# Histopathological and Clinical Characteristics of Testicular Germ Cell Tumors- Experience at Prince Hussein Urology and Transplant Center, Jordan

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## ABSTRACT

**Objective:** To investigate the clinical and histopathological characteristics of testicular germ cell tumours in a sample at Jordanian population, and to compare it with worldwide findings.

**Methods:** The data of 75 patients who had undergone radical orchiectomy for the germ cell tumor at Prince Hussein Urological Center between 2010 and 2014 were collected. They were retrospectively analyzed according to clinical and histopathological parameters.

**Results:** 62% of the cases,(47 patients), were found to be seminomas, with the mean age being 36 years (22-80) with most of the cases were of classical seminoma. 38% of the cases (28 patients) had Non-Seminomatous Germ Cell Tumor (NSGCT). Although only 14% (4 patients) of the cases were of pure form, the rest were of mixed NSGCT. Yolksac and teratoma were found to be the most common histological types among Mixed NSGCT and the median age was 32 years (range 20-48). Overall, the average period that patients stayed before seeking medical attention was about 4 months, which ranged from 3 weeks to one year.

**Conclusion:** The age at presentation and the histopathological type of testicular germ cell among Jordanian patients are similar to those currently published in the world records. However, the diagnosis is delayed; this implies that the concerned stakeholders should emphasize the need of patient education and physician awareness.

**Key words:** Clinical characteristics, Histology, Germ cell tumor, Testicular.

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## Introduction

Testicular Germ Cell Tumors (TGCT) include a variety of types including seminoma, yolk sac tumor, teratoma, choriocarcinoma and embryonic carcinoma or mixed variants made up of components of the aforementioned types.[1] Although testicular tumors are rare tumors, representing about 1% of all cancers, they are the most common types of tumors in males aged between 20 and 40.[2] Most studies have indicated that delays in seeking diagnoses and accompanying treatments have been causing negative impacts in their

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managements.[3,4] TGCT being considered as a prototype of cancer of high cure and survival rate if properly managed.[5] We think that it is important to study the trend of this cancer in a given country (Jordan) to find out if there are specific characteristics of it among its population. It is expected that the study will be helpful in finding out certain risk factors so that outcomes can be monitored. In this retrospective study, we evaluated data of a sample of 75 Jordanian patients who had undergone radical orchiectomy at Prince Hussein Urology Centre/ Medical Service, a tertiary major referral center that serves patients from all the provinces in Jordan, between from 2010 to September 2014 to configure histopathological patterns of this treatable and yet potentially lethal cancer. In this regard, too, the study aimed at comparing the findings with those in the worldwide studies.

## Methods

After the review and approval by the ethical committee, retrospectively, pathological reports were reviewed between January 2010 and September 2014 in a bid to obtain radical orchiectomy specimens that had germ cell testicular tumors for analyses. In this regard, the specimens were analyzed in respect with variable clinical and histopathological parameters. All cases that had no germ cell tumors were excluded (two cases: one with lymphoma and the other with sertoli cell tumor). Moreover, all cases of pediatric GCT were excluded because of the apparent differences in the behaviour and natural history between male adults and male children. Finally, a total of 75 patients with germ cell tumors were identified and their data taken for analyses with respects to type, stage, site and presence of IGTN and age of patient and time of definite initial treatment.

## Results

Seminoma was the most common tumor sub-type of GCT that was identified among patients, and was represented by about 62% (47 patients), with the average age being 36 years (22-80). However, the average maximum diameter of the tumor size was about 5.07 cm (from all cases that ranged from 0.7 to 11cm). Whilst 28 cases of the seminoma were at stage T1, 17 were at T2 (Table I). Cases that involved right side were 63% and left side cases were 37%. Notably, however, no case had bilateral involvement. Classical seminoma was the most dominant variant, at 95%. Two cases were varients form of seminoma : one case of seminona with syncytiotrophoblastic elements, the other was spermatocytic seminoma. Most common presentations were painless masses at 91%. However, there were also other less common presentations such as advance disease, pain and hydrocele.

38% of the cases (28 patients) had NSGCT, and the average age for this group was 32 years ranging (20-48) The average size of the maximum diameter of the cancerous size was 5.7 cm (from 1.7-11cm). 53% of the NSGCT patients were at T1 stage, whilst the remaining ones, (47%) were at stage T2. Twelve (43%) of NSGCT involve the right side, and left side in 15 cases (57%).

