Balanced Reciprocal Translocation t(17;22)(p11.2;q11.2) and 10q23.31 Microduplication in a Infertility Male Suffering from Teratospermia

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Research

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Abstract

We describe the first case of two chromosomal abnormalities, balanced reciprocal translocation t(17;22) (p11.2;q11.2) and a microduplication in the region 10q23.31, in an infertility man suffering from teratospermia. Several genes located on the translocation breakpoints or the region of duplication show rich expression in the tissue of testis. They have been reported to be associated with developmental disorder and retardation, which might also be the risk factors affecting in spermatogonial differentiation and spermatogenesis. More studies should be carried out for identification of new genes associated with semen quality. Our case might support the opinion that haploinsufficiency of the testis-expressed gene could be the cause of sperm immotility and abnormal sperm morphology. The two chromosomal abnormalities that carry additional reproductive risks, is apparently harmful with regard to the male infertility, and could contribute to the genomic instability resulting in disease.

Introduction

It has been observed that declining fertility rates is among the most salient features of global demography over the last decade. Male infertility, affecting approximately 50% of the couples with problems to have children, is getting more and more concern(1). It is highly vary for the causes of male infertility, which can be related to the acquired, congenital or idiopathic factors that impair spermatogenesis. Despite many health conditions and lifestyle factors can affect fertility, the diagnosis in around 40% of infertility men remain to be elucidated, which might be underlying genetic causes(2). So far, recognized genetic causes of spermatogenic failure include karyotype abnormalities, Y-chromosome microdeletions, systemic syndromes, and gene mutations. The formation of normal bivalents during the meiosis is disrupted in these patients resulting in an inefficient spermatogenesis. To investigate, one of the routinely genetic tests to be performed in infertility patients is karyotype analysis. Besides numerical abnormalities, chromosome structural defects are detected 5–10 times more frequently in infertile men(3)(4). There are some potential pathogenic mechanisms related to effects on the expression of genes, when they are targets of chromosomal rearrangements (such as deletions, duplications and breakpoints). The presence of structural chromosomal abnormalities in the sperm increases the risk of aneuploidy and unbalanced chromosomal complements in the fetus. The most frequent structural abnormalities are translocations, especially reciprocal translocations (1.3–1.4%), being more common in oligozoospermic males than in azoospermics(2)(5) (6). In carriers of an apparently balanced reciprocal translocation, it could be an increased risk of reproductive issues. Reciprocal translocations t(17;22) with different breakpoints have been published in two cases with infertility male in the literature(7)(8). The existence of multiple independent structural abnormalities and resulting phenotypes are often more complex than expected. We report clinical, cytogenetic and copy number variations(CNVs) findings for the first man who suffers from teratospermia, and has both a balanced reciprocal translocation t(17;22)(p11.2;q11.2) and a microduplication in the region 10q23.31. In view of assisted reproductive techniques, it is especially important to gain information about the genetic causes of male infertility, as these defects can be transmitted across generation(s).

Materials And Methods

Study samples

The patient came to the hospital for infertility and genetic counseling. The study protocol was approved by the Ethics Committee of the First Affiliated Hospital of Guangxi Medical University, and written informed consent was
obtained from the patient.

Semen analysis

Briefly, semen analysis was performed according to the method recommended by the fifth edition of the World Health Organization guidelines(9). Semen samples were collected twice for patient with an interval of 2-7 days after abstinence. Sperm motility was calculated by counting more than 200 spermatozoa.

Karyotypes analysis

The peripheral blood cells were treated with colchicine for 1.5 hour, incubated in hypotonic solution and fixed with methanol-acetic acid solution, according to the laboratory standard program. The karyotype analysis were carried out with 400-550 bands in G-banding of metaphase chromosomes. Twenty metaphase counts and eight karyotypes were analyzed. The karyotypes were described according to the International Human Cytogenetic Nomenclature System (ISCN 2020)(10).

Molecular analysis

Y-microdeletion studies were performed using a multiplex PCR amplification based method(11). In brief, DNA was extracted using standard techniques followed by two separate multiplexed PCR reactions. The patient was considered to have Y-microdeletion, if a deletion was detected in at least one marker within the verification marker set.

