

Prenatal diagnosis of a fetus with a ring chromosome 20 characterized by array-CGH

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Summary

Objective: a fetus with a ring chromosome 20 is presented.

Methods: at 16 weeks' gestation, ultrasound examination evidenced no apparent structural malformation. Amniocentesis was performed for maternal anxiety.

Results: chromosome analysis identified a ring chromosome 20 and array-CGH demonstrated that the ring including micro-deletion of the short arm in 20p13, that was extended for about 632.2 kb and a micro-deletion of the long arm in 20q13.33 region.

Conclusion: this is the first case of a ring chromosome 20 diagnosed prenatally. This reinforces the importance of offering amniocentesis with a-CGH to make more accurate prenatal diagnosis.

Key words: ring chromosome, array-CGH.

Introduction

Ring chromosome 20 [r(20)] syndrome is a rare disease characterized by neurological abnormalities expressed by moderated mental retardation, behavioral disorders, refractory epilepsy (1). Ring chromosomes are usually formed by fusion of the deleted telomere ends of both

chromosome arms, but there are reports of cases in which there was integrity of both chromosome ends (2). Two genes, CHRNA4 and KCNQ2, mapped to 20q13.2e13.3 have been identified to be implicated in the mechanism underlying seizure disorders and were considered as candidate gene in the generation of neurologic manifestation of r(20) syndrome.

To our knowledge no cases of [r(20)] have been described prenatally.

Methods

A 33 year-old nulliparous woman was referred to Artemisia Fetal-Maternal Medical Centre at 17th week of gestation. She underwent to amniocentesis for maternal anxiety. Her past medical history was negative. Both parents were healthy and non-consanguineous. The pregnancy was uncomplicated. Previously, as a routine practice, our medical equipe performed ultrasound examination of the fetus.

Results

Ultrasound examination showed a di-amniotic, di-chorionic, twin pregnancy with regular fetal growth and no apparent structural malformations, for both feti. Then, amniocentesis was performed. Metaphase analysis of amniocytes revealed a normal karyotype of 46,XY for the first fetus and a karyotype of mos 46 XX, r(20)[44]/45,X,-20[6] for the second fetus. Examination revealed in 12% of examined metaphase plates a condition of monosomy of chromosome 20. To confirm the findings of the classic cytogenetic and to determine the exact amounts of euchromatin present in the ring derived from chromosome 20, array CGH was performed on DNA extracted from amniocytes. The result demonstrated a micro-deletion of the short arm of chromosome 20 in 20p13, extended for about 632.2 kb and a micro-deletion of the long arm of the same chromosome in the 20q13.33 region, extended for about 779.9 kb.

Woman opted for the termination of pregnancy.

Discussion

To our knowledge, this is the first case of prenatal diagnosis of r(20). Ring(20) syndrome is characterized by phenotypic variability, particularly concerning dysmorphism, malformations, mental retardation and behavioral disturbances. The severity of clinical features has been ascribed to high percentages of r(20) chromosome abnormal cells, ring instability and presence or absence of chromosome 20 deleted regions (1).

R(20) was described only in post-natal life with over 60 cases reported in the literature, mostly resulting in refractory epilepsy and cognitive problems (3).

In our case mosaicism was present in 12%. FISH, and more specifically a-CGH, revealed that the ring chromosome derived from micro-deletions of both short and long arm. The ring chromosomes are unstable during mitosis which explains that people have a mosaic karyotype with normal cells and cells containing the ring chromosome. The percentage of cells affected by the anomaly appears to correlate at the age of goal seizures, the IQ of patients and the existence of malformations (4).

Two epilepsy genes *CHRNA4* and *KCNQ2* mapped to 20q13.2-13.3 and located within 1 Mbp of 20qter were considered as responsible for epilepsy generation if deleted (5).

In our case, deletion was at the site of the genes in question, so probably fetus would develop severe epileptic symptoms.

However, to our knowledge, there are four described cases of a ring chromosome 20 patient who has the typical severe epilepsy disorder but not deleted subtelomeric regions. Elghezal supports that clinical features of ring chromosome 20 syndrome are caused essentially by the loss of the ring chromosome 20 involving mosaic chromosome 20 monosomy and not because the mere deletion of the two epilepsy-associated genes *CHRNA4* and *KCNQ2* located at 20q 13.3. However, in this case, CGH analysis was not performed to confirm the absence of possibly submicroscopic chromosome rearrangements (6). The a-CGH technique is an efficient and practical approach to the molecular characterization of chromosomal arrangement and permits to better describe the genes involved in this mechanism. In fact, in addition to the conventional cytogenetic analyses and FISH, it permits an accurate identification of the origin and content of marker chromosomes, contributing to a more informed prenatal counselling and patient follow-up.

In conclusion we believe that the introduction of a-CGH analysis when ring were found during the prenatal period, will permits in the future a better identification of a genotype/phenotype correlation providing for an efficient approach to identifying the origin and extent of deleted and duplicated material in chromosomal rearrangements.

Declaration of interest

The authors report no declarations of interest.

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