Original Article

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Scrotal Pain in Testicular Cancer: Analysis of Its Association with Clinicopathological Features

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Abstract

Objective: In our study, we aimed to determine the prevalence of scrotal pain at initial presentation in patients with testicular cancer (TC) and to investigate the association of scrotal pain with the clinical, histological, and pathological features of TC.
Materials and Methods: Patients who underwent radical inguinal orchiectomy with a pathology of TC between 2015 and 2024 at two training and research hospitals were retrospectively analyzed. Data on patients' age, initial presenting complaints, side of cancer, preoperative alpha-fetoprotein, human chorionic gonadotropin, and lactate dehydrogenase levels, stage, presence of rete testis/lymphovascular/hilar invasion, tumor size, number of tumor foci, and histological subtypes were recorded. Patients were categorized into two groups based on whether they reported scrotal pain at the initial presentation. The relationship between scrotal pain and the aforementioned factors was statistically analyzed.
Results: A total of 129 patients with TC were included, 63 (48.8%) reporting scrotal pain and 66 (51.2%) without pain. The primary complaints at presentation were-62 patients (48.1%) with painless scrotal swelling/irregularity, 48 patients (37.2%) with painful scrotal swelling/irregularity, and 15 patients (11.6%) with scrotal pain only. Additionally, two patients (1.6%) were diagnosed after abdominal masses were detected on computed tomography for abdominal pain, one (0.8%) was diagnosed during imaging for flank pain, and one (0.8%) was diagnosed during an infertility workup with scrotal ultrasonography. The mean age of the patients was 34 years. Pathology showed 61 (47.3%) seminoma and 68 (52.7%) non-seminoma cases. Rete testis invasion was present in 36 (27.9%) of cases and absent in 93 (72.1%) of cases. Lymphovascular invasion was present in 40 patients (31%) and absent in 89 patients (69%). Cancer staging classified 77 (59.7%) as stage 1, 42 (32.6%) as stage 2, and 10 (7.8%) as stage 3. Statistical analysis showed no significant association between scrotal pain and examined factors ($p>0.05$).
Conclusion: The signs and symptoms of TC should be well understood by all male patients and clinicians. It is important to keep in mind that scrotal pain can be observed in nearly half of TC patients. Prospective studies involving larger populations are needed to better understand the relationship between scrotal pain and TC.
Keywords: Orchiectomy, pain, signs and symptoms, testis cancer

Introduction

In recent years, there has been a significant increase in the incidence of testicular cancer (TC), particularly in industrialized societies, although the exact cause remains unclear. The incidence of TC peaks in the 20-40 age range, making it one of the most commonly diagnosed cancers in men within this age group (1,2). If diagnosis and treatment are initiated early in the development of TC, the five-year survival rate for patients can reach up to 99%. Although treatment options have significantly advanced, the survival rate for patients diagnosed at the metastatic stage of TC can decrease to as low as 78%. Furthermore, patients undergoing chemotherapy are at a high risk of experiencing side effects that could impact their quality of life (2-4). To prevent late diagnosis in TC patients, it is crucial that all men, as well as clinicians, are familiar with the signs and symptoms of TC (4,5). As stated in the European Association of Urology (EAU) guidelines, the general consensus in the literature is that TC is typically diagnosed as a "painless testicular mass or an incidental finding on ultrasound (US)" (6). A review of

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previous literature shows that scrotal pain is reported in only 0.01-10% of TC cases (7). Additionally, TC is listed under "painless masses" in the guidelines for primary healthcare services, that patients first approach (8). However, recent studies emphasize that pain can be a common symptom in patients with TC (2,7,9). The cause of scrotal pain in TC is thought to be related to hemorrhage or infarction within the tumor (7). A key topic of debate in the research is whether the presence of scrotal pain in TC can predict or reflect the stage of the cancer.

In our study, we aimed to determine the prevalence of scrotal pain at the time of initial presentation in patients with TC and investigate the relationship between scrotal pain and the clinical, histological, and pathological features of TC.

Materials and Methods

Our research was initiated after obtaining approval from the Scientific Research Evaluation and Ethics Committee of University of Health Sciences Türkiye, Ankara Etlik City Hospital (approval number: AEŞH-BADEK-2024-834, date: 11.09.2024). The data of patients who underwent radical inguinal orchiectomy with a preliminary diagnosis of TC between January 2015 and January 2024, at Dışkapı Yıldırım Beyazıt Training and Research Hospital and University of Health Sciences Türkiye, Ankara Etlik City Hospital were retrospectively reviewed from the hospital's information management system. Patients under the age of 18, those with a pathological diagnosis other than TC, sex cord stromal or adnexal tumors, primary extragonadal tumors, those who underwent orchiectomy due to an extratesticular mass, undescended testis, partial orchiectomy, a history of previous TC; and those with incomplete data in the records were excluded from the study. The surgical decisions for all patients were made by specialized urologists based on physical examination, scrotal Doppler US, tumor markers, and, when necessary, magnetic resonance imaging results. Additionally, all patients were provided with information about the inguinal orchiectomy procedure, and written consent was obtained.