Microarray analysis

CNVs analysis was performed in the illumnia NovaSeq 6000 (Illumnia Inc, USA). Experiments were carried out with the NovaSeq 6000 S4 Reagent Kit and the S4 flowcell, according to the manufacturer's protocol. The NovaSeq 6000 PE150 was used for genotype calling, quality control and CNVs identification. For annotation of genes in the deleted or duplicated genomic segments, the public databases including Database of DGV, ClinGen, OMIM, gnomAD, GeneReview and DECIPHER were used for interpretation and classification of the clinical significance of candidate CNVs.

Bioinformatics analysis

The data on expression levels in different normal tissues of candidate genes, which located on the breakpoints of translocation and duplication, were extracted from NCBI gene database(https://www.ncbi.nlm.nih.gov/gene/) and the projects of human protein atlas (HPA)(12)(http://www.proteinatlas.org). The functions of these genes were obtained from the published literature and the neXtProt knowledgebase(13)(https://www.nextprot.org). The interaction network of genes was performed in GeneMANIA(14)(https://www.genemania.org).

Results
A 35-year-old male who came to the department of prenatal and genetic diseases in our hospital for consultation during miscarriage of his wife, was referred for karyotype analyses. Physical examinations were practically normal in the couples. The medical history was unremarkable regarding some risk factors of infertility: no exposure to roentgen radiation or toxins, and no trauma of the tests were known. Two different semen analyses of the patient showed asthenospermia and teratospermia. The results of the normal sperm count of 20.1×10⁶/ml (≥15×10⁶/ml), lower progressive motility sperms 27.7% (A+B≥32%), and abnormal sperm morphology 100% (>96%) were observed, according to the guidelines for semen analysis from the fifth edition of World Health Organization (9). Normal spermatozoa from fertile men have elongated shape with a 2.4/1 length to transversal diameter ratio. The acrosome covers approximately 2/3 of the head surface, which closely attaches to the head. In contrast, spermatozoa from the cases possessed conspicuous head-shaped and acrosomal anomalies (Fig. 1AB). Sperm heads were close to the ratio of 1/1 spherical with absent or minute acrosomes. Others were pyriform or irregularly ovoid and had small acrosomes, not well attached to the nuclear surface or completely disengaged from it (acrosome hypoplasia). Unfortunately, we didn’t get medical information from their family members.

The cytogenetic analysis (G-banding) showed that patient’s karyotype was 46,XY,t(17;22)(p11.2;q11.2) (Fig. 2) and his wife’s karyotype was 46, XX. No microdeletion was found in AZF regions (sy84, sy86, sy127, sy134, sy254 and sy255) in the Y chromosome analysis. CNVs showed a microduplication approximately 224.98-kb in size, and the result described as seq[GRCh37]dup(10)(q23.31q23.31) chr10:g.91371499_91596485dup. However, this microduplication was not mentioned in any public database before (Fig. 3).

**Discussion**

Previously, reciprocal translocation between chromosome 17 and chromosome 22 had been described in two male patients with reproductive problems of repeated spontaneous abortions in his wife (Table 1). Interestingly, the two involving chromosomes are characterized by the presence of chromosome-specific low copy repeats (LCR)(15)(16). The enrichment of LCR precipitated a high frequency of nonallelic homologous misalignments and unequal recombination during the meiosis, leading to the instabilities in the region of the chromosome 17 and chromosome 22. It is well known that, duplication of chromosome 17p11.2 results in Potocki-Lupski syndrome (PTLS), while its reciprocal deletion leads to Smith-Magenis syndrome (SMS)(17). In addition, alteration of gene dosage on part of 22q is responsible for the aetiology of a number of human congenital anomaly disorders including cat eye syndrome (CES) and DiGeorge syndrome/velocardiofacial (DGS/VCFS)(18)(19). The dosage change of significant genes could play an important role in several distinct processes such as transcription, cell differentiation, and DNA repair. When translocation occurs, although the genome may change in balance, it will also have a serious impact, such as t(15;17) occurring in acute myeloid leukemia, and t(9;22) occurring in chronic myeloid leukemia (20)(21). Recent epidemiological studies have identified an association between male infertility and cancer, and some ‘male infertility-cancer genes’ have been established as risk factors in cancer progression (22). Some shared biological processes could explain the shared etiology of cancer and male infertility, such as cell survival, cell fate, and genome maintenance (Fig.4). Disruption in any of these pathways would be expected to lead to loss or damage of germ cells and the associated expression of male infertility.

