Original Article

Clinicopathological and Demographic Analysis of Testicular Tumors: Single-Center Experience

Testis Tümörlerinin Klinikopatolojik ve Demografik Analizi: Tek Merkez Deneyimi

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ABSTRACT

Introduction: Testicular cancers rank among the most prevalent solid tumors in young males. The majority of these cases involve germ cell tumors, with seminomas emerging as the predominant histological subtype. This study aims to investigate both the clinical-demographic profiles of patients diagnosed with testicular tumors and the distribution of histopathological subtypes within this cohort.
Materials and Methods: Patients aged 18 and over who were diagnosed with testicular tumors other than secondary malignancies and were followed up in our clinic between 2008 and 2022 were included in the study. Comprehensive clinical and pathological data were meticulously recorded for each patient. Survival outcomes were compared using the Kaplan-Meier method with the log-rank test.
Results: Germ cell tumors exhibited a median onset age of 29. Among the cases, non-seminomatous tumors constituted 55.9%, while seminomas accounted for 44.1%. Within the non-seminomatous tumor category, mixed germ cell tumors stood out as the most frequently encountered subtype, comprising 45.4% of cases. Testicular involvement was noted predominantly in the right-side testis (56.7%), followed by the left-side testis (42.3%), and bilateral involvement was rare (1%). The percentage of patients diagnosed at stage 1 was 56.7%.
Conclusion: Germ cell tumors are primary testicular malignancies and remain a significant health problem among young men. Although seminomas have historically predominated, there has been an increase in the rates of non-seminomatous tumors in recent years. Early and accurate diagnosis remains the most important step towards the successful treatment of these tumors.

Keywords: Testicular cancer, Epidemiology, Germ cell neoplasms, Seminoma, Nonseminomatous germ cell tumor

ÖZET

Amaç: Testis kanserleri, genç erkeklerde en yaygın görülen solid tümörler arasında yer almaktadır. Bu vakaların büyük bir kısmını germ hücreli tümörler oluşturmakta ve seminomlar en yaygın histolojik alt tip olarak öne çıkmaktadır. Bu çalışma, testis tümörü tanısı konulan hastaların klinik-demografik profillerini ve bu grup içindeki histopatolojik alt tiplerin dağılımını incelemeyi amaçlamaktadır.
Gereç ve Yöntemler: Çalışmaya, 2008-2022 yılları arasında testis tümörü tanısı alan ve kliniğimizde takip edilen 18 yaş ve üstü hastalar dahil edildi; ikincil kötü huylu tümörler dışarıda bırakıldı. Her bir hastanın kapsamlı klinik ve patolojik verileri titizlikle kaydedildi. Sağkalım analizleri için Kaplan meier metodu kullanıldı ve log rank analizi yapıldı.
Bulgular: Germ hücreli tümörlerin median tanı yaşı 29 olarak belirlendi. Vakaların içinde, non-seminomatöz tümörler %55.9, seminomlar ise %44,1 oranında bulundu. Non-seminomatöz tümörler içinde, en sık rastlanan alt tip, vakaların %45,4'ünü oluşturan mix germ hücreli tümörler olarak

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belirlendi. Testis tutulumu çoğunlukla sağ testiste (%56,7) görülürken, sol testis (%42,3) ve çift taraflı tutulum nadirdi (%1). Evre 1'de tanı konulan hastaların oranı %56,7 olarak saptandı.
Sonuç: Germ hücreli tümörler primer testis maligniteleridir ve genç erkekler arasında önemli bir sağlık sorunu olmaya devam etmektedir. Tarihsel olarak seminomlar baskın olsa da, son yıllarda non-seminomatöz tümörlerin oranlarında bir artış görülmektedir. Erken ve doğru teşhis bu tümörlerin başarılı tedavisine yönelik en önemli adım olmaya devam etmektedir.

Anahtar Kelimeler: Testis tümörü, Epidemiyoloji, Germ hücreli tümör, Seminom, Nonseminomatöz germ hücreli tümör

Introduction

Testicular cancers are the most common solid tumors observed in young males[1]. The vast majority (>95%) of testicular cancers comprise testicular germ cell tumors. According to the current WHO classification system, germ cell tumors are classified into two main subgroups: seminomas and non-seminomatous tumors. Approximately 50% of these cases are seminomas. Non-seminomatous tumors encompass embryonal carcinoma, choriocarcinoma, yolk sac tumor, teratoma, and mixed germ cell tumors formed by various combinations of these elements[2]. The majority of cases occur in young men aged 15 to 40 [3].

