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Original Research Article

Correlation of histopathological findings in azoospermic males undergoing microsurgical testicular sperm extraction and sperm retrieval rate: a retrospective study

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ABSTRACT

Background: Male factor is the sole cause of infertility in 20% cases, and a contributory cause in 30-40% cases of infertility. Azoospermia is the absence of sperms in semen and it affects around 1% males. With the advent of procedures like testicular sperm aspiration (TESA) and microsurgical testicular sperm extraction (M-TESE), surgical sperm retrieval (SSR) has been made possible and such men can father their own genetic offspring with the help of*In vitro*-fertilization-intra-cytoplasmic sperm injection (IVF-ICSI). Tissue can also be cryopreserved for use in future. Histopathological evaluation of testicular tissue obtained on diagnostic testicular biopsy/ M-TESE can help to predict the probability of finding sperms, the underlying etiology of azoospermia and also to establish obstructive (OA) cause when in doubt.
Methods: This is a retrospective analysis of database of 34 azoospermic males who underwent MTESE between year 2015- 2023 and for whom histopathology was done.
Results: In this study, SSR rate was 41.17%. The most common histopathological finding was Sertoli cell only syndrome in 41.1% cases (sperm retrieval rate 14.2%) followed by normal spermatogenesis in 17% cases (sperms found in 100% cases). Maturation arrest was found in 11.7% cases with sperms found in 25% cases. The study is limited by small sample size.
Conclusions: The histopathology of testicular tissue can provide valuable insights into predicting SSR rate and establishing diagnosis of OA etiology in azoospermia.

Keywords: Azoospermia, Histopathology, M-TESE, SSR rate

INTRODUCTION

In western world, azoospermia affects around 1% men and 10% of infertile men.[1] WHO 2010 defines azoospermia as the complete absence of spermatozoa in the ejaculate post centrifugation on at least 2 occasions. In 40% cases, etiology is unknown.[2] Azoospermia can be OA and non-OA (NOA). The diagnosis of OA and NOA can be made based on patient's history, physical examination, hormonal profile-FSH, LH, testosterone, TSH, prolactin, semen analysis, scrotal ultrasound, transrectal ultrasound and genetic tests including karyotype and Y chromosome microdeletion if indicated. In OA azoospermia, spermatogenesis is normal but due to obstruction along the male reproductive tract, sperms cannot be found in ejaculate. The obstruction can be at the level of epididymis, vas deferens or ejaculatory ducts.[3] NOA comprising of about 60% cases of azoospermia is intrinsic, often idiopathic testicular impairment leading to failed spermatogenesis. In cases of NOA, focal areas of spermatogenesis can be found.[4]

Several techniques of SSR are available like TESA, PESA (percutaneous epididymal sperm aspiration) M-TESE. Sperms can easily be found in cases of OA using TESA or PESA depending on the site of obstruction. In cases of NOA, if sperms are not found on TESA, microdissection technique can be used for MTESE. It has the advantage of identifying dilated tubules called "high probability zones" from where probability of finding sperms is higher.[5,6] Viable sperms found by SSR can be used for IVF- ICSI and also can be cryopreserved for use in future.[7,8]

Another advantage of sending testicular tissue for histopathology is that it can help us to find etiopathogenesis and suggest underlying cause. Parameters like hormonal levels, testicular volume, histology, Y chromosome microdeletion assessment can help with appropriate management.[9] Testicular histopathology is a reliable predictive factor for successful SSR in NOA patients.[10]

A major limitation of testicular biopsy is that it may not be representative of the whole testis as focal changes in spermatogenesis can be there. Sending biopsies from multiple sites in the testis can damage the testicular architecture leading to hormonal abnormalities.[11]

The present study was done with an aim to correlate the Histopathological findings in azoospermic males undergoing MTESE with sperm retrieval rate.

METHODS

Study design

It was retrospective, observational study.

Population

The data of 34 azoospermic patients who underwent MTESE (done following TESA, if no sperms were found in TESA) followed by histopathological evaluation from 2017-2023 in Bansal hospital Bhopal was evaluated. The study was approved by the Institutional ethics committee (MP/0429), IRB on April 13, 2024.

Inclusion criteria

Azoospermic males in the age group of 26-55 years undergoing MTESE were included.

Exclusion criteria

Cases where histopathogy was not done and those where sperms were found on TESA and MTESE was not required.

Technique

patients underwent micro-TESE which involves delivering testicle through small scrotal incision on medial raphe. Transverse tunical incision was given and testicular tissue retrieved. Tissue was immediately delivered to embryologist in media. One such sample was also sent for histopathology. Tunica subsequently closed with running prolene 4-0 suture. Skin closure done with monocryl 3-0.

Histological assessment

For histopathology, tissue sections were stained with hematoxylin and eosin. At least 100 sections were examined. The histopathological findings were categorized as follows:[12] Normal Spermatogenesis: The seminiferous tubules are healthy and lined by a thin basement membrane. The germinal epithelium shows normal progression from spermatogonia to spermatocytes. Abundant spermatids and spermatozoas are seen. Hypospermatogenesis: The germinal epithelium is seen along with all the stages of germ cells till spermatozoa but the number of germ cells is reduced. Germ cell maturation arrest: Here the process of spermatogenesis is arrested at a specific cell stage, usually at primary or secondary spermatocyte stage. Sertoli cell only syndrome: Here the Seminiferous tubules contain only Sertoli cells. No other cells of spermatogenesis are seen. On H and E staining, Sertoli cells appear as oval shaped cells perpendicular to basement membrane. Seminiferous tubule hyalinization: Here the tubules are lined by a thick basement membrane. Tubules have a smaller diameter along with collagen deposition. Germinal epithelium is absent. Mixed pattern: Here a combination of two or more histopathological patterns is seen in the same testicular biopsy specimen. Testicular atrophy-absence of seminiferous tubules with tubular sclerosis. Leydig cell hyperplasia-here Leydig cells infiltrate between seminiferous tubules without displacing or obliterating them.

