Rare association of multiple etiologies in a severe oligoasthenospermic male

Vineeth V.S.[1], Mohsen Najafi[1], Sreenivasa G.[1], Sharath Kumar C.[2], Suttur S. Malini[1,*]

[1] Department of Studies in Zoology, University of Mysore, Manasagangothri, Mysore, Karnataka, India.
[2] Mediwave IVF and Fertility Research Hospital, Mysore, India.

*Corresponding Author: email address: drssmalini@gmail.com (S.S. Malini)

ABSTRACT

We report a rare case of a 30 year old man diagnosed with severe oligoasthenospermia, where the infertile condition is traced back to a multiple etiologies. Routine semen analysis and sperm function tests followed by hormone analysis are carried out to diagnose the condition as well as the severity. The initial findings prompt us to perform Ultrasound scanning of testis and Trans Rectal Ultrasound Scanning (TRUS) to check the anatomical and functional status of the accessory reproductive organs. Semen analysis and sperm function tests provide an insight into the severity of the condition. The hormonal analysis, Ultrasound scanning of testis and TRUS of accessory reproductive glands confirms the association of hormonal imbalance, testis and accessory gland defects which results in the observed infertile condition with severe sperm defects. A thorough investigation of infertile subjects is essential for appropriate diagnosis and effective personalized treatment owing to the probability of multiple etiologies. Incomplete diagnosis can have adverse effects in treatment and Assisted Reproductive Techniques (ART).

Keywords: Oligoasthenospermia, TRUS, Sperm function test.

INTRODUCTION

Male causes for infertility are found in 50% of couples who undergo diagnostic tests to elucidate the underlying causative factor (Dohle et al., 2005). The etiology of the male factor infertility is multifactorial and these affect spermatogenesis, which is a complex cascade of events governed by several genes and hormones. Male infertility can be the result of congenital and acquired urogenital abnormalities, infections of the genital tract, increased scrotal temperature, endocrine disturbances, genetic abnormalities and immunological factors. In majority of cases, accounting for 60-75%, no causal factor is found and is classified as idiopathic infertility (WHO, 2000)

CASE PRESENTATION

A 30-year-old male, who had come for fertility assistance at one of the Infertility clinics at Mysore, was subjected to routine examination. Basic semen analysis, which involves physical and microscopic examination of semen, enables to identify the infertile condition. Diagnosis of the infertile condition is solely based on these semen parameters assessed namely count, motility, morphology etc (American Urological Association, 2004). Sperm function tests helps to identify specific defects of acrosome, plasma membrane and chromatin packaging. This is vital to diagnose the type of male subfertility and plan treatment measures accordingly (Charles, 2000). Semen

biochemical assay provides an insight to the functional status of the accessory reproductive glands. Karyotyping helps to rule out any chromosomal aberrations. Apart from these any underlying endocrinopathy is made evident through hormonal assay of the reproductive hormones namely LH, FSH, Testosterone and Estradiol. In addition to all these Ultrasound scanning of testis and Trans Rectal Ultrasound Scan (TRUS) for the examination of the internal sex organs reveals any pathological condition associated with the testis and accessory reproductive glands.

MATERIALS AND METHODS

Genetic register was maintained for the patient to look for possible environmental and lifestyle factors that could contribute to the observed condition. Pedigree analysis was done employing standard symbols with a minimum of 2-3 rounds of interaction with the patient. Conventional semen analysis was done and parameters like semen volume, sperm count, sperm morphology, color, liquefaction, odor, coagulation and pH were recorded (WHO, 2000). Sperm function tests namely Acrosomal Intactness (AI) test (Gopalkrishnan, 1995), Hypo-Osmotic Swelling (HOS) test (Misro and Chaki, 2008) and Nuclear Chromatin Decondensation (NCD) test (Gopalkrishnan, 1995) were performed to check the status of acrosome, plasma membrane intactness, and sperm chromatin integrity.