Importantly, in this study, Intratubular Germ Cell Neoplasia (ITGCN) was present in 35% of seminoma cases whilst 42% in the NSGCT cases, resulting to an overall presentation of 37% of all people that had ITGCN. The study also revealed the rate of testis invasion as 17% (from 8 cases) for cases of seminoma, and 10% (from 3 cases) for cases that involved NSGCT. Overall, painless masses were the most common presentation, at 91%. In addition, no bilateral cases were identified.

Remarkable too, 85% of the NSGCT cases were of mixed forms, with most common types being yolk sac tumor and teratoma. The study also identified 4 cases of pure NSGCT: 2 cases of embryonal carcinoma, one case of yolk sac tumor and the other choriocarcinoma.

Notably, the average time for definitive treatment was 4 months and 3 months for seminoma and NSGCT respectively, ranging from 3 weeks to 12 months.

## Discussion

Germ Cell Tumors (GCT) are classified by two systems: WHO histopathological system which divides the GCT into pure or mixed form and the clinical based classification that broadly classifies the GCT into seminoma or non-seminoma types.[6] The clinical based classification system has been so because the two subtypes, as seminoma GCT and non-seminoma (NSGCT), have been showing very noticeable differences in their natural history, prognosis and management guidelines.[7,8] TGCT being considered as a prototype of cancer of high cure and survival rate if properly managed, up to 95% of cases excpected to be cured.[9-11]

**Table I:** Descriptive features of Seminoma and NSGCT tumors.

| Rete testis invasion | ITGCN* | Right VS left | T2 tumors | T1 tumors | Average size (Cm) | Average Age (Years) | Number of cases | Type |
|---|---|---|---|---|---|---|---|---|
| 8cases (17%) | 16(34%) | Right 30 (63%) Left 17 (37%) | 18(39%) | 29 (61%) | 5.07 | 36 | 47(62%) | SEMINOMA |
| 3cases (10%) | 12(42%) | Right 12 (43%) Left15 (57%) | 13(47%) | 15(53%) | 5.7 | 32 | 28(38%) | NSGCT * |

*Non Seminomatous Germ Cell Tumor..

**Table II:** T (Staging) Of Testicular Germ Cell Tumor

| No evidence of primary tumor | pT0 |
|---|---|
| *CIS | pTis |
| Tumor is limited to the testis and epididymis without vascular/lymphatic invasion; tumor may invade into the tunica albuginea but not the tunica vaginalis. | pT1 |
| Tumor is limited to the testis and epididymis with vascular/lymphatic invasion, or it is simply tumor extending through the tunica al buginea with involvement of the tunica vaginalis | pT2 |
| Tumor invades the spermatic cord with or without vascular/lymphatic invasion | pT3 |
| Tumor invades the scrotum with or without vascular/lymphatic invasion | pT4 |

*Carcinoma In Situ: Intra Tubular Germ Cell Neoplasm.
American Joint Committee on Cancer. Cancer Staging Education 2014

Seminoma is the most common germ cell tumor that occurs at an older age group that it is the NSGCT.[12,13] Seminoma is further divided into sub-types: classical seminoma, syncytiotrophoblastic seminoma, spermatocytic seminoma and seminoma with anaplastic features.[12] Non-seminomatous germ cell tumors (NSGCT) include embryonal carcinoma, yolk tumor, teratoma and choriocarcinoma.[14] The NSGCT types can exist either alone in pure forms or as combinations of mixed GCTs with or without subtypes of seminoma.[15] However, most NSGCTs occur as mixed tumors composed of two or more GCT subtypes. In this study, the GCTs that contain both seminoma and NSGCT subtypes are classified as NSGCTs.[16.8]

In this study, about 62% of cases were seminoma; most cases of seminoma were classical seminoma; 2 of the seminoma cases too, had variants with syncytiotrophblastic elements. Further, of the seminoma cases, one case of spermatocytic seminoma was identified. The average age of the seminoma patients was 36 years, and 25% of them had diffuse involvement of the testis.

Of all the cases, 38% of the patients had NSGCT, with most of them having mixed germ cell tumor.

Only 4 cases were established as pure NSGCT; two cases were of embryonal carcinoma, with one yolk sac tumor whilst the other as choriocarcinoma. The most

common type of the NSGCT, was teratoma. However, the most frequent types that were present in the mixed tumor were yolk sac tumor and teratoma followed by seminoma at 60%, 57% and 50%, respectively. As already mentioned, the average age of patients with NSGCT was 32 years, which is lower than the mean age of the seminoma patients.

