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Original Research Article

Histopathological Patterns of Testicular Biopsies in Azoospermic Infertile Males

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ABSTRACT

Introduction: Testicular biopsy is important in categorizing patients with Azoospermia and provides useful information and guidelines for further treatment. Histopathological findings of testicular biopsies are of significant importance in making decision for selection of cases for Intracytoplasmic sperm injection (ICSI) in patients with non-obstructive azoospermia.
Objective: To categorize histopathological patterns of testicular biopsy specimens from Azoospermic infertile males to Modified Johnson scoring system.
Methodology: Testicular biopsies from male patients with history of infertility and azoospermia were included in this study. All biopsies were received in 10% Bovian fixative and routinely processed and stained with Haematoxylin and Eosin (H and E). Clinical data was obtained and recorded on a proforma. All cases were examined microscopically and various histological patterns were evaluated and categorized according to the histopathological patterns and Modified Johnson scoring was performed.
Results: A total 32 cases of testicular biopsies from Azoospermic males were evaluated. Most frequent pattern found was of Seminiferous tubule hyalinization (34.375%), further categorized as Johnson score 1. The second most frequent was Germ cell maturation arrest (25%), further categorized as Johnson score 8-3.The third common was Sertoli cell only syndrome (18.75%), further categorized as Johnson score 2. There were 3 cases that showed mixed pattern and 2 case showed discordant pattern.
Conclusion: This study outlines the different histopathological patterns of testicular biopsies in cases of male infertility in our setup and identifies seminiferous tubule hyalinization as the most common pathological finding amongst various histopathological patterns.

Key Words: Testicular biopsy, hypospermatogenesis, male infertility

INTRODUCTION

Infertility is defined as inability to conceive after one year of unprotected intercourse. [1] Male infertility is one of the important causes of infertility among couples and it contributes to significant number of infertility cases. [2] It is estimated that around 1% of total male population and 10% of men seeking infertility treatment are affected by testicular failure. [3] Evaluation by testicular biopsy in cases of azoospermia provides reliable information regarding spermatogenesis which can further be categorized into various histopathological patterns. [4] This provides valuable

information to the clinician for the purpose of prognosis and treatment. [5]

Diagnostic testicular biopsy is used to determine testicular histopathological patterns and to foresee the possibility of finding sperms in the testis. [6] Histopathological findings of testicular biopsies are of significant importance in making decision for selection of cases for Intracytoplasmic sperm injection (ICSI) in patients with non-obstructive azoospermia. [7]

Andrologists when treating Azoospermic infertile patient considered testicular biopsy of great value for diagnostic and prognostic purposes. Other tests such as Hormone levels and microdeletions tests cannot differentiate between obstructive azoospermia (OA) and non-obstructive azoospermia (NOA) and also cannot guide regarding success in mature sperm retrieval during Testicular Sperm Extraction (TESE). [8]

The present study was undertaken to evaluate histopathological patterns of testicular biopsy specimens from Azoospermic infertile males and to categorize each case according to Modified Johnson scoring system.

MATERIALS AND METHODS

After Institutional ethical approval, testicular biopsy specimens were collected during a period of 1 and half year from March 2017- July 2018. Testicular biopsies from male patients with history of infertility and azoospermia were included in this study. This study included 32 men with bilateral biopsy that is 64 samples. Patients with undescended testis, history of infection were excluded from the study.

Clinical data was obtained and recorded on a proforma. All biopsies were received in 10% Bouin's fluid and routinely processed and stained with Haematoxylin and Eosin (H and E). All slides were examined microscopically and various histological patterns were evaluated and categorized according to the histopathological patterns and Modified Johnson scoring was performed.

The testicular biopsies were categorized into different histopathological patterns [9] as follows:-

1. Normal Spermatogenesis
2. Hypospermatogenesis
3. Germ cell maturation arrest
4. Sertoli cell only syndrome
5. Seminiferous tubule hyalinization
6. Mixed pattern
7. Discordant pattern

Normal Spermatogenesis: The seminiferous tubules are lined by thin basement membrane and the germinal epithelium shows normal progression from spermatogonia to spermatocytes along with spermatids and spermatozoa as shown in figure 1.

