Original Article

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Pathology Section

Clinicopathological Study of Testicular Lesions in a Tertiary Care Centre of Dakshina Kannada, India

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ABSTRACT

Introduction: Testicular biopsies are performed for both diagnostic and therapeutic purposes. Diagnostic testicular biopsies are usually performed as a part of a male infertility work-up. Therapeutic testicular excision biopsies are performed for a wide range of disorders, including neoplastic lesions, inflammatory lesions, cryptorchidism, testicular trauma, and as a part of prophylactic treatment of carcinoma prostate.

Aim: To evaluate the indications for orchidectomy and diagnostic testicular biopsies and to understand the histopathological spectrum of testicular lesions and concordance with clinical diagnosis.

Materials and Methods: This was a retrospective study conducted in the Department of Pathology, Father Muller Medical College, Mangalore, Karnataka, India. The study period is from July 2017 to June 2020. Data was collected and analysed in August 2020. All testis' biopsies, including excision and diagnostic biopsies, are included in the study. Histopathological findings and the clinical diagnosis were evaluated for concordance. Data were tabulated and statistically evaluated for age distribution, laterality, and frequency using Microsoft Excel 2021. Percentages for the variables and concordance rate were calculated.

Results: A total of 139 cases (mean age 54.5 years) were included in the study. Prophylactic orchidectomy for carcinoma prostate (64/139=46.04%) was the most common clinical indication. Non neoplastic lesions account for 48.20% (67/139). Frequent non neoplastic lesions are testicular torsion (23/139=16.55%) and abscess (12/139=8.63%), followed by cryptorchidism (9/139=6.47%). Left-sided lesions are more frequent than right-sided lesions. Histopathology confirmed two cases of suspected male infertility and Androgen Insensitivity Syndrome (AIS). Neoplastic lesion accounts to 6.47% (9/139). Frequent neoplasm in the study was seminoma (3/139=2.16%), followed by lymphoma (2/139=1.44%). Other neoplasms included in the study were mixed germ cell tumours, post-pubertal teratoma, and spermatocytic tumour. Testicular tuberculosis accounts to 1.44% (2/139) in the present population.

Conclusion: Non neoplastic lesions were common compared to testicular neoplasms. Testicular torsion, followed by abscess, was the most common indication for orchidectomy. Testicular Tuberculosis can mimic a neoplasm on clinical and radiological work-up. Hence, careful evaluation has to be performed in young suspected cases of tuberculosis.

Keywords: Androgen insensitivity syndrome, Cryptorchidism, Germ cell neoplasm, Orchidectomy, Teratoma, Testicular neoplasm, Seminoma

INTRODUCTION

The testis is a paired organ with reproductive function and is involved in producing hormones [1]. It is suspended by a spermatic cord and lies within the scrotum [2]. Testis produces spermatozoa and also secretes testosterone [3]. Testicular lesions include neoplastic and non neoplastic lesions [4]. Non neoplastic lesions of the testis are frequent. Neoplastic testicular lesions account for only 1% of all malignancies in males worldwide [5,6]. However, they are the fourth most common cause of malignancy-related deaths in young males [7,8].

Testicular lesions usually present as a scrotal mass, pain in the groin, or an abdominal mass [9]. Non neoplastic lesions include cryptorchidism, atrophic testis, trauma, torsion testis, and infections [10]. Testicular malignancies commonly occur in the second to fourth decade of life [11,12]. Also, the incidence of malignancy reduces with the advancement of age [13,14]. About 95% of testicular malignancies are germ cell tumours, with many predisposing factors such as cryptorchidism, strong family history, Klinefelter syndrome, and the presence of germ cell tumours in the contralateral testis [15].

Testicular swellings are considered to be malignant until proven otherwise [16]. Hence, imaging studies play an essential role in the initial assessment along with the history and examination [17]. Ultrasonography and doppler studies help to diagnose neoplasms as well as infectious lesions with secondary changes. Assessing the blood supply status helps detect testicular torsion in children early. In case of inconclusive ultrasonographic findings, magnetic resonance imaging can opt for a better understanding [18]. Despite advanced imaging studies and tumour marker assays, the most reliant diagnosis is based on histopathological examination [19].