Chromosomal analysis of the individual was carried out on peripheral blood lymphocyte culture by using the standard protocol as per Seabright (1971) with slight modifications. G banded metaphase plates were analyzed by automated Leica Karyo software and karyotyped according to the International System for Human Cytogenetic Nomenclature (2005). Hormonal analysis employing ELISA was carried out to quantify Estradiol, LH, FSH, and Testosterone levels in the subject. Ultrasound scanning of testis was performed to check the functional status of the testis. Biochemical analysis of the semen reflected abnormalities with the functioning of the accessory reproductive glands prompting us to perform TRUS for the patient.

RESULTS

Pedigree analysis revealed no history of infertility, consanguinity, miscarriage or still births in the family of the individual. Physical examination of the semen recorded decrease in volume when compared to the low reference value (WHO 2000). Barring pH, which was observed to be slightly increased, all other parameters studied exhibited normal condition. Microscopic examination revealed low count and low motility of the sperms (Table 1). Sperm function tests confirmed the severe abnormality as low values were observed with regards to AI, HOS and NCD test. These reflect abnormalities in the acrosome, plasma membrane intactness, and sperm chromatin integrity (Table 2). Chromosome analysis did not reveal any aberrations. Table 3 records the increased levels of LH and testosterone observed in the individual. Abnormal condition identified through Ultrasound scanning includes bilateral testicular hypoplasia where the volume of the right testis is 9.89cc and left testis is 7.84cc (Figure1.a and 1.b). TRUS

results showed varied pathological conditions in the accessory reproductive glands (Table 4).

Table 1: Spermiogram.

Parameters	Normal condition	Observation
Coagulation	Semisolid coagulated mass	Coagulated.
Liquefaction Time	60 min.	30 min.
Color	Grayish white	Grayish white
pH	7.2-8.0	8.3
Volume	1.5ml (low reference value)	1ml
Sperm count	20 million/ml	6 million/ml
Motility	30-50%(forward progressive)	20%

Table 2: Sperm function tests

Sperm Function Tests	Normal range	Response of the patient
Hypo-Osmotic Swelling test	60%	40%
NuclearChromatin Decondensation test	70%	50%
Acrosome Intactness test	50%	55%

Table 3: Hormonal assay

Hormones	Observed reading	Normal range
FSH	2.7 mIU / mL	2-14 mIU / mL
LH	15.1 mIU / mL	1.5 – 8 mIU/ml
Testosterone	8.2 ng/ dl	2 - 6.9 ng/d1
Estradiol	28 pg/ml	10 – 36 pg/ml

Table 4: Trans Rectal Ultrasound Scan

Organ	Condition observed	Normal volume	Observed volume
Testis	Hypoplasia	15-20 cc	Right testis: 9.89cc, Left testis: 7.84cc
Seminal Vesicle	Right SV small, Left SV dilated	1.2-1.4 cc	Right SV: 0.71cc Left SV: 4.82cc
Prostate	Hypoplasia	25-35 cc	7.17cc

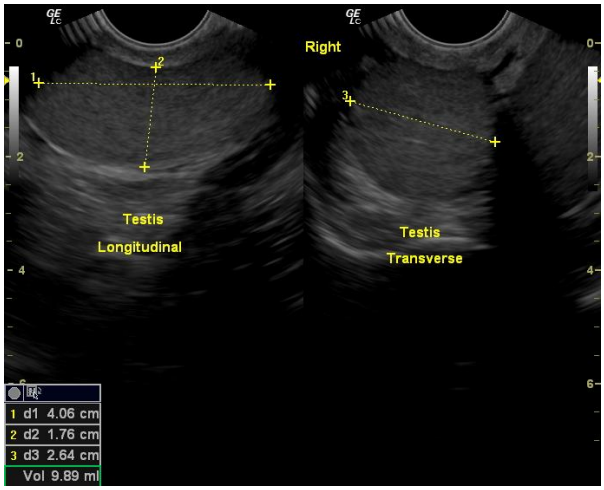

Figure 1.a): Hypoplasia of right testis of the patient. The volume of the right testis is found to be 9.89cc

