



Testicular Tumors: A 15-Year Archive Review and Histopathological Evaluation

Testis Tümörleri: 15 Yıllık Arşiv Taraması ve Histopatolojik Değerlendirilmesi

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Abstract

Aim: Testicular tumors are one of the most common malignancies in men in the age group of 15-40 years, although they are rarely observed. In our study, it was aimed to evaluate their histopathological features by retrospectively examining of the cases diagnosed as testicular tumor in our department.

Material and Method: Age, tumor localization, tumor size, pathological stage, tumor type and frozen information of 65 cases diagnosed as testicular tumor in the Department of Medical Pathology at Tokat Gaziosmanpaşa University Faculty of Medicine between 2006-2020 were examined.

Results: The mean age of 65 cases diagnosed as tumor was 37.9±17.73 years. Their ages ranged from 1 to 78 years. Macroscopic tumor diameter was an average of 4.6±2.36 cm, 36 (55.4%) of them were located in the right and 29 (44.6%) of them were located in the left testis. Histopathological diagnosis was germ cell tumor in 53 (81.7%) cases and non-germ cell tumor in 12 (18.3%) cases. The most common tumor was seminoma with 22 (33.9%) cases and the second was mixed germ cell tumor with 19 (29.3%) cases. In components forming mixed germ cell tumors, embryonal carcinoma was the most commonly seen. Intraoperative frozen section examination was performed in 17 cases, it was determined that 10 cases were malignant and 7 cases were benign.

Conclusion: The histopathological and general features of our series of testicular tumor was determined to be compatible with the literature to a great extent. Intraoperative frozen section examination is an important auxiliary diagnostic method in terms of organ preserving surgery.

Keywords: Testis, tumor, germ cell, frozen section examination, testis preserving surgery

Öz

Amaç: Testis tümörleri nadir görülmekle birlikte, 15-40 yaş grubundaki erkeklerde en sık görülen malignitelerden biridir. Çalışmamızda bölümümüzde testis tümörü tanısı almış olguların retrospektif olarak incelenip, histopatolojik özelliklerinin değerlendirilmesi amaçlandı.

Gereç ve Yöntem: 2006-2020 yılları arasında Tokat Gaziosmanpaşa Üniversitesi Tıp Fakültesi Tıbbi Patoloji Anabilim Dalı'nda testis tümörü tanısı alan 65 olgunun yaş, tümör lokalizasyonu, tümör boyutu, patolojik evre, tümör tipi ve frozen bilgisi incelendi.

Bulgular: Tümör tanısı alan 65 olgunun yaş ortalaması 37,9±17,73 yılı idi. Yaşları 1-78 yıl arasında değişmekteydi. Makroskopik tümör çapı ortalama 4,6±2,36 cm olup, 36'sı (%55,4) sağ, 29'u (%44,6) sol testis lokalizasyonlu idi. Histopatolojik tanı 53 olguda (%81,7) germ hücreli tümör ve 12 olguda (%18,3) germ hücreli dışı tümördü. En sık görülen tümör 22 olgu (%33,9) ile seminom ve ikinci sıklıkta 19 olgu (%29,3) ile mikst germ hücreli tümördü. Mikst germ hücreli tümörleri oluşturan komponentlerde en sık embriyonel karsinom görüldü. İntraoperatif frozen kesit inceleme 17 olguda yapılmış olup, 10 olgunun malign, 7 olgunun benign olduğu saptandı.

Sonuç: Testis tümörü serimizin histopatolojik ve genel özelliklerinin büyük oranda literatür ile uyumlu olduğu saptanmıştır. İntraoperatif frozen inceleme organ koruyucu cerrahi açısından önemli bir yardımcı tanı yöntemidir.

