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The Frequency of Chromosomal Abnormalities in Men With Azoospermia and Oligoasthenoteratozoospermia: a Preliminary Study

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Abstract: The aim of this study is to investigate the frequency of chromosomal abnormalities in men with severe andrological infertility. In 50 men with azoospermia and severe oligoasthenoteratozoospermia (OAT), who referred for our intracytoplasmic sperm injection program, a cytogenetic study has been prospectively carried out. Peripheral blood lymphocytes were cultured for chromosomal analysis and for each proband 30 metaphases were analyzed by GTG banding technique. Major chromosomal abnormalities were detected in 4 of cases (8%). There were 3 sex-chromosome abnormalities, 46

XXY in all 3 cases, and one autosomal chromosomal abnormality 46 XY, t (1;7) (P32;Q32). Although the sample size is small, the high frequency of chromosomal abnormalities detected in this preliminary study emphasizes the importance of chromosomal analysis in subfertile men. As prenatal diagnosis is indicated if an infertile man with an abnormal karyotype fathers a child, it is particularly important to know this fact before providing infertility treatment.

Key Words: Male infertility, chromosomal abnormalities

Introduction

Many survey has clearly shown an increased incidence of chromosomal abnormalities in subfertile males and it is estimated that the incidence of chromosomal abnormalities among the population of infertile males is 4 to 5 % compared with 0.5 to 0.7 % in general population (1-4). In addition to the recognizable structural abnormalities of the sex chromosomes and autosomal chromosomes, specific gene mutations and nonspecific genetic syndromes may be associated with male infertility (1). Although the exact mechanism is not clear, it has been suggested that a wide variety of chromosomal anomalies exert an adverse effect on spermatogenesis, resulting in azoospermia or severely impaired semen parameters (5). Today, intracytoplasmic sperm injection (ICSI) is the treatment of choice for andrological subfertility, allowing fertilization and pregnancy rates close to those of natural conception. However, since infertility treatment with ICSI is mainly aimed at a male population with particular risk for chromosomal anomalies and injection of a chromosomally abnormal sperm increases the incidence of chromosomal abnormality in offspring, screening for karyotype abnormalities in males with severe andrological subfertility is recommended in the male partner prior to ICSI (4). This allows the appropriate patient counseling and also provides in-

formation about patients in whom prenatal diagnosis should be indicated.

The purpose of this study is to investigate the frequency of chromosomal abnormalities in 50 men who referred to our ICSI program due to azoospermia or severe oligoasthenoteratozoospermia.

Materials and Methods

In 50 men with azoospermia and oligoasthenoteratozoospermia (OAT), who referred to Assisted Reproductive Technologies and Reproductive Endocrinology Unit of Sevgi Hospital for evaluating their chances of micromanipulation, a prospective study was carried out to detect the frequency of chromosomal abnormalities. Thirty-three of patients were azoospermic and 17 have had OAT. Patients with OAT had a progressive motile sperm count with a normal morphology below 0.5 million/ml. The morphology was evaluated as defined by Kruger et al (6). All patients were initially evaluated by urologist and conventional diagnostic work-up including patient's history, genital examination, ultrasonography and hormone analysis were performed. For chromosomal analysis, peripheral blood lymphocytes were cultured and for each proband 30 metaphases were analyzed by Trispsin-Giemsa (GTG) banding technique.

	Number of patients	Sex-chromosome abnormalities	Autosomal chromosome abnormalities	Total
Azoospermia	33	3 (9 %)	-	3
OAT	17	-	1 (5.8 %)	1
Total	50	3	1	4

Table 1. Chromosome analysis of men with andrological infertility

OAT : Oligoasthenoteratozoospermia

Results

Four (8 %) of the 50 men examined were found to have chromosomal anomalies. Three of these were sex chromosome abnormalities, 46 XXY in all 3 cases and another patient was diagnosed as having an autosomal chromosomal abnormality 46 XY, t(1;7)(p32;q32). Table 1 shows the general results. The frequency of abnormal karyotype in azospermic patients was 9 % (3/33) and all affected the sex chromosomes. In the OAT group, the frequency of chromosomal abnormality was 5.8 % (1/17) and it was detected in autosomal chromosome.

Discussion

Male factor is responsible in approximately 40 % of infertility (1,7). Among the many causes of male subfertility, chromosomal anomalies are well-documented and known factors. There are many reports indicating that the incidence of chromosomal anomalies in the male subfertile population is significantly increased (1-3,8,9). It has been reported that mean sperm count are significantly lower in chromosomally abnormal men than in men with a normal karyotype and the severity of spermatogenic impairment and the incidence of chromosomal abnormalities seem to be positively correlated (4,8). The incidence of chromosomal abnormalities has been reported to increase up to 15.4 % in azospermic males whereas it is approximately 6 to 7 % in oligospermic men with a sperm count below 10 million/ml. (3,4). Retief et al (9) reported a 7.1 % frequency of major chromosomal abnormalities in his study of 496 infertile males in whom 21 % were azospermic. Bourrouillou et al (3) found higher incidence (10.3 %) in 952 infertile males but in this study 40 % of patients were azospermic. All these studies pointed out that the frequency of chromosomal abnormalities are higher in the azospermia group than in those the oligospermia group and more than 90 % of abnormalities affects

sex chromosomes in azospermic patients whereas the autosomal chromosome abnormalities are more frequent in patients with oligozoospermia. Our findings support these reports and three sex chromosome abnormalities detected in our study were seen in azospermic patients and one patient with OAT had autosomal abnormality.

The recent introduction of intracytoplasmic sperm injection (ICSI) by Palermo et al (10) opened a new era for men with extremely poor semen parameters. This followed by the use of epididymal and testicular spermatozoa for ICSI in patients with obstructive and non-obstructive azoospermia and this offered hope to azospermic patients for fathering a child, even in patients with mosaic Klinefelter's syndrome (2). Currently, ICSI in the treatment of severe male factor infertility allows fertilization and pregnancy rates close to those of natural conception. However, as infertility treatment with ICSI is mainly applied for male subfertility and these men have an increased risk for chromosomal abnormality, there is an increased risk for having an chromosomally abnormal offspring. The results of prenatal karyotype and prospective follow-up of children born after ICSI do not indicate an increase in congenital malformations and it seems that using spermatozoa from chromosomally normal males does not increase the risk of fetal chromosomal abnormalities. Therefore some centers do not recommend strict prenatal diagnosis on the basis of ICSI alone unless the woman carries an independently increased risk. On the other hand, due to the fact of increased rate of chromosomal abnormality in the presence of andrological infertility, screening for karyotype abnormalities should be part of the diagnostic work-up carried out in the male partner prior to ICSI. Baschat et al (4) performed chromosomal analysis on the male partners of 32 couples with andrological infertility before ICSI and found 2 constitutional chromosomal translocations (6.4 %). In one of these two couples with paternal translocation, a twin pregnancy was achieved and amniocentesis revealed an un-

balanced 22, Y translocations in one fetus. This study emphasized the importance of pre-treatment cytogenetic investigation of male partner.

In conclusion, ICSI is currently the treatment of choice for male subfertility. However, when spermatozoa from men with a pathological karyotype are used for ICSI, the offspring may have an increased risk for chromosomal abnormality. Therefore, routine cytogenetic analysis of a male partner prior to ICSI should be advocated for both the appropriate coun-

seling of patients and also selecting the patients who will be candidates for prenatal diagnosis.

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