

RE: TESTICULAR HISTOPATHOLOGICAL DIAGNOSIS AS A PREDICTIVE FACTOR FOR RETRIEVING SPERMATOZOA FOR ICSI IN NON-OBSTRUCTIVE AZOOSPERMIC PATIENTS

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Int Braz J Urol. 2005; 31: 338-341

Dear Editor,

ICSI has allowed some couples to have genetic offspring using a small number of spermatozoa from the testes. It seems that these patients have small foci of spermatogenesis in the testes even though remaining azoospermic. It is possible that they present a minimum quantitative threshold of spermatogenesis which must be exceeded for any spermatozoa to reach the ejaculate, estimated to be 4 to 6 mature spermatids per tubule (1). Conventional teaching has been that men with azoospermia and serum follicle-stimulating hormone concentrations more than 2 to 3 times normal have severe testicular failure not amenable by any conventional therapy. However, Kim et al. demonstrated that, 30% of those men who were previously advised against testicular biopsy if atrophy was present, were potentially able to initiate a pregnancy in the era of testicular sperm extraction with advanced micromanipulation techniques (2).

We have read with great interest the recent article by Glina et al. showing that the percentage of patients with positive sperm retrieval according to histological testicular pattern was 50% in patients with hypospermatogenesis, 33% in patients with maturation arrest, and 40% in patients with Sertoli cell only syndrome. Even though differences in sperm retrieval compared to other series (80% for hypospermatogenesis, 50% for maturation arrest and 20% for Sertoli cell only syndrome) have been brought to our attention, an important message was delivered by their article. The pregnancy rate was only 3/16 procedures, (18.75%) in patients with non-obstructive azoospermia. This does not differ from a previous study that showed a pregnancy rate of 22% in patients with non-obstructive azoospermia (3).

Non-obstructive azoospermic patients may be suffering from a genetic defect or a genetically determined barrier to reproduction. Therefore, it is not surprising that, despite succeeding in extracting live spermatozoa in non-obstructive cases of azoospermia, the pregnancy rates are significantly lower when compared to those with obstructive azoospermia (4).

Y-chromosome microdeletion screening is recommended in cases of severe spermatogenetic impairment by numerous societies (Société Française de Génétique Humaine, European Society of Human Reproduction and Embryology, European Association of Urology and American Urological Association). Investigators identified different chromosomal regions containing independent loci related to male gametogenesis and azoospermia (azoospermia factors, or AZFs). More specifically, at least 3 non-overlapping regions of Yq (called AZFa, AZFb, and AZFc) have been firmly related to male infertility, which may be related with the possibility of sperm retrieval for assisted reproductive techniques. Consequently, molecular diagnosis of Y-chromosome microdeletions is now available and routinely indicated in subfertile patients with low sperm concentrations ($< 5 \times 10^6/\text{mL}$). As many cases of male infertility are likely to be of a genetic origin, the potential risk of transmitting infertility to future generations is of great concern. In fact, any patient with secretory azoospermia should undergo a Karyotype and Y chromosome microdeletion search. Therefore, the authors should state the reason for not asking for Y microdeletion evaluation.

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Respectfully,

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REPLY BY AUTHORS

We fully agree with Dr. Pasqualotto that any man with severe oligospermia or non-obstructive azoospermia that would be submitted to ICSI should undergo a complete genetic screening. This includes karyotype and Y chromosome microdeletion search

and this is part of our routine work-up. However, we did not report that in our paper because the objective was to learn, in our experience, the role of previous histological testicular pattern as a prognosis for sperm retrieval in non-obstructive azoospermic men.