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AZFc partial microdeletion and microduplications on idiopathic oligozoospermic patients

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Abstract/Resumo

Several studies have shown a strong relationship between genetic factors and infertility, however, the causes of oligozoospermia remain unclear. The application of molecular technologies is bringing important advances in the infertility field by enabling the detection of changes at the genetic and genomic levels in patients, such as mutations and copy number variations (CNVs). In this study we chose to characterize genomic alterations of the Y-chromosome in oligozoospermic men, to identify specific CNVs that were associated with the phenotype. The experimental group comprised 18 idiopathic oligozoospermic patients without an AZF deletion (analyzed using multiplex PCR) and 5 proven fertile men were part of the control group. Analysis of whole genome copy number changes was performed by 4x180K (Agilent, US) microarray comparative genomic hybridization (aCGH) which included CNV and single nucleotide polymorphism (SNP) probes. In this study only Y-chromosome alterations were analyzed. An apparently benign gain in AZFc region involving only DAZ1 and DAZ4 genes was detected in nine patients and four control subjects. However, other copy number changes in the AZFc region, possibly related to the oligozoospermia phenotype, were detected in three patients (16,7%). The alterations included extensive duplications and deletions involving, among other genes, the four copies of the DAZ gene. Some studies relate subdeletions of AFZc with infertility, while others do not observe this association. The most common AZFc partial microdeletions involves two copies of the DAZ genes, and one or two copies of CDY1 and BPY2 genes. However, there has been no previous report of patients with partial AZFc deletions involving four copies of the gene. The consequences of minor CNVs on Y chromosome could be further studied in bigger cohorts. Also, the determination of breakpoints and extent of the Y chromosome CNVs detected by the technique could be validated by higher resolution techniques for a better genotype-phenotype correlation.

Keyword/Palavras-chave: Male infertility; array-CGH; Copy number variation; Y chromosome; Spermatogenesis

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