Abstract

Infertility affects approximately 7% of men worldwide, and among these 50% of the cases are idiopathic. It is expected that most of the idiopathic male infertility may have a genetic origin. Even though some genes have been proposed or functionally verified to be responsible for male infertility, the genetic causes in many cases remain to be elucidated. The current study was designed to identify the genetic cause of infertility in a Pakistani family.

In the recruited family two brothers were suffering from infertility. The semen analysis revealed that they are suffering from oligo-asthenozoospermia with very poor forward progression of sperms. We analyzed the sperm morphology from the patient's semen smear slides and found out that they are suffering from multiple morphological abnormalities of sperm flagellum (MMAF). Whole-exome sequencing demonstrated a novel homozygous frameshift mutation, c.911_914AA, p.E305Gfs*14 in *DDX25/GRTH* gene. Subsequently, the identified mutation was confirmed through Sanger sequencing which endorsed the fact that the mutation in *DDX25/GRTH* gene is co-segregating with MMAF phenotype in the family and also following the Mendelian law of inheritance. Since pathogenic mutation in *DDX25/GRTH* has already been identified as a recurrent cause of male infertility, thus, altogether the results indicate that mutation (c.911_914AA, p.E305Gfs*14) in *DDX25/GRTH* gene is the genetic reason underlying asthenozoospermia in our subject family.