Case Report

Diagnostic dilemmas in the management of a case of azoospermia due to adult onset hypogonadotropic hypogonadism along with posttubercular epididymal obstruction

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Abstract

Adult-onset idiopathic hypogonadotropic hypogonadism (HH) is one of the rare but reversible cause of male infertility. It is one of the few causes of non-obstructive azoospermia (OA). In very rare situations, obstructive azoosperima is also seen along with non-OA. We report our experience with the management of such a case of male infertility – a case of adult-onset HH with posttubercular epididymal obstruction. Index case was a 33-year-old male diagnosed with adult-onset HH. He had persistent azoospermia after 6 months of gonadotropins therapy. On further evaluation, he was also found to have OA (posttubercular epididymal obstruction). The *in vitro* fertilization (IVF)-Embryo Transfer (ET) with percutaneous epididymal sperm aspiration was successful in achieving a pregnancy.

Keywords: Azoospermia, hypogonadotropic hypogonadism, intracytoplasmic sperm injection, *in vitro* fertilization-et, percutaneous epididymal sperm aspiration, testicular sperm extraction

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INTRODUCTION

Adult-onset idiopathic hypogonadotropic hypogonadism (HH) is an uncommon cause of azoospermia, leading to male infertility. In such cases, gonadotropin therapy can restore the spermatogenesis and reverse infertility. The incidence of congenital HH is approximately 1 to 10:100,000 live births, and one-third of the cases are idiopathic.[1]

Infertility, in cases of genitourinary tract tuberculosis (GTB), is caused by distortion of the normal anatomy by fibrosis involving the reproductive tract structures. In most of the cases, epididymis is involved, leading to obstructive azoospermia (OA). We report a case of adult-onset HH who also had OA following GTB.

CASE REPORT

An infertile couple presented with 5 years of primary infertility with male partner having azoospermia. The male partner was a 32-year-old businessman, nonsmoker, and nonalcoholic. He had attained normal puberty with well-developed secondary sexual characters. He denied any history of sexual dysfunction. He had a history of abdominal tuberculosis at the age of 17 years, and antitubercular treatment was given for 9 months.

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On clinical examination, no abnormality was detected and external genitalia were normal. He already had fine-needle aspiration cytology (FNAC) of both testes. There was no evidence of spermatogenesis in FNAC report as told by the patient. Serum levels of testosterone were low normal, that is, 4.22 ng/mL (normal range = 3.4–11.2 ng/mL). Follicle-stimulating hormone (FSH) was also below normal range, that is, 0.97 mIU/mL (normal range = 2.0–15 mIU/mL). Karyotype was normal. On ultrasonography (USG), the size of right testis was 36 × 21 mm and left was 38 × 21 mm (normal range). The peak systolic velocity (PSV) of right testis was 5 cm/s and resistive index (RI) was 0.56, whereas PSV of left testis was 6 cm/s and RI was 0.47. Bilateral seminal vesicles were symmetrical and small in size. On the basis of all above parameters, provisional diagnosis of adult-onset HH was made.

Female partner was 27 years old with average built (body mass index = 20). On infertility evaluation, she was found to have polycystic ovarian syndrome with anti mullerian hormone (AMH) of 8.87 ng/mL.

Male partner was given human menopausal gonadotropins (HMG) 75 IU and human chorionic gonadotropin (HCG) 2000 IU biweekly for 3 months. Repeat semen examination at 3 and 6 months also showed azoospermia but serum FSH (4.7 IU/ml) and Serum Testosterone (12.7 ng/ml) were in normal range.

In view of persistent azoospermia with normal serum FSH and testosterone levels, the patient was further evaluated. On repeat scrotal USG, the size of right testis was increased from 36 × 21 to 42 × 21 mm, but left testis almost remained the same (39 × 21 mm). There was a significant improvement in vascularity of both the testes. The PSV of right testis increased from 5 to 8 cm/s. The PSV of left testis was 9 cm/s, which was 6 cm/s earlier. Few areas of calcification were also appreciated in left epididymis and in prostatic parenchyma which were not mentioned in earlier USG. Seminal vesicles were small in size with calcification. All these findings were probably the sequelae of previous infection. In view of improved FSH, testosterone, vascularity, and testicular volume, he was advised FNAC. FNAC showed normal maturation up to spermatozoa stage. Diagnosis of OA along with treated HH was carried out.

