Consanguinity in a Turkish Family with Thrombocytopenia with Absent Radii (TAR) Syndrome

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Summary. Two sibs with TAR syndrome and whose parents are blood relatives are described. To our knowledge this is the first report of consanguinity in TAR syndrome.

Introduction

The association of thrombocytopenia and aplasia of the radii as a syndrome has been well documented by Gross et al. (1956), Shaw and Oliver (1959), Nilson and Lundholm (1960), Hall et al. (1961), Dignan et al. (1967), Haarmann et al. (1975), McKusick (1978; McK 27400), and others. The TAR syndrome consists of hypomegakaryocytic thrombocytopenia and bilateral aplasia of the radii in 100% of cases. Frequently other anomalies are associated. The hands are probably abnormal in all patients and show limited extension, radial deviation, and hypoplastic carpals and phalanges, but thumbs are always present. The ulnae, usually somewhat shorter and malformed, are bilaterally absent in 20% and unilaterally absent in 8% (Hall 1979). Humeri are abnormal in at least half the cases and absent in 5%, resulting in phocomelia. Skeletal malformations of the lower limbs include dislocated hips, tibial torsion, ankylosis of the knees, patellar dislocation, valgus and varus foot deformities, and abnormal toe placement. Hypoplasia or aplasia of the lower limbs has been demonstrated by Pfeiffer and Maintz (1973), Temtamy and McKusick (1978), and Ray et al. (1980). The typical facial appearance was pointed out by Hays et al. (1982).

Leukemoid blood pictures in newborns with TAR syndrome were described by Emery et al. in 1957. The frequency of cardiac defects is increased, but not that of renal malformations. TAR syndrome shows the pattern of autosomal recessive inheritance. Surprisingly, consanguinity has not been reported. In this paper TAR syndrome associated with blood relationship of the parents is described.

Case Report

The parents, a 43-year-old Turkish man and a 35-year-old Turkish woman, are first cousins once removed. The family pedigree is shown in Fig. 1. The first child (V,1) of this family was born in 1968 with bilateral aplasia of the forearms. Her hands had five fingers but originated directly from shortened humeri. Easy bruisibility was reported. The girl died in Turkey at the age of 6 months; the cause of death is unknown. Thereafter one girl and three boys (V,2–V,5) were born without any malformations. The sixth child (V,6) was a premature male baby who died within 1 h of birth because of immaturity. His birth weight was 900 g; deformities were not observed.

The child who was presented to our hospital was an 18-month-old boy (V,7; Fig. 2). Pregnancy was normal until 38 weeks, when hydramnios and placental insufficiency developed. At birth in the 41st week, the child was slightly asphyxiated. Birth weight was 3500 g, length 50 cm, and head circumference 35.5 cm. The baby had deformities of both arms with almost no forearms and radially deviated hands with five fingers. X-rays revealed bilateral absence of the radii, hypoplasia of the ulnae distally, and marked brachymesophalangia V (Figs. 3 and 4). Further malformations were not observed. A chromosomal abnormality or metabolic disturbance could be excluded. Genitals were without pathological findings.

The blood picture on the first day of life showed a leukocytosis of 81,200/mm³ and thrombocytopenia of 70,000/mm³. There were no signs of neonatal infection. In the first weeks of life, leukocytosis ranged from 25,000 to 50,000/mm³ and thrombocytes from 15,000 to 50,000/mm³. Bone marrow puncture revealed only few and small megakaryocytes. Major bleeding has not occurred, but petechiae and easy bruisingility have often been noticed. Now and then an eczema has been present on the cheeks. During the first year of life, clinical treatment was required because of a bacterial pneumonia and two subcutaneous abscesses.

At the age of 18 months he was presented to our hospital for treatment of genu varum to be due to rickets. However, radio-

Fig. 1. Family pedigree
graphy revealed this anomaly as part of the syndrome (Fig. 5). His prominent forehead and small jaw (Fig. 1) gave him the typical facial appearance.

Discussion

This boy (V,7) showed the typical features of the TAR syndrome: bilateral aplasia of the radii, radially deviated hands with five fingers, hypomegakaryocytic thrombocytopenia, and leukemoid blood picture in the first days of life. As far as we can judge, the first girl of this family (V,1) also suffered from TAR syndrome. This malformation can be delimited from other syndromes with aplasia of the radii such as Fanconi’s pancytopenia syndrome, Holt-Oram syndrome, fetal thalidomide syndrome, trisomy 18 syndrome, Robert’s syndrome, Aase syndrome, and SC-phocomelia.

The genetics of TAR syndrome is not quite clear. The incidence of the condition for autosomal recessive inheritance in sibs of probands agrees fairly well with the expected. However consanguinity or specific ethnic group involvement has not been noted so far, which one would expect more often in such a rare hereditary disease. Possibly the true occurrence is much higher, but underestimated due to the early demise of some probands or to incomplete diagnosis.

Other ways of hereditary transmission are discussed in the literature. Lenz (1973) presented a concept for a possible genetic relation between TAR syndrome and Fanconi’s pancytopenia syndrome. This idea was later used by Herrmann and Opitz (1977) to elucidate a relationship of Robert’s syndrome and SC-phocomelia. Based on these reports, Aldenhoff and Waldenmaier (1979) considered a common genetic cause of Robert’s syndrome, SC-phocomelia, and TAR syndrome by the following formal interpretation: There are two alleles, $a_1$ and $a_2$, of a normal allele $a_0$. Homozygotes for $a_1$ would have Robert’s syndrome, and homozygotes for $a_2$ would show SC-phocomelia. Heterozygote conditions would be responsible for TAR syn-