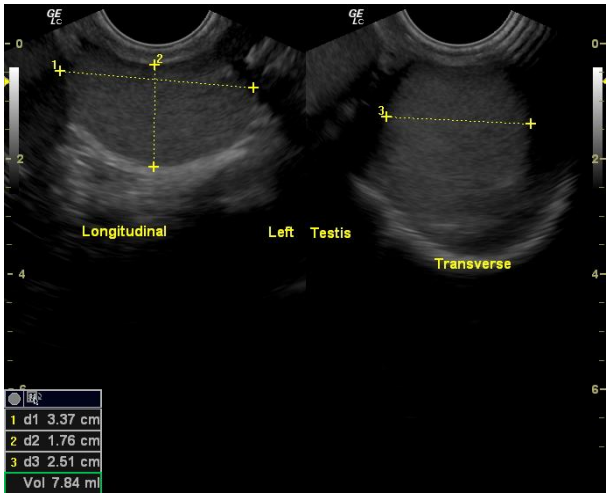

Figure 1.b): Hypoplasia of left testis of the patient. The volume of the left testis is found to be 7.84cc.

Dilation of left seminal vesicle with increased volume 4.82cc (Figure 2.a) and hypoplasitic condition of right seminal vesicle with volume 0.71cc is evident in the figure 2.b. Figure 3 shows the hypoplastic condition of prostate gland where the volume is 7.17cc. All the above analyses carried out revealed associated testicular and accessory glands abnormalities, which coupled with endocrine disruption, have led to the severe infertile condition.

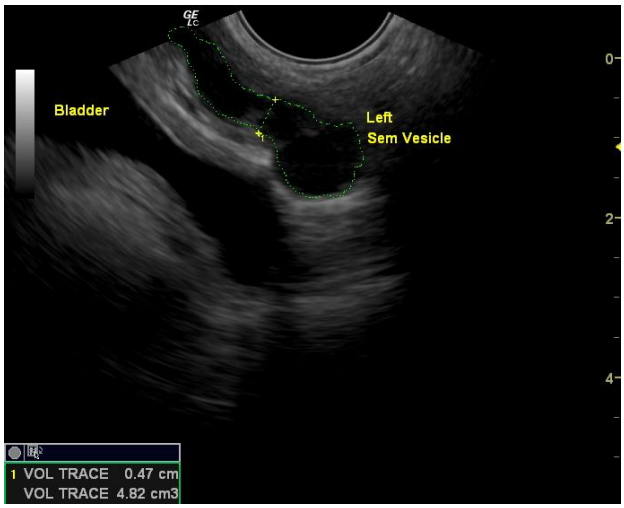

Figure 2.a): The left seminal vesicle was found to be dilated with volume recorded as 4.82cc

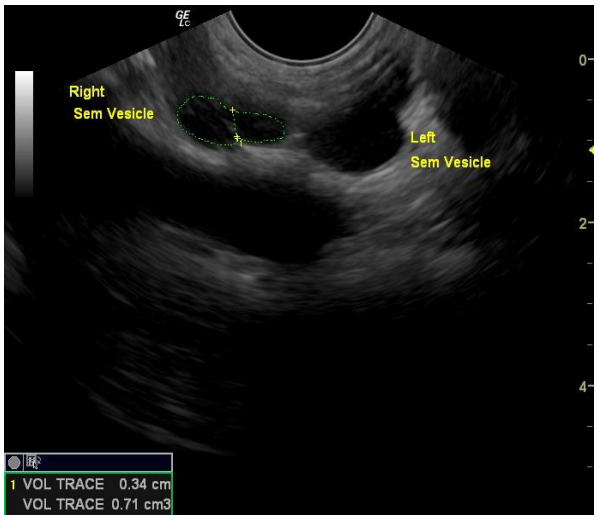

Figure 2.b): Hypoplasitic condition exists in right seminal vesicle with an observed volume of 0.71c

