Commentary

Molecular cytogenetics of recurrent missed abortions

Cytogenetic analysis of reproductive wastage is an important stage in understanding the genetic background of early human development. It is well established that about 50-60 per cent of spontaneous abortions have chromosome abnormalities. However, the role of karyotype imbalance in the aetiology of some nosologic forms of pregnancy loss remains unclear. Recurrent miscarriage is usually defined as the loss of three or more consecutive pregnancies before 20, or even 28 wk. It is considered as a multifactorial problem with different presumptive causes including genetic, anatomic, endocrine, autoimmune and others factors. At the same time, role of chromosome abnormalities in the aetiology of recurrent spontaneous abortions (RSA) is still unclear. Several studies have revealed a frequency of chromosomal abnormalities as high as 51-60 per cent in RSA, while others reported a significantly low incidence i.e., 5-29 per cent. This variability reflects the complex nature of recurrent miscarriages. It is suggested that the role of chromosomal abnormalities is lower with increasing number of pregnancy loss. On the other hand, differences in the frequency of aberrations may be related with some difficulties in conventional cytogenetic analysis of products of conceptions. Maternal cell contamination, cell culture failures, low level chromosomal mosaicism are the main problems of such studies. Use of molecular cytogenetic techniques helps avoid these problems due to possibility of analysis of non-cultured embryo cells. Current progress in molecular cytogenetic approaches significantly adds to our knowledge in the field of prenatal genetics and reproductive medicine. Introduction of interphase fluorescent in situ hybridization (FISH), comparative genomic hybridization (CGH) and array-CGH into analysis of spontaneous abortions has revealed previously underestimated abnormalities in first trimester human embryos such as rare types of aneuploidy (autosomal monosomies, double or triple aneuploidies), structural rearrangements, and a high rate of chromosomal mosaicism.

From this point of view, the study of Halder and Fauzdar in this issue has a noticeable significance. It is an attempt to investigate the karyotype of recurrent spontaneous abortions by molecular cytogenetics methods, such as interphase FISH and CGH. Several aspects of this study should be underlined. First of all, the authors point out a relatively low rate of aneuploidy. This finding is confirmed by results of other studies on RSA by conventional cytogenetic techniques. On the other hand, four from 10 spontaneous abortions have revealed a suspected partial gain/loss of different chromosomes after CGH. Further investigations of these cases would be very interesting in the light of recently discovered phenomenon of copy number polymorphism in the human genome. It is possible that role of segmental aneuploidy in pregnancy loss among couples with recurrent miscarriages will be re-estimated soon owing to introduction of array-CGH.

Another finding is related with skewed sex ratio among spontaneous abortions. The prevalence of female embryos is a common feature of early pregnancy loss. Several hypotheses are widely discussed in order to explain sex-specific embryo elimination. But the true factors of this fact remain unclear. One of the possible mechanisms is related with disturbances of epigenetic processes (namely, X-inactivation or genomic imprinting) in early...
embryos. However, the prevalence of epigenetic abnormalities, mechanisms of their origin as well as role in human prenatal selection are not investigated yet. The first showings are coming from assisted reproductive technologies. It is possible that some cases of idiopathic recurrent spontaneous abortions are related with aberrations of epigenetic genome reprogramming in parent’s gametes or in early embryos. In spite of long history of cytogenetic examinations of human spontaneous abortions, further studies are required for understanding of genetic mechanisms of prenatal selections and improving the medical counselling of couples with recurrent pregnancy loss.

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References