Anahtar Kelimeler: Testis, tümör, germ hücre, frozen kesit inceleme, testis koruyucu cerrahi



INTRODUCTION

Testicular tumors are one of the most common seen malignancies in men in the age group of 15-40 years, although they are rarely observed. It constitutes 1-2% of all malignancies in men. The age standardized incidence rate of testicular cancer was 1,5 per 100000 people in the world. It is more commonly seen in developed countries and its incidence is increasing day by day. As the highest incidence rate is 7.2-8.7 in Europe, the lowest incidence rate is 0.3-0.6 in Africa and 0.4-1.7 in Asia.^[1,2] Etiopathogenesis has not been fully elucidated. However, environmental and genetic factors are blamed in the etiology. Family history, undescended testis, testicular microlithiasis, inguinal hernia, low birth weight, maternal smoking during pregnancy, high-fat diet, obesity, occupational exposures are supposed among the risk factors.^[3,4] Patients with testicular tumors usually present with a unilateral painless mass. The tumors are more commonly observed in the right testis than the left one. The incidence of bilaterality is reported to be at rate of 1-4%.^[5,6] Germ cell tumors (GCTs) constitute 95% of testicular tumors. GCTs are divided into two main groups as seminomatous and nonseminomatous GCTs. Seminomas make up 50% of all GCTs. Nonseminomatous GCTs include embryonal carcinoma (EC), yolk sac tumor (YST), choriocarcinoma (CC) and teratoma (T). Non-germ cell tumors (NGCTs) of the testis are classified as sex cord-stromal tumors paratesticular tumors, mesenchymal tumors of the spermatic cord and testicular adnexa, hematolymphoid tumors and metastatic tumors.^[3,4] In The World Health Organization (WHO) 2016 classification of testicular tumors, different from the WHO 2004 classification, germ cell tumors are defined as the tumors derived from germ cell neoplasia in situ and the tumors unrelated to germ cell neoplasia in situ.^[3,7]

In our study, we aimed to examine the age, tumor location, tumor size, pathological stage, tumor type and frozen information of cases diagnosed as testicular tumor in our department between 2006-2020, and to evaluate them in the light of literature information.

MATERIAL AND METHOD

A total of 65 cases who were diagnosed as testicular tumor by performing histopathological examination in the Department of Medical Pathology between 2006-2020, were analyzed after obtaining the approval of the Clinical Research Ethics Committee (20-KAEK-320) at Tokat Gaziosmanpaşa University Faculty of Medicine for our study. Pathology reports of the cases were analyzed retrospectively by scanning the pathology archive. Hematoxylin-eosin stained preparations of the cases were reviewed and classified according to the WHO 2016 classification. Age, tumor localization, tumor size, tumor type, pathological stage and frozen information of the cases were registered from the pathology reports and the records in the automation system. The obtained data were evaluated in the light of literature information.

Statistically, categorical measurements were specified as numbers and percentages, and continuous measurements were expressed as mean and standard deviation (median and minimum-maximum where necessary). SPSS 22 package software was used for the analysis.

RESULTS

Testicular tumors were detected in 65 (42.8%) of 152 orchiectomy materials from 2006-2020, which were retrospectively detected from our department archive. The ages of 65 patients diagnosed as tumor ranged from 1 to 78 years and the mean age was found to be 37.9 ± 17.73 years. The age range distribution of the patients was given in **Figure 1**. Macroscopic tumor diameters ranged from 0.8 to 10 cm, with an average of 4.6 ± 2.36 cm. 36 (55.4%) of the tumors were located in the right, 29 (44.6%) of them were located in the left testis. Bilateral testicular involvement was not present in any of the patients. Fifty three (81.7%) of our cases were diagnosed as GCT and 12 (18.3%) of them as NGCT. The histopathological distribution of our cases diagnosed as testicular tumor was given in **Table 1**. The most common tumor among our cases was seminoma with 22 (33.9%) cases (**Figure 2**) and the second most common tumor was mixed GCT with 19 (29.3%) cases. In the components forming mixed GCTs, EC (**Figure 3**) was the most common seen. The distribution of mixed GCTs and constituent components was shown in **Table 2**. In our series, there were 17 cases who underwent intraoperative frozen section examination. The characteristics of these cases were given in **Table 3**. Intraoperative frozen section examination was performed in 17 cases, it was determined that 10 cases were malignant and 7 cases were benign. All cases diagnosed as epidermoid cyst were the cases which underwent intraoperative frozen section examination. Of the cases with pathological tumor staging, 31 were found to be pT1, 18 were pT2, and 4 were pT3. Six of our patients became exitus. Two of them had a diagnosis of GCT and the others consisted of one patient each who had a diagnosis of lymphoma, leiomyosarcoma, adenomatoid tumor and malignant melanoma metastasis.

