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Testicular Tumors

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CLINICOPATHOLOGICAL PATTERN OF TESTICULAR TUMORS A 3-YEARS EXPERIENCE AT A TERTIARY CARE UROLOGY CENTER

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ABSTRACT

Objective: To evaluate the clinical presentation of testicular tumors and their histological pattern present in our setup.
Study Design: Case series.
Place and Duration of Study: Armed Forces Institute of Urology (AFIU) Rawalpindi, from Jul 2016 to Jun 2019.
Methodology: The documents of all the cases of testicular tumors presenting in the last 3 years were retrieved and their relevant clinical detail: age, clinical presentation, side of involvement, operative procedure conducted and the histopathology report were documented.
Results: Thirty two patients of testicular tumors were documented over a period of three years, making 10.66 cases reporting per year. The mean age was 30.10 ± 15.42 years, with the youngest 3 months old infant and the eldest being 58 years of age. The tumors were commonest on the right (59.3%) with 81.2% presentation as swelling of testis. Radical orchiectomy was performed in 90.6% of the cases and retro peritoneal lymph node dissection (RPLND) in 6.2%. Germ cell tumors were found in 71.8% cases with mixed germ cell tumorbeing the commonest histopathology seen in 31.2% of the cases followed by the seminoma (25%) and non-Hodgkin lymphoma (12.5%).
Conclusion: Testicular tumors were relatively uncommon in our part of the world with a limited number of cases presenting to a tertiary care urology center. The presentation was variable but a rising trend in non-Hodgkin lymphoma results in a decrease in the overall number of germ cell tumors.

Keywords: Germ cell tumor, Radical orchiectomy, Seminoma, Undescended testis.

INTRODUCTION

In developed countries, testicular tumour is the most commonly diagnosed cancer in males aged 15-44 year[1]. According to the American Cancer Society, the cancer statistics of 2016 reported that approximately 8720 new cases of testicular tumor were diagnosed in 2016, but only estimated 380 individuals would die of it[2]. Testicular tumors constitute around 1-1.5% of the male neoplasms[3]. As far as the urological tumors are concerned, testicular tumors represent 5% of the above. According to Vechhia *et al*[4], in the western countries, 3-10 new cases of testicular tumors/100000 males/year, are being reported. The rising trend in testicular tumors has not been seen in the Asian countries, whereas the increasing incidence of these tumors have been recorded in the US and Europe[5], especially in the Caucasian and Hispanic men in United States. Interestingly Ghazarian *et al*[6], has even projected a rising incidence in the next decade in United States. Despite of the rising trend in testicular tumors, the mortality has decreased due to advances in the treatment modalities. Indeed early and accurate diagnosis is important for successful management of testicular tumors as a delay in diagnosis relates with higher and advanced stage at the time of presentation for management.

A lot of research has been reported from the west about the testicular tumors, however the publications from Asian countries have been scarce. The main aim of this study was to highlight the mode of presentations of testicular tumors in our setup alongwith the operative procedures, the histological pattern and compare it with other national and international studies with the intention to specify the peculiar issues and patterns encountered in our circumstances.

METHODOLOGY

This retrospective case series study was conducted at the Department of Urology, at the Armed Forces Institute of Urology (AFIU) Rawalpindi, from July 2016 to June 2019. Due approval was acquired from the Institutional Ethics Review Board (Ref no: Uro-Adm-Trg-1/IRB/2016/106). All the 32 patients presenting to the Armed Forces Institute of Urology, Rawalpindi with testicular tumor were included in this study by non-probability convenience sampling with no specific exclusion criteria. Their documents were retrieved and critically analyzed regarding the age, mode of presentation (including signs and symptoms), tumor markers

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(β-HCG, α-FP, LDH) and operative procedures, while the histopathology reports were procured from the documents as well as from the Armed Forces Institute of Pathology (AFIP) Rawalpindi. The descriptive quantitative data analysis was conducted using the SPSS-21. The frequencies, percent-ages and the mean with standard deviations were calculated.

