Two brothers with Martsolf's syndrome

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SUMMARY Two brothers affected by a syndrome consisting of short stature, hypogonadism, and severe mental retardation are reported. The syndrome shares the features of that described by Martsolf et al1 in two brothers born to a consanguineous Polish Jewish couple. Although our patients' parents are Sephardic Jews, they deny consanguinity. These observations and personal knowledge of another affected Jewish boy raise the question of whether Martsolf's syndrome is a new entity that should be included in the group of those that affect mainly Jewish people, and whether its pattern of inheritance is X linked recessive or autosomal recessive limited to males.

In 1978, Martsolf et al1 described two brothers born to consanguineous Polish Jewish parents. The boys were affected by a syndrome that had never been reported before. It consisted of severe mental retardation, cataracts, short stature, and primary hypogonadism. To our knowledge no further cases have been reported since. We describe here a family with two affected sons, in order to (a) clarify the clinical delineation of this syndrome; (b) list the symptoms according to their frequency; and (c) help determine its mode of inheritance, which is still controversial.

Case reports

CASE 1 (III.5, FIG 1)
The patient, a male, the second child of a Sephardic Jewish mother and father, aged 24 and 28 respectively, was born in December 1974. Although the couple denied being consanguineous, some of their ancestors were from the same village in Syria and therefore a certain degree of kinship might exist between them. The product of the first pregnancy was a girl (III.4) with congenital dislocation of the left hip, but who was otherwise normal. A son (III.8) of one of the mother's sisters had hypoplasia and one of the father's sisters had a daughter (III.1) with bilateral dislocation of the hips, and another had a son (III.2) with no physical anomalies but with psychomotor delay. The pedigree is illustrated in fig 1. The proband was the product of a normal pregnancy and delivery. Birth weight was 2980 g. At 45 days total bilateral cataracts were diagnosed. At 2 months of age he was referred for genetic evaluation. Physical examination showed: weight 4600 g (50th centile), height 54 cm (50th centile), and head circumference 35 cm (5th centile). He had a high forehead, flat superciliary ridges, epicantus, bilateral cataracts, micrognathia, very high palate, low set and posteriorly rotated ears with a small lobe on the right, and prominent antihelices. The fingers were tapered. In the feet metatarsus varus and proximally inserted second to fifth toes were noted. He also had bilateral cryptorchidism and a small phallus. Dermatoglyphs showed whorls on all the fingers. By that time several studies such as x-ray, cardiovascular and urinary examinations, G banded karyotype,2 and TORCH and metabolic screenings had already been performed with normal results. At 3 months of age a neurological evaluation revealed psychomotor delay. At 3½ he was operated on for cataracts, but two months later a second operation was necessary to correct

Received for publication 17 September 1984.
Accepted for publication 26 September 1984.
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bilateral secondary glaucoma. When he was 6 months an electroretinogram showed that in the right eye there was a subnormal a wave, a scotopic b wave, and absence of oscillatory potentials. In the left eye there were normal a and b waves and subnormal oscillatory potentials. Four months later a new neurological evaluation revealed psychomotor development corresponding to the age of 6 months. A pneumoencephalogram showed microencephaly with cortical and central atrophy (mainly on the left side), and slightly dilated but not displaced lateral ventricles. At 10 months of age there were frank extrapyramidal signs. At 17 months a biopsy of the brain showed a normal cerebral structure. At that time his head circumference was 43 cm (<5th centile) and his height was 74 cm (25th centile). Chromosomal defect, antenatal viral infections, and inborn errors of metabolism were also excluded. However, a specific diagnosis could not be made, and therefore no risk of recurrence was given.

In November 1976, the boy was re-examined by us after his mother had asked for genetic counselling because she was pregnant. He showed marked psychomotor delay and spasticity which affected mainly the legs, but also the arms. He had brachyplagiocephaly (probably positional), low set and posteriorly rotated ears, very high palate, complete dentition with malaligned inferior incisors, prognathism, thoracic scoliosis, left cryptorchidism, hypoplasia of the nails on hands and feet, and sparse hair. His weight was 8200 g, height 79 cm, and head circumference 44 cm; these values are all below the 5th centile. Once more it was impossible to give the risk of recurrence. Six months later, his mother had a normal female baby. Eventually, the proband acquired some speech, was able to hold his head up due to psychomotor stimulus, and became more responsive to his environment.