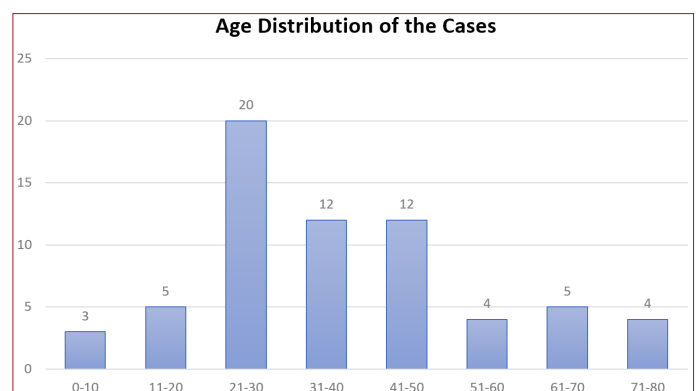


Figure 1. The age distribution of the patients with testicular tumors

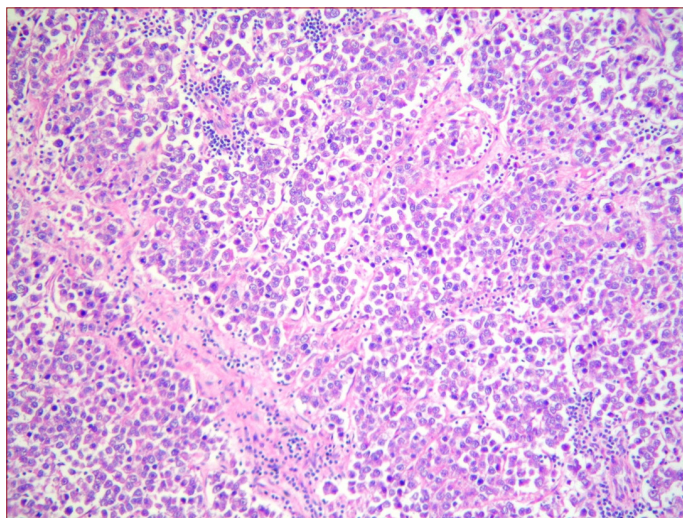


Figure 2. Seminoma. Lymphocytic infiltration between polygonal shaped tumor cells with prominent nucleoli and eosinophilic cytoplasm. (HE x 100)

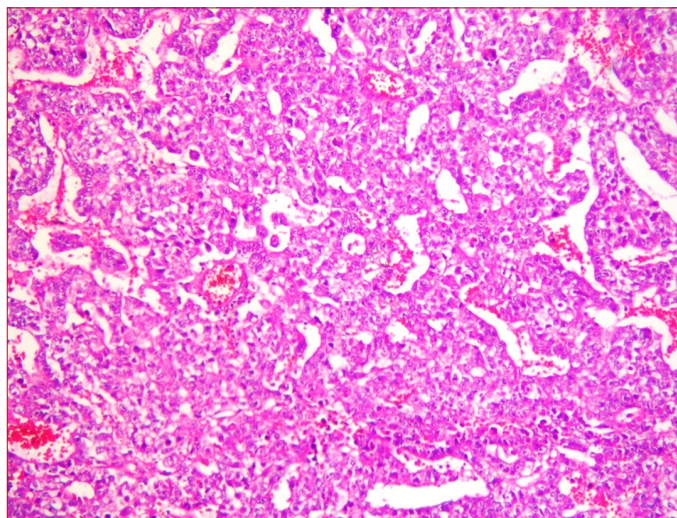


Figure 3. Embryonal carcinoma. Glandular pattern of columnar-shaped tumor cells. (HE x 100)