RESULTS

A total of 32 cases of testicular tumors were recorded during this period. This constituted 10.66 cases documented per year at our setup. The age ranged from 3 months to 58 years (mean 30.10 ± 15.42 years). Testicular tumors were found mostly in the third and fourth decade of life, constituting 18 cases (56.25%) in these two decades. This was followed by the sixth decade which showed 15.6% of the patients. The tumors were more common on the right side (19 cases 59.3%) with 10 cases on the left (31.25%) and 3 (9.3%) bilateral (fig-1).

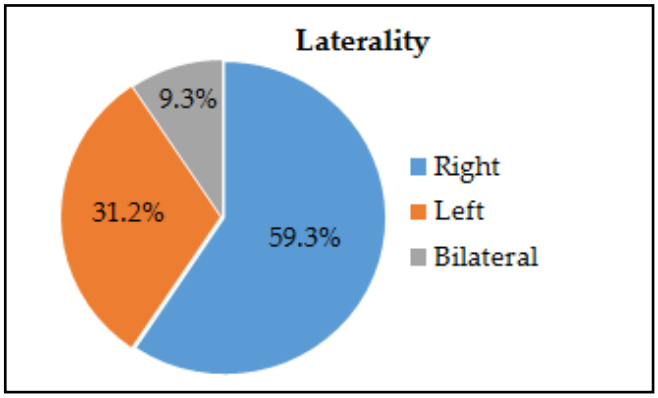

Figure-1: Side predilection.

Figure-2: Ulcerating testicular tumor with maggots.

The commonest clinical presentation was swelling of testis found in 26 cases (81.2%) of the patients. This was followed by dragging pain in 17 (53.1%) (table-I). Two (6.2%) cases presented with bilateral testicular swellings, while the third case of bilateral lesions infact had bilateral tumors in intraabdominal testes. Two (6.2%) had abdominal mass at presentation along with cryptorchidism. One patient (3.1%) had a past history of radical orchiectomy and was lost to follow up. He presented with a fungating/ulcerating inguino-scrotal lesion along with maggots (fig-2).

As far as the tumor markers are concerned, amongst the seminomas (8 cases), 1 (12.5%) showed a raised β-HCG level. However in non seminomatous germ cell tumors (15 cases), α FP was raised in 9 cases (60%) and β HCG in 8 cases (53.3%) of patients. Amid the total testicular tumors (32 cases), LDH was raised in only 5 cases (15.6%).

Among the 32 patients, radical orchiectomy was performed in 29 (90.6%). Two (6.2%) cases had cryptorchidism who developed the tumors in the intra-abdominal testes with one having bilateral intra-abdominal testes with tumors in both the testes. Due to obstructive uropathy secondary to abdominal lymphadenopathy, one of these required ureteric stenting prior to the diagnosis. In one patient (3.1%) who presented with an inguinoscrotal ulcerating lesion, he was subjected to incisional biopsy of the lesion. Retro peritoneal lymph node dissection (RPLND) was performed in 2 cases (6.2%).

Table-I: Clinical presentation of the patients (n=32).

Presentation	n (%)
Swelling of testis	26 (81.2)
Dragging Pain in testis	17 (53.1)
Severe Pain in testis	3 (9.3)
Bilateral testicular swelling	2 (6.2)
Hydrocele	4 (12.5)
Cryptorchidism	2 (6.2)
Abdominal Mass	2 (6.2)
Weight Loss	3 (9.3)
Inguino-scrotal Ulcer with Maggots	1 (3.1)
Family History	1 (3.1)

Germ cell tumors were commonest among the lesions, seen in 23 cases (71.8%). In detail it was the mixed germ cell tumor which was seen in 10 cases (31.2%), followed by seminomas in 8 cases (25%) and then diffuse large B cell lymphoma in 4 (12.5%). A variety of other lesions were also seen. Interestingly one 6 years old boy was referred by the paediatrich-aem-oncologist for radical orchiectomy in a known case of acute lymphoblastic leukemia (ALL) who had already undergone bone marrow transplant and developed a relapse in the testis (table-II).

Table-II: Histopathological diagnoses.