Testicular biopsies are performed for both diagnostic and therapeutic purposes. Diagnostic testicular biopsies are performed as a part of a male infertility work-up [1]. Therapeutic testicular excision biopsies are performed for a wide range of disorders that includes neoplastic lesions, inflammatory lesions, cryptorchidism, testicular trauma, and as a part of prophylactic treatment of carcinoma prostate [6].

This study is undertaken to evaluate the indications for orchidectomy and diagnostic testicular biopsies. And also aims to understand the histopathological spectrum of testicular lesions along with evaluating the concordance with the clinical diagnosis. This aids pathologists in providing a histopathological diagnosis with clinical significance.

MATERIALS AND METHODS

This was a retrospective study conducted in the Department of Pathology, Father Muller Medical College, Mangalore, Karnataka, India. The study period is from July 2017 to June 2020. Data was collected and analysed in August 2020. The study was initiated after obtaining ethical clearance. (FMIEC/CCM/431/2020).

Inclusion criteria: All testicular biopsies received in the pathology department during the study are included.

Exclusion criteria: Para-testicular biopsies are excluded from the study.

Sample size calculation: Estimated minimum sample size is 120, with a confidence interval of 95% and attributable error of 5%.

Procedure

Specimens were fixed in 10% formalin, and multiple representative sections were obtained from the testis. After tissue processing, slides were stained with haematoxylin and eosin. Relevant clinical details like age, laterality and clinical diagnosis were recorded. Histopathological analysis of the tissue was performed, and the findings were recorded. Further, the histopathological findings and their concordance with the clinical diagnosis were evaluated.

STATISTICAL ANALYSIS

Data were tabulated and statistically evaluated for age distribution, laterality, and frequency using Microsoft Excel 2021. Percentages for the variables were calculated. The concordance between histopathological diagnosis and clinical diagnosis was evaluated using tables. And then the corcordance rate was calculated.

RESULTS

This study includes 139 cases received in the department of pathology for a period of three years. Majority of the cases were in the age range of 61 to 70 years (41/139=29.5%), followed by 71 to 80 years (24/139=17.27%). The mean age was found to be 54.5 years. The age range and frequency is depicted in [Table/Fig-1].

Age range (years)	Frequency (n)	Percentage (%)
<10	3	2.16
11-20	21	15.11
21-30	7	5.04
31-40	8	5.76
41-50	9	6.47
51-60	15	10.79
61-70	41	29.50
71-80	24	17.27
81-90	10	7.19
> 90	1	0.72
Total	139	100

[Table/Fig-1]: Age distribution of all study participants.

Among the 139 cases included in the study, 49% (68/139) of the cases underwent bilateral orchidectomy. Majority of the these procedures were performed in association with treatment for carcinoma prostate. Left-sided orchidectomy accounts to 27% (38/139) and right-sided orchidectomy accounts to 23% (33/139).

Orchidectomy is performed for a wide variety of clinical indications in the present study. Bilateral orchidectomy as a part of prophylaxis in patients with carcinoma prostate (64/139=46.04%) was the most common clinical indication, followed by torsion testis (21/139=15.11%), pyocele (10/139=7.19%) and testicular neoplasm (10/139=7.19%). Other clinical indications were cryptorchidism, epididymo-orchitis, hydrocele, testicular trauma, abscess, and tuberculosis. Histopathological evaluation was solicited to confirm the clinical diagnosis of AIS in two cases (1.44%). The single diagnostic testicular biopsy received was evaluated for the cause of male infertility. Frequency of clinical diagnosis is depicted in [Table/Fig-2].

