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Preconception, Preimplantation and Prenatal Genetic Diagnosis (CoGEN)

A complex approach in the diagnostics of Y-chromosome cytogenetic aberrations

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Introduction

Cytogenetic aberrations of Y-chromosome (reaY) is one of the most significant reasons for azoospermia in men. The aim of the study was to determine reaY types, point out the importance of a complex of methods for the correct diagnostics, search for biological effects of reaY presence.

Methods: GTG-, CBG-banding; FISH (fluorescence in situ hybridization); AZF testing; chromosomal microarray (CMA).

Materials: cultures of blood lymphocytes, amniotic fluid, chorionic villus samples.

Results

In total 46 postnatal (men with azoospermia (n=27), women (n=5) and children (n=13) with sex dysfunction and growth retardation, random case in male (n=1)) and 15 prenatal (with high risk for chromosomal disorders) karyotypes with reaY were detected. Combination of standard karyotyping, FISH, molecular genetic methods allows to differentiate reaY types (Figure 1). 72.1% among the all reaY karyotypes occurred in the mosaic karyotype with 45,X clone (Figure 2). The most common aberration is isoYp (Figure 3). ReaY without size change are the most difficult to detect at the first line genetic diagnostics – karyotyping. So the main features of the abnormal structure were identified in GTG-banding: changes in the Yp/Yq size, the "folded" Y chromosome shape, dynamic mosaicism, 45,X clone presence, in CBG-banding: changes in Yq12 localization, delYq12, two centromeres presence. FISH and AZF tests were used as additional diagnostic methods. Also no cytogenetically normal Y-chromosome with delAZFbc/abc was identified. So, it can be assumed delAZFbc/abc while the medium size of the Y-chromosome retention in GTG is the indirect sign to suspect reaY. CMA was additionally used for the psuisoY diagnostics.

