

Testicular sperm extraction (TESE) and intracytoplasmic sperm injection (ICSI) for non-obstructive azoospermia

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SUMMARY

The use of prior diagnostic testicle biopsy to predict success or failure of testicular sperm extraction (TESE) with ICSI in patients with non-obstructive azoospermia caused by testicular failure.

INTRODUCTION

The discovery that azoospermic men with germinal failure often have tiny foci of intact spermatogenesis somewhere in their testes has brought hope that these men could now father a child by virtue of testicular sperm extraction (TESE) and intracytoplasmic sperm injection (ICSI) (Silber et al., 1994 and Silber et al., 1995a). There has also been some hope expressed that early round spermatids could be found and used for ICSI in patients who have no sperm recoverable. We wish to present our results and our analysis. Furthermore, we

wished to determine what impact deletions in the Y chromosome might have on the type and severity of testicular defect and on the pregnancy rate (Silber et al., 1995b).

MATERIALS AND METHODS

One hundred twenty-four (124) azoospermic men with biopsy-documented testicular failure caused by Sertoli cell only or maturation arrest, and 35 severely oligospermic men ($< 1 \times 10^6$) underwent Y chromosomal STS (sequence tagged site) mapping. Forty-nine of the Y-tested azoospermic men, and 28 of the Y-tested severely oligospermic men, underwent testicular sperm extraction (TESE) and intracytoplasmic sperm injection (ICSI). In addition, 74 men with non-obstructive azoospermia (who were not Y-tested) caused by germinal failure underwent TESE-ICSI. Forty-five patients with non-obstructive azoospermia caused by testicular failure underwent diagnostic testicle biopsy prior to a subsequent TESE-ICSI procedure. The diagnostic testicle biopsy was analyzed quantitatively, and correlated to the results of subsequent attempts at TESE-ICSI (Table 1).

Table 1

	# Patients With or Without Mature Spermatids Found on Histology	# Patients With Sperm Found at TESE-ICSI	# Pregnant (Ongoing) or Delivered)
With Sperm	26	22 (85%)	12 (55%)
Without Sperm	19	1 (5%)	0 (0%)
Total	45	23 (51%)	12 (52%)

RESULTS

Spermatogoa and elongated spermatids were recoverable in 46 (62%) of the 74 azoospermic couples. Neither embryo transfer rate (58%), 2PN fertilization rate (39%), cleavage rate (81%), nor the delivered pregnancy rate (23%) per initiated cycle was affected by whether the pathology was Sertoli cell "only," maturation arrest, post-chemotherapy, or cryptorchid atrophy (Silber, 1995 and Silber et al., 1995c).

In the 28 men (38%) in whom no sperm was found at TESE, round spermatids were not found, either in the TESE procedure itself, or in a subsequent examination of histologic sections. Round spermatids were never found in the absence of elongated spermatids or sperm.

However, success or failure of TESE was predictable by prior testis biopsy (Silber and Rodriguez-Rigau, 1981; Silber et al., 1995a). Seventeen (11%) of the 159 infertile men had deletions of the DAZ region of the Y chromosome. None of the 100 controls with normal spermatogenesis, and none of the fathers of DAZ-deleted infertile men (six tested) had DAZ deletions.

The site and size of the Y deletion did not correlate in azoospermic men with a specific finding of Sertoli cell only or of maturation arrest. However, smaller Y defects were associated with finding some sperm at TESE, and larger Y defects were associated with finding no sperm at TESE. Of the total of 17 Y-deleted men, 12 had deletions limited to interval 6, and 10 of those (83%) had sperm in the testis. Five had deletions extending beyond the bounds of interval 6, and none (0%) of those had any sperm at all in the testes. When sperm were recoverable, there was no difference in pregnancy rate with ICSI whether the man was Y-deleted (40%) or Y-intact (50%).

CONCLUSIONS

The specific pathology of azoospermic germinal failure (Sertoli cell "only," maturation arrest, cryptorchidism, etc.) had no effect on the likelihood of finding sperm with TESE-ICSI or on the pregnancy rate. In the absence of elongated spermatids or sperm, round spermatids could not be found. We further found that a large series of infertile men continues to demonstrate deletions of the DAZ region of the Y chromosome (12% with azoospermia and 6% with severe oligospermia). In addition, the presence of Y deletions does not preclude the finding of sperm sufficient for ICSI in the testes of azoospermic men. Larger deletions of the Y are associated with the total absence of testicular sperm, but smaller deletions are associated with small numbers of sperm that are sufficient for ICSI. Thus, prior diagnostic testicle biopsy analyzed quantitatively is extremely useful for predicting which patients will have success or failure with TESE-ICSI.

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