

Case report

Trisomy 8 mosaicism syndrome

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Abstract: Authors present the case of a 15-year-old boy assessed for Marfan syndrome for many years. The child was treated because of skeletal defects, mild mental deficiency and dysmorphic features of face. Chromosomal analysis showed a trisomy 8 mosaicism.

Key words: mosaic karyotype, trisomy 8.

Trisomy 8 mosaicism (T8M) is a relatively common chromosomal abnormality but because of extremely variable phenotypic and cytogenetic expression quite often it is undiagnosed. The estimated frequency is about 1:25,000 to 50,000 births. There is at least a 5:1 male predilection (GORLIN et al. 1990). Patients with trisomy for a C-group autosome have been recognised since 1963 but trisomy 8 mosaicism was first reported in 1971 by Grouchy (FINEMAN et al. 1975). There is no significant difference in phenotype between the so-called pure trisomy 8 and trisomy 8 mosaicism. The abnormal cell line tends to disappear from lymphocytes with age. In older patients aneuploidy can sometimes be demonstrated in fibroblast cultures only (SCHINZEL 1984, JORDAN et al. 1998). Causes of chromosomal nondisjunction are still unknown. KARADIMA et al. 1998 performed a molecular study on trisomy 8 and trisomy 8 mosaicism. They reported the results of analyses of 26 probands (and parents) using 19 microsatellite DNA markers mapping along the length of chromosome 8. The results of the nondisjunction studies show that 20 cases were probably due to mitotic (postzygotic) duplication,

Received: December 28, 2001. Accepted:

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as reduction to homozygosity of all informative markers was observed and no third allele was ever detected. Only two cases were due to maternal meiotic nondisjunction and in four cases it was not possible to detect the extra chromosome due to a low level of mosaicism. Those results are in contrast to the common autosomal trisomies, where the majority of cases are due to errors in maternal meiosis (KARADIMA et al. 1998).

Life expectancy of patients with T8M is usually normal. Most infants have normal birth weight for gestational age. Mean parental ages at birth of the probands are increased (father 32 years, mother 29 years). Particularly characteristic is the combination of the following: normal or advanced growth, multiple skeletal abnormalities (spinal deformity, absent or hypoplastic patella, contractures of fingers and toes), deep longitudinal plantar furrows, limitation of motion in multiple joints, absence of the corpus callosum, and moderate mental retardation with disproportionally delayed language. The face shows a high and prominent forehead, hypertelorism with broad-based nose, full lips, and micrognathia. The trunk is relatively long and slender with narrow shoulders and pelvis. The neck is short or sometimes webbed. About 25% of patients have congenital heart defects and 10% have cleft palate. Renal malformations are probably present in at least every second case. Due to limited joint restriction, the children characteristically start to walk on their toes (BEIGHTON et al. 1999, KURTYKA et al. 1988).

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The reported patient was born on 28 November 1985. His mother was 29 years old, father was 31 years old, both were healthy and unrelated. Elder and younger siblings were normal. The boy was a child from the 5th pregnancy, 4th delivery (the 1st pregnancy finished as a spontaneous abortion). He was born after 40 weeks of pregnancy, with birth weight 4450 g, length 61cm, head circumference 40 cm, trunk circumference 36 cm and 9 points in Apgar scale. The boy has been under clinical observation since the newborn period but without any genetic examination. During the first year of life he suffered from recurrent respiratory system infections. A mild psychomotor retardation and hypotonicity was observed, with tendency to poor coordination and delayed speech. Because of many skeletal defects: abnormal scapula, scoliosis, camptodactyly of second, third and fifth fingers and toes, ectopic wandering patella and joint contracture, he was hospitalised several times in the orthopedic ward. Additionally, he had hypospadias. For the whole period he was treated as Marfan syndrome because of long, slender trunk and spinal deformity. At the age of 15 years he was sent for the first time for genetic counselling. He was then 162 cm high and weighed 44 kg, and his head circumference was 57 cm. His face was long and narrow, lips were full. He had a webbed neck and typical features for T8M of the trunk: long, narrow shoulders,



Figure 1. Phenotype of a patient with trisomy 8 mosaicism

winged scapula and scoliosis. The most striking features were contractures of toes and fingers and typical deep creases on both soles (Figure 1). Because of wandering hypoplastic patella the boy was operated and the patellapexy was done. After a year the patella was wandering again. Because of contracture of the big toe of the left foot, which made him unable to walk, the arthrodesis of the toe was done. His speech is still delayed although he has undergone speech therapy for many years. On the basis of USG, echocardiography, CT and NMR, congenital defects of internal organs were excluded.

Chromosomal analysis was done on peripheral blood lymphocytes according to conventional techniques. The analysis revealed a mosaic karyotype: 47,XY,+8 [7]/46,XY [43]. Unfortunately the parents did not agree to a cytogenetic diagnosis based on fibroblasts.

The characteristic skeletal thoracic abnormalities are present in almost every patient with T8M. We believe that trisomy 8 mosaicism can be suspected with a high probability in mentally retarded patients if the disorder is known to the observer. Our patient's case was an example of wrong diagnosis because of abnormalities suggesting Marfan syndrome. We think that in each case of mental retardation and skeletal abnormalities, especially with joint contractures, it is nec-

essary to make a cytogenetic analysis. It is still a problem that in too many cases with somatic abnormalities and dysmorphic features the genetic investigation is unnecessarily postponed.

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