A Mentally Retarded Child with Convulsions, Agenesis of the Corpus Callosum, and a Translocation Involving Chromosomes 2 and the B Group

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Many instances of autosomal translocations in man have now been recorded. This report concerns a male infant with mental retardation, fits, and agenesis of the corpus callosum, and who, on cytogenetic study, appeared to have a translocation between part of the long arm of a No. 2 chromosome on to the long arm of a B group chromosome 46,XY,t(2q-;Bq+).

Case Report

The second child of parents aged 30 years, who are not consanguineous, was born in 1966. There was no relevant family history, and gestation was normal. At birth the baby's condition was said to be good despite foetal bradycardia lasting 1½ hours during the second stage of labour.

He was first seen at St. Bartholomew's Hospital, Rochester, at 11 weeks, with a four-week history of fits. The seizures appeared to be mostly typical clasp-knife spasms, but some focal seizures with twitching of the right arm and face were noted.

On admission to The Hospital for Sick Children, Great Ormond Street, at 19 weeks of age, the appearance of the child was not thought to be abnormal. The head circumference was 41 cm., with flattening of the occiput. The bridge of the nose was slightly broad and flattened, with almond-shaped eyes and well-developed epicanthic folds. The palate was broad and shallow; ears and hair-line were normal (see Fig. 1 and 2). The hands appeared normal and there were no dermatoglyphic abnormalities.

The eyes were persistently turned to the right, and

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there were also superimposed coarse nystagmoid jerks to the right. It was thought that he was blind, but well-defined optic atrophy was not distinct until several months later.

He responded to loud noises by blinking. A Moro response was not obtained. Tendon jerks were, and still remain, symmetrically elicitable. Feeding from the bottle and spoon was satisfactory.

Electroencephalograms at 11 and 19 weeks of age were similar and showed severe generalized abnormalities, with frequent multifocal discharges and a patchy asymmetry between the activities of the two hemispheres. Several prolonged seizures, including brief massive spasms occurred during the recordings, with corresponding EEG changes.

Radiology. The skull was small and brachycephalic. A lumbar air encephalogram at 19 weeks showed that the cisterna magna was large, but the fourth ventricle and aqueduct appeared normal. The third ventricle was dilated and projected upwards, separating the bodies of the lateral ventricles and also their anterior horns, the appearances of agenesis of the corpus callosum. The occipital horns of the lateral ventricles were large, the left being larger than the right, and there were some wide sulci over the right hemisphere.

Routine haematological investigations were normal; plasma sodium, potassium, chloride and TCO₂, blood urea, plasma calcium, phosphate, and alkaline phosphatase levels were also normal. The spinal fluid was unremarkable. Urinary chromatography disclosed a normal amino acid pattern; a slight rise in urinary lactose and sucrose excretion was thought to be consistent with recent ACTH treatment.

Treatment and Progress. Treatment with ACTH (10 units daily for 2 weeks) at 12 weeks of age was not accompanied by any significant improvement in fit control but conventional anticonvulsants (phenytoin 60 mg., phenobarbitone 30 mg. daily) seemed to confer some benefit.

At 15 months, according to his mother, he was 'not doing anything' beyond smiling at his mother and sister. His head circumference was 44.5 cm. and no new neuro-

FIG. 3. Results of cytogenetic studies.
logical features had emerged, but he had had numerous attacks of bronchitis, presumably due to inhalation of food and secretions.

Cytogenetic Studies

A buccal smear from the propositus showed no sex chromatin in 200 suitable nuclei.

Chromosome studies were carried out on the propositus and both parents, using lymphocyte culture from peripheral blood (Moorhead et al., 1960). The chromosome complements of 30 cells of the propositus were 46,XY,t(2q-;Bq+) (see Fig. 3). Each cell analysed showed only one chromosome No. 2 and three chromosomes in the B Group. An additional chromosome resembling No. 3 and an additional long submetacentric chromosome were also present. These are interpreted as resulting from a reciprocal translocation between the long arm of No. 2 and the long arm of a B chromosome. Though accurate measurements were not made, this additional material appeared to correspond in length to the deleted section of the abnormal chromosome of the pair No. 2.

The chromosome complements of 20 cells from each parent were normal: mother 46,XX; father 46,XY, and no non-modal cells were observed.

Discussion

The most probable explanation of the cytogenetic findings in the propositus is that he has a reciprocal translocation between part of the long arm of one chromosome No. 2 and the long arm of a member of the group 4-5. In the absence of any evidence of mosaicism in the propositus, or either parent, and assuming natural paternity, it is most likely that the translocation arose in gametogenesis. It is not possible to say if the phenotypic abnormalities observed in the propositus are due to the chromosome abnormality or to genetically determined or congenital factors. The translocation appears to be balanced and, if this is the case, then apart from the possibility of a gene position effect, it is unlikely that the phenotypic and chromosomal abnormalities are related.

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REFERENCE