The etiopathogenesis and risk factors associated with testicular cancers remain not fully elucidated. However, undescended testis (cryptorchidism) is a prominent risk factor, increasing the risk of testicular cancer development by fivefold[4]. Additionally, diet, environmental factors, infertility, and history of testicular cancer in the contralateral testis are acknowledged as risk factors for new testicular cancer development [3].

Approximately 70% of patients are diagnosed at an early stage (normal tumor marker levels, absence of lymph node involvement or distant metastases), while around 30% receive a diagnosis at an advanced stage[5]. In the metastatic stage, the International Germ Cell Cancer Collaborative Group's (IGCCCG) risk classification system stratifies patients into good, intermediate, and poor risk groups. Patients in the poor-risk group have a worse prognosis[6, 7].

This study aims to investigate epidemiological data, histopathological characteristics, and survival rates by screening patients diagnosed with testicular cancer at our hospital over the past 15 years.

Material and Methods

Medical records of patients who were under follow-up in our Medical Oncology Clinic between 2008 and 2022 were screened. Patients aged 18 and above diagnosed with testicular cancer were included in the study. Patients with metastasis to the testis from another cancer were excluded. The total number of patients enrolled in the study was 95. Patient data were retrieved from the hospital database and patient follow-up records. Data such as age, pathological diagnoses, histopathological subgroups, tumor location, tumor stage, current status, and last follow-up or dates of death were recorded.

Statistical analyses were conducted using IBM SPSS Statistical Software (IBM SPSS Statistics version 22.0, IBM SPSS, USA). Descriptive analysis was used to analyze the clinical and demographic characteristics of the patients. Categorical and numerical variables were presented as numbers and percentages (n, %). Continuous data were reported as means ± standard deviation if they followed a normal distribution; otherwise, they were presented as median and range. Survival outcomes were assessed using the

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Table 1. General characteristics of the patients

	n	%
Age (median, range)	29 (18-79)	
Smoking history		
Yes	51	53.7
No	44	46.3
Alcohol consumption		
Yes	10	10.5
No	85	89.5
Comorbidity		
Yes	6	6.3
No	89	93.7
Germ cell tumors	93	97.9
Non-germ cell tumors	2	2.1
Laterality		
Right	54	56.8
Left	40	42.2
Bilateral	1	1
Stage at diagnosis		
Stage 1	55	57.9
Stage 2	23	24.2
Stage 3	17	17.9

Kaplan-Meier method with the log-rank test (univariate analysis) or the Cox proportional hazards regression model (multivariate analysis). A p-value of <0.05 was considered statistically significant for all analyses.

The study received ethics committee approval from the local ethics committee The study was conducted in compliance with the principles outlined in the 1964 Declaration of Helsinki.

Results

A total of 95 patients were included in the study, with a median age of 29 (18-79) years. The number of patients with a history of smoking and alcohol consumption was 51 (53.7%) and 10 (10.5%), respectively. The majority of patients (93.7%) had no comorbidities. Of the patients, 93 (97.9%) were diagnosed with germ cell tumors. The general characteristics of the patients are presented in Table 1.

Table 2. Histopathological distribution of testicular tumors

	n	%
Seminoma	41	43.2
Non-seminoma (%54.7)		
Embryonal carcinoma	7	7.4
Mix germ cell tumor	44	46.3
Yolc sac tumor	1	1
Leydig cell tumor	2	2.1
Total	97	100

Non-seminomatous tumors were the most common germ cell tumor subtype (55.9%). Only two patients had Leydig cell tumors classified as non-germ cell tumors. The histopathological subtypes of the tumors are presented in Table 2.

Among the patients, 54 (56.8%) had tumors located in the right testis. At diagnosis, 55 patients (57.9%) were in stage 1, while 23 (24.2%) were in stage 2. Among the stage 1 patients, 12(21.8%) received one cycle of carboplatin (area under the curve=7), 11(20%) received one cycle of bleomycin/ etoposide/ cisplatin(BEP), and 5(9.1%) received three cycles of BEP, while 27(49.1%) patients did not receive any treatment. Among the stage 2 patients, 20(87%) received three cycles of BEP, while three(13%) received four cycles of BEP. Among the stage 3 patients, 13(76.5%) received three cycles of BEP, while four(23.5%) received four cycles of BEP.

The median overall survival had not been reached yet. The 5-year overall survival was 89% for the entire patient group, with rates of 98%, 94%, and 57% for stages 1, 2, and 3, respectively. Kaplan-Meier curves according to stages are presented in Figure 1.