Hypospermatogenesis: The germinal epithelium shows all the stages of germ cells but the number is reduced as shown in figure 2.

Germ cell maturation arrest: At a specific cell stage the process of spermatogenesis is arrested usually at the level of primary or secondary spermatocytes. Further it can be complete as shown in figure 3 or incomplete as shown in figure 4.

Sertoli cell only syndrome: The tubules contain only Sertoli cells and no other cells of spermatogenesis as shown in figure 5.

Seminiferous tubule hyalinization: The tubules have much thickened basement membrane with a smaller diameter along with tubular collagenisation. There is no germinal epithelium as shown in figure 6.

Mixed Pattern: There is variation in the histopathological pattern in the same testicular biopsy. Germ cell maturation arrest along with Sertoli Cell Syndrome as shown in figure 7 and seminiferous tubule along with hyalinization Germ cell maturation arrest as shown in figure 8.

Discordant pattern: There is variation in the histopathological pattern of right and left testis.

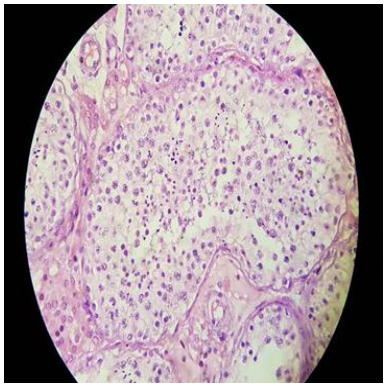

Figure 1. Normal Spermatogenesis

Figure 2. Hypospermatogenesis

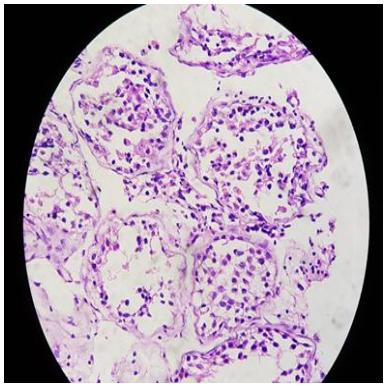

Figure 3. Complete Maturation Arrest

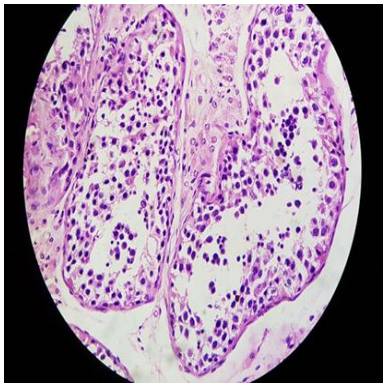

Figure 4. Incomplete Maturation Arrest

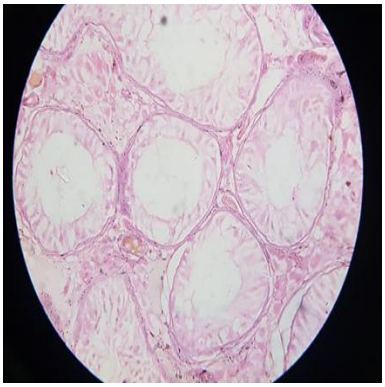

Figure 5.Sertoli cell only syndrome

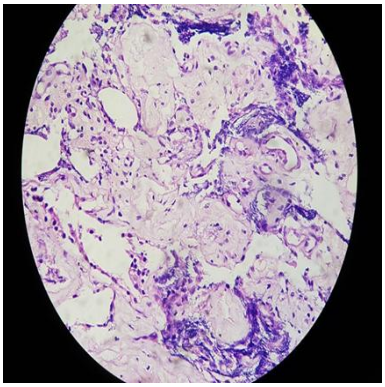

Figure 6. Seminiferous tubule hyalinization

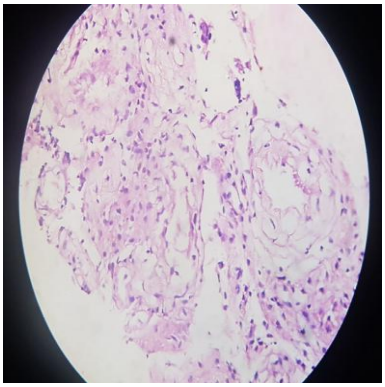

Figure7. Mixed pattern, Left side Sertoli cell and Right tubule shows maturation arrest at spermatogonia