Table 1. Histopathological distribution of testicular tumors		
Diagnosis	n	%
Germ cell tumors		
Seminoma	22	33.9
Embryonal carcinoma	1	1.5
Yolk sac tumor	3	4.7
Choriocarcinoma	1	1.5
Teratoma	1	1.5
Mixed GCT	19	29.3
Spermatocytic tumor	1	1.5
Epidermoid cyst	5	7.8
Sex cord-stromal tumor		
Leydig cell tumor	2	3.1
Hematolymphoid tumors		
Diffuse large B-cell lymphoma	4	6.2
Paratesticular tumors		
Adenomatoid tumor	1	1.5
Mesenchymal tumors of the spermatic cord and testicular adnexa		
Leiomyoma	1	1.5
Leiomyosarcoma	1	1.5
Hemangioma	1	1.5
Metastatic tumors		
Malignant melanoma metastasis	1	1.5
Renal cell carcinoma metastasis	1	1.5
Total	65	100

Table 2. Distribution of mixed GCTs		
Tani	n	%
EC+YST+T	6	31.5
S+EC	4	21
S+EC+YST	3	15.7
EC+YST	1	5.3
EC+T	1	5.3
S+YST	1	5.3
S+YST+T	1	5.3
S+EC+YST+T	1	5.3
S+EC+T+CC	1	5.3
Total	19	100

EC: Embryonal carcinoma, YST: Yolk sac tumor, T: Teratoma, S: Seminoma, CC: Choriocarcinoma

Table 3. Testicular tumors which intraoperative frozen section examination were performed in				
Age	Localization	Tumor size (cm)	Frozen section diagnosis	Final diagnosis
78	Left	3	Malignant	Seminoma
38	Right	2.5	Malignant	Mixed GCT (EC+S)
21	Left	3	Malignant	Mixed GCT (EC+YST)
19	Right	2	Malignant	Embryonal carcinoma
49	Right	10	Malignant	DLBCL
1	Left	5	Malignant	Yolk sac tumor
9	Right	0.8	Benign	Epidermoid cyst
25	Right	4	Malignant	Seminoma
41	Left	1	Malignant	Teratoma
21	Left	1	Benign	Epidermoid cyst
64	Right	1.5	Benign	Hemangioma
6	Right	1.5	Benign	Epidermoid cyst
62	Right	3	Benign	Leiomyoma
16	Right	1.5	Benign	Epidermoid cyst
25	Right	7.5	Malignant	Seminoma
22	Left	3	Malignant	Yolk sac tumor
68	Right	3	Benign	Epidermoid cyst

GCT: Germ cell tumor, EC: Embryonal carcinoma, S: Seminoma, YST: Yolk sac tumor, DLBCL: Diffuse large B-cell lymphoma

DISCUSSION

Testicular cancer is the most common cancer of the genital system in men. Approximately 50000 new cases and 10000 deaths are detected every year in the world.^[2] In the last few decades, an increase has been observed in the incidence of testicular cancer all over the world, mainly in European countries. However, with early diagnosis, standardization of tumor management and advances in treatment, a significant decrease in mortality rates has been detected. It is seen that the five-year survival rates have increased from 63% to over 90%.^[1] The etiology of testicular tumors is not clear, and environmental and genetic factors play a role. Cryptorchidism is one of the most important risk factors and the rate of development of testicular cancer is 2.9-6.3%.^[8] Age, family history of testicular tumor, the white race,

high socioeconomic level, testicular microlithiasis, trauma, infection, exposure to in utero diethylstilbestrol, mother's smoking during pregnancy, occupational exposures, chemicals, diet rich in fat and dairy products are among the risk factors.^[2,3,8] Testicular tumors are most common in the 15-40 years age range. The mean age of the patients in our series was 37.9 years, and it was consistent with the literature.^[1,2] Right side testicular tumor involvement is more common than the left side. The frequency of bilateral testicular tumor involvement is 1-4%. Bilateral tumors can be observed simultaneously (synchronous) or at different times (metachronous).^[6] Right side involvement was more common in our cases, and bilateral testicular involvement was not observed.