We analyzed patients' age, cancer laterality, preoperative levels of alpha-fetoprotein (AFP), human chorionic gonadotropin (hCG), and lactate dehydrogenase (LDH), contrast-enhanced thoracoabdominal computed tomography findings, and histopathological reports, including histological subtypes (seminoma vs. non-seminoma), tumor sizes (mm), number of tumor foci (unifocal or multifocal), and the presence of rete testis, lymphovascular, or hilar invasion. The pathological stage and prognostic groups of the patients were determined according to the 2016 tumor, node, metastasis (TNM) classification system of the International Union Against Cancer (10). Additionally, the initial complaints of patients presenting to the emergency department or urology outpatient clinic were reviewed. However, in patients who reported scrotal pain at initial presentation, the severity of the pain could not be quantified due to the retrospective design of our study.

Statistical Analysis

Descriptive statistics were used to report the characteristics of the study groups, which were classified based on the presence or absence of scrotal pain. Continuous variables and their distribution patterns were evaluated for normality using the Shapiro-Wilk test. Variables that did not meet the assumptions for parametric tests were reported as medians and interquartile ranges (Q1-Q3) and compared using the Mann-Whitney U test. Categorical variables were summarized as frequency distributions and percentages, and comparisons were made using chi-square tests. In our study, a type 1 error level of 0.005 was considered, and all analyses were performed using IBM SPSS Statistics for Windows, version 22.0 (IBM Corp., Armonk, New York, United States of America).

Results

Following a review of the information management systems of our hospitals, data from 163 patients were collected. After applying the exclusion criteria, data from 129 patients with TC were included in the analysis. Among these, 63 patients (48.8%) reported scrotal pain at their initial presentation, while 66 patients (51.2%) did not experience pain. The primary complaints at presentation were identified as follows: 62 patients (48.1%) had painless scrotal swelling or irregularity, 48 patients (37.2%) had painful scrotal swelling or irregularity, and 15 patients (11.6%) presented with scrotal pain only. Additionally, 2 patients (1.6%) were diagnosed after abdominal masses were detected on computed tomography performed for abdominal pain, and 1 patient (0.8%) received a diagnosis during imaging performed due to flank pain. Lastly, 1 patient (0.8%) was diagnosed with a TC during an infertility workup involving scrotal Doppler ultrasonography. The initial presenting complaints of the patients are summarized in Table 1.

The mean age of the patients was calculated as 34 years [standard deviation (SD): ±11.84; median: 30 (Q1: 25, Q3: 40)]. TC was located in the right testis in 67 (51.9%) patients; in the left testis in 62 (48.1%) patients; with no cases of bilateral TC. The preoperative mean AFP level was 351.1 ng/mL SD: ±1693.3, median: 3.7 (Q1: 2.21, Q3: 53.65), hCG level was 2224.7 mIU/mL (SD: ±23233.94, median: 1.74 (Q1: 0.2, Q3: 31.79), and LDH level was 392.5 U/L (SD: ±1170.11, median: 221 (Q1: 190.75, Q3: 229.5).

Pathologically, the mean tumor size was 43.4 mm [SD: ±23.7; median: 40 (Q1: 25, Q3: 58.5)]. Among the patients, 61 (47.3%) were diagnosed with seminoma, while 68 (52.7%) had non-seminoma histology. Tumors were unifocal in 105 (81.4%) patients and multifocal in 24 (18.6%). Rete testis invasion was present in 36 (27.9%) patients, while 93 (72.1%) patients had

Table 1. Initial presenting complaints of patients with testicular cancer

Complaints	(n, %)
Painless scrotal swelling-irregularity	**62 (48.1%)**
Painful scrotal swelling-irregularity	**48 (37.2%)**
Only scrotal pain	15 (11.6%)
CT for abdominal pain	2 (1.6%)
CT for flank pain	1 (0.8%)
USG for infertility	1 (0.8%)

CT: Computed tomography, USG:Ultrasonography

no invasion. Lymphovascular invasion was detected in 40 (31%) patients and was absent in 89 (69%). Additionally, hilar invasion was present in 13 (10.1%) patients, and absent in 116 (89.9%).

Based on the TNM staging system, the prognostic classification results were as follows: 77 (59.7%) patients were stage 1, 42 (32.6%) were stage 2, and 10 (7.8%) were stage 3. The clinical and pathological data of the patients are summarized in Table 2.