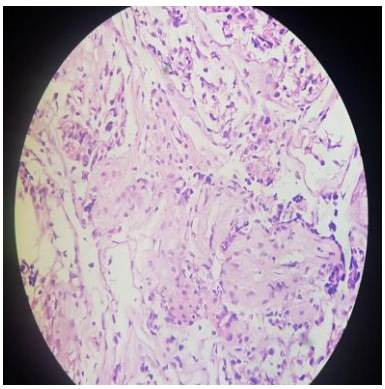

Figure 8. Mixed Pattern, Left lower atrophic and upper two shows maturation arrest

Later samples were scored as Modified Johnson scoring [10]

Score 10: There is full spermatogenesis
Score 9: Incomplete spermatogenesis with many late spermatids
Score 8: There are less than 5 spermatozoa per tubules and a few late spermatids
Score 7: There are many early spermatids but no spermatozoa or late spermatids.
Score 6: There are few early spermatids but no spermatozoa or late spermatids
Score 5: there are many spermatocytes but no spermatozoa or spermatids
Score 4: There are few spermatocytes but no spermatozoa or spermatids
Score 3: There are only spermatogonia
Score 2: Only presence of Sertoli cells and no germinal epithelial cells
Score 1: There is no seminiferous epithelium

OBSERVATIONS

A total 32 cases of testicular biopsies from Azoospermic males were evaluated. Bilateral testicular biopsy after written informed consent.

The number of cases and their percentages for various histopathological patterns were calculated as shown in table1. According to Johnson scoring testicular biopsies were categorized as shown in table 2.

Table 1. Histopathological classification of testicular biopsies in infertile men

Histopathological classification	No of cases-32 (Samples=64)	%
Normal spermatogenesis	1	3.125
Hypospermatogenesis	1	3.125
Germ cell maturation arrest	8	25
Sertoli cell only syndrome	6	18.75
Seminiferous tubule hyalinization	11	34.375
Mixed Pattern	3	9.35
Discordant pattern	2	6.25
Total	32	100

Table 2. Categorization of testicular biopsies according to Johnson scoring system

Johnson scoring	No of cases-32 (Samples=64)	%
10	1	3.125
9	5	15.625
8	4	12.5
7	0	0
6	0	0
5	1	3.125
4	0	0
3	5	15.625
2	6	18.75
1	10	31.25
Total	32	100

RESULTS

In histopathology of testicular bilateral biopsies in Azoospermic infertile males most frequent pattern was of seminiferous tubule hyalinization (34.375%), followed by Germ cell maturation arrest (25%), followed by Sertoli cell only syndrome (18.75%).

Out of 32 cases, 3 that showed mixed pattern and 2 case showed discordant pattern.

There were 3 cases that showed mixed pattern, 2 cases showed Germ cell maturation arrest along with Sertoli Cell Syndrome as shown in figure 7 and one case showed Seminiferous tubule along with hyalinization Germ cell maturation arrest as shown in figure 8.

2 cases showed discordant pattern, one of subjects showed Incomplete Maturation arrest upto spermatids on right side and left testis showed Hypospermatogenesis. Another case showed Sertoli cell only syndrome on right and Germ cell maturation arrest on left side.

On categorization of testicular biopsies according Johnson scoring system, the most frequent pattern was of seminiferous tubule hyalinization (34.375%) and they were correlated to Johnson score 1.

