Dual Causes Of Primary Infertility In A Patient With Cystic Fibrosis

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Citation

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Abstract

The Case Report of a 32-year-old male patient with cystic fibrosis and primary infertility is reported. The patient had unilateral absence of the vas deferens, evidence of azoospermia on semen analysis, and rare evidence of spermatogenesis on testicular sperm extraction (TESE). This Case Report illustrates the importance of TESE in evaluation and diagnosis of male infertility, in the setting of cystic fibrosis.

INTRODUCTION

Infertility in a couple is commonly defined as inability of conception despite frequent unprotected intercourse for a one-year period ([1]). Congenital bilateral absence of the vas deferens (CBAVD) is thought to account for approximately 1% of patients first seen with male infertility ([2]). Several studies have demonstrated that CBAVD has a strong association with mutations in the cystic fibrosis transmembrane conductance regulator (CFTR) gene on chromosome 7, thus it is strongly linked to cystic fibrosis (CF) ([3]). Almost all patients with CF have been determined to have CBAVD that result in obstructive azoospermia unable to be corrected surgically ([4]). Nearly 80% of Caucasian patients with CBAVD have at least one gene mutation in CFTR, with the most common mutation being ΔF508 ([3]).

It has long been thought that men with cystic fibrosis undergo normal spermatogenesis, and infertility is solely due to obstruction, or CBAVD ([3]). There is no doubt that most men with CBAVD have obstructive infertility, but recent literature reviews report rare cases of men with CBAVD and concomitant abnormal spermatogenesis. We present the case report of a male with CF, unilateral absence of the vas deferens and primary infertility whose testis biopsy revealed few tubules with spermatogenesis and no active sperm noted.

CASE REPORT

A 32-year-old Caucasian male was first seen with a three-year history of primary infertility. His medical history was significant for cystic fibrosis (diagnosed at six weeks), pancreatic insufficiency, and gastroesophageal reflux disease. In the past, DNA studies have determined the patient to be homozygous for the ΔF508 gene. The patient's wife tested negative for the presence of the CF gene. No history of childhood cryptorchidism, radiation, varicocele, or sexually transmitted disease was noted to explain the infertility. The patient denied any history of alcohol abuse or tobacco use. No significant family history of fertility problems was noted. The patient's surgical history was significant for an umbilical hernia repair.

After three years of inability to achieve a pregnancy, the patient decided to pursue a fertility work-up. A semen analysis was performed that showed azoospermia. Serum follicle-stimulating hormone (FSH), luteinizing hormone (LH), prolactin, and testosterone levels were within normal limits.

Physical examination demonstrated a well-developed male with normal secondary sexual characteristics. Genitourinary (GU) examination showed testicles descended bilaterally and were of normal consistency with no palpable masses. The right vas deferens was not palpable. However, a small left sided tubular structure in the spermatic cord was palpable which could represent a small scarred vas deferens or an agenetic vas deferens. The rectal examination showed no abnormalities. Scrotal ultrasound was negative for varicocele, but did show significant tubular ectasia bilaterally.

The patient underwent TESE for evaluation of

spermatogenesis and storage for possible future intracytoplasmic sperm injection. Seminiferous tubules were harvested and noted to be gray in appearance. Specimens were then sent for cytological analysis. Findings concluded that few tubules exhibited moderately active spermatogenesis, whereas most others appeared to be hyalinized. Finally, significant portions were indeterminate in appearance, and no viable sperm were present. The patient, and wife, were appraised of the above results and chose to use donor sperm for artificial insemination.

DISCUSSION

This Case Report illustrates the rare scenario when two separate defects, congenital absence of the vas deferens and abnormal spermatogenesis, both likely contribute to primary male infertility. Well-known is that patients with cystic fibrosis commonly have obstructive azoospermia due to CBAVD ([5]). Also assumed for years is that patients with CBAVD are infertile solely due to obstruction of sperm, and that spermatogenesis in these patients is normal ([3]). Recent review of the literature makes this a controversial subject in limited reports of patients with CBAVD and concomitant abnormalities in spermatogenesis.

Multiple studies of patients with CBAVD suggest that spermatogenesis is normal. Okada and colleagues noted that spermatogenesis was not significantly impaired on examination of testicular biopsy in ten patients with CBAVD ([6]). Goldstein and Schlossberg reported slight hypospermatogenesis in two patients, with CBAVD and normal spermatogenesis in seven men ([7]). These studies led to the idea that men with cystic fibrosis and CBAVD have normal sperm function and could use TESE successfully to obtain sperm for intracytoplasmic sperm injection (TESE). This process would allow these patients with CBAVD to potentially achieve a successful pregnancy.

More recent studies suggest an association exists between patients with CBAVD and abnormal spermatogenesis. Larriba and colleagues reported that CBAVD, combined with the related 5T variant in the CFTR gene, may lead to decreased spermatogenesis ([8]). This Case Report supported the possibility that mutations in the CFTR gene can lead to both obstructive and non-obstructive causes of azoospermia on the basis of the pathologic findings described above. In the Okada and colleague study, 30% of patients with CBAVD exhibited concomitant hypospermatogenesis histologically ([6]). Meng and colleagues' reported that 12% of the cohort studied with CBAVD had abnormal spermatogenesis ([3]).

Studies are limited in describing fertility in male patients with cystic fibrosis. Men with CBAVD are presumed to be sterile due to the inability to transport sperm from the vas deferens to the urethra. TESE and ICSI have made it possible for men with CBAVD to father a child. McCallum and co-workers reported that 62.5% of the cohort studied with CBAVD achieved a pregnancy in their trial ([4]). Their study affords men with CBAVD the opportunity to have children if they do not have abnormal spermatogenesis.

Apparent is that conflicting information exists regarding the possibility of a link between CBAVD and abnormal spermatogenesis. Significant implications exist to these studies regarding the chance of conceiving a child for these patients. Also, important to note is that one should not make the assumption that patients with CBAVD uniformly have normal spermatogenesis. Patients with CBAVD carry the possibility of having a genetic reason for abnormal spermatogenesis, but future research needs to be conducted in this area to better define the cause of this problem.

This Case Report illustrates that patients with primary male infertility can have multiple problems that prohibit them from achieving a pregnancy. Patients with absent vas deferens and an abnormal semen analysis who desire assisted reproduction should be offered a TESE with cytological analysis. Technologic advances of TESE and ICSI make achieving a successful pregnancy possible for these patients. The female partner of these patients should undergo genetic testing to determine CF status to provide the parents with the most accurate information possible about having a child with cystic fibrosis. In this Case Report, the patient's wife tested negative for the CF gene. Future research needs to be conducted in patients with CBAVD with abnormal spermatogenesis to offer them more accurate information regarding their chance of success in achieving a pregnancy.

CONCLUSION

This Case Report illustrates the rare scenario when two separate defects, congenital absence of the vas deferens and abnormal spermatogenesis, both likely contribute to primary male infertility in this patient. Patients with CBAVD and an abnormal semen analysis who desire assisted reproduction should be offered a TESE with cytological analysis. Technologic advances of TESE and ICSI make achieving a successful pregnancy possible for these patients.

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