On microscopic evaluation, 45.32% (63/139) cases were found to have a normal histomorphology. Bilateral orchidectomy was performed in majority of these cases, as a part of prophylactic treatment for carcinoma prostate. Non neoplastic pathologies were identified in 48.20% (67/139) cases. The most common

Clinical diagnosis	Frequency	Percentage (%)
Undescended testis	9	6.47
Torsion testis	21	15.11
Testicular trauma	2	1.44
Hydrocele	6	4.32
Inguinal hernia repair	2	1.44
Carcinoma Prostate prophylaxis	64	46.04
Infertility	2	1.44
Androgen Insensitivity Syndrome (AIS)	2	1.44
Carcinoma penis	1	0.72
Epididymo-orchitis	5	3.60
Scrotal filariasis	1	0.72
Testicular abscess	3	2.16
Pyocele	10	7.19
Tuberculosis testis	1	0.72
Testicular neoplasm	10	7.19
Total	139	100

[Table/Fig-2]: Clinical diagnosis.

non neoplastic lesion was testicular torsion (18/139=17.99%), followed by testicular abscess (12/139=8.63%). A 74% of testicular torsion was found in patients below 20 years. Epididymo-orchitis (9/139=6.47%) and cryptorchidism (9/139=6.47% were not uncommon in the study.

Neoplastic testicular pathologies accounts to 6.47% (9/139). Classical seminoma (3/139=2.16%), followed by lymphoma (2/139=1.44%) were the common neoplastic lesions in the current study. Histopathological diagnosis and their frequency are detailed in [Table/Fig-3].

Histopathology diagnosis	Number of cases	Percentage (%)
Bilateral orchidectomy with normal histology	63	45.32
Non neoplastic lesions (67/139=48.20%)		
Atrophic testis	5	3.60
Androgen Insensitivity Syndrome (AIS)	2	1.44
Testicular torsion/Infarction	25	17.99
Testicular abscess	12	8.63
Non specific epididymo-orchitis	9	6.47
Incomplete maturation arrest	2	1.44
Granulomatous Epididymo-orchitis	2	1.44
Germ cell aplasia	1	0.72
Cryptorchid testis	9	6.47
Neoplastic lesions (9/139=6.47%)		
Classical seminoma	3	2.16
Lymphoma	2	1.44
Teratoma-postpubertal	1	0.72
Spermatocytic seminoma	1	0.72
Mixed germ cell tumour	1	0.72
Leydig cell tumour	1	0.72
Total	139	100

[Table/Fig-3]: Histopathology diagnosis and frequency.

Histopathological and clinical diagnosis was evaluated to assess the concordance of diagnosis. Calculated concordance rate was 99.22%. Majority of the clinical diagnosis were in concordance with the histopathological diagnosis, with a single discordant case. [Table/Fig-4] depicts the concordance between histopathology and clinical diagnosis of all testicular lesions.

Among the 64 cases (64/139=46.04%), who underwent bilateral orchidectomy as a part of carcinoma prostate prophylactic treatment, 61 were found to have normal histomorphology.

Clinical diagnosis	Histopathology diagnosis												
	Normal histology	Testicular atrophy	AIS	Torsion testis	Infarction	Cryptorchidism	Non Specific epididymo-orchitis	Granulomatous Epididymo-orchitis	Testicular abscess	Incomplete maturation arrest	Germ cell aplasia	Testicular neoplasm	Total
Undescended testis	-	-	-	-	-	9	-	-	-	-	-	-	9
Torsion testis	-	-	-	21	-	-	-	-	-	-	-	-	21
Testicular trauma	-	-	-	-	2	-	-	-	-	-	-	-	2
Hydrocele	-	5	-	1	-	-	-	-	-	-	-	-	6
Inguinal hernia repair	1	-	-	-	-	-	1	-	-	-	-	-	2
Carcinoma prostate	61	-	-	-	-	-	3	-	-	-	-	-	64
Infertility	-	-	-	-	-	-	-	-	-	1	1	-	2
Androgen Insensitivity Syndrome (AIS)	-	-	2	-	-	-	-	-	-	-	-	-	2
Carcinoma penis	1	-	-	-	-	-	-	-	-	-	-	-	1
Epididymo-orchitis	-	-	-	1	-	-	4	-	-	-	-	-	5
Scrotal Filariasis	-	-	-	-	-	-	-	-	-	1	-	-	1
Testicular abscess	-	-	-	-	-	-	-	-	3	-	-	-	3
Pyocele	-	-	-	-	-	-	1	-	9	-	-	-	10
Tuberculosis testis	-	-	-	-	-	-	-	1	-	-	-	-	1
Testicular neoplasm	-	-	-	-	-	-	-	1	-	-	-	9	10
Total	63	5	2	23	2	9	9	2	12	2	1	9	139

