RESEARCH ARTICLE

Clinicopathological Features and Survival of Young Turkish Patients with Testicular Germ Cell Tumors

Alpaslan Ozgun*, Bulent Karagoz, Tolga Tuncel, Levent Emirzeoglu, Serkan Celik, Oguz Bilgi

Abstract

Background: Testicular germ cell tumors (TGCTs) are a relatively common malignancy in young men. The aim of this study was to investigate the clinicopathological features and survival of young Turkish patients with TGCT. Materials and Methods: In this retrospective study, the clinical and pathological characteristics of young Turkish patients with TGCT who were monitored by the Department of Medical Oncology of a military hospital between 2008 and 2013 were investigated. Overall survival data were analyzed. Results: Ninety-six patients were included in the study. The mean age was 26.4 years. Among the patients, 17.7% had seminoma and 43.8% had mixed non-seminomatous germ cell tumors. Some 46.9% were Stage I, 30.2% were Stage II, and 22.9 were Stage III. Of the patients, 83.3% received chemotherapy, 25% underwent retroperitoneal lymph node dissection (RPLND), 3.1% received radiotherapy, and 12.5% were followed-up without treatment. In addition, 18.8% of the patients were administered salvage chemotherapy due to relapse or progression. The 5-year overall survival rate was 90.2% for all patients. The 2-year overall survival rate was 100% for Stage I patients, 94% for Stage II patients, and 70.2% for Stage III patients. The difference between the survival curves of stages was statistically significant (p=0.029). Conclusions: In young Turkish patients with TGCT, good results were obtained with appropriate treatment, most receiving chemotherapy. The prognosis of the disease was good even in the advanced stage.

Keywords: Testicular germ cell tumor - young Turkish patients - treatment - prognosis

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Introduction

Testicular germ cell tumor (TGCT) is the most common malignant tumor among men between 15-35 years of age. Response to cisplatin-based chemotherapy is very good and a cure rate of 80% can be achieved even in patients with metastatic disease at the time of diagnosis (Dewesa et al., 1995; Sant et al., 2004).

The aim of this study was to investigate the clinicopathological features and survival data of young Turkish patients with TGCT. For this purpose, the clinical and pathological characteristics of young Turkish patients were retrospectively analyzed.

Materials and Methods

In this retrospective study, the clinical and pathological characteristics of 96 patients with TGCT who were monitored by the Department of Medical Oncology of Istanbul Gulhane Military Medical Academy Haydarpasa Training Hospital between 2008 and 2013 were analyzed. Survival analyses were performed. For this purpose, patients' follow-up charts at our clinic and examination results recorded in the hospital automation system were used. All of the patients were young soldiers on active military duty. All patients had undergone orchiectomy and had TGCT as the pathological examination results. The final status of the patients (alive or dead) was determined based on their final status on June 13, 2013. In order to determine the final status on this date, the telephone numbers of the patients recorded in the system were contacted and the final status of the patients who could be contacted by phone was recorded. The patients were retrospectively analyzed backwards from this date.

Approval was obtained from the ethics committee of our hospital before the study. As the staging system, AJCC Cancer Staging Manual 7th Edition 2010 TNM Staging System was used. The statistical analyses were performed by using the SPSS software package version 20. Overall survival curves were generated using the Kaplan-Meier analysis and the statistical difference between the survival curves of stages was calculated using the log-rank analysis. Cases with a Type 1 error level of <5% were considered statistically significant.

*Department of Medical Oncology, Gulhane Military Medical Academy, Haydarpasa Training Hospital, Istanbul, Turkey *For correspondence: alpozgun@yahoo.com*

Results

Ninety-six patients with TGCT were included in the study. The mean age of the patients was 26.4 years. The minimum age was 18 years and the maximum age was 50 years. All patients were Caucasian. The ECOG performance status scores of the patients at the time of diagnosis was 0 in 90 patients (93.8%) and 1 in 6 patients (6.2%).

When all patients were evaluated with respect to tumor localization, it was observed that tumors were equally located in both testes (in the right testis in 50% of the patients and in the left testis in 50% of the patients). However, tumors were more frequently in the left testis in patients with pure seminoma (in the left testis in 58.8%, in the right testis in 41.2%). Sixty-five patients (67.8%) had mixed germ cell tumors (42 patients (43.8%) had mixed non-seminomatous germ cell tumors, 23 patients (24%) had mixed seminoma+non-seminomatous germ cell tumors), 17 patients (17.7%) had pure seminoma, 9 patients (9.4%) had pure embryonal cell carcinoma, 3 patients (3.1%) had pure yolk sac tumors, and 2 patients (2.1%) had pure teratoma. Forty-five patients (46.9%) were Stage I, 29 patients (30.2%) were Stage II, and 22 patients (22.9%) were Stage III at the time of diagnosis. The demographics and clinicopathological characteristics of the patients are summarized in Table 1.