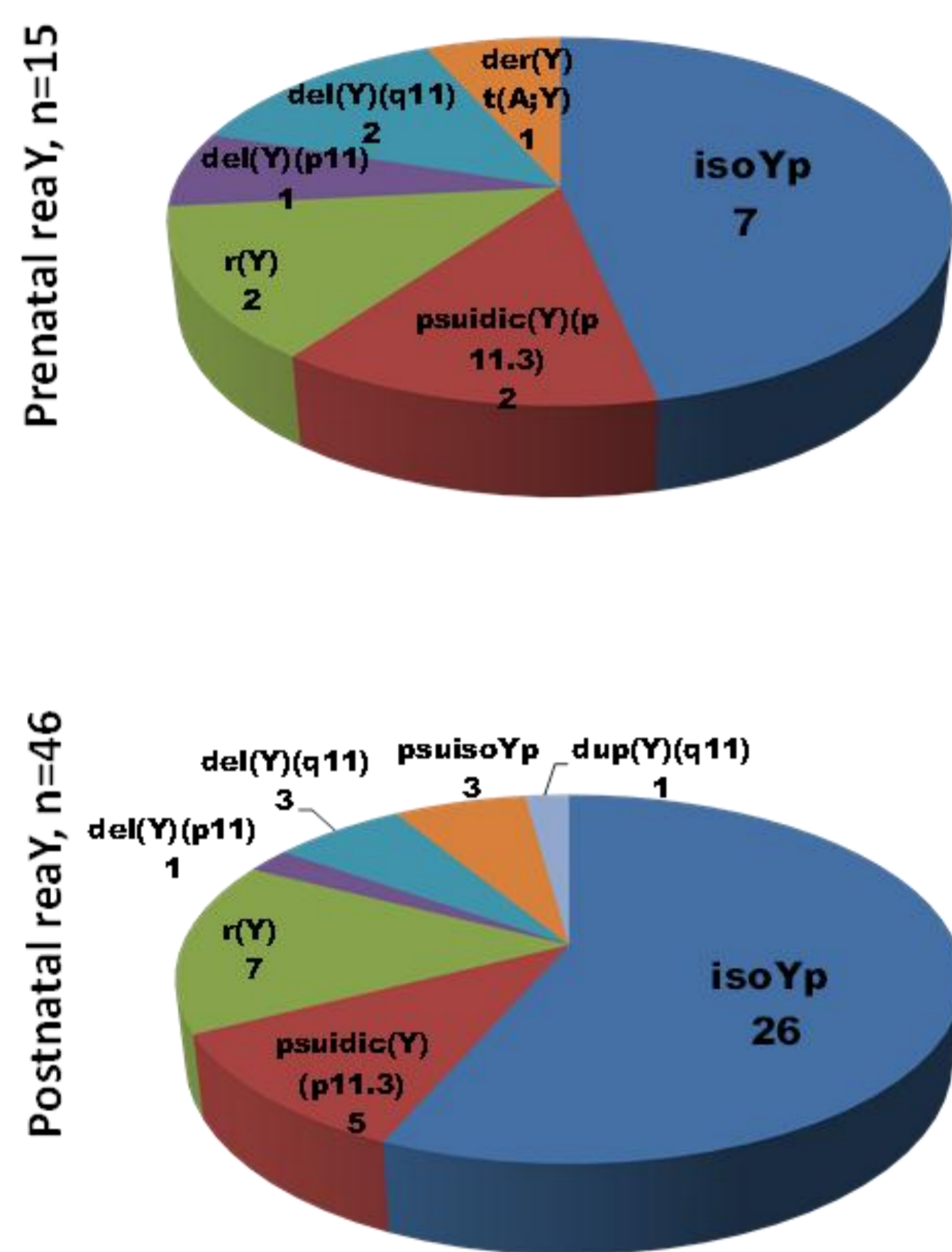


Figure 1 reaY types in pre- and postnatal karyotypes

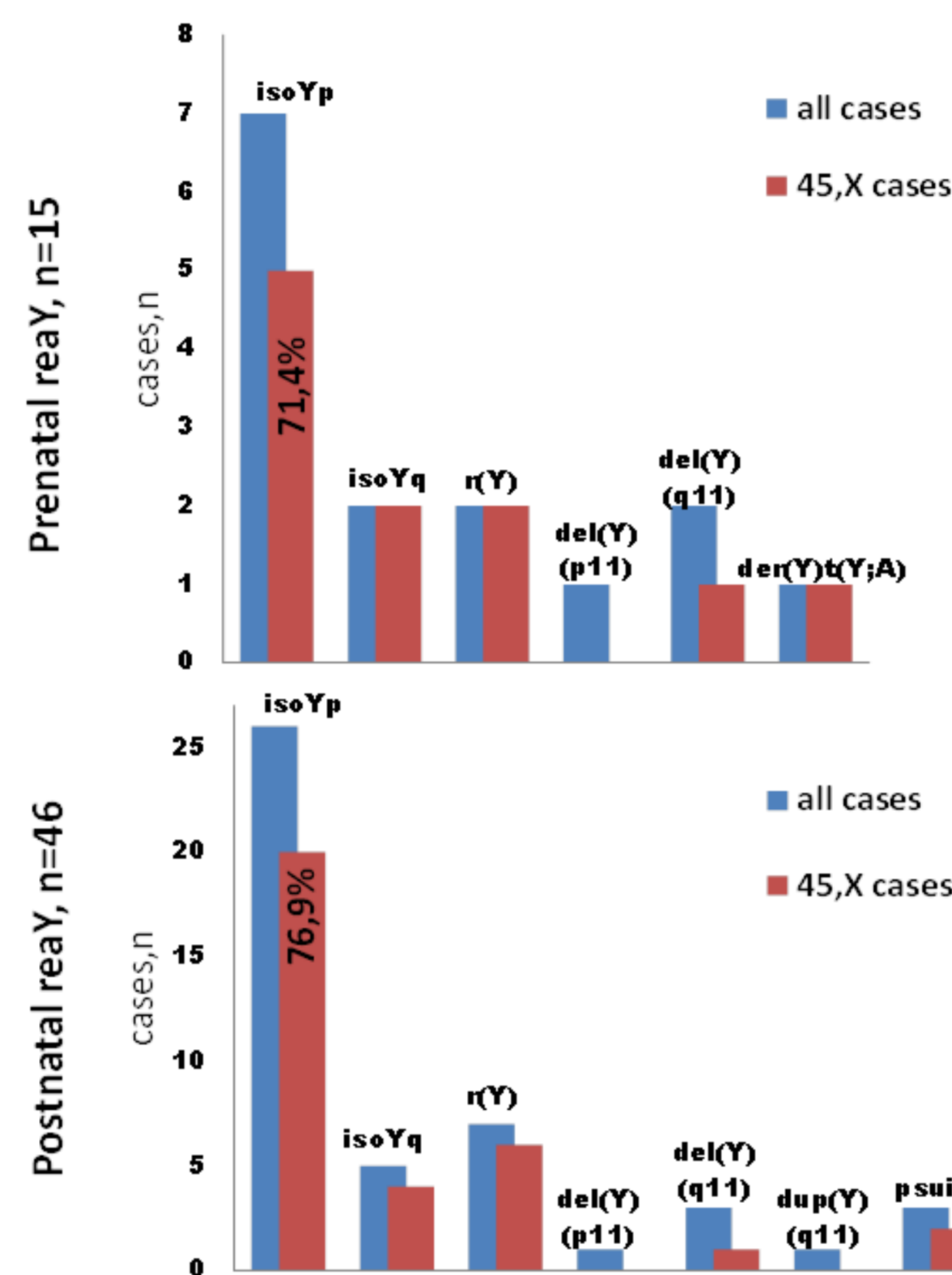


Figure 2 The frequency of 45,X mosaicism in reaY karyotypes

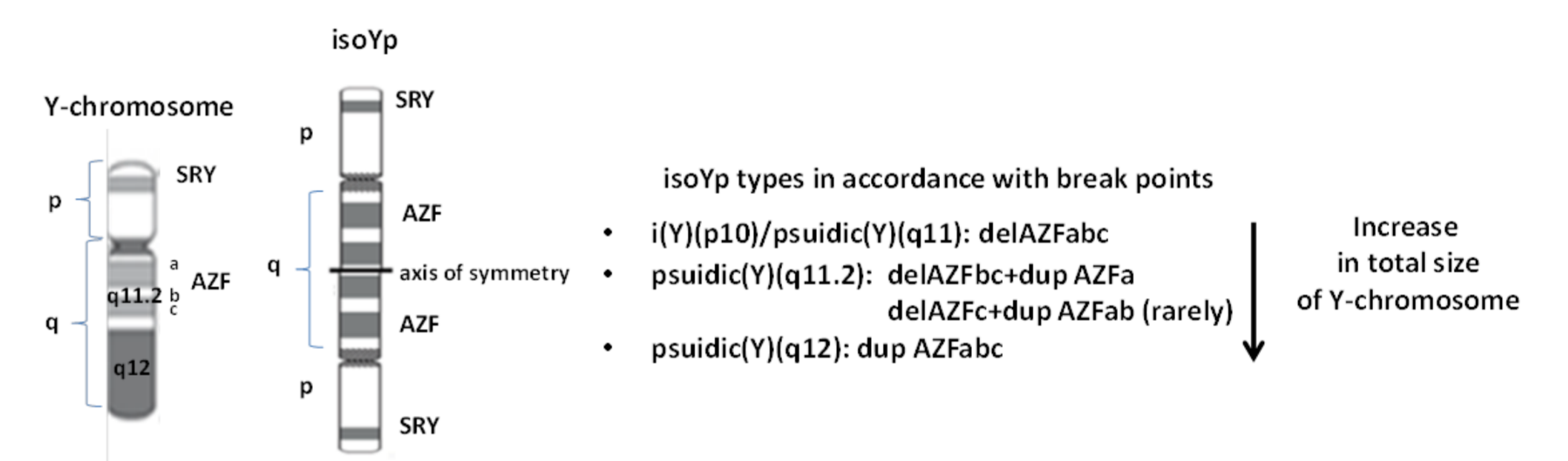


Figure 3 The localization of the Y-chromosome regions in normal morphology and during the formation of isoYp

Conclusion

It is necessary a complex approach for the correct Y-chromosome diagnostics. Cytogenetic abnormality is the cause of the subsequent loss of Y-chromosome (45,X clone) and interstitial delAZF. These facts lead to the corresponding patient phenotype and male infertility, that is important to use when conducting medical genetic counseling.

References

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