[Table/Fig-4]: Concordance between histopathology and clinical diagnosis.

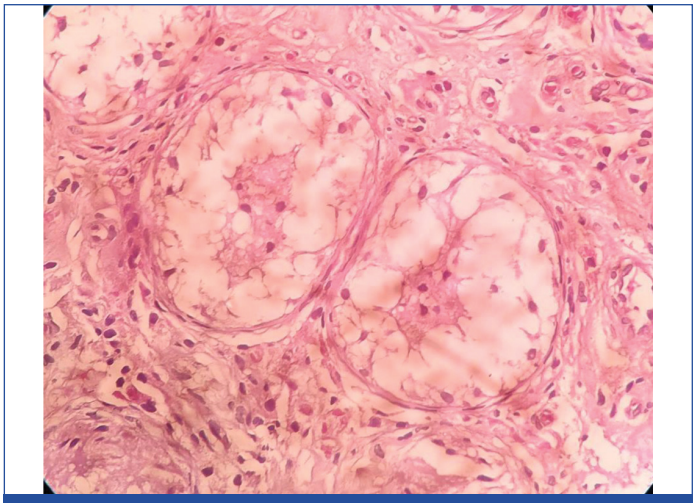
Rest of the three cases shows features of epididymo-orchitis. Orchidectomy performed during inguinal hernia repair and penectomy also showed normal histomorphology. All cases of cryptorchid testis (9/139=6.47%) evaluated were negative for Germ Cell Neoplasia In- Situ (GCNIS) or any malignancy. Among the cases of hydrocele, a majority (5/6) bear testicular atrophy, and one case showed features of testicular torsion. A majority (9/10) of clinically suspected cases of pyocele were diagnosed to have a testicular abscess.

Cases for infertility evaluation (2/139=1.44%) were validated to have germ cell aplasia and incomplete maturation arrest. Germ cell aplasia is characterised by decreased diameter of tubules and absence of maturing germ cell layers. [Table/Fig-5] show the microscopic view of germ cell aplasia. Another case of filarial hydrocele was diagnosed to have incomplete maturation arrest.

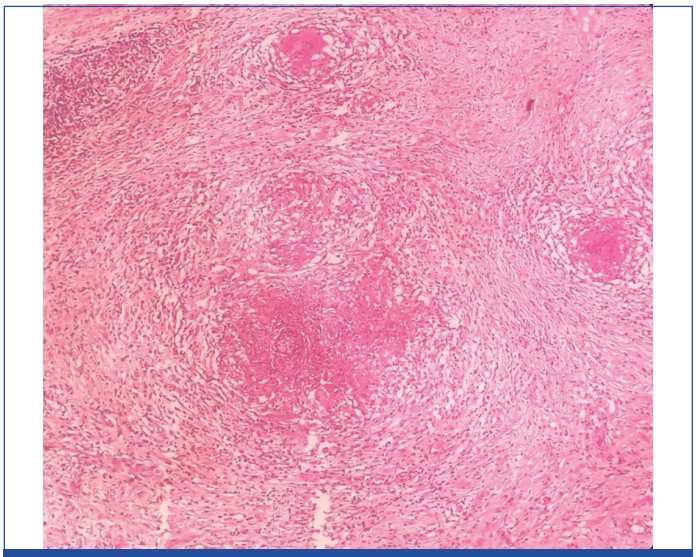
The clinical diagnosis of AIS was confirmed in both cases with histopathology. Two cases of granulomatous epididymo-orchitis were noted; one of them was clinically evaluated as a testicular neoplasm.This was the single case in the study which has discordance between clinical and histopathological diagnosis. [Table/Fig-6] shows the discordant case which was clinically diagnosed as testicular neoplasm. Granulomatous inflammation with central necrosis is shown.