Moreover, it seems that both right side and left side involvement are almost equal (as right 54%, and left 46%). There is no significant difference in prognoses between the two sites.[17] However, right side and left side tumors require different surgical templates if retroperitoneal lymph node dissection is needed due to the differences in the primary lymphatic landing zones between left and right sided tumors.[18,19] The mean size of the tumor for seminoma was 5.07 cm, ranging from 0.7 to 11 cm. For NSGCT, it was 5.7 cm, ranging from 1.7 to 11cm. The Rete testis invasion was identified in 8 cases of seminoma (17%) and 3 case of NSGCT (10% of cases). Overall, 15% of study population had Rete testis invasion.

The most common presentation of the Testicular Germ cell tumor has been painless mass.[4] Similarly, most common presentaion in our patients was painless mass (91%). Most invasive GCTs arise from a precursor lesion called Intratubular Germ Cell Neoplasia (ITGCN).[20,21] The ITGCN consists of undifferentiated germ cells located basally in the seminiferous tubules.[21,22] Men with the ITGCN have had a significant increase in risk of developing invasive GCT. Presence of ITGCN in the orchiectomy specimen does not increase the risk of relapse in patients with GCT.[21] In this study, ITGCN was present in 35% of cases of seminoma. In NSGCT, it was found in 42% of all the cases; thus, in overall 37% of the cases had ITGCN.

In 1997, the American Joint Committee on Cancer (AJCC) and the Union for International Cancer Control (UICC) reached a consensus in developing the classification criteria for the GCT that would recognize clinical stages of the disease based on histopathological findings, pathologic stage of the primary tumor, postorchiectomy serum tumor marker levels, and presence and extent of metastatic diseases as determined by physical examination and staging imaging studies.[23] (See Table II)

In this study, the extent of the primary tumor was included as the data were collected from the pathological reports. Most cases identified (57%) were at T1 stage. Cases at T2 were found to be 40%. However, incomplete data prevented researchers from including lymph node and distant metastasis staging in the study. Impliedly, early diagnoses were of paramount importance for the successful management of the disease. Delays in diagnoses and hence associated management could lead to adverse impacts, especially on prognosis.[24] The meantime for one to receive definitive initial management, that is radical orchiectomy, from the development of the symptoms was 4 months and 3 months for seminoma and NSGCT respectively (ranging from 3 weeks up to 12 months).

It was clear that the patients manifested significant delays before seeking diagnoses. In this regard, it was noted that both patients and physicians did not play their roles significantly. Thus, health authorities have to create awareness on physicians and education programs on patients about the significance of early diagnoses. Studies have regarded testicular cancer as a model of successful treatment of other cancers, especially those that are solid. Even during advanced stage, high doses of chemotherapies and rescue bone marrow transplantation can improve prognoses.[25,26] In addition, techniques of radical retroperitoneal dissection have been found to improve the effectiveness of GCT treatment, and reduce adverse complications.[27] Indeed, more studies should be done on Jordanians so that outcomes of this type of cancer can be realized, especially regarding delayed diagnoses. Fortunately, here at Prince Hussein Urology and Transplant Center, Jordan, data collection and management is now becoming computerized, and it is expected that monitoring and evaluating trends of this type of cancer will be easier. However, more prospective studies are needed for follow-up of patients with germ cell tumor, and to evaluate the current management of this curable cancer in our

institution and in Jordan as well. Although, the overall incidence of the disease is increasing, innovations in chemotherapeutics and radiotherapy and surgical therapies are marked to improve its management and patient survival.

The major limitation of this study is that, levels of tumor markers both preoperative and post radical orchiectomy have not been included due to incomplete data. Further, we did not follow patients' outcomes, and we did not also study the impacts of delays of diagnoses and initiations of the management. It is hoped that future studies will take these limitations as their concern to render more ameliorations on this subject.

## Conclusion

From this study it can be elucidated that the histopathological type and the age of patients with testicular germ cell tumors are comparable to those that are published in studies worldwide. Our patients manifested delays in diagnoses, and are at the age risk (20-45), therefore, patients should be encouraged to do testicular examination. Moreover, primary care physicians should be educated about such types of tumors.

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