

Chapter 12

MALE INFERTILITY AND TREATMENT WITH ASSISTED REPRODUCTIVE TECHNIQUES

Gizem KÖPRÜLÜLÜ KÜÇÜK¹

Introduction

There have been many years of research about gender formation, the process of development of infants in the womb, and sex chromosomes which are object of curiosity for humans. Various theories have been produced in this subject. At early 20th century, when it became clear that sex chromosomes play a key role, this subject reached enlightenment. Thus, many ideas about this issue were disproved.

Sex formation process is a difficult and complex stage. It can occur as healthy if successive processes proceed smoothly. Problems that may arise from a disruption in the process can cause infertility.

Sex Cells Formation in Humans

Sex- specific, different characteristics develop both in women and men. The most obvious of this is the presence of eggs in women and the presence of sperms in men. These cells are generally called “gamet” and they are produced in gonads. Gamet producing process is called gametogenesis and has 4 steps:

1. Outer embryonic origin of sex cells and migration of these cells to gonads
2. Increase the number of sex cells through mitosis
3. Reduction of chromosomal numbers of sex cells by meiosis
4. Structural and functional maturation of sex cells

Although first step is observed both in women and men, there is sex-specific differences in other 3 steps.

Origin of sex cells and migration

The earliest forms of gametes in the embryonic process are called primordial germ cells (PGC). These cells first form outside the gonads and then migrate to the gonads to form sex cells. If primordial germ cells migrate to other stages where are expect the gonads, they will usually die. However, in the case of life, they develop as teratoma (Figure 1). Teratomas are amorphous structures containing differentiated tissues such as hair, skin, teeth, cartilage.

¹Lecturer, Istanbul Şişli Vocational School, gizem.koprululu@sisli.edu.tr

Although ICSI spreads on worldwide in last years, only last period there are possible risks because of random using of ICSI. These worries especially have recently emerged as result of recent advances in genetically determined male infertility.

ICSI is more fearful for emerging offspring in transmitting genetic anomalies than other forms of supporting reproduction techniques. Because an active spermatozoon which is necessary to begin all mechanism for oocyte penetration and to be exposed normal capacitation and acrosome reaction skips all physiological steps associated with fertilization. With skipping of these steps ICSI allows egg fertilization by a modified spermatozoon. Thus risk of genetic damage will increase in the offspring.

Mulhall and colleague are reported first time that fertilization and pregnancy are obtained by using ICSI with testicular spermatozoon from azoospermic patients which have deletion on DAZ region. This case is demonstrated that spermatozoon which carries deleted Y chromosome are completely effective on fertilization.

After that the same group are reported that birth of male children via ICSI from a male which has AZF deletion and also other workers are obtained the same results at the end of their studies. Following the Mendel possibilities, all of male childrens are inherited Y chromosome which has deletion.

In vitro fertilization (IVF) is a technique based on artificial fertilization of an egg by sperm under the in vitro conditions.

IVF is an important therapy method when other therapy methods are failed. Briefly IVF procedure includes; to follow the spawning period of a female, to obtain egg from the ovary and to fertilize this egg with a sperm in in vitro conditions in the laboratory environment and to transfer the zygote which is a fertilized egg for a successful pregnancy in the uterus.

Spermatozoon with deleted Y chromosome also transmits deletions to male childrens via IVF. In fact this case indicates that the spermatozoon obtained from an oligozoospermic subject which carries deletion on long arm can fertilize oocyte in in vitro conditions.