Histopathological Pattern	n (%)
Germ Cell Tumors (GCTs)	23 (71.8)
Seminomatous GCTs	8 (25)
Non-seminomatous GCTs	15 (46.8)
Embryonal Carcinoma	1 (3.1)
Yolk Sac Tumor	3 (9.3)
Malignant Teratoma	1 (3.1)
Mixed GCT	10 (31.2)
Stromal/ Non-specific stromal Tumors	9 (28.1)
Leydig cell Tumor	3 (9.3)
Lymphoma	4 (12.5)
ALL	1 (3.1)
Angiomyxoma	1 (3.1)

DISCUSSION

The majority (90-95%) of the testicular tumors constitute germ cell tumors (GCT)[4]. Their etiology is not exactly known but the old hypothesis persists that the tumor process starts in the fetal life with involvement of abnormal proliferation of primordial germ cell. Testicular tumors are associated with certain risk factors like cryptorchidism, family history (first degree relative with testicular tumors), infertility, Klinefelter's syndrome and even trauma and hormonal changes. Cryptorchidism has 5-10 fold increased risk of evolving a testicular tumor. Likewise around 11% of these tumors are associated with cryptorchidism[4], with seminoma being the commonest. In cases of cryptorchidism, the contralateral testis can also develop a testicular tumor. In our study we had only 6.2% association with cryptorchidism and both the cases developed testicular tumor in the intra-abdominal testes. Interestinglythe white collar workers have been found to be at higher risk of germ cell tumors as compared to the blue collar workers. Thus associationwith higher socioeconomic status cannot be ignored.

Amongst the testicular tumors, the non-seminomas have a peak incidence in 3rd decade while seminomas peak in 4th decade of life. In our study we reported a combined 56.25% tumors in the third and fourth decade of life. Testicular tumors are a shade common on the right side which reflects the increased incidence of undescended testis on the right. Beigh *et al*[7], reported 70.3% right sided tumors and Deotra *et al*[8], 60% as compared to 59.3% on right in our study. Bilateral tumors are seen in 1-2% with about half associated with undescended testis. However we had 9.3% bilateral tumors with one out of three having cryptorchidism.

In 1987, Jafarcy and Zaidi[9], reported testicular tumors as 3.8% of all malignancies in Pakistan. While in 2007 Mushtaq *et al*[10], reported an incidence of 1.24% testicular tumors of all male malignancies. The germ cell tumors are considered as the commonest variant of around 90-95% preponderance[4]. However Mushtaq *et al*[10], reported 67.3% germ cell tumors (seminoma: non-seminoma ratio of 11:14) and interestingly lymphoma as the second commonest 18.7% amongst the patients of Northern Pakistan. They also found no increasing pattern of testicular tumors in Pakistan as compared to the tumor registry of 1991[11]. Similar to Mushtaq *et al*[10], Chakrabarti *et al*[12], from Central India reported germ cell tumor (77.1%) as the commonest tumor followed by lymphoma (17.1%). In two other studies from Pakistan the incidence of germ cell tumors has been found to be 87%[13], and >90%[14]. However in our study we had 71.8% germ cell tumors as the commonest testicular tumor. In all the children we documented the presence of yolk sac tumor except one who was a known case of acute lymphoblastic leukemia treated with bone marrow transplant but developed a relapse in one of his testes. We found lymphoma in 12.5% cases, as the second most common tumor after germ cell tumors and all were diffuse large B cell variant which has a relatively poorer prognosis. Testicular lymphoma is a rare disease comprising approximately 1-2% of all non-Hodgkin Lymphoma and about 5% of testicular tumors, and is primarily a disease of the elderly. Apart from lymphomas, amongst the stromal tumors, Leydig cell tumors were seen in 9.3% of the cases in our study. These tumors may have endocrine abnormalities like loss of libido and gynaecomastia[15], which were not seen in our patients. Earlier these were considered as rare tumors, however in the recent studies they have been reported as high as 3-22% of the testicular tumors[16,17].

The testicular tumors are quite uncommon in underdeveloped areas like Pakistan, India and African countries as compared to the industrialized countries with higher socioeconomic status. An enormous difference can be appreciated from the fact that the maximum documented cases reporting in a year was seen in United Kingdom by Horwich *et al*[18], which was 64.9 per year followed by Walschaerts *et al*[19], from France with 53.2 per year, as compared to 1.5 from Nigeria[20], and 7.4 from India[7]. In our study we documented 10.66 cases reporting in a year while in another study from Pakistan Mushtaq *et al*[10], reported 21.4 cases in a year.

