A New Case of a Complex Small Supernumerary Marker Chromosome: A Der(9)t(7;9)(p22;q22) due to a Maternal Balanced Rearrangement

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J Pediatr Genet 2015;4:199–200.

Abstract

Complex small supernumerary marker chromosomes (sSMCs) constitute one of the smallest subsets within the patients with an sSMC. Complex sSMCs consist of chromosomal material derived from more than one chromosome, for example, the derivative der(22)t(11;22)(q23;q11.2) in Emanuel syndrome. Here, a yet unreported case of a complex sSMC formed due to a t(7;9)(p22;q22)mat is presented.

Keywords

- complex small supernumerary marker chromosomes (sSMCs)
- genotype-phenotype correlation
- partial trisomy 9
- partial trisomy 7

Introduction

As defined in 2004, small supernumerary marker chromosomes (sSMCs) are structurally abnormal chromosomes that cannot be identified or characterized in detail by banding cytogenetics, are generally about the size of or smaller than a chromosome 20, and molecular cytogenetic techniques are necessary for their comprehensive characterization.[1] It is suggested that there are approximately 3 million of sSMC carriers in the human population of 7 billion individuals, and only one-third of the sSMC cases are associated with clinical abnormalities.[2] Apart from few specific syndromes (Pallister-Killian- = i(12p)-, isochromosome-18p, i(18p), cat-eye- i (22p∼q)-, idic(15)- and Emanuel- or derivative-chromosome-22 der(22)t(11;22)-, syndrome), for the remaining sSMC cases only first steps toward genotype-phenotype correlations were done by now.[2,3]

Complex sSMCs are such consisting of chromosomal material derived from more than one chromosome.[1] Emanuel- or derivative-chromosome-22- (der(22)t(11;22), OMIM #609029) syndrome is the most frequently occurring of the so-called complex sSMCs.[4] Besides many single case reports and Emanuel syndrome, there are still two additional recurrent complex sSMCs identified:

1. der(22)t(8;22) syndrome (OMIM #613700)[5]
2. der(13)t(13;18)(q11;p11.21) or der(21)t(18;21)(p11.21; q11.1) syndrome[4]

Here we report a new complex sSMC case, based on a balanced maternal translocation of chromosomes 7 and 9.

received
April 22, 2015
accepted after revision
April 28, 2015
published online
October 20, 2015

DOI http://dx.doi.org/10.1055/s-0035-1565270.
ISSN 2146-4596.

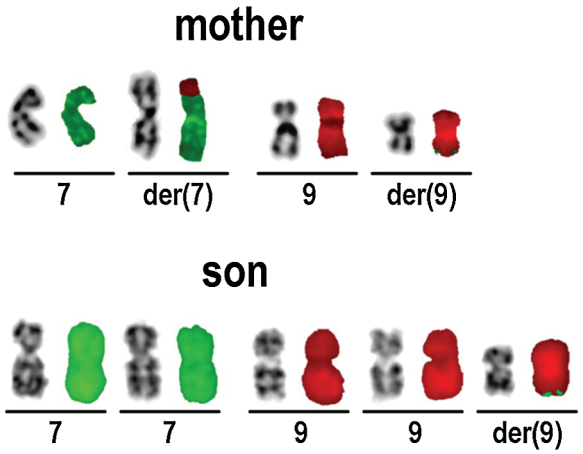

Fig. 1 The results from banding cytogenetics in mother and son (not shown) were substantiated by whole chromosome painting probes for chromosomes 7 (green) and 9 (red). Here the results of FISH together with inverted DAPI-banding are depicted.

Case Report

The male patient was born by cesarean section with a birth weight of 1,940 g and a length of 44 cm. His birth was from the fifth pregnancy of his mother, who had experienced three spontaneous abortions before; besides, the patient had an older healthy brother.

The patient was born hypotrophic, with full and wavy hair; a prominent forehead (middle facial part); microcephaly; low-set abnormal ears; hypertelorism; narrow, short eye slits; antimongoloid eye slant; broad, flat nasal bridge; bulbous nasal tip; microretrognathia; high palate; macrostomia; short neck; hollow stomach; short upper and lower extremities; bilateral clinodactyly of second and fifth fingers; thumbs and first toes are positioned far from other fingers (sandal gap); hypoplasia of toes nails; single transverse palmar crease; hypoplastic aortic arch; and hypoplastic lungs. He died 1½ days after birth.

Banding cytogenetic analysis of the mother revealed a balanced karyotype 46,XX,t(7;9)(p22;q22). For the first and healthy son the karyotype was 46,XY,t(7;9)(p22;q22). In this reported patient the karyotype was unbalanced and revealed a 47,XY, + der(9)t(7;9)(p22;q22), which was confirmed by fluorescence in situ hybridization (FISH) using homemade whole chromosome painting (WCP) probes[6] (►**Fig. 1**).

Discussion

Here we report a new case of a complex sSMC leading to partial trisomy 7pter to 7p22 and 9pter to 9q22. This case belongs to the 64% of complex sSMCs formed due to parental balanced translocations, and is, as known for the majority of sSMCs,[2] a maternally derived one. No cytogenetic studies were performed in the three spontaneous abortions of the mother of the reported patient. Thus, it can only be speculated that they might have been due to other reasons or due to unbalanced karyotypes such as 46,XN,der(7)t(7;9)(p22;q22), 46,XN,der(9)t(7;9)(p22;q22), 47,XN, + der(7)t(7;9)(p22;q22), or 47,XN, + der(9)t(7;9)(p22;q22). Also, uniparental disomy of chromosome 7 or 9 could have complicated these pregnancies additionally.[3]

The present case emphasizes our recent statement that complex sSMCs are most likely much more frequent than originally suggested.[4] When detecting a centric minute-shaped sSMCs, in approximately 40% of the cases such an sSMC is complex. Like in other complex sSMCs also, the der(9) reported here was present in 100% of the cells. As noncomplex centric minute-shaped sSMCs tend to be there rather in mosaic, this may be used also as another hint on the presence of a complex sSMC. Finally, in clinically abnormal patients with a centric minute-shaped sSMCs present in 100% of the cells, a complex sSMCs should be considered.[4]

In summary, we report a new complex sSMC formed due to a balanced maternal translocation t(7;9)(p22;q22). As molecular studies were not possible due to lack of parental DNA, it can only be speculated about possible mode of formation for the karyotype observed in the patient. Most likely is a monosomic rescue event, that is, the duplication of one paternal chromosome 9. Overall, this case underlines the importance of the full determination of structure and origin of sSMCs, as only such comprehensive studies can help understand more about the mechanisms of their formation.

Acknowledgments

Supported in parts by the Else Kröner Fresenius Stiftung (2011_A42) and the DAAD.

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