The second was Germ cell maturation arrest (25%) and they were correlated to Johnson score from 8-3.

The third common was Sertoli cell only syndrome (18.75%) and correlated to Johnson score 2.

Hypospermatogenesis represented 3.125% cases and they correlated to Johnson score 9.

Normal spermatogenesis (3.125%) and they were correlated to Johnson score 10.

DISCUSSION

The occurrence of male infertility and the consequent histological findings in testicular biopsies contrast because of a few fundamental etiological elements including social propensities, hereditary causes and ecological conditions, for example, hidden

contaminations, synthetic concoctions, radiation and presentation to warm. [11,12]

In spite of the fact that a fundamental male fertility assessment requires an extensive history and physical examination alongside semen investigation, testicular biopsy remains the key examination for every single testicular reason for infertility. [13]

The present outcomes demonstrated concurrence with some International investigations and disparities with others and these outcomes are analyzed as pursue: Normal spermatogenesis represented 3.125 % out of the all 32 cases. This is practically like the outcome reported by Meinhard et al, 5%. [14] Different investigations detailed higher frequency Nagpal et al. detailing 16%, [15] and Haddad et al., at Jordon who revealed 11.2% for obstructive azoospermia, [16] Brannen and Roth detailed (35%). [17] The contrast between the present investigation and others gathering could be because of their gathering of patients as they considered scores 10 and 9 as ordinary, while in the present examination, score 10 was viewed as typical and 9 was considered as hypospermatogenesis.

Spermatogenic arrest: In the present examination, spermatogenic arrest were additionally subdivided into two gatherings: Complete and Incomplete. All tissue tests indicating spermatogenic arrest spoke to 25% which is equivalent with concentrate done by Rashed et al (2008) who detailed spermatogenic capture at a recurrence of 28% in Egyptian guys, [2] Glina et al (2005) revealed a higher occurrence contrasted with referenced investigations (37.5%) in Brazil, [6] however there are studies with outcomes lower as compared to our studies, Brannen and Roth (1979) indicated (12.5%) in United States [17] Al-Rayess and Al-Rikabi (2000) concluded (11%) for Soudian network [18] and Thomas (1990) revealed (5%) in Nigeria, [19] while Haddad et al (2004) announced an exceptionally low frequency of spermatocyte development capture (1.7%) in Jordon. [16]

Sertoli cell in our study amounted 18.75 %, this outcome was low contrasted with the 34% noted by M. Rashed et al, [2] yet is equivalent with 12.5% announced by Brannen and Roth examine. [17] Haddad et al (2004) recorded a low occurrence for SCOS which was; 2.9%. [16] SCO may result from various causes, for example, cryptorchidism, cytotoxic medications, or light. Be that as it may, much of the time the etiology is obscure. The nonattendance of germ cells might be because of variables present amid fetal life. [20]

The no germ cells no Sertoli cells group was represented a percentage (34.375%) which is the highest in our study. On comparison incidence of 28.4% was reported in Haddad et al study, [20] and 23% in Thomas study (1990). [18] May the higher percentage in our study is inclusion of severe Oligospermic and Azoospermic males is the cause.

This blended outcomes might be because of some hereditary variables and also inclusion criteria of only Azoospermic infertile males. More investigations and bigger number of testicular samples are expected to understand the numerous patterns brought from this heterogeneity.

CONCLUSION

Biopsy of Testis is vital diagnostic test in determining the gonadal causes of azoospermia, reproductive prognosis and therapeutic considerations for Azoospermic men. This is a requirement for higher classification, diagnosis, prognosis and treatment of men presented with non-obstructive azoospermia.

In this respect, testicular biopsy diagnostic test is gaining additional price as a golden normal tool for medical diagnosis and also for the recovery of mature spermatozoon from men with either non-obstructive or obstructive azoospermia who are opting for ICSI treatment to conceive. For ICSI the surgeon need to understand that there can Discordant and mixed pattern so for retrieval of germ cells multiple site of

both the testis will definitely increase chances of success.

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