CASE 2 (III. 7)

In July 1983, the mother had another son after a normal pregnancy and delivery. Birth weight was 3380 g. During the neonatal period he presented with icterus due to ABO incompatibility. He was given two O type blood transfusions. On the third day of life an ophthalmological examination showed punctiform pupils due to iridocrystalline adherencies and bilateral cataracts. The cornea and iris were normal. One week later an electroretinogram revealed absence of waves. The patient had microcephaly (head circumference 33 cm), low set and posteriorly rotated ears, high palate, microretrognathia, unilateral cryptorchidism, small phallus, thumbs adducted in the palms, and pes talus with abnormal implantation of the toes. The boy died suddenly at 15 days of age. Necropsy was not performed.

Our first patient was re-examined for the last time when he was 9 years old (fig 2). At that age his weight was 11.3 kg, height (in supine position) 110 cm, and head circumference 46 cm (below the 5th centile). He also showed brachycephaly, a low posterior hairline, simplified, protruding, low set ears, high palate, big central upper incisors, flat maxilla, prognathism, long neck, flat chest, wide depressed sternum, bilateral cryptorchidism, and slender, relatively long limbs. The hands showed short palms with long fingers. Small scapulae and thoracic scoliosis were observed. The feet were cavus.

Discussion

Despite some differences, it is evident that our patients are affected by the syndrome described by Martsolf et al 1 (table). In our patients, both of prepubertal age, hypogonadism was expressed by cryptorchidism and a very small phallus, and cataracts were diagnosed before 3 months of age. Martsolf's patients had normal phallus, but small soft testes,
and cataracts were diagnosed when the boys were 10 years old. At the last examination our case 1 could not stand by himself. Although the parents said that when he was 3 he had had very severe pneumonia which might have contributed to his psychomotor retardation, we think he was more severely affected than Martsolf’s patients even before that. The dermatoglyphic patterns in patient BS of Martsolf et al and our case 1 were similar: the former had whorls on eight fingers and the latter on all of them. The parents of Martsolf’s patients were Polish Jews and our patients were Sephardic Jews. It is possible that some of our patients’ ancestors had migrated to Syria from Europe (their father is blonde). No other affected cases were recorded in either of the two families. Dr María del Valle Torrado (personal communication, 1984) had the opportunity of seeing another male patient at the Jewish Hospital in Buenos Aires who also presented with this syndrome and it is possible that this syndrome affects only males of Jewish descent born to unaffected parents. Only in one case were the parents consanguineous. This suggests two possible patterns of inheritance: (1) X linked recessive inheritance, and (2) autosomal recessive inheritance (with expression limited to males?).

The fact that all the reported patients were males supports the first hypothesis. Several factors support the second hypothesis.

(a) The parents of Martsolf’s patients were consanguineous and, although it has not been proved, it is possible that our patients are consanguineous because some of their ancestors came from the same village in Syria.

(b) If it is proved that this syndrome affects predominantly or only Jewish people, it is well known that their genetic diseases are almost without exception of autosomal recessive inheritance.

(c) There were no other affected persons in the parents’ sibships nor in previous generations.

(d) The fact that only males were affected could be explained by accepting that the expression of the syndrome is limited by sex, although the mechanism by which this happens is unknown. The fact that only males seem to be affected might be a coincidence, since very few cases have been reported. Another possibility is that as in infancy hypogonadism is more obvious in males than in females, isolated cases of affected females could have gone unnoticed. However, this problem, so important for genetic counselling, will not be solved until new families have been reported. The different level of severity with which the syndrome expressed itself in the two families favours variable interfamilial expression with low variability in the same family.

References


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doi: 10.1136/jmg.22.4.308

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