On the other hand, the family history was found to be negative as regards the first generation.

MATERIALS AND METHODS

Cultures of peripheral blood were set up according to the standard method. Some of the preparations were subjected to the action of trypsin [10] in order to obtain banding of the chromosomes and hence a precise identification of all the pairs of homologous chromosomes.

RESULTS AND DISCUSSION

Using standard Giemsa staining, 25 cells of the mother of the child (II, 1) and 28 cells of the father (II, 2) were examined. Whereas all the cells of II, 1 showed a normal 46 XX karyotype those of II, 2 showed an abnormal

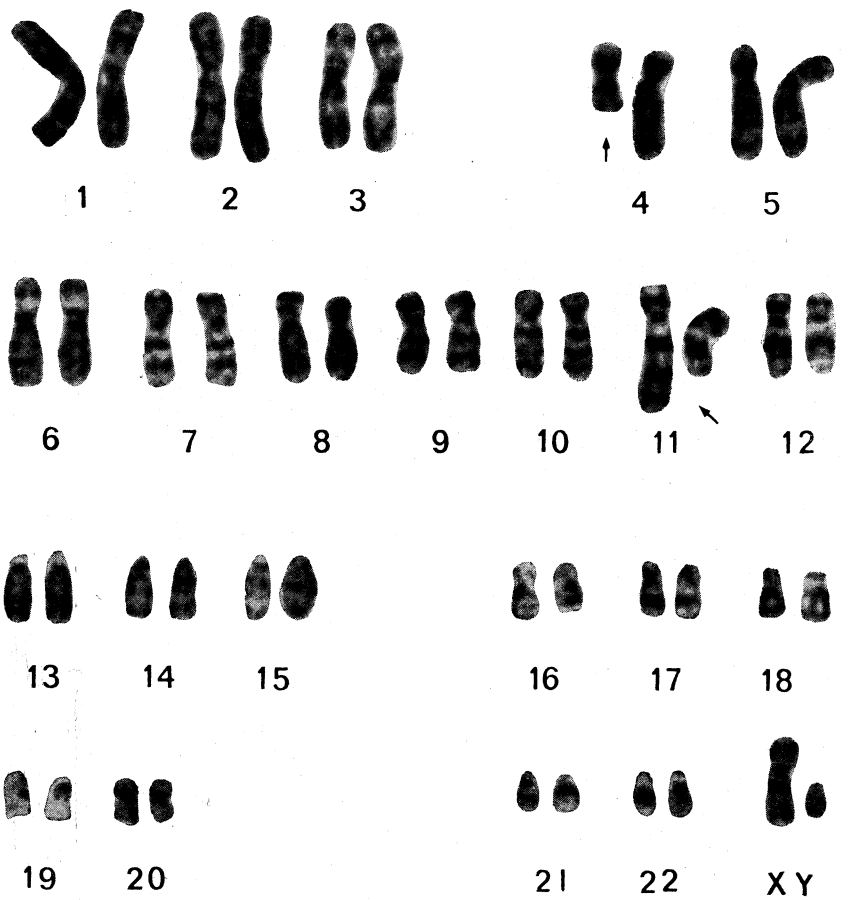

Fig. 2. – Karyotype of II, 2 obtained from metaphase treated with trypsin, showing the translocation $4q^{-}/11q^{+}$.

karyotype. In fact, a detailed analysis revealed the presence of a metacentric chromosome slightly smaller than a no. 16 and of a chromosome of group B having the long arm of greater length than that of a normal group B chromosome; in addition, there was one C-group chromosome missing. In order to identify the chromosomes involved in this structural rearrangement, some preparations were subjected to treatment with trypsin in order to obtain G-bands. Examination of the karyograms obtained in this way showed that there was a balanced translocation between sections of the long arms of chromosome no. 4 and of chromosome no. 11. About 2/3 of the long arm of chromosome no. 4 were translocated on the long arm of chromosome no 11, which consequently came to assume the morphology of a B group chromosome, while the deleted chromosome came to have the size of a small metacentric chromosome carrying at the distal end of its long arm a very short section of the long arm of chromosome no. 11 (fig. 2). According to the trypsin band and interband numbering laid down at the 1971 Paris conference, the karyotype of II, 2 therefore was: 46 XY, *t* (4; 11) (*q* 22; *q* 24) (fig. 3). The

