Familial inversion translocation (8;13) with partial trisomy 13 in several family members

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Abstract. A partial trisomy 13q was observed in siblings with hexadactyly, hypertelorism, haemangiomas and severe psychomotor retardation. It originated from a maternal inversion translocation 46,XX,inv(8)(q23q241),t(8;13)(q241;q32). The family showed a pedigree pattern typical for the segregation of a chromosomal translocation. In spite of this the diagnosis was delayed several years, because the bands involved from the two chromosomes were of great similarity. This stresses the importance of reinvestigating families with a clinical suspicion of a chromosomal syndrome, preferentially with prometaphase chromosomes. The identification of a chromosomal rearrangement is essential for genetic counselling and prenatal diagnosis.

Key words: Chromosome inversion translocation – Partial trisomy 13 – Prometaphase chromosomes – Genetic counselling – Congenital malformations – Mental retardation

Introduction

Partial trisomies 13 rarely occur de novo [13,8] but usually result from adjacent segregation of a parental translocation. The first report of a trisomy for the distal part of chromosome 13 came from Stalder et al. in 1964 [12]. Since then, a number of partial trisomies 13 have been reported and have been used for karyotype-phenotype correlation studies [9].

We want to report a large family with a number of malformed infants, two of them chromosomally studied, showing a partial trisomy 13, originating from a familial (8;13) translocation. It is of special interest that the chromosome analysis of the first infant was interpreted as normal. It was after the first malformed child, was born and the chromosomes of the infant and the parents were examined with Q and R banding. When a partial trisomy 13 was found in the proband, the chromosomes of her elder brother (IV,1) were evaluated again on the stored microphotographs. He was found to have the same chromosomal aberration as the proband. The mother carried a complicated balanced (8;13) translocation, so did the maternal grandfather. In generation II, seven malformed children died in early infancy. In generation III, two malformed infants died and there was one abortion. Medical records were available for three individuals in generation II (II,3,II,7 and II,9) and for two individuals in generation III (III,1,III,4). The information on generations II and III was collected from hospital records, family records, midwife records and parish files. The data from the two affected children in generation IV, were recorded in detail.

Case reports

The proband (IV,2) was a 16-day-old female infant, referred for chromosome studies because of multiple anomalies, Fig. 2. She was the product of a full term normal delivery as the second child of a 32-year-old healthy woman. The father was 34 years old at the birth of the proband. The parents were not related.

The clinical examination showed birth weight 3160g; length 49 cm, apgar score unknown but she was perinatally asphyxiated with base excess: -20.5. She was treated with NaHCO3. Her caput was trigonocephalic with a prominent metopic suture. There was a broad bridged nose and a haemangioma on the face. Other salient features included large, low set ears, high arched palate, long filtrum, retrognathia, low posterior hairline and short neck. There was an extra dimple next to the fifth finger on the left hand. It was removed by surgery shortly after birth. Bilateral simian creases were also present and there was a lack of extension in the left elbow. The great toes were broad with a wide space between the first and second toes and the feet were held in a metatarsus-varus position. She was universally hypotonic. Since her third living month she had often been hospitalized because of severe psychomotor retardation, infections and epileptic seizure. She is now 3 years old and severely retarded, unable to sit or stand without support. She is hypotonic and cannot crawl. Her gaze does not fix. Her height is within the normal range but the weight is 2 S.D. below normal [6,7]. Emotions are limited to her smiling when touched. She has no speech and does not react when talked to.
he developed symptoms of heart failure and heart catheterization was done when he was three weeks old. It showed a Steno-Fallot's tetralogy and he was digitalized and treated with diuretics. In spite of therapy he got worse and died when 4 months old in intractable apnoeic spells. He was mentally and physically retarded; at 10 weeks old there was no eye contact and he was severely hypotonic. At the same time he was reported to the Service for the Mentally Retarded. The clinical features were similar to those described in his sister (the proband). The face was asymmetrical. He had an extra finger on the ulnar side of both hands and simian lines in the palms. Inguinal and umbilical herniae were present. The testes were not descended and both great toes were broad with wide spaces between the first and second toes. The inguinal hernia was life threatening several times because of incarcerations, but it was always possible to reduce them manually and avoid operation. EKG showed ventricular enlargement and right bundle branch. Heart catheterization showed Steno-Fallot's tetralogy. X-ray examination showed dextrocardia, scoliosis cranii, normal skeletal configuration except bilateral hexadactyly. The autopsy confirmed the heart defect described and also showed cerebral and cerebellar hemiatrophy with a tiny falx cerebri.

**Case 3.** The older sister of the mother (Fig. 1) (III,1) died when three weeks old with symptoms of pyloric stenosis and marasmus. The infant showed hypoplasia of the left eye and aplasia of the thenar on both hands. She had malformed genitalia, not further specified (atresia ani?) and bilateral metatarsus varus.

**Case 4.** The mother's brother (Fig. 1) (III,4) died when two years old. The pregnancy was normal and the mother was 31 years at the time of delivery. The father was 29 years old. The birth weight was 2950 g, length 51 cm. The infant was described as having a prominent metopic ridge and flat occiput. The head was microcephalic; less than −2 S.D. [6, 7]. Hexadactyly on both hands and a slit-formed opening in the sacral region was observed. He had convulsions, cyanotic spells and failure to thrive (−2 S.D. in length, −3 S.D. in weight at 16-months-old) and died institutionalized at 18 months old, severely mentally and physically retarded. No heart failure was seen. X-rays showed an oxycephalic head with flat occiput. The thorax was