Translocations involving chromosome 17 have been thought to be harmful for the fertility of the carrier (7). The breakpoint of chromosome 17p11.2, also the critical region of SMS, was contained genes involved in several pathogenesis of cancers and reproductive physiology processes. ALKBH5 (alkB homolog 5) was an ubiquitously expressed protein in testis and brain, and was described as a cancer/testis gene (Table 2)(23). In the animal study,
ALKBH5 resulted in impaired fertility by affecting meiotic metaphase-stage spermatocytes apoptosis(24). Stained testis and epididymis sections of ALKBH5 knockout male mice, observed to contain no mature sperm, but germ cells of degeneration resembling round, elongating, or elongated spermatids(25). In our patient, sperm morphology supported this result as well. Besides, DRC3 (Dynein regulatory complex subunit 3) was a critical hub for the control of flagellar motility, which was also key component of the N-DRC (nexin-dynein regulatory complex). DRC3 regulated to the waveform of flagella together with dynein g, and its mutant caused decreasing the movement speed(26). In addition, COP9S3 (COP9 signalosome subunit 3), known as CSN3, is a component of the COP9 signalosome complex (CSN), which involved in various cellular and developmental processes(27). CNS3 knockout mice could not finish meiosis phase I. Meanwhile, PLD6 (phospholipase D family member 6), also known as MitoPLD, is the endonuclease that plays a critical role in PIWI-interacting RNA (piRNA) biogenesis during the spermatogenesis(28). The destruction of UBB (Ubiquitin B) gene was related to the low expression of many proteins involving in spermatogenesis and the reducing of germ cell number(29). UBB gene knockout mice were infertility, because of the structure destruction in gonad and reproductive organ, resulting in unformed gametes(30). Some other genes, such as CCDC144NL-AS1, LLGL1, FLII, TOP3A and ULK2, were involved in important functions like cell proliferation(31), embryonic development(32)(33)(34) and autophagy(35). Genes exhibit multiple physiological and pathological functions depending on the tissue and/or cell type where they are expressed(36). Thus, genes that highly expressed in testis might probably play roles in the process of sperm function and male fertility. There are still several genes, including GID4, SPECC1 and PRPSAP2, expressed highly in testis. Resulting haploinsufficiency of these genes from translocation could produce an increased risk of male infertility. Since the role of some genes remain unexplored in the development of male reproductive, studies in this direction would be very interesting in the future.

Among the individuals associated with translocation of chromosome17, the rate of unbalanced gametes was up to 81% in the case of t(17;22)(q11;q12), most of others were around 50%(37). This suggested that together with chromosome 17 and chromosome 22 might be a risk factor for abnormal meiotic segregation. Genes mapped within or just adjacent to the breakpoint region of 22q11.2 had been identified to be involved in hematological malignancies such as chronic myeloid leukemia and other disorders in development(19)(21). Among them, there was a gene, SPECC1L(sperm antigen with calponin homology and coiled-coil domains 1 like), expressed highest in testis compare to other tissues(table2). This gene was first identified to be disrupted by a balanced translocation t(1,22)(21.3;q11.23) in a female patient with bilateral oromedial-canthal (Tessier IV) clefts(38). It encoded a ‘cross-linking’ protein that functionally interacts with both microtubules and the actin cytoskeleton, which was necessary for cell adhesion and migration(39). It was also found in the cases of Opitz G/BBB syndrome, SPECC1L mutations could cause syndromic forms of facial clefting which support the original correlation to chromosome 22q11.2(40). Another gene CDC45 (cell division cycle 45) was a member of the pre-initiation complex in DNA replication, which was important for early steps of DNA replication in eukaryotes. Biallelic mutations of CDC45 caused a spectrum of phenotypes including isolated short stature and craniosynostosis(41)(42). Meanwhile, it might promote hepatocellular carcinoma (HCC) or non-small cell lung cancer (NSCLC) and correlated with worse prognosis in patients(43)(44). Another well-studied gene, T-box transcription factor 1(TBX1), had been reported that its haploinsufficiency caused abnormal growth and remodeling in the pharyngeal apparatus and related structures(45). Same as, haploid 22q11 gene insufficiency in the patients disrupt orofacial and cranial nerve development by modifying retinoic acid-modulated anterior–posterior hindbrain differentiation(46)(47). These disruptions likely contributed to dysphagia in infants and young children with 22q11DS. Several other genes in the 22q11 region had been implicated in the pathogenesis of developmental disorders. It had been reported that gene PI4KA was implicated in the pathogenesis of cerebellar hypoplasia and arthrogryposis(48). Ess2 (also termed
Dgcr14) was a nuclear protein that bridged transcriptional regulators and spliceosomal complexes via distinct interacting domains, which might impact in the pathogenesis of DiGeorge syndrome(49). Gene SNAP29 has been shown to be involved in formation of primary cilia, epidermal differentiation, membrane fusion and autophagy, which implicated in a number of pathological conditions such as recessive neurocutaneous cerebral dysgenesis, neuropathy, ichthyosis, and keratoderma(50). Gene DGCR8 encodes a subunit of the microprocessor complex which mediates the biogenesis of microRNAs from the primary microRNA transcript. It could enhance Tri-negative breast cancer cell migration and invasion via targeting TGF-β(51). Taken these together, genes mention above were associated with developmental disorder and retardation, which also the shared biological processes of cancer and infertility, might also affect in spermatogonial differentiation and spermatogenesis.