Nine neoplastic lesions are included in the study. Malignant lesions are found to be more common than benign lesions. Germ cell tumours (6/9) are found to be the most common neoplasm in the present study. They include seminoma (3/9), mixed germ cell tumour (1/9), postpubertal teratoma (1/9) and spermatocytic tumour (1/9). Other neoplastic lesions are testicular lymphoma (2/9) and leydig cell tumour (1/9). Leydig cell tumour, which is a sex cord stromal tumour is the only benign neoplasm included in the study.

Microscopy of seminoma has tumour cells in sheets or lobules separated by fibrous septae with lymphocytic infiltrates. Lymphoma comprises of discohesive, pleomorphic malignant cells with

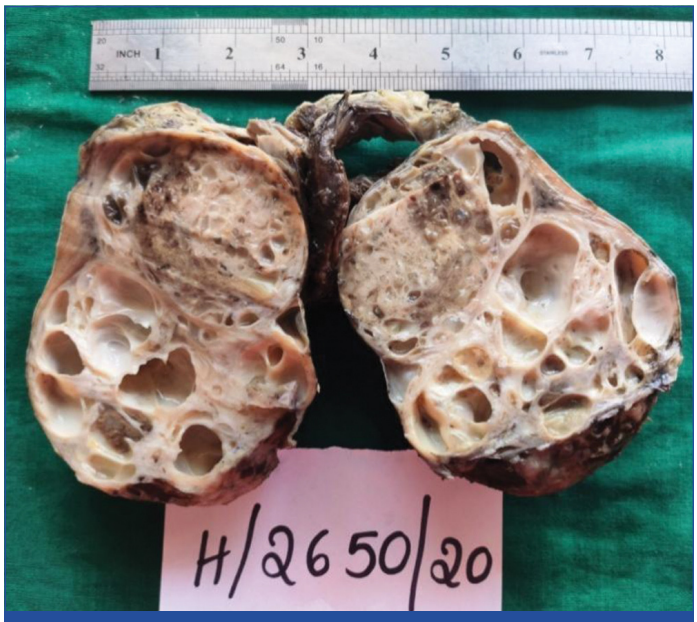


[Table/Fig-5]: Germ cell aplasia in a case of male infertility (H & E, 400x).

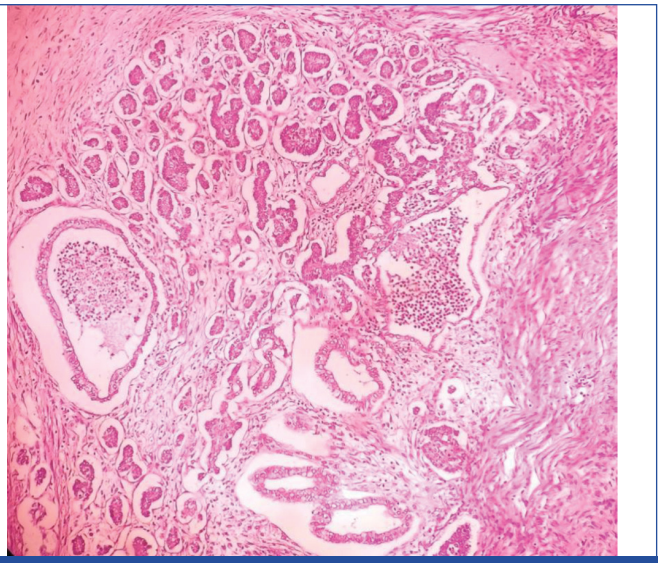


[Table/Fig-6]: Granulomatous inflamation (H & E, 100x).

irregular nuclei and prominent nucleoli. Mixed germ cell tumours commonly have a combination of embryonal carcinoma and yolk sac tumour. Postpubertal teratoma has a heterogenous cut surface with solid and cystic components [Table/Fig-7]. Microscopy shows multiple cyst lined by glandular/squamous epithelium and GCNIS component. Mesenchymal, neuro-ectodermal and neural tissue can also be seen. [Table/Fig-8] shows the gross and microscopic appearance of postpubertal teratoma.