A painless swelling of one testis is the commonest presentation of testicular tumors[13], reported 67.5% by Beigh *et al*[7], 100% by Tan *et al*[21], as compared to 81.2%

in our study. Indeed testicular self-examination, which is to be performed in men >15 years of age once a month after warm bath, can be helpful in early detection of these painless testicular swellings[22]. Other symptoms/signs encountered may be a dull dragging pain, pain with epididymo-orchitis, hydrocele, cryptorchidism, abdominal mass, scrotal ulceration and even infertility. We reported a case extensive inguino-scrotal ulcer alongwith maggots. He was infact a case who had lost to follow up after undergoing radical orchiectomy and presented after three years with this complication.

Raised tumor markers are not only diagnostically important but also play a prognostic role. Their importance in the follow up of these patients cannot be underestimated. α-fetoprotein (AFP) is produced in the fetus in yolk sac (endodermal sinus), intestine and liver. AFP is raised in yolk sac tumor, its increased level correlates with the amount of yolk sac tumor present in the mixed germ cell tumor and to a lesser extent by embryonal carcinomas and teratomas. It can be found in up to 20-25% of teratomas and is associated with mucinous glands and hepatoid differentiation. In one large cohort study of Germa-Lluch *et al*[23], of 1490 cases of testicular tumor, >60% of patients with non seminomatous germ cell tumors had raised AFP levels, making it the most commonly elevated tumor marker in testicular cancer. This figure was similar to our study where 60% cases of non seminomatous germ cell tumors showed elevated α-fetoprotein.

On the other hand β-human chorionic gonadotrophin is raised in choriocarcinoma and at times in seminoma and mixed germ cell tumor with syncytiotrophoblastic cells. The extent of its rise depends on histologic tumor type and the overall tumor burden. Elevations of β-hCG can also be seen in approximately 10-20% of patients with stage I seminoma and up to 30-50% of disseminated seminoma secondary to the existence of syncytiotrophoblastic components within the tumor. In our study, 12.5% seminomas showed an elevated β-hCG as compared to 53.3% in non seminomatous germ cell tumors. Beigh *et al*[7], showed elevated AFP and β-hCG levels in 8.1% and 43.24% respectively.

Serum lactic dehydrogenase (LDH) may be higher in seminomas and non-seminomas. It has relatively low specificity for germ cell tumors. LDH is elevated in 40–60% of men with testicular germ cell tumors. LDH has limited sensitivity and specificity for seminoma, but LDH levels >2000 U/L are more reliable with bulky disease, and increasing levels are a precise pointer towards recurrence. In our study serum LDH was found to be raised in 15.6% of the cases. An increased serum LDH level may be the singular biochemical aberration in 10% of patients with persistent or recurrent non seminomatous germ cell tumors. Rarely hormone producing tumors may cause hyperthyroidism, hypercalcaemia and even precocious pseudopuberty.

Radical orchiectomy was the main operative procedure (90.6%) performed in our study. We had two cases of testicular tumor in the intra-abdominal testes. After initial diagnosis with trucut biopsy, these were managed by chemotherapy followed by exploration, excision of abdominal lesions along with the RPLND for the residual lymph node masses. We had no case of testis sparing surgery. However recent studies are supporting the concept of surgical exploration and frozen section assessment in indeterminate small testicular tumors and testis sparing surgery in order to avoid radical orchiectomy in certain patients[24,25].

CONCLUSION

The presentation was variable but the association of cryptorchidism with testicular tumors was also quite evident. The latter group indeed requiring major interventions like retro peritoneal lymph node dissection. The incidence of testicular tumors in our Asian population is low as reflected by the number of cases reporting to a tertiary care urology center in Pakistan. In addition the number of non-Hodgkin lymphoma seen in the testis was also high thus reducing the overall incidence of germ cell tumors as compared to the rest.

CONFLICT OF INTEREST

This study has no conflict of interest to be declared by any author.

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