PIEBALD TRAIT IN A RETARDED CHILD WITH INTERSTITIAL DELETION OF CHROMOSOME 4

To the Editor: In 1974, Funderburk and Crandall [1] reported a 3-year-old boy with moderate mental retardation, short stature, and integumentary pigment changes typical of the autosomal dominant piebald syndrome. The patient's chromosomes showed a reciprocal translocation and an intercalary band deletion of one of the no. 4 chromosomes. We have encountered a similar case that supports the association of the piebald trait with an interstitial deletion of the long arm of chromosome no. 4.

The patient, T.B., was a 13-month-old black girl born to a healthy 17-year-old primapara after a 36 week normal pregnancy. Birth weight was 1.9 kg. A small white forelock, areas of hypopigmentation on the legs, and other minor anomalies were noted at birth. Shortly after birth a chromosome analysis was performed using peripheral blood lymphocytes. Giemsa-trypsin bands were obtained using Seabright's improved method [2]. Thirty cells were examined, and a 46,XX,del(4)(q11q21) karyotype [3] was established. This diagnosis was confirmed by a second chromosome analysis 1 year later.

At 13 months, psychomotor development was noticeably delayed; the patient sat alone at 10 months but was still unable to stand unaided. Her height was 72 cm; weight, 9.0 kg; and head circumference, 45.3 cm. Unusual facial features included a broad, flat nasal bridge with epicanthus and pseudohypertelorism (interpupillary distance was 43 mm, within normal limits). Ears were low set. The patient's hands showed short, incurved fifth fingers, a simian crease on the left hand, transversal main lines with zygodactyly triradius (bc) on the left hand, and a tiny vestigial pattern in the third interdigital area on the right hand. Both axial triradii were in intermediate position. Hand X-rays confirmed bone age at a low-normal limit and clinodactyly of both fifth fingers. The patient had inspiratory stridor while sleeping, but both lungs were clear. Examination of the parents revealed no physical dermatoglyphic or chromosomal abnormalities.

The clinical and chromosomal findings in our patient were similar to those of Funderburk and Crandall [1] who reported a translocation and a deletion. Our case, however, revealed only a deletion. Any further rearrangement of the middle of the abnormal chromosome was not detected. We therefore assume that the interstitial deletion of band q13 of chromosome no. 4 is the cause of this syndrome. Although we cannot rule out a very small translocation in our case, the abnormalities described are satisfactorily explained by the deletion. Normal chromosome complements found in both parents suggest that the chromosomal aberration in their daughter probably originated in a parental gamete.

It is of interest that the deleted segment in this case was adjacent to centromeric heterochromatin, making position effect a possible mechanism of pathogenesis [4]. Recent observations in plants and *Drosophila* suggest that the change in gene action could be due to repositioning of genetic material [5]. Excesses of apparently balanced

rearrangements in retarded children may indicate the presence of a similar effect in humans [6].

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ADENOSINE DEAMINASE DEFICIENCY: ANOTHER FAMILY WITH A "SILENT" ADA ALLELE AND NORMAL ADA ACTIVITY IN TWO HETEROZYGOTES

To the Editor: In a previous paper [1], we reported the existence of an adenosine deaminase "silent" allele (designated as ADA^0) in a family with a child who died of severe immunodeficiency disease (SCID). The assignment of the ADA^0 allele was determined by the unusual transmission of the ADA phenotypes and quantitative assays of the enzyme in family members. Since then, a total of four families with a similar transmission of ADA phenotypes have been found [2, 3]; one was found in a normal family and the other in families with SCID. We would like to document another SCID family in which the silent allele could be traced through 3 generations and to reemphasize that heterozygotes for the silent allele may, on occasion, have normal ADA activity in their red cells.

In accordance with the previous report [1], the pedigree (fig. 1) shows the ADA phenotype, the presumed genotype, and ADA activity in each of the family members. The ADA phenotypes of the parents of the proband (II-1 and II-2) were ADA 1 and ADA 2; however, their children had four different phenotypes—ADA 2 (III-1), ADA 2-1 (III-2), ADA 1 (III-3), and no detectable ADA (III-4). It seems apparent that each parent carries a "silent" gene which was transmitted as allelic to the normal ADA^1 or ADA^2 in the family. Therefore, the genotypes of their children should be ADA^2/ADA^0, ADA^2/ADA^1, ADA^1/ADA^0 and ADA^0/ADA^0, respectively.

An important observation from this pedigree is that two of six heterozygotes