Approximately 90-95% of testicular tumors consist of GCTs. In our series, 53 (81.7%) of 65 cases were GCT. Seminomas are the most common observed among testicular tumors. Seminomas constituted 22 (33.9%) of our cases (**Figure 2**), in addition they were found at a rate of 58% of the components that made up mixed GCTs (**Table 2**). Radiotherapy is used for the treatment of seminomas and has no place for the treatment of other GCTs, so in the presence of testicular tumor, correct diagnosis of seminomas is important in terms of treatment and prognosis. It has been reported that the biological behaviors of anaplastic seminomas with high mitotic activity do not change the prognosis and treatment of the patient and therefore do not need to be specified in pathology reports.^[9,10] Although the rate of embryonal carcinoma in mixed GCTs is over 80%, its pure form is rarely seen (2-10%).^[5,9] Pure embryonal carcinoma was detected in one of our cases (1.5%) and embryonal carcinoma was available in 89.7% of mixed GCTs in our cases. Although yolk sac tumor is rarely seen (1%), it is the most common observed testicular tumor of the prepubertal period. In children, its pure form is seen. Its pure form is rare in adults and it is found as a component of mixed GCTs, with a rate of 40%.^[11] One of our three cases diagnosed as yolk sac tumor was in the prepubertal period and he was 1 year old, the others were 22 and 38 years old. In 68.4% of our mixed GCT cases, yolk sac tumor component was available. Pure form of choriocarcinoma is rare and accounts for less than 1% of testicular tumors. Finding the vital tumor area becomes difficult due to the widespread presence of bleeding and necrosis. Vascular invasion is an important feature of choriocarcinoma.^[11,12] In one of our cases, pure choriocarcinoma was seen and choriocarcinoma was available as a component of mixed GCT in our another case. The age of our pure choriocarcinoma case was 21 years. He was diagnosed as lung metastasis before, and then it was detected that the primary was testis. Microscopic examination revealed that the entire testis was hemorrhagic and necrotic in appearance, there were tumor cells with pleomorphic bizarre nuclei in limited areas, frequent mitosis and widespread vascular invasion (**Figure 4**). Teratomas are rarely seen as pure and constitute 2-3% of GCTs. They

accompany mixed GCTs at a rate of approximately 50%. In our series, pure teratoma was observed in a 41-year-old patient. The rate of teratoma accompanying mixed GCTs was 52.7% in our cases. While prepubertal teratomas show benign behavior, it is considered that postpubertal teratomas show malignant behavior.^[10,11] Mixed GCTs, which are composed of different combinations of GCT subtypes, constitute approximately half of the testicular GCTs. In our series, the rate of mixed GCTs to all testicular tumors was low, with the rate being 29.3% (**Table 1**). Among the most common combinations there are embryonal carcinoma+teratoma, embryonal carcinoma+seminoma, embryonal carcinoma+yolk sac tumor+teratoma, embryonal carcinoma+teratoma+choriocarcinoma. Embryonal carcinoma is the most common accompanying component to combinations (**Figure 3**).^[3,11] In our series, combination of embryonal carcinoma+yolk sac tumor+teratoma was the most frequently observed (**Table 2**). Spermatocytic tumor constitutes 1-2% of GCTs. Average age of occurrence is 52-59 years.^[3] In our series, one case (1.5%) with a diagnosis of spermatocytic tumor was available and the age was 47 years. Epidermoid cyst accounts for 1-2% of all testicular tumors and is the most common benign tumor of the testicle. It is frequently seen between the second and fourth decades. It has an average diameter of 2 cm and is mostly observed in the right testicle. It is difficult to distinguish from malignant tumors clinically, and the definitive diagnosis is made by histopathological examination. Intraoperative frozen section examination is useful in determining radical orchiectomy or testicular preserving surgery option for treatment of epidermoid cyst.^[13] Four of our five cases diagnosed as epidermoid cyst were localized in the right testicle, and the mean tumor diameter was 1.6 cm. Intraoperative frozen section examination was performed in all of our cases, and testicular preserving surgery was performed because their frozen section diagnoses were benign.