It was known that the chromosomal rearrangement associated with other chromosomal changes, particularly those involving segmental duplications, might contribute to a very genomic instability(5)(52). Many implicated risk genes in CNVs were responsible for different cellular processes, including cell signaling, sensing and repair(53). Impairment of these genes was expected to disrupt the functions specifically involved with cellular development and lead to cause diseases. In addition to the reciprocal translocation, the array analysis also revealed a novel 224.98-kb microduplication in chromosome 10q23.31. Reports of 10q duplication with other chromosomal abnormality are uncommon, and two cases with breakpoints in 10q23.31(chr10:91371499-91596485) had been reported so far. DECIPHER Patient 341717 documented with growth delay, intellectual disability and emotional lability, detected an overlapped CNVs of 8.52Mb(chr10:90100579-98618234). Similarly, DECIPHER Patient 252137 documented with phenotypes including: delayed puberty obesity, autism, cognitive impairment, intellectual disability, and abnormality of limbs, head and neck, detected an overlapped CNV of 2.63Mb(chr10:89584411-92213522).

In current study, we identified a previously unreported copy number variation at 10q23.31(chr10:91371499-91596485). This microduplication encompassed approximately four genes, FLJ37201, KIF20B, LINC00865 and PANK1(table2). None of these genes were identified in OMIM as disease causing. By now, it is unknown whether one of these genes could be dosage sensitive and responsible for the male infertility. FLJ37201 was described as tigger transposable element derived 2 pseudogene. Although pseudogenes were considered to be evolutionally conserved, they were found to act as a gene reservoir that might allowed the genome to carry out novel functions effectively(54). It was reported that pseudogenes might be present in reproductive cells more than in somatic cells(55). Moreover, transposable elements could create chromosomal insults or rearrangements and impacted gene expression, which were recognized as contributors to genomic innovations as well as genome instability(56). In this view, with a higher expression in testis, FLJ37201 could be regarded as a new candidate gene for recognizing mechanisms in male infertility. LINC00865 was a member of long noncoding RNAs (IncRNAs). IncRNAs with sequence lengths over 200 nucleotides, were considered to be regulators of many cellular processes, particularly in tumorigenesis and cancer progression(57). It had been revealed that IncRNAs could be regulated in both gene level and transcription level, and induce both cell-cycle arrest and apoptosis(58). Difference with other IncRNAs, LINC00865 was indicated highly expression in the tissue of testis, which could be recognized as a cancer/testis gene. Since its role remain unexplored in male reproductive, studies in this direction would be very interesting.