The couple was planned for *in vitro* fertilization with intracytoplasmic sperm injection (IVF-ET/ICSI) with percutaneous epididymal sperm aspiration (PESA) or microtesticular sperm extraction. Stimulation was done with antagonist protocol. A total of 10 oocytes were retrieved. PESA was performed. Adequate and motile sperms (70 million with 40% motility) were obtained. ICSI was done and seven embryos were formed. Two embryos of grade I were transferred on day 3. Beta-HCG on day 14 postembryo transfer was 354 IU/mL. At 6-week ultrasound, a single live pregnancy was confirmed. At 30 weeks of gestation, patient developed preeclampsia. Pregnancy was terminated at 32 weeks. A male baby of weight 1.4 kg with Apgar score of 6.8 was born. There was no obvious congenital malformation. The baby's growth and development at 1-year follow-up is normal.

DISCUSSION

Azoospermia is defined as the absence of spermatozoa in at least two different ejaculated semen samples (including the centrifuged sediment).[2,3] The incidence of azoospermia in infertile couples is approximately 10 to 15%. Clinically, azoospermia is classified as obstructive (posttesticular) and nonobstructive (pretesticular or testicular). Rarely, both these components occur in a same individual known as mixed genesis azoospermia.

Mixed genesis azoospermia is a challenging situation to diagnose as well as manage. The differentiation of OA from non-OA (NOA) is very important as both these conditions require different treatment approaches.

Initially, index case was diagnosed as adult-onset HH, a type of NOA. Adult-onset HH usually manifest as loss of libido, sexual dysfunction, hot flashes, and infertility. Because of sufficient androgen production, these individuals have normal puberty and secondary sexual characters. Most of the adult-onset HHs are diagnosed when semen analysis is done as a part of infertility work-up.

Adult-onset HH with infertility has treatment options of exogenous gonadotrophins or pulsatile gonadotropin-releasing hormones to restore the normal spermatogenesis. Gonadotropins can be given as a combined or sequential regimen. In combined regimen, both HCG and HMG are given together. In sequential regimen, HCG is given first for 3 months to initiate spermatogenesis followed by HMG. Combined regimen was opted in index case. In literature, most of the men with HH attained testicular function in the first year of hormonal therapy. The median time to initiation of spermatogenesis ranges between 6 and 9 months in different studies.[4-6] Burris *et al.*[7] have even

mentioned longer duration of therapy, up to 24 months in patient with low testicular volume, that is, less than 3 mL, to initiate spermatogenesis. Spontaneous conception is usually achieved within 6 to 9 months of gonadotropin therapy. Pregnancies have been reported even after 2 years of therapy.[8] Most of these patients have sperm count below normal range and usually require ART to achieve pregnancy.

In index case, diagnosis of OA in treated case of HH was made with a suspicion of associated obstructive pathology. The FNAC of bilateral testes was done, which showed normal maturation up to spermatozoa stage.

Tuberculous infection of the seminal vesicles or the prostate may diffuse and usually results in calcification of seminal vesicles, prostate, and the vas deferens with azoospermia or aspermia. Paick et al.[9] reviewed 50 men with infertility. Seventeen men had atrophic seminal vesicles on trans rectal ultra sound (TRUS) and 15 of them had a history of pulmonary tuberculosis. Index case also had abdominal tuberculosis and now presented with OA with atrophic seminal vesicles and calcification. Many studies have recommended that patients with atrophic seminal vesicles and history of tuberculosis should not be given the option of surgical management and to be treated with artificial reproductive technique (ART).[9,10] PESA was performed for our patient, and his wife conceived in first cycle.

In conclusion, adult-onset HH usually responds well with hormone therapy. In case of persistent azoospermia after gonadotropins therapy, possibility of mixed genesis azoospermia should be kept in mind. IVF with testicular sperm gives excellent results in such cases.

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Conflicts of interest

There are no conflicts of interest

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