[Table/Fig-7]: Gross appearance of postpubertal teratoma.



[Table/Fig-8]: Postpubertal teratoma (H & E, 100x)

DISCUSSION

Non neoplastic lesions (93.52%) of the testis are more common than neoplastic lesions. Testicular torsion (16.55%), followed by a testicular abscess (8.63%), and cryptorchidism (6.47%) are the most common non neoplastic lesions in the current study. Similar observations were made in earlier studies by Reddy H et al., and Dhawle M et al., [5,8].

Male factors contribute to 20% of the causes of infertility. Hypospermatogenesis, maturation arrest, and germ cell aplasia are the common histological changes found in male infertility. The present study includes two cases of male infertility under evaluation. Germ cell aplasia with focal spermatogenesis and incomplete maturation arrest was noted in those cases. Correlation with sperm count and morphology helps in the evaluation of these cases. Oligospermia is noted in incomplete maturation arrest, and azoospermia is in complete maturation arrest. A recent autopsy study has found that men with severe SARS-CoV-2 infection have developed impaired hormonal function and fertility-related issues. The histological findings include lymphocytic infiltrate, thickening of the tubular basement membrane, scarcity of Leydig cells, and decreased spermatogenesis. The present study includes a case of filarial hydrocele for which orchidectomy was performed as a part of the treatment. Histopathological evaluation of the testis revealed incomplete maturation arrest. The majority of the hydrocele cases in the current study are noted to have an atrophic testis on microscopic evaluation. Hence, these factors also contribute to male infertility [1,20].

Testicular tuberculosis is relatively rare and amounts to 3% of genital tuberculosis. On ultrasound imaging, testicular tuberculosis presents as diffusely enlarged heterogenous or homogenous hypoechoic lesions, which mimics a neoplasm. Thus, testicular neoplasms should be considered a differential diagnosis in suspected cases. The present study includes two (1.44%) cases of granulomatous epididymo-orchitis with caseous necrosis. One among them was clinically evaluated as a testicular neoplasm. Zeihl-Neelsen stain was performed in both cases but was found negative for Acid-Fast Bacilli (AFB). Similarly, Das A et al., observed that it is highly uncommon to find the presence of AFB in testicular tuberculosis. Polymerase Chain Reaction (PCR) studies opted for confirmation. Das A et al., suggest opting for Fine Needle Aspiration Cytology (FNAC) as the preliminary investigation before testicular biopsy or orchidectomy in young suspected cases of testicular tuberculosis. Sample can be obtained for PCR studies as well during the procedure. Thus the patient receives treatment at the earliest [21].

According to Chaudry S et al., AIS cases have a risk of developing GCNIS in early adulthood and frank malignancies after thirty years. Benign lesions include sertoli cell adenoma and hamartoma. The present study includes two cases of AIS. On histopathological evaluation, Sertoli cell adenoma composed of small tubules populated by immature Sertoli cells, an increase in tubular density, and a relative decrease in Leydig cells were noted in these cases. The recent trend is to perform gonadectomy soon after puberty due to the risk of GCNIS in AIS. However, retaining the gonads till adulthood can improve the quality of life since natural testosterone is peripherally aromatised with oestrogen. Chaudry S et al., support the current recommendation of retaining gonads till adulthood [22].

Cryptorchidism is a common congenital anomaly of the testis. It is associated with infertility and an increased risk of testicular malignancy. Hence, components of GCNIS, which are usually associated with germ cell tumours are to be searched for during histopathological evaluation. In the present study, cryptorchidism contributes to 6.47% of the cases. On histopathological evaluation, maturation arrest and atrophic changes were noted in these cases. GCNIS components were not identified in any of these cases [11].