The relationship between scrotal pain and various clinical and pathological factors was analyzed. Statistical evaluations showed no significant association between scrotal pain and patient age, tumor laterality, tumor size, number of tumor foci, presence of rete testis invasion, lymphovascular invasion, hilar invasion, preoperative AFP, hCG, LDH levels, disease stage, and histological subtype of the tumor (p-values: 0.188, 0.725, 0.532, 0.501, 0.237, 0.848, 0.763, 0.728, 0.948, 0.296, 0.303, and 1, respectively). Detailed statistical results are presented in Table 3.

Table 2. Clinical and pathological information of patients with testicular cancer

Age (years) (median: Q1-Q3)	30 (25-40)
Side (n, %)	
Right	67 (51.9%)
Left	62 (48.1%)
Scrotal pain (n, %)	
Absent	66 (51.2%)
Present	63 (48.8%)
Total tumor size (mm) (median: Q1-Q3)	40 (25-58.5)
Number of tumors (n, %)	
Single	105 (81.4%)
Multiple	24 (18.6%)
Rete testis invasion (n, %)	
Absent	93 (72.1%)
Present	36 (27.9%)
Lymphovascular invasion (n, %)	
Absent	89 (69%)
Present	40 (31%)
Hilus invasion (n, %)	
Absent	116 (89.9%)
Present	13 (10.1%)
AFP (ng/mL) (median: Q1-Q3)	3.7 (2.21-53.65)
hCG (mIU/mL) (median: Q1-Q3)	1.74 (0.2-31.79)
LDH (U/l) (median: Q1-Q3)	221 (190.75-229.5)
Stage (n, %)	
1	77 (59.7%)
2	42 (32.6%)
3	10 (7.8%)
Histology (n, %)	
Seminoma	61 (47.3%)
Non-seminoma	68 (52.7%)

Q1: 1st quartile, Q3: 3rd quartile, AFP: Alpha-fetoprotein, hCG: Human chorionic gonadotropin, LDH: Lactate dehydrogenase, mIU: Milli-international unit, U/l: Unit per liter

Discussion

With advancements in modern diagnostic and treatment methods, TC exhibits one of the highest survival rates among all cancer types, however, delays in diagnosis often result in the detection of TC at more advanced clinical stages. Consequently, this necessitates intensive chemotherapy, leading to increased morbidity and mortality that is associated with the TC (4). According to the United States National Cancer Institute's Surveillance, Epidemiology, and End Results database, the

Table 3. Statistical analysis of possible factors causing scrotal pain in testicular cancer

Factors	Scrotal pain		p-value
	Absent	**Present**	
Age (years) (median; Q1-Q3)*	29.5 (24-40)	35 (25-41)	0.188
Side (n, %)			
Right	33 (49.3%)	34 (50.7%)	0.725
Left	33 (53.2%)	29 (46.8%)	
Total tumor size (mm) (median; Q1-Q3)*	40 (29.5-60)	40 (22-55)	0.532
Number of tumors (n, %)			
Single	52 (49.5%)	53 (50.5%)	0.501
Multiple	14 (58.3%)	10 (41.7%)	
Rete testis invasion (n, %)			
Absent	**45 (48.4%)**	**48 (51.6%)**	0.237
Present	21 (58.3%)	15 (41.7%)	
Lymphovascular invasion (n, %)			
Absent	**47 (52.8%)**	**42 (47.2%)**	0.848
Present	19 (47.5%)	21 (52.5%)	
Hilus invasion (n, %)			
Absent	**59 (50.9%)**	**57 (49.1%)**	0.763
Present	7 (53.8%)	6 (46.2%)	
AFP (ng/mL) (median; Q1-Q3)*	3.84 (2.22-51.36)	3.64 (2.14-60.4)	0.728
hCG (mIU/mL) (median; Q1-Q3)*	1.9 (0-36.3)	0.98 (0.2-14.7)	0.948
LDH (U/l) (median; Q1-Q3)*	232 (195-308)	219 (184.5-299)	0.296
Stage (n, %)			
1	**36 (46.8%)**	**41 (53.2%)**	0.303
2	25 (59.5%)	17 (40.5%)	
3	5 (50%)	5 (50%)	
Histology (n, %)			
Seminoma	**34 (55.7%)**	**27 (44.3%)**	1
Non-seminoma	32 (47.1%)	36 (52.9%)	

*: Mann-Whitney U test, Q1: 1st quartile, Q3: 3rd quartile, AFP: Alpha-fetoprotein, hCG: Human chorionic gonadotropin, LDH: Lactate dehydrogenase, mIU: Milli-international unit, U/l: Unit per liter
Chi-square test

prognosis of TC worsens as the stage at diagnosis becomes more advanced (11). When TC manifests with pain, it may be misdiagnosed as more prevalent benign conditions, like epididymo-orchitis or scrotal trauma, leading to potential delays in its diagnosis. A survey conducted among patients diagnosed with TC revealed that 95% initially sought care from family physicians, and 54% were misdiagnosed at the time of their initial presentation. A broader study reported a misdiagnosis rate of 13% in primary care centers. In both studies, TC was most commonly mistaken for epididymitis (4,12). These findings highlight a lack of adequate awareness regarding the symptoms of TC, one of the most common malignancies in young men, among both patients and primary care physicians.