Reports of the histopathology were retrieved and the findings were correlated with sperm retrieval rate.

Statistical analysis

Data collected on prepared proforma, entered into excel 2016 sheet and analyzed with SPSS ver. 20 (IBM Corp., Armonk, NY, USA). Results reported as number (%).

RESULTS

Data from men who underwent sperm retrieval by MTESE and tissue was sent for histopathology was collected. The age group ranged from 26-55 years. Majority of patients belonged to 31–40-year-old age group (Table 1) and middle-class strata according to modified Kuppuswamy scale (Table 2).

Table 1: Age distribution of subjects.

Age (in years)	N (%)
3rd decade (21-30)	6 (17.6)
4th decade (31-40)	15 (44.1)
5th decade (41-50)	13 (38.2)

Table 2: Socioeconomic distribution of subjects according to modified Kuppuswamy scale.

Score	Socioeconomic class	N (%)
26-29	Upper (I)	4 (11.7)
16-25	Upper middle (II)	10 (29.4)
11-15	Lower middle (III)	12 (35.2)
5-10	Upper lower (IV)	6 (17.6)
<5	Lower (V)	2 (5.8)

The most common histopathological finding was Sertoli cell only syndrome comprising 41.1% cases, here the SSR rate was found to be around 14.2% The second most common finding was normal spermatogenesis comprising 17% cases with sperm retrieval rate of 100%. Maturation arrest was found in 11.7% cases with a sperm retrieval rate of 25%. Germ cell aplasia, Leydig cell hyperplasia and Spermatocytic arrest comprised 5.8% cases each with sperm retrieval rates of 50%, 50% and 100% respectively. Disorganized Spermatogenesis was found in 2.9% cases with 100% sperm retrieval rate. Granulomatous orchitis, testicular atrophy and hypospermatogenesis comprised 2.9% cases each with no sperms retrieved in all three categories (Table 3).

Table 3: Histopathological findings.

Histopathology	N	Total population (%)	Sperms found, N (%)
Normal spermatogenesis	6	17	6 (100)
Maturation arrest	4	11.7	1 (25)
Disorganised spermatogenesis	1	2.9	1 (100)
Sertoli cell only	14	41.1	2 (14.2)
Granulomatous orchitis with sertoli cell only	1	2.9	0
Testicular atrophy/ sclerosis	1	2.9	0
Germ cell aplasia	2	5.8	1 (50)
Leydig cell hyperplasia	2	5.8	1 (50)
Spermatocytic arrest (complete/incomplete)	2	5.8	2 (100)
Hypospermatogenesis	1	2.9	0 (0)

However, due to the small sample size of this study, more such studies are needed to find the true predictive values of each of the histopathological findings.

DISCUSSION

Over 70 million couples in the world are affected by infertility.[13] Male infertility is a significant contributor to cases of infertility. Azoospermia affects 1% males. With advancement in surgical techniques and technology, procedures like TESA, MTESE, PESA can be offered to azoospermic men, giving them an opportunity to father their own children. Diagnostic testicular biopsies can predict the chance of successful sperm retrieval with techniques like MTESE.

In this study, most patients were in the age group of 31-40 years. Normospermatogenesis, suggestive of an OA etiology was found in 17% cases, which was the second most common histopathological finding in OA azoospermia, viable sperms are present in the testis, but a blockage along the male reproductive tract prevents their passage in the semen. Various factors such as recurrent infections followed by fibrosis, vasectomy, testicular torsion are contributory causes. Previous studies have found similar outcomes.[14,15] In a study by Mushtaq et al from Islamabad histopathology of testicular biopsy of 53 infertile males was evaluated and the most frequent pattern was found to be Sertoli cell only syndrome (30.1%) followed by hypospermatogenesis (18.8%). Normal spermatogenesis was found in 16.9%.[16]

In our study, the most common pattern in histopathology was Sertoli cell-only syndrome accounting for 41.1% cases. It is irreversible and can be caused by underlying conditions like chemotherapy, radiotherapy, orchitis, cryptoorchidism or structural abnormalities in the long arm of Y chromosome.[16]

Maturation arrest was found in 11.7% cases with SSR rate of 25%. In a similar study from Hyderabad, India by Veeramachaneni et al testicular biopsy of 141 males with infertility 30.5% exhibited normal histopathology, followed by Sertoli cell syndrome in 26.24%, complete spermatocytic arrest in 9.93% patients and testicular atrophy in 9.2% patients.[17]

Other histological findings were granulomatous orchitis, testicular atrophy/ sclerosis, maturation arrest, disorganized spermatogenesis, hypospermatogenesis + maturation arrest, germ cell aplasia. Sperm retrieval rates vary according to histopathological findings. Genetic, environmental, demographic and cultural factors may contribute to differences in histopathological findings observed in different studies.

The limitation of this study is the small sample size. More such studies are needed to better ascertain the true predictive values of histopathological findings for SSR rates and live birth rates.

CONCLUSION

Histopathological findings help guide management of male infertility patients by predicting SSR rates when diagnostic testicular biopsy is undertaken. It can help patient to decide whether to go microdissection SSR or donor sperm. It can also help in establishing diagnosis of OA azoospermia when in doubt and planning corrective surgery accordingly.

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