Testicular neoplasms are the most common malignancies in young males, and the majority is of germ-cell origin. According to Globocan-2020 by World Health Organisation (WHO), the age-standardised incidence rate of testicular malignancy in the world is 1.8%. Based on the literature, seminoma, teratoma, and embryonal carcinoma are common in young adults, and spermatocytic tumours and lymphoma are common in the elderly. Malignant lesions of the testis are more common than benign ones. Similarly, the present study includes eight malignant lesions and one benign Leydig cell tumour [23].

Among the nine neoplastic lesions included in the study, the most common malignancy was seminoma (3/9=33%), followed by lymphoma (2/9=22%). Similar observation was given by Baidya R et al., [10]. According to Reddy H et al., and Shruti G et al., teratoma is more common than lymphoma. Surhonne SP et al., and Abdulkadir A et al., observed that mixed germ cell tumour is the second most common neoplastic lesion after classic seminoma [Table/Fig-9] [8-10,12,14]. No age predilection was observed for seminoma in the current study. Primary testicular lymphoma usually presents in the sixth decade of life. Similarly, both lymphoma cases were included in the current study presented in the sixth decade [8-10,12,14].

Neoplasm	Shruti G and Alok S [14] 2015	Reddy H et al., [8] 2016	Baidya R et al., [10] 2017	Surhonne SP et al., [12] 2018	Abdulkadir A et al., [9] 2019	Present study 2022
Classic Seminoma	42%	42.90%	44.44%	32%	50%	(3/9=33)%
Mixed germ cell tumour	6%	7.20%	22.22%	19%	16.60%	(1/9=11%)
Teratoma	10%	28.60%	11.11%	6.80%	-	(1/9=11%)
Spermatocytic tumour	2%	-	-	3.40%	16.70%	(1/9=11%)
Leydig cell tumour	2%	-	-	-	8.30%	(1/9=11%)
Non Hodgkin Lymphoma	6%	-	22.22%	8.50%	-	(2/9=22%)

[Table/Fig-9]: Comparison of types of testicular neoplasms in various studies [8-10,12,14].

Post-pubertal testicular teratoma is a malignant germ cell tumour and accounts for 2.7% to 7% of germ cell tumours. It has a higher risk of metastasis and is usually seen in young adults. These are firm and nodular tumours with heterogenous solid cystic cut surfaces. Similarly, in the present study, the case of post-pubertal teratoma presented before 20 years, with a similar gross appearance [24].

Mixed germ cell tumours are malignant tumours with more than one germ cell component. These are clinically regarded as non seminomatous regardless of the presence or absence of seminomatous components. They are usually present by 30 years of age. The common combinations include embryonal carcinoma, seminoma, and yolk sac tumour. In the current study, the patient presented at 25 years with a 45% embryonal carcinoma component, 30% yolk sac tumour component, and 25% teratoma component. The presence and percentage of embryonal carcinoma are associated with a high-risk of metastasis and poor prognosis.

A spermatocytic tumour is a germ cell tumour unrelated to GCNIS. It usually presents in the fifth decade with an excellent prognosis. Tumours were presented in the fifth decade in the present study as well. These tumours rarely metastasise. OCT4 and MAGEA4 markers aid in differentiating spermatocytic tumours from typical seminoma [10,11,24].

Limitation(s)

The number of testicular neoplasms included in the study is relatively less. Hence, the neoplastic spectrum and age predilection of the tumours couldn't be assessed well.

CONCLUSION(S)

Non neoplastic lesions of the testis are more common than neoplastic lesions. Testicular torsion and abscess formation are the most common lesions amounting to orchidectomy in the study population. Though, prevalance of testicular tuberculosisis was less in the present study population. This lesion of infective aetiology can be misdiagnosed as a neoplasm with clinical and radiological findings. Hence, in a young suspected case, FNAC with PCR studies can be done as a preliminary investigation before testicular biopsy and orchidectomy.

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