KIF20B (previously called MPHOSPH1 or MPP1) was a member of the Kinesin-6 family, which had been involved in cerebral cortex growth and midbody organization of neural stem cells in mouse(59). It could accelerate or coordinate midbody maturation, and regulate later steps of maturation in a human cell line. Meanwhile, KIF20B was found to serve important roles in multiple types of cancer, which could function as cancer-testis antigen specific to
human bladder cancer (60). It also regulated cell proliferation, apoptosis and tumor growth in hepatocellular carcinoma associating with the tumor suppressor p53 (61)(62). Similarly, gene PANK1 (pantothenate kinase 1) worked as a p53 transcriptional target, played an importance role in metabolic regulation, as well as modulates energy balance in the adaptive(63). Taking these into account, this 10q23.31 duplications most likely represents a risk factor for sperm immotility and abnormal sperm morphology. Increasing dosage of the four duplicate genes might disrupt diverse cellular processes, and implicated in the pathogenesis of male infertility. Since there was no evidence of a phenotypically well-defined syndrome resulting from 10q23.31 duplication so far, and its clinical significance remains unclear. Combined with the balanced reciprocal translocation t(17;22), 10q23.31 duplication could have more severe consequences for gametogenesis, and could be treated as a risk factor in our infertility patient.

**Conclusion**

In this study, we have identified two chromosomal abnormalities, a balanced reciprocal translocation t(17;22) (p11.2;q11.2) and a microduplication in the region 10q23.31, in our patient suffering from teratospermia. Genes located in the translocation breakpoints or the region of duplication show the highly expression in the tissue of testis, which are associated with developmental disorder and retardation. They might be risk factors in spermatogonial differentiation and spermatogenesis. The haploinsufficiency of these genes in our case could be the cause of sperm immotility and abnormal sperm morphology. The two chromosomal abnormalities is apparently harmful with regard to infertility, could contribute to the genetic instability resulting in disease. In the long run, it is important to accumulate more cases and investigate the genes affect by structural chromosomal abnormalities, regardless of the severity or the absence of manifestations. It could be better to understand about the mechanisms which lead to varied phenotypes, and provide improved genetic counseling.

**Abbreviations**

CNVs: Copy Number Variations  
PCR: Polymerase Chain Reaction  
DGV: Database of Genomic Variants  
ClinGen: Clinical Genome Resource  
OMIM: Online Mendelian Inheritance in Man  
gnomAD: genome aggregation database  
DECIPHER: Database of Chromosomal Imbalance and Phenotype in Humans Using Ensembl Resources  
LCR: Low Copy Repeats  
PTLS: Potocki-Lupski Syndrome  
SMS: Smith-Magenis Syndrome  
CES: Cat Eye Syndrome
DGS: DiGeorge Syndrome
VCFS: Velocardiofacial
ALKBH5: AlkB homolog 5
DRC3: Dynein regulatory complex subunit 3
COPS3: COP9 signalosome subunit 3
PLD6: Phospholipase D family member 6
UBB: Ubiquitin B
LLGL1: LLGL scribble cell polarity complex component 1
CCDC144NL-AS1: Coiled-coil domain containing 144NL antisense RNA 1
FLII: FLII actin remodeling protein
TOP3A: DNA topoisomerase III alpha
ULK2: Unc-51 like autophagy activating kinase 2
GID4: GID complex subunit 4 homolog
SPECC1: Sperm antigen with calponin homology and coiled-coil domains 1
PRPSAP2: Phosphoribosyl pyrophosphate synthetase associated protein 2
SPECC1L: Sperm antigen with calponin homology and coiled-coil domains 1 like
TBX1: T-box transcription factor 1
CDC45: Cell division cycle 45
PI4KA: Phosphatidylinositol 4-kinase alpha
Ess2: Ess-2 splicing factor homolog
SNAP29: Synaptosome associated protein 29
DGCR8: DGCR8 microprocessor complex subunit
FLJ37201: Tigger transposable element derived 2 pseudogene
KIF20B: Kinesin family member 20B
LINC00865: Long intergenic non-protein coding RNA 865
PANK1: Pantothenate kinase 1
Declarations

Ethical Approval and Consent to participate: This study was approved by the Ethics Committee of the First Affiliated Hospital of Guangxi Medical University. Informed consent was obtained from all participants before the start of this study.

Consent for publication: The patient signed informed consent regarding publishing their data and photographs.