The distribution of patients according to the subtypes of stages was follows: 22 patients (22.9%) Stage IA, 13 (13.5%) Stage IB, 10 (10.4%) Stage IS, 20 (20.8%) Stage IIA, 8 (8.3%) Stage IIB, 1 (1%) Stage IIC, 13 (13.5%) Stage IIIA, 2 (2.1%) Stage IIIB, and 7 (7.3%) Stage IIIC (Table 2). Among the pure seminoma cases, 11 patients (64.7%) were Stage I, 4 (23.5%) were Stage II, and 2 (11.8%) were Stage III at the time of diagnosis. Of the mixed non-seminomatous germ cell tumors 19 (45.2%) were Stage I, 12 (28.6%) were Stage II, and 11 (26.2%) were Stage III. Twenty-two patients (22.9%) had metastatic disease at the time of diagnosis. Among the patients with metastatic disease 13 patients (59.1%) were in the good-risk group, 2 (9.1%) were in the moderate-risk group, and 7 (31.2%) were in the poor-risk group. Of the metastatic patients, 11 (50%) had mixed non-seminomatous germ cell tumors and 2 (9.1%) had pure seminoma. Among the metastatic patients, 17 (77.3%) had lung metastasis, 2 (9.1%) had liver metastasis, and 3 (13.6%) had other organ metastases.

Twelve patients (12.5%) (a part of patients with Stage IA disease) were followed-up without treatment. Among patients under follow-up, 5 patients relapsed. Only 3 (3.1%) among all patients were administered only pelvic radiotherapy as treatment; these patients had Stage IA seminoma. Twenty-four patients (25%) had retroperitoneal lymph node dissection (RPLND). The lymph node pathological results for the patients undergoing RPLND were reactive hyperplasia in 12 patients (50%), teratoma in 7 patients (29.2%), and necrosis in 5 patients (20.8%).

Eighty patients (88.3%) received chemotherapy. Among patients who were administered chemotherapy, 33 patients (41.3%) received 3 courses of BEP, 21 (26.3%) received 4 courses of BEP, 12 (15%) received 2 courses of

Table 1. Patient Demographics and Clinicopathologic Characteristics (n=96)

Characteristic		n	%
Age, years	Median	26.4	
	Range	18-50	
Race	White	96	100
ECOG Performance status	0	90	93.8
	1	6	6.2
Site of tumor	Right testis	48	50
	Left testis	48	50
Histology	Seminoma	17	17.7
	Embryonal carcinoma	9	9.4
	Yolk sac tumor	3	3.1
	Teratoma	2	2.1
	Mixed nonseminomatous germ cell tumor	42	43.8
	Mixed germ cell tumor	65	67.8
Stage	I	45	46.9
	II	29	30.2
	III	22	22.9
Presence of metastasis		22	22.9
Site of metastasis	Lung	17	77.3
	Liver	2	9.1
	Others	3	13.6
Radiotherapy	3	3.1	
RPLND	24	25	
Chemotherapy	80	83.3	
Relapse	13	13.5	
Sites of relapse	Retroperitoneal lymph nodes	6	46.2
	Lung	3	23.1
	Others	4	30.7

Table 2. The Distribution of Patients According to the Subtypes of Stages (n=96)

Stage	n	%	Stage	n	%	Stage	n	%
I: IA	22	22.9	II: IIA	20	20.8	III: IIIA	13	13.5
IB	13	13.5	IIB	8	8.3	IIIB	2	2.1
IS	10	10.4	IIC	1	1	IIIC	7	7.3

Table 3. The Distribution of Patients Who were Administered Chemotherapy and Salvage Chemotherapy According to the Chemotherapy Protocols (n=80)

		n	%
Chemotherapy protocol	3 courses of BEP	33	41.3
	4 courses of BEP	21	26.3
	2 courses of BEP	12	15
	4 courses of EP	8	10
	6 courses of EP	2	2.5
	6 course of Carboplatin	2	2.5
	3 courses of EP	8	8.3
	3 courses of EP	1	1.3
	2 courses of VIP	1	1.3
Salvage chemotherapy protocol	3 courses of VeIP	4	22.2
	3 courses of VIP	3	16.7
	3 courses of TIP	3	16.7
	2 courses of EP	3	16.7
	4 courses of BEP	2	11.1
	2 courses of BEP	2	11.1
	3 courses of BEP protocol	1	5.7

Table 4. Response to Salvage Chemotherapy (n=18)

Response	n	%
Complete response	5	27.7
Partial response	4	22.2
Stable disease	5	27.7
Progression	4	22.2

BEP, 8 (10%) received 4 courses of EP, 2 (2.5%) received 6 courses of EP, 2 (2.5%) received 6 course of Carboplatin, 1 (1.3%) received 3 courses of EP, and 1 (1.3%) received 2 courses of VIP protocol (Table 3). Tumor marker levels remained elevated following chemotherapy in 13 patients (13.5%).