References

- Affara, NA. (2001). *The Role of the Y Chromosome in Male Infertility*, Expert Reviews in Molecular Medicine., Cambridge University Press, Cambridge, England,1-16.
- Akdere, H., Burgazli, M. (2013). *Erkek İnfertilitesine Genetik Yaklaşım*. Erkek Üreme Sağlığı. 15(54), 207-211
- Altıntaş, R., Durmaz, A., Karamazak, S., Tavmergen, E., Onay, H., Altay, AB. (2011). *Testiküler sperm ekstraksiyonu sonuçlarının AZF gen mutasyonları ile ilişkisi*. Turkish Journal of Urology, 37(3), 229-234.
- Ambulkar, PS., Waghmare, JE. and Tarnekar, AMA. (2013). *Cytogenetic and Molecular Analysis of Y Chromosome Microdeletions in Idiopathic Cases of Human Male Infertility*, 1-7.
- Calogero, AE., Garofalo, MR., Barone, N., Longo, GA., DePalma, A., Fichera, M., Rappazo, G., D'Agata, R., Vicari, E. (2002). *Spontaneous transmission from a father to his son of a Y chromosome microdeletion involving the deleted in azoospermia (DAZ) gene*. Journal of Endocrinological Investigation, 7(4), 631-634.
- Elsaid, H., Babiker, E., Abu, D., Alhassan, EA. and Abushama, H. (2014). *Detection of Y chromosome microdeletion in AZFb and AZFc loci using sequence tagged sites (STSs)*. 2(6), 384-388.

- Ender, A. and Ondes, B. (2012). *Approach to the Infertile Couple and Choice of the Optimum Patient for In Vitro Fertilization*. Journal of Academic Research in Medicine, 1(2), 57–60.
- Ferlin, A., Raicu, F., Gatta, V., Zuccarello, D., Palka, G. and Foresta, C. (2007). *Male infertility: role of genetic background*. Reproductive biomedicine online, 14(6), 734–745.
- Forti, G., Corona, G., Vignozzi, L., Krausz, C., Maggi, M. (2010). *Klinefelter's syndrome: a clinical and therapeutical update*. Sex Dev, 249–58.
- Gaddum-Rosse, P., Blandau, J. (1972). *Comparative Studies on the Proteolysis of Fixed Gelatin Membranes by Mammalian Sperm Acrosomes*. AM. J. ANAT. 133-144
- Gartner, LP, Hiatt, JL. (1997). *Colot Textbook of Histology*. WB Saunders Company. 406-412
- Gillbert, FS. (2003). *Developmental biology*, Seventh Edition, Sinauer Associates, Inc. Publishers, Sunderland, Massachusetts.
- Girardi, SK., Melnik, A., Schlegel, PN. (1997). *Submicroscopic deletions in the Y-chromosome of Infertile Men*. Human Reproduction, 12(5) 1635-1641.
- Guo Q, Lan, F, Xu L, Jiang Y, Xiao L, Huang H. and Zhou, Y. (2012). *Quadruplex real-time polymerase chain reaction assay for molecular diagnosis of Y-chromosomal microdeletions*. Fertility and Sterility, 97(4), 864–869.
- Güney, Al., Javadova, D., Kirac, D., Ulucan, K., Koc, G., Ergec, D., Tarcan, T. (2012) *Detection of Y chromosome microdeletions and mitochondrial DNA mutations in male infertility patients*. Genetics and Molecular Research, 11(2), 1039–1048.
- Hanley, N. A., Ball, S. G., Clement-Jones, M., Hagan, D. M., Strachan, T., Lindsay, S., Wilson, D. I. (1999). *Expression of steroidogenic factor 1 and Wilms' tumour 1 during early human gonadal development and sex determination*. Mechanisms of Development, 87(1–2), 175–180.
- Johnson, MD. (1998) *Genetic risks of intracytoplasmic sperm injection in the treatment of male infertility: recommendations for genetic counseling and screening*. Fertil Steril, 70:397-411.
- Kao, SH., Chao, HT. and Wei, YH. (1998). *Multiple deletions of mitochondrial DNA are associated with the decline of motility and fertility of human spermatozoa*. Molecular human reproduction, 4(7), 657–66.