Availability of supporting data: The datasets used and analysed during the current study are available from the corresponding author on reasonable request.

Competing interests: The authors report no conflict of interest.

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Authors’ Contributions: SH participated in the project development and manuscript writing, HW, YQ analyzed and interpreted the data, LW, XL performed the experiments, YH reviewed and edited the manuscript. All authors read and approved the final manuscript.

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**Tables**

**Table 1.** the carriers of the reciprocal translocation t(17;22)

| Karyotype of the carrier                                    | Clinical outcome of the translocation | Reference          |
|-------------------------------------------------------------|--------------------------------------|--------------------|
| 46,XY,inv(1)(p13;q21),t(17;22)(p11:p11)                      | Recurrent abortion                   | (Kim et al. 2011)  |
| 46,XY,t(17;22)(q11;q12)                                     | Miscarriage;                         | (Geneix et al. 2002) |
|                                                             | Oligoteratozoospermia                |                    |

**Table 2.** Genes located at the breakpoint(17p11.2 and 22q11.2) and the duplicated region(10q23.31)
| Number | Genes       | Description                                      | Location          | Expression (the first / the second)                                                                 | function                                                                 |
|--------|-------------|--------------------------------------------------|-------------------|-----------------------------------------------------------------------------------------------------|--------------------------------------------------------------------------|
| 1      | ALKBH5      | alkB homolog 5                                   | 17p11.2           | Testis / Brain                                                                                     | Spermatogenesis(GO:0007283); Cell differentiation(GO:0030154)           |
| 2      | DRC3        | dynein regulatory complex subunit 3              |                   | Testis / Thyroid                                                                                   | Protein binding (GO:0005515)                                            |
| 3      | COPS3       | COP9 signalosome subunit 3                       | 17p11.2           | Testis / Bone marrow                                                                               | In utero embryonic development (GO:0001701); Protein binding (GO:0005515); Protein deneddylation (GO:0000338) |
| 4      | PLD6        | phospholipase D family member 6                  | 17p11.2           | Testis / Prostate                                                                                  | DNA methylation involved in gamete generation (GO:0043046); Meiotic cell cycle (GO:0051321); Spermatid development (GO:0007286) |
| 5      | UBB         | ubiquitin B                                      | 17p11.2           | liver / Testis                                                                                     | Male meiosis I (GO:0007141), Seminiferous tubule development (GO:0072520); Positive regulation of intrinsic apoptotic signaling pathway by p53 class mediator (GO:1902255) |
| 6      | LLGL1       | LLGL scribble cell polarity complex component 1  | 17p11.2           | Brain / Testis                                                                                     | Regulation of establishment or maintenance of cell polarity (GO:0032878); Regulation of protein secretion (GO:0050708) |
| 7      | CCDC144NL-AS1 | coiled-coil domain containing 144NL antisense RNA 1 | 17p11.2           | Testis / Placenta                                                                                  | knockdown of CCDC144NL-AS1 was related to conversion of human pluripotent stem cells. Knockdown of CCDC144NL-AS1 dramatically altered the distribution of cytoskeletal filamentous actin (F-actin) stress fibers compared to the negative control group treatment. |
| 8      | FLII        | FLII actin remodeling protein                    | 17p11.2           | Testis / Spleen                                                                                     | Multicellular organism development (GO:0007275); Actin binding (GO:0003779) |
