Copy number variations in spermatogenic failure patients with chromosomal abnormalities and unexplained azoospermia

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Received June 16, 2015
Accepted September 29, 2015
Published December 7, 2015
DOI http://dx.doi.org/10.4238/2015.December.7.17

ABSTRACT. Male infertility is mostly caused by spermatogenic failure. Currently, routine genetic analyses of unexplained azoospermia or oligoazoospermia are limited to the investigation of Y chromosomal microdeletions and chromosome karyotype analyses. The aim of this study was to find spermatogenic failure genes in patients with chromosomal abnormalities and unexplained azoospermia caused by copy number variations in order to provide a theoretical basis for further research. Spermatogenic failure patients consisting of 13 males with chromosomal abnormalities and 20 with unexplained azoospermia were enrolled. The subjects underwent high-throughput genome-wide sequencing to find copy number variants (CNVs), and the results were analyzed using the Database of Genomic Variants, Online Mendelian Inheritance in Man database, and PubMed. The results showed that 16 CNVs were detected in 11 patients with chromosome abnormalities, and 26 CNVs were found in 16 males with azoospermia. Our data showed CNV-involved loci including: three times on 11p11.12 and 14q11.2 and twice on 6p21.32, 13q11, 15q11.11, 16p12.2,
and 21q22.3. Some CNVs may involve changes in genetic structure and function or gene mutations, which may affect gene expression in testicular tissues and lead to spermatogenic failure. The involved genes include \textit{EDDM3A}, \textit{EDDM3B}, \textit{HLA-DRB1}, \textit{HLA-DQA1}, \textit{POTE B}, \textit{GOLGA8C}, \textit{DNMT3L}, \textit{ALF}, \textit{NPHP1}, \textit{NRG1}, \textit{RID2}, \textit{ADAMTS20}, \textit{TWF1}, \textit{COX10}, \textit{MAK}, and \textit{DNEL1}. By applying high throughput genome-wide sequencing to determine CNVs, we provide a number of candidate genes possibly contributing to spermatogenic failure.

**Key words:** Copy number variations; Spermatogenic failure; Chromosomal abnormalities; Y-chromosomal microdeletions; Azooospermia; Oligozoospermia