IN VITRO FERTILIZATION WITH TESTICULAR SPERM EXTRACTION IN A MALE WITH CYSTIC FIBROSIS AND CONGENITAL BILATERAL ABSENCE OF THE VAS DEFERENS BEFORE AND AFTER ELEXACAFTOR/TEZACAFTOR/IVACAFTOR

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OBJECTIVE

To report a case of in vitro fertilization (IVF) with testicular sperm extraction (TESE) in a male with cystic fibrosis (CF) and congenital bilateral absence of the vas deferens (CBAVD) before and after initiation of elexacaftor/tezacaftor/ivacaftor (ETI; Trikafta), examining the impact of CFTR modulator therapy on reproductive outcomes.

BACKGROUND

Cystic fibrosis (CF) is an autosomal recessive disorder with a US prevalence of approximately 7.97 per 100,000. Historically, median survival was in the mid-30s, but with highly effective CFTR modulators, life expectancy now surpasses 50 years. As patients with CF live longer, healthier lives, more are pursuing parenthood.

In males with CF, infertility is most commonly due to congenital bilateral absence of the vas deferens (CBAVD), leading to obstructive azoospermia, though spermatogenesis is typically preserved. Data on the impact of CFTR mutations on sperm function are conflicting; some evidence indicates men with CF have lower sperm quality, greater difficulty with retrieval, and worse ICSI outcomes compared with CBAVD-only patients. Many rely on assisted reproductive technologies (ART) such as TESE with ICSI, with cohort studies reporting sperm-retrieval success >98% and live-birth rates above 75% when IVF is pursued.

In females, CFTR dysfunction can thicken cervical mucus and alter pH, hindering sperm transport and fertilization. CFTR modulators — particularly elexacaftor/tezacaftor/ivacaftor (ETI; Trikafta) — appear to *enhance* female fertility, with increased pregnancy rates likely due to improved cervical mucus hydration and normalized pH.

Clinical Gap: The reproductive benefits of CFTR modulators in females are increasingly recognized, but data on their impact on male fertility — spermatogenesis and sperm quality — remain lacking. No studies to date have compared pregnancy outcomes using TESE before and after initiation of ETI in male CF patients.

DESIGN & METHODS

Study Type: Retrospective case report.

Patient: A 39-year-old male with CF and CBAVD and his 36-year-old female partner with recurrent pregnancy loss.

Comparison: IVF/TESE cycles performed *prior to* ETI initiation were compared to a subsequent cycle *after* ETI initiation.

Outcomes Assessed:

- Androgenization (serum testosterone)
- Semen analysis parameters
- Oocyte retrieval & fertilization
- Blastulation rates
- Preimplantation genetic testing (PGT) results

Analysis: Descriptive comparison given the case report design.

RESULTS

Three IVF/TESE cycles were performed: two prior to ETI initiation and one following ETI initiation.

Parameter	TESE #1 (Pre-ETI, Age 31)	TESE #2 (Pre-ETI, Age 35)	TESE #3 (Post-ETI, Age 36)
Oocytes Retrieved	**22**	**16**	**Pending**
Blastocysts Vitrified	7	—	—
Embryos Biopsied (PGT)	6	2	2
Euploid Embryos	1	2	Pending
Mosaic Embryos	1	0	Pending
Azoospermia (Post-ETI)	—	—	Persistent (Ejaculate 0.1 mL)
Serum Testosterone	—	—	436 ng/dL

Key Finding: Despite ETI initiation, persistent azoospermia was confirmed on semen analysis (ejaculate volume 0.1 mL). Androgenization was appropriate (testosterone 436 ng/dL), indicating ETI did not negatively affect androgen production.

CONCLUSIONS

While ETI confers substantial systemic benefits in males with CF, this case demonstrates no clear improvement in ART outcomes following initiation of CFTR modulator therapy, evidenced by:

- Persistent azoospermia on post-ETI semen analysis
- Continued poor blastulation across all cycles

The female partner's advancing age (31 to 36 years across cycles) may independently affect oocyte quality and embryo outcomes — an important confounder when interpreting differences between pre- and post-ETI cycles.

As more individuals with CF pursue parenthood due to improved survival with CFTR modulators, prospective studies are needed to define the reproductive implications of ETI and other CFTR modulators in males.

SUPPORT

None to declare.