Discussion

It is widely acknowledged that cancer incidence is progressively rising worldwide. In 2020, a total of 74,500 new cases of

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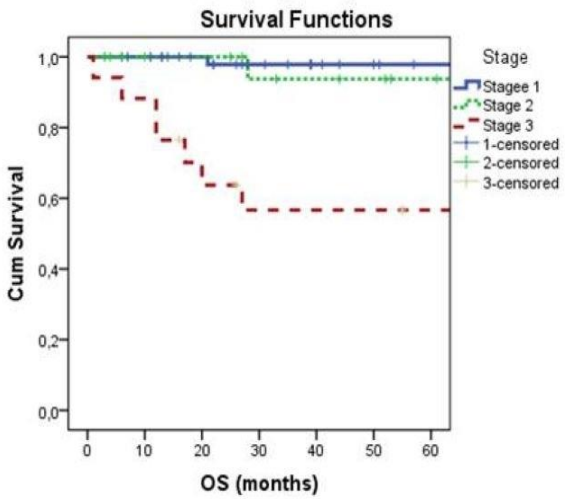

Figure 1. Kaplan-Meier plot according to tumor stage

testicular cancer were reported globally, positioning testicular cancers as the 20th most prevalent malignancy[8]. However, when focusing on the younger age group, the landscape shifts. Testicular tumors reaching their peak incidence within the 15-40 age range are recognized as the most frequent solid cancers in this demographic[3]. This trend is also evident in retrospective studies conducted in Turkey. In the study of Çalışkan et al., the mean age was 36.9, while Yalçınkaya et al. reported a mean age of 32.9[9, 10]. Similarly, Gürsoy et al. noted the most frequent occurrence within the 26-32 age bracket[11]. Our study, consistent with this trend, determined a median age of 29, aligning with the age range where testicular tumors are most commonly observed. Despite slight variations across series, the consistency in the age group with the peak incidence remains globally coherent.

Existing literature suggests a lower prevalence of non-seminomatous tumors[12]. However, studies conducted in our country indicate a higher occurrence of non-seminomatous tumors. Both Gürsoy et al. and Çalışkan et al. reported a higher incidence of non-seminomatous tumors compared to seminomas[9, 11]. Similarly, in our study, non-seminomatous tumors constituted 54.7% of all testicular tumors. While challenging to fully elucidate this discrepancy in retrospective Turkish series compared to the literature, genetic, sociocultural differences, and spesific environmental exposures may contribute to these variations.

Regarding subtypes within non-seminomatous tumors, mixed germ cell tumors are the most frequent. They are the second most common type of germ cell tumor in adults, following seminomas. Embryonal carcinoma constitutes the second most common non-seminomatous subtype. Teratomas and yolk sac tumors are less frequently encountered[11]. Our study similarly found the highest prevalence of mixed germ cell tumors within non-seminomatous tumors, with embryonal carcinoma being the second most frequent subtype.

Irrespective of histopathological subtypes, germ cell tumors exhibit a greater predilection for the right testis. Analyzing laterality, the studies previously mentioned and conducted in our country consistently report a higher prevalence of right testicular tumors compared to left testicular tumors. This phenomenon can be attributed to the higher frequency of undescended testes in the right testis. Additionally, while bilateral testicular tumors are reported to range between 1-7% in the literature, our study observed a bilateral occurrence rate of 1%[13].

Testicular cancers are recognized as chemosensitive tumors, thereby rendering survival outcomes generally favorable, whether in the adjuvant or metastatic setting. Gürsoy et al. reported a 5-year overall survival rate of 88% across the entire patient group[11]. In our study, the 5-year survival rate for the entire patient cohort was 89%, while stage 3 patients exhibited a rate of 57%. These data underscore the significance of administering adjuvant chemotherapy to patients at risk for recurrence or metastasis in

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terms of enhancing survival. Furthermore, the 5-year survival rate was 92% for seminomas and 89% for non-seminomatous tumors in our study. Despite a numerical distinction, statistical significance was not observed.

Several limitations are inherent to our study. Primarily, being a single-center and retrospective study, inherent biases are unavoidable. Secondly, the relatively limited number of cases may impact the study's power to provide comprehensive epidemiological insights. Additionally, the lack of information on salvage treatments for patients who experienced relapse is another limitation. Therefore, when interpreting the study's outcomes, it is advisable to consider these factors.

Conclusion

Germ cell tumors constitute the majority of testicular malignancies. While their incidence within the general population might be relatively low, they stand out as the most prevalent solid organ tumors among young men. Historically, seminomas have been reported to dominate among germ cell tumors; however, recent studies have indicated an increasing prevalence of non-seminomatous tumors. Treatment outcomes, particularly in the early stages, demonstrate near-optimal results. Hence, early and accurate diagnosis remains the pivotal step towards successful management in these tumors..

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