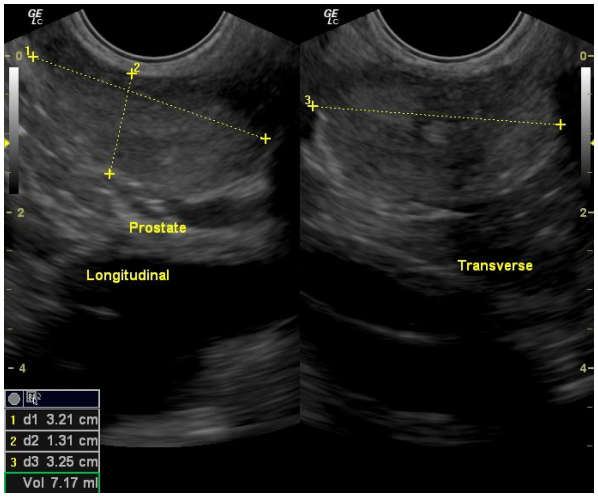

Figure 3: Hypoplasia of prostate gland is evident in the patient with a recorded volume of 7.17cc.

DICSUSSION

In the present study pedigree analysis clearly rules out any prevalence of infertile condition in the family. Semen analysis reflects poor quality of semen in this individual and the sperm function tests carried out confirms the severity of the sperm defects. It also serves to reveal the risk for following Assisted Reproductive Techniques (ART) like In Vitro Fertilization (IVF), Intra Uterine Insemination (IUI) and Intra Cytoplasmic Sperm Injection (ICSI), as the success rates will be affected owing to the sperm defects.

The FSH levels were normal but increased levels of testosterone and LH was observed which confirms mild androgen resistance, as the patient has got normal external genital organs. This hormonal imbalance observed could be the reason for the low sperm count observed (Geidam et al., 2008). Spectrum of accessory gland disorders and also that of testis was observed in the patient reported here. In the subject studied the size of the testis was found to be smaller than the normal size. The size of the testis influences the total number of spermatozoa per ejaculate (Andersen et al., 2000; Behre et al., 2000). Hence the low count and abnormal morphology of the sperms observed can be attributed to the decreased spermatogenic activity, owing to the small size of the testis (Holstein et al., 2003).

In the present study the left seminal vesicle hyperplasia observed is due to the blockage in the vesicle resulting in hyperplasia of seminal vesicle. The condition results in semen devoid of fructose, which is the source of energy for the sperms. Low

fructose levels have been positively correlated to low count, motility and high chromatin stability affecting the fertilizing capacity of the sperms (Saeed et al., 1994; Gonzales et al., 1997)**.** The right seminal vesicle hypoplasia observed leads to low secretion thereby decreasing the semen volume. Gonzales et al (2001) observed low seminal fluid fructose concentration in patients with fertility disorders.

Secretions of the prostate are very much essential for the maintenance of the alkaline nature of the semen. This in turn helps in neutralizing the acidic nature of vagina thereby facilitating movement of the sperms in the female reproductive tract. The hypoplasia of prostate identified by TRUS, in association with testicular hypoplasia and other accessory glands disorder, hampers the semen quality leading to reduced fertility potential.

CONCLUSION

Male infertility being a multifactorial disorder requires extensive analysis for precise diagnosis. That being the case the rare occurrence of conditions involving multiple etiologies like hormonal imbalance, accessory gland defects, sperm function defects etc poses a challenging task for providing effective personalized treatments. Analysis of the ejaculate alone does not reveal all the defects of spermatogenesis nor the ability of the spermatozoa to perform the events preceding fertilization and finally to fertilize the oocyte.

Thus, effective diagnosis and treatment for male infertility is only possible through thorough and precise analysis of all the possible factors that can lead to the observed condition.

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