- Kent-First, M., Muallem, A., Shultz, J., Pryor, J., Roberts, K., Nolten, W., Grosch, J. (1999). *Defining regions of the Y-chromosome responsible for male infertility and identification of a fourth AZF region (AZFd) by Y-chromosome microdeletion detection*. Molecular Reproduction and Development, 53(1), 27–41.
- Koşar PA. ve Özçelik N. Erkek infertilitesinde genetik değerlendirme, 2007; 14(3), 48–52.
- Kozina, V., Cappallo-Obermann, H., Gromoll, J., Spiess, AN. (2011). *A one-step real-time multiplex PCR for screening Y-chromosomal microdeletions without downstream amplicon size analysis*, 6(8).
- Krausz, C., McElreavey, K. (1999) *Y chromosome and male infertility*. Front Biosci, 4(1), 1-8
- Krausz, C., Hoefsloot, L., Simoni, M. and Tuttelmann, F. (2014). *EAA/EMQN best practice guidelines for molecular diagnosis of Y-chromosomal microdeletions*. Andrology, 2(1), 5–19.
- Li, ZA. (2012). *New Molecular Diagnostic Approach to Assess Y Chromosome Microdeletions in Infertile Men*, 40(1), 237–248.
- Mulhall, JP, Reijo, R., Alagappan, R., Brown, L., Page, D., Carson R. (1997). *Azoospermic men with deletion of the DAZ gene cluster are capable of completing spermatogenesis: fertilization, normal embryonic development and pregnancy occur when retrieved testicular spermatozoa are used for intracytoplasmic sperm injection*. Human Reproduction. 503-8.
- Pazarba, A. (2011). *Erkek İnfertilitesinin Sitogenetiği*, 230–245.
- Plaseski, T., Noveski, P., Trivodalieva, S., Efremov, GD., Plaseska- Karanfilska, D. (2008). *Quantitative fluorescent-PCR detection of sex chromosome aneuploidies and AZF deletions/ duplications*. Genet Test, 595-605
- Poongothai, J., Gopenath, TS. and Manonayaki, S. (2009). *Genetics of human male infertility*. Singapore medical journal, 50(4), 336–347.
- Prasad, SV., Skinner, SM., Carino, C., Wang, N., Cartwright, J., Dunbar, BS. (2000). *Structure and function of the proteins of the mammalian Zona pellucida*. Cells Tissues Organs 166(2):148-164.
- Rolf, C., Gromoll, J., Simoni, M., Nieschlag, E. (2002) *Natural transmission of a partial AZFb deletion of the Y chromosome over three generations*. Human Reproduction, 9(4), 2267-2271.
- Rowe, PJ. and Griffin, PD. (2002) *Current Practices and Controversies in Assisted Reproduction*. World Health, 01 – 381.
- Salicioni, AM., Platt, MD., Wertheimer, EV. (2007). *Signalling pathways involved in sperm capacitation*. Soc Reprod Fertil Suppl, 245-59.
- Sevinç, D., Zehir, A., Biricik, A., Sertyel, S., Kahraman, S., Güney, I. (2002). *The relationship between human Y chromosome microdeletions and sperm morphology*, Marmara Medical Journal , 227-232.

Shah, K., Sivapalan, G., Gibbons, N., Tempest, H. and Griffin, DK. (2003). *The genetic basis of infertility*. *Reproduction*, 13–25.

Stouffs, K. and Lissens, W. (2012). *X chromosomal mutations and spermatogenic failure*. *Biochimica et Biophysica Acta (BBA) - Molecular Basis of Disease*, 1822(12), 1864–1872.

Tagliarini, E. B., Assumpção, J. G., Scolfaro, M. R., de Mello, M. P., Maciel-Guerra, A. T., Guerra Júnior, G., & Hackel, C. (2005). *Mutations in SRY and WT1 genes required for gonadal development are not responsible for XY partial gonadal dysgenesis*. *Brazilian Journal of Medical and Biological Research*, 38(1), 17–25.

Thielemans, BF, Spiessens, C., D'Hooghe, T., Vanderschueren, D. and Legius, E. (1998). *Genetic abnormalities and male infertility*. *European journal of obstetrics, gynecology, and reproductive biology*, 81(2), 217–225.