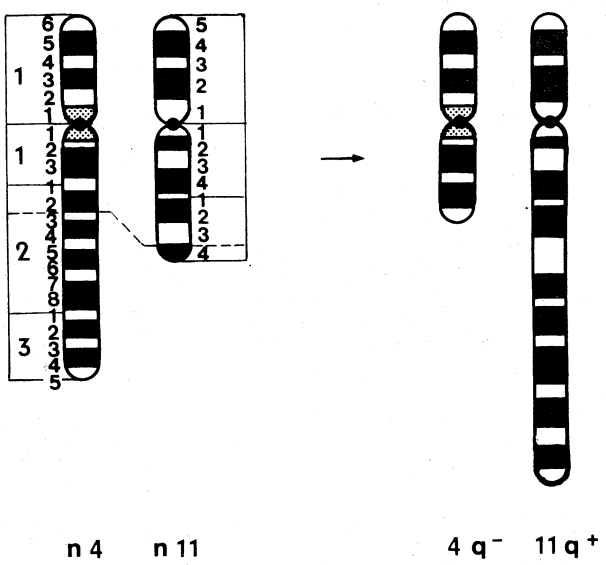

Fig. 3. – Mechanism of formation of the translocation.

chromosome analysis of the relatives of II, 2 was then carried out in order to ascertain the possibile presence of other carriers. From the analysis of 31 cells of the sister (II, 5) and 50 cells of the mother (I, 2) a normal 46 XX karyotype was found in both, whereas the study of 26 cells of the father (I, 1) showed the presence of the same abnormal chromosomes observed in II, 2. A study of the trypsin banding pattern confirmed that I, 1 was a carrier of the same balanced translocation that had been found in his son (fig. 4).

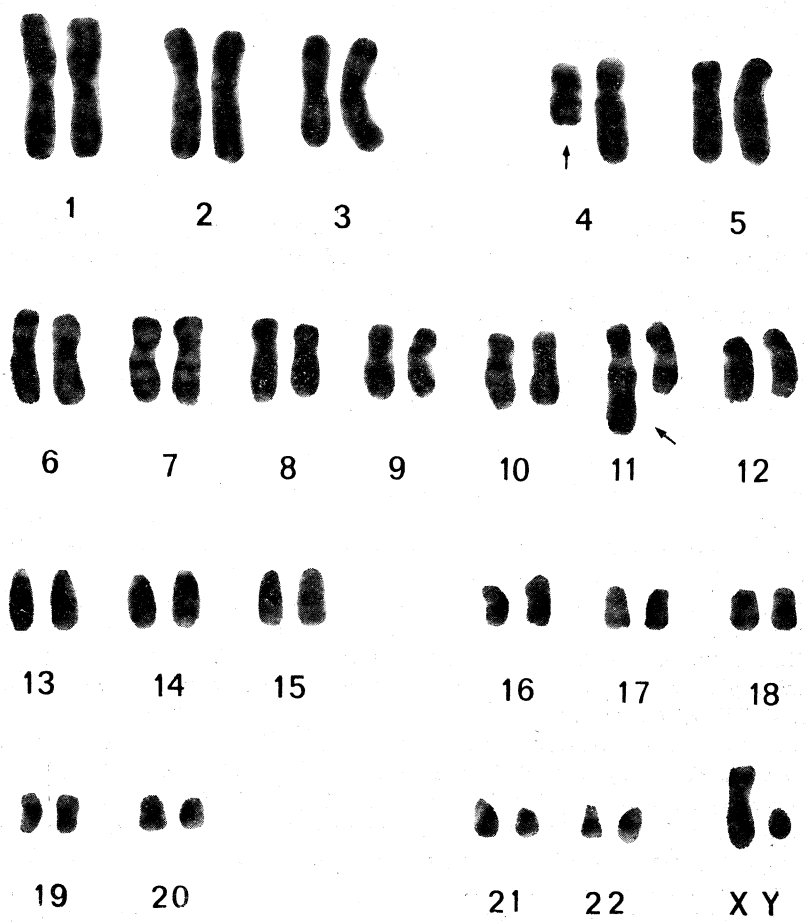

Fig. 4. – Karyotype of I, 1 obtained from a metaphase treated with trypsin, showing the same translocation as that found in II, 2.

Examination of the pedigree revealed that two individuals belonging to the second generation (II, 3 and II, 4) had died in the perinatal period owing to unstated causes. Since they were both children of a carrier (I, 1) it is reasonable, even in the absence of clinical and cytogenetic data, to think that one or both of them might have been carriers of an unbalanced chromosome set.

As regards the child (III, 1), the clinical picture, as revealed by the medical card, does not resemble the symptomatology described by other authors [1, 2, 4, 3, 7, 11, 12, 8], in cases of partial trisomy or monosomy of the long arm of chromosome n. 4. We are therefore unable to put forward any hypothesis about the possibility that he might have been the carrier of monosomy or trisomy of the long arm of this chromosome. Moreover, it is necessary to mention that in our case the section of chromosome n. 4 translocated is larger than in some of the above mentioned cases and that, unlike all these, a chromosome of pair n. 11 is involved. To all this it must be added that the

extremely abnormal course of the mother's pregnancy may have somehow affected the development of the embryo and have complicated the clinical picture, which might therefore be only partly due to chromosomal alteration.

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