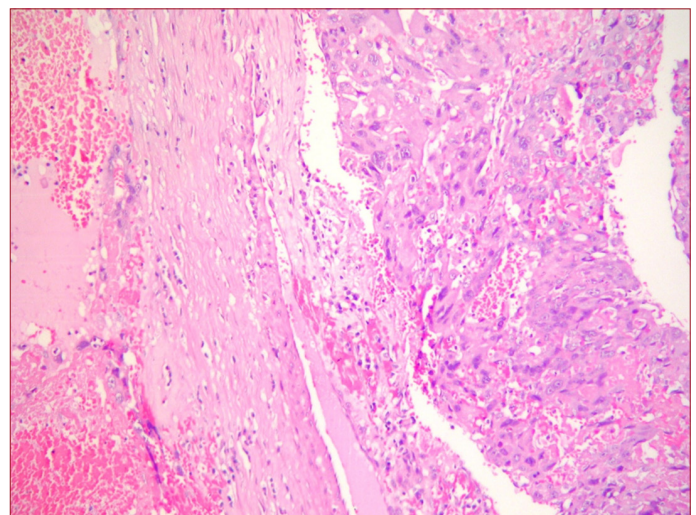


Figure 4. Choriocarcinoma. Hemorrhage, areas of necrosis and vascular invasion of pleomorphic tumor cells. (HE x 100)

Sex cord-stromal tumors account for 8% of all testicular tumors. Leydig cell tumor, which is the most common seen in this group, constitutes 1-3% of all testicular tumors.^[11,14] Leydig cell tumor was detected in 2 (3.1%) of our cases, but other tumor types were not observed. Lymphomas are the most common testicular neoplasms of patients over the age of 60 years. It is seen in 1-9% of all testicular tumors. The most common type is diffuse large B-cell lymphoma with a rate of 80-90%.^[15] Diffuse large B cell lymphoma was observed in 4 (6.2%) of our cases. Three of these cases were over 60 years old. In our series, an adenomatoid tumor located in the paratesticular area was observed in one case who was sent for consultation. Adenomatoid tumor is the most common paratesticular neoplasm. It accounts for approximately 30% of all paratesticular masses.^[3,16] Mesenchymal tumors may develop from interstitial mesenchymal cells and endothelial cells of the spermatic cord and testicular adnexa. In our series, one case each with a diagnosis of hemangioma, leiomyoma and leiomyosarcoma was observed. Secondary tumors of the testis are extremely rare, they are seen at a rate of 0.06-3.6%. The most common metastasis to the testicle originate from the prostate, gastrointestinal tract, kidney, lung, malignant melanoma and urinary tract. In children, neuroblastoma, Willms tumor and rhabdomyosarcoma metastases are seen.^[3] In our cases, malignant melanoma metastasis was observed in a 76-year-old patient and renal cell carcinoma metastasis in a 56-year-old patient.

Most of the testicular tumors are GCTs diagnosed with clinical and radiological findings before surgery. With the increasing use of scrotal USG, the diagnosis of small-sized and nonpalpable testicular lesions has increased. It has been shown that 80% of these lesions are benign. Scrotal ultrasonography does not have sonographic features to precisely distinguish intratesticular tumors as benign and malignant. The correct and definite distinction between benign and malignant lesions is only possible with histopathological examination. Frozen section examination is a very sensitive and specific intraoperative procedure to distinguish testicular and paratesticular tumors as benign and malignant. There are few studies suggesting that frozen section examination can be accurate and effective to avoid radical orchiectomy. Silverio et al. retrospectively analyzed frozen section examination results and the biopsy permanent sections of 170 patients diagnosed as testicular lesions during fourteen years. As a result, they determined that frozen section examination helped to prevent unnecessary radical orchiectomy in 46 (88.5%) of cases with non-malignant lesions.^[17,18] Frozen section examination is an important diagnostic method in determining the preference of organ-preserving surgery or radical orchiectomy surgical methods for childhood testicular tumors.^[19] In our series, frozen section examination was performed in 17 cases, and organ preserving surgery was performed in 7 cases whose frozen diagnosis was benign (**Table 3**).

CONCLUSION

As a result, the majority of our series of 65 cases with testicular tumors in our 15-year archive consisted of GCTs by being in accordance with the literature, and most of these were seminomas and mixed GCTs. We think that further studies should be done to emphasize that intraoperative frozen section examination is an important diagnostic method in terms of organ preserving surgery.

ETHICAL DECLARATIONS

Ethics Committee Approval: For this research; Tokat Gaziosmanpaşa University Faculty of Medicine Clinical Research Ethics Committee approval was obtained (Date: 28.01.2021, number 20-KAEK-320)

Informed Consent: Because the study was designed retrospectively, no written informed consent form was obtained from patients.

Referee Evaluation Process: Externally peer-reviewed.

Conflict of Interest Statement: The authors have no conflicts of interest to declare.

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