Our study demonstrated that, contrary to common belief, scrotal pain is not a rare symptom in patients with TC. In addition to scrotal pain being the sole complaint in some cases, nearly half of the patients with TC experienced this symptom. Similar to our findings, Rovito et al. (2) in a survey involving 569 TC patients, reported that 44.3% of their patients experienced scrotal pain during the initial clinical examination. Additionally, Wilson and Cooksey (7) emphasized the significance of scrotal pain as a symptom in TC patients. Although some previous studies have reported lower rates of scrotal pain, they also concluded that scrotal pain is not a rare occurrence in patients with TC (12,13). Although the EAU guidelines describe TC as a "painless testicular mass or an incidental finding on US" in our study, only one patient was diagnosed incidentally with TC during scrotal ultrasonography performed for another reason (6).

The number of studies investigating the mechanism by which TC causes scrotal pain is limited. Similar to our findings, Wilson and Cooksey (7) did not find a significant relationship between the presence of scrotal pain at presentation and the histological subtype or stage of TC. On the other hand, Rovito et al. (2) reported that the frequency of scrotal pain increases as the stage of TC advances. Our study is the first to examine the relationship between scrotal pain at initial presentation and TC-specific factors such as tumor size, number of tumor foci, rete testis invasion, lymphovascular invasion, hilar invasion, preoperative AFP, hCG, and LDH levels. In our study, we found that the presence of scrotal pain does not predict the presence of TC-specific factors.

An increasing number of healthcare consumers are turning to the internet as a primary source of information, with many individuals considering online searches as a step that precedes consulting a physician (14). Particularly among younger patients, the internet is highly likely to serve as a key source of health-related knowledge. Therefore, understanding which websites patients access, how they filter the information, and what criteria they use to assess its reliability is crucial, as it ultimately affects the quality of the information obtained. Given these factors, it is reasonable to anticipate that suspicions regarding a potential cancer diagnosis may lead to heightened anxiety.

Pain, including cancer-related pain, is now widely recognized as a complex biopsychosocial phenomenon influenced by multiple factors (15). Cancer pain may stem from a variety of biological factors, including both disease-related and treatment-related mechanisms (16). However, it is not limited to purely physiological or biological causes; psychological elements such as anxiety and fear also play a significant role in shaping the pain experience (17). In our current study, while clinical and pathological factors associated with pain were examined, no psychometric tools were used to assess psychological contributors. The high frequency of reported pain may be a psychosomatic manifestation triggered by anxiety associated with the possibility of a testicular tumor diagnosis.

Study Limitations

Since our study was conducted retrospectively using the hospital information management system, the severity of scrotal pain could not be assessed. Consequently, the relationship between the degree of scrotal pain severity and the stage of TC could not be evaluated. Moreover, the impact of initial scrotal pain on the prognosis of TC patients could not be investigated during follow-up. Another limitation of our study is the lack of evaluation of individual tumor components such as yolk sac and teratoma, as well as pathological findings that may contribute to scrotal pain, such as necrosis and infarction.

Conclusion

In conclusion, the signs and symptoms of TC should be well understood by all male patients and clinicians. It is important to keep in mind that scrotal pain may be present in approximately half of patients with TC. Prospective studies involving larger populations are needed to better understand the relationship between scrotal pain and TC.

Ethics

Ethics Committee Approval: Scientific Research Evaluation and Ethics Committee of University of Health Sciences Türkiye, Ankara Etlik City Hospital (approval number: AEŞH-BADEK-2024-834, date: 11.09.2024).

Informed Consent: All patients were provided with information about the inguinal orchiectomy procedure, and written consent was obtained.

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Footnotes

Authorship Contributions

Surgical and Medical Practices: B.Y.E., E.H., M.A., A.N.K.,Concept: M.Y., T.C.Ş., M.A., Design: M.Y., E.H., A.N.K., Data Collection or Processing: B.Y.E., E.H., T.C.Ş., Analysis or Interpretation: B.Y.E., T.C.Ş., M.A., Literature Search: M.Y., T.C.Ş., A.N.K., Writing: B.Y.E., M.A., A.N.K.,

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