| 9      | TOP3A       | DNA topoisomerase III alpha                      | 17p11.2           | Testis / Bone marrow                                                                               | Chromosome separation (GO:00051304); Meiotic cell cycle (GO:0051321); DNA topoisomerase activity (GO:0003916) |
| 10     | ULK2        | unc-51 like autophagy activating kinase 2        | 17p11.2           | Testis / Brain                                                                                     | Protein serine/threonine kinase activity (GO:0004674); Cellular response to DNA damage stimulus (GO:0006974); Neuron projection development (GO:0031175); Autophagy (GO:0006914) |
| 11 | GID4 | GID complex subunit 4 homolog | 17p11.2 | Testis / Esophagus | Ubiquitin protein ligase activity (GO:0061630); Protein ubiquitination (GO:0016567) |
| 12 | SPECC1 | sperm antigen with calponin homology and coiled-coil domains 1 | 17p11.2 | Brain / Testis | Actin cytoskeleton organization (GO:0030036) |
| 13 | PRPSAP2 | phosphoribosyl pyrophosphate synthetase associated protein 2 | 17p11.2 | Lymph node / Testis | Protein binding (GO:0005515); Negative regulation of catalytic activity (GO:0043086); 5-phosphoribose 1-diphosphate biosynthetic process (GO:00006015) |
| 14 | SPECC1L | sperm antigen with calponin homology and coiled-coil domains 1 like | 22q11.2 | Testis / Thyroid | Protein binding (GO:0005515); Cell adhesion (GO:0007155); Cell cycle (GO:0007049); Cell division (GO:00051301) |
| 15 | TBX1 | T-box transcription factor 1 | 22q11.2 | Testis / Prostate | DNA-binding transcription factor activity, RNA polymerase II-specific (GO:0000981); Cell population proliferation (GO:0008283); Negative regulation of cell differentiation (GO:0045596); Positive regulation of transcription, DNA-templated (GO:0045893) |
| 16 | CDC45 | cell division cycle 45 | 22q11.2 | Testis / Bone marrow | Single-stranded DNA binding (GO:0003697); Mitotic DNA replication preinitiation complex assembly (GO:1902977); Double-strand break repair via break-induced replication (GO:0000727); Regulation of chromatin silencing at telomere (GO:0031938) |
| 17 | PI4KA | phosphatidylinositol 4-kinase alpha | 22q11.2 | Brain / Testis | Phosphatidylinositol kinase activity (GO:0052742); Signal transduction (GO:0007165); Phosphatidylinositol-mediated signaling (GO:0048015) |
| 18 | Ess2 | ess-2 splicing factor homolog | 22q11.2 | Testis / Bone marrow | Protein binding (GO:0005515); mRNA splicing, via spliceosome (GO:0000398); Nervous system development (GO:0007399) |
| 19 | SNAP29 | synaptosome associated protein 29 | 22q11.2 | Testis / Brain | Protein binding (GO:0005515); Protein transport (GO:0015031); Synaptic vesicle fusion to presynaptic active zone membrane (GO:0031629) |
| 20 | DGCR8 | DGCR8 microprocessor complex subunit | 22q11.2 | Testis / Placenta | Primary miRNA processing (GO:0031053); Protein homodimerization activity (GO:0042803); Protein-RNA adaptor activity (GO:0140517) |
| 21 | FLJ37201 | tigger transposable | 10q23.31 | Testis | More present in reproductive |
| 22 | KIF20B   | kinesin family member 20B | 10q23.31 | Testis / Lymph node | Cell cycle arrest (GO:0007050); Cell division (GO:0051301); Positive regulation of cell population proliferation (GO:0008284); Positive regulation of cytokinesis (GO:0032467) |
| 23 | LINC00865 | long intergenic non-protein coding RNA 865 | 10q23.31 | Testis / Urinary bladder | Regulator of cellular processes |
| 24 | PANK1    | pantothenate kinase 1      | 10q23.31 | Liver / Kidney        | Coenzyme A biosynthetic process (GO:0015937); Phosphorylation (GO:0016310); Protein homodimerization activity (GO:0042803); Pantothenate kinase activity (GO:0004594) |

**Figures**

Figure 1

Morphology sperm images of our case. (A) Black arrow indicates a rounded acrosomeless head. White arrow indicates pyriform sperm head and midpiece comments are thick. (B) Black arrow indicates round without acrosome. White arrow indicates pyriform sperm head and less than 40% of the head is occupied by the acrosome.
Figure 2

Cytogenetic images of chromosome karyotype (from peripheral blood sample): 46, XY, t (17; 22) (p11.2; q11.2).
Copy number variations (CNVs) analysis was performed on the case. A microduplication 10q23.31 (chr10:91371499-91596485) had been shown, affecting genes of FLJ37201, KIF20B, LINC00865 and PANK1.

The network of genes located on the breakpoints of translocation and duplication (available from GeneMANIA). We used GeneMANIA to perform an interactome analysis the set of candidate genes obtained from the breakpoints and investigate the relationships among these genes within the combined genetic functional network.