Transmission of a ring chromosome 18 from a mother with 46,XX/47,XX,+r(18) mosaicism to her daughter, resulting in a 46,XX,r(18) karyotype

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Abstract

A 6 month old patient is reported with a ring chromosome 18 confirmed by cytogenetic studies and in situ hybridisation. Her clinical features were similar to previous cases of ring chromosome 18 syndrome. The ring chromosome was inherited from the phenotypically and mentally normal mother with a mosaic 46,XX/47,XX,+r(18) karyotype.

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The phenotypic and clinical features of patients with a ring chromosome 18 syndrome probably depend on the extent of deletion of the short or long arm and on rearrangements leading to loss or duplication of chromosome 18 sequences.¹ Transmission of ring chromosome 18 has rarely been reported.²⁻⁶ In these families one normal chromosome 18 is generally replaced by the ring chromosome 18. In our study we describe a woman with partial trisomy 18 mosaicism caused by an additional ring chromosome 18, resulting in a 46,XX,r(18) karyotype in her daughter.

Case report

The patient was born at 42 weeks of gestation by normal spontaneous delivery. She was 49 cm long, had a head circumference of 32 cm, and a birth weight of 3150 g. The mother was 28 years old and the father 24 years old. The girl was their first child. There were no previous abortions. When examined at the age of 1 week, she had a broad nasal bridge and a flat occiput. The ears were low set with poorly developed helices but prominent antihelices. The neck was short. She had talipes calcaneus. There was low implantation of both thumbs and overlapping second and third toes

on the left foot. Cardiac examination showed a complex heart defect (tetralogy of Fallot, peripheral pulmonary stenosis, small patent ductus arteriosus, atrial septum defect secundum, and hypoplastic pulmonary artery system).

The parents were phenotypically and mentally normal and there was no heart disease in the family.

CYTOGENETIC STUDIES

Chromosome analysis of the patient was performed on PHA stimulated lymphocytes using standard trypsin-Giemsa banding techniques. All 100 cells studied showed a 46,XX,r(18) karyotype with the breakpoints approximately at p11 and q23. The ring had a monocentric single appearance (fig 1). Chromosome analysis of peripheral lymphocytes from the mother showed a normal karyotype in 98 cells and an additional ring chromosome 18 in two metaphases (fig 2). The cytogenetic pattern of the ring chromosome was comparable to the ring chromosome 18 of the daughter. Chromosome analysis of fibroblasts was not possible. The father had normal chromosomes. A cell line is not available from the patient.

IN SITU HYBRIDISATION

The α satellite biotin labelled DNA probe of chromosome 18 (Onkor) was used. The conditions used for hybridisation and detection of the resultant signal by an antibody/peroxidase system were as described by Stock *et al.*⁷ Two

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Figure 1 Partial karyotype from peripheral lymphocytes of the patient showing the normal chromosome 18 and the ring chromosome 18.

Figure 2 Metaphase from peripheral lymphocytes of the mother showing the two normal chromosomes 18 and the ring chromosome 18.

Figure 3 Metaphase of the patient after in situ hybridisation with the α satellite biotin labelled DNA probe of chromosome 18.

strong hybridisation signals were observed in the patient. They showed a normal chromosome and the ring chromosome with a chromosome 18 centromere (fig 3).

Discussion

Our patient with a non-mosaic 46,XX,r(18) karyotype presented the characteristic symptoms of the ring chromosome 18 syndrome.¹ The phenotypically and mentally normal mother had a low percentage of partial trisomy 46,XX/47,XX,+r(18) mosaicism in her peripheral lymphocytes and had transmitted the ring chromosome 18 to her daughter. At least two of her cell lines were affected: peripheral lymphocytes and germ cells. In accordance with various published data the mosaicism in the mother may have originated from a trisomic zygote generating normal diploid cell lines through mitotic non-disjunction events.^{8,9}

So far, only four cases with full trisomy 18 mosaicism and one case with an additional small ring chromosome 18 in peripheral lymphocytes/fibroblasts, combined with normal intelligence and non-specific dysmorphism, have been described.¹⁰⁻¹⁴ The significance of the trisomy 18 may depend on the cell line in which the genes are expressed.

In summary, no previously published case has shown a syndrome with a ring chromosome 18 which was transmitted from a phenotypically and mentally normal mother with a 46,XX/47,XX,+r(18) karyotype. Careful chromosome analysis should rule out parental mosaicism which may contribute to a recurrent risk of giving birth to a child with either

partial trisomy or monosomy of different regions of chromosome 18.

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