A case of de novo, double, balanced translocations (distal 9p to 3p, distal 18q to 3q)

The patient, born in 1973 to a 24 year old G2, P1, A0 black woman, was the 2820 g product of an uncomplicated pregnancy and delivery. At the age of 10 weeks, the infant was started on phenobarbital for seizure activity and remained on anticonvulsants for the next four years. Development has been characterised by psychomotor delay with growth parameters falling below the 3rd centile. At the age of 3 years she had an IQ of less than 30 on the Cattell Infant Intelligence Scale.

On physical examination this child had a variable right esotropia, simian creases on both palms, a high arched palate, and bilateral hallux valgus and plantar valgus deformities. In the past, she has been variously described as both hypo- and hypertonic, having an abnormally shaped head, hyperreflexia in the lower extremities, and athetoid movements in all extremities.

The patient's family consists of the parents and a 15 year old sister, all of whom are physically normal and of normal intelligence.

Cytogenetic study of this patient's peripheral blood showed 44 autosomes and two X chromosomes. G banding revealed partial loss of the short arm of chromosome 9, partial loss of the long arm of chromosome 18, and extra material on both arms of chromosome 3. The distal short arm of chromosome 9 appeared to be translocated onto the short arm of chromosome 3, while the distal long arm fragment of 18 was attached to the long arm of chromosome 3 (figure). The breakages in the chromosome arms were at 9p22 and 18q21. It was assumed that the breakage points in chromosome 3 were p27 and q29. Assuming de novo, balanced, reciprocal translocations, the karyotype is thus: 46,XX,t(3;9)(3;18)(p27;q29;p22;q21). The karyotypes of both parents are normal.

Despite the apparent preservation of the entire complement of both chromosomes 9 and 18 through translocation, this patient had definite phenotypic abnormalities. In fact, it may be more than just coincidence that her defects are reminiscent of some of those found in the 9p- syndrome (retardation, delayed speech, abnormal skull, hypotonia),¹ as well as the 18q- syndrome (retardation, short stature, deformities of the extremities).² Unfortunately, the phenotypic anomalies are non-specific and appear as part of many other chromosomal disorders. Although small deletions could have been generated by loss of parts of the translocated segments of 9 and 18, of greater theoretical interest is the possibility that no genes have been lost in this complex rearrangement. The physical abnormalities and retardation could be the result of position effects after

FIGURE Partial karyotype, with arrows showing how the distal 9p and 18q are translocated to 3p and 3q, respectively.

removal of genes from their usual chromosomal environment. A precedent for this idea is found in the six cases of balanced, non-Robertsonian translocations reported among a group of 455 mentally retarded children,³ an incidence of translocation much higher than among a group of 1679 non-retarded children. None of these cases, however, involved more than two chromosomes.

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