Thirteen patients (13.5%) relapsed. Among these patients, relapse localization was the retroperitoneal lymph nodes in 6 patients (46.2%) and the lungs in 3 patients (23.1%), and 4 patients (30.7%) had other organ metastases. The mean time-to-relapse was 20.7 months. The shortest and longest times to relapse were 3 months and 65 months, respectively. Of the patients with relapse, 7 (53.8%) had seminoma and 2 (15.4%) had mixed non-seminomatous germ cell tumors. Among the patients with metastatic disease at the time of diagnosis, 6 patients (27.3%) achieved a complete response, 3 patients (13.6%) achieved a partial response, 7 patients (31.8%) had stable disease, and 6 patients (27.3%) had progression.

Salvage chemotherapy (second-line chemotherapy) was administreted in cases with sustained high levels of tumor markers after chemotherapy, in cases with relapse and in patients who had metastatic disease at the time of diagnosis and progressed after chemotherapy. Eighteen patients (18.8%) received second-line chemotherapy. Among patients who were administered second-line chemotherapy, 4 patients (22.2%) received 3 courses of VeIP, 3 (16.7%) received 3 courses of VIP, 3 (16.7%) received 3 courses of TIP, 3 (16.7%) received 2 courses of EP, 2 (11.1%) received 4 courses of BEP, 2 (11.1%) received 2 courses of BEP, and 1 (5.7) received 3 courses of BEP protocol (Table 3). Following second-line chemotherapy, 5 patients (27.7%) achieved a complete response, 4 (22.2%) achieved a partial response, 5 (27.8%) had stable disease, and 4 (22.2%) had progression (Table 4). Four patients received third-line chemotherapy. As the third-line chemotherapy, one patient received VIP protocol, one patient received VeIP protocol, one patient had Paclitaxel+Gemcitabine and one patient received Gemcitabine+Oxaliplatin treatment. Two patients achieved a partial response and 2 patients had progression after third-line chemotherapy. Three patients received fourth-line chemotherapy. As the fourth-line chemotherapy, one patient received TIP protocol, one patient received Paclitaxel+Gemcitabine, and one patient was administered Gemcitabine+Oxaliplatin treatment. After chemotherapy, progression was observed in all patients who received fourth-line chemotherapy. Two patients received fifth-line chemotherapy. As the fifth-line chemotherapy, the patients received Gemcitabine+Oxaliplatin treatment. After chemotherapy, progression was observed in all patients who received fifth-line chemotherapy.

In this study, the mean follow-up was 39.3 months. The minimum and maximum follow-up times were 1 month and 210 months, respectively. Out of 96 patients included in the study, 7 patients (7.3%) died. Among the patients who died, 5 patients (71.4%) had mixed germ cell tumor and 2 patients (28.6%) had pure seminoma. Among the patients who died, 4 patients (57.1%) had Stage III disease, 2 patients (28.6%) had Stage II disease, and one patient (14.3%) had Stage I disease at the time of diagnosis. The 5-year overall survival rate was 90.2% and the 2-year overall survival rate was 92.3% for all patients. The 2-year overall survival rate was 100% for Stage I patients, 94% for Stage II patients, and 70.2% for Stage III patients. The median survival has not been reached. The difference between the survival curves according to stage was statistically significant (p=0.029) (Figure 1). There was no statistically significant difference between the survival curves in terms of histopathological type (p=0.811) (Figure 1).

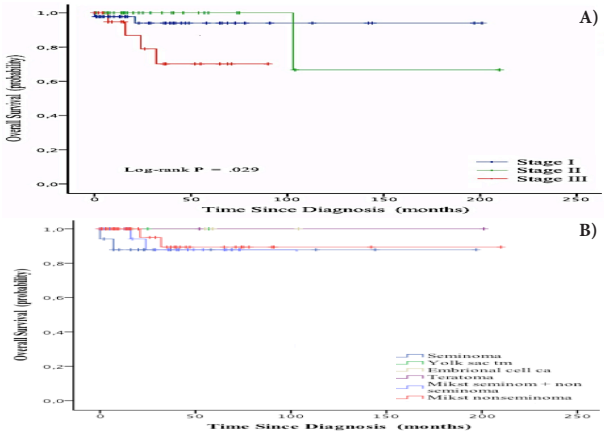

Figure 1. Kaplan-Meier Curve for Overall Survival of Patients with Testicular Germ Cell Tumor According to A) The Stage of the Disease; and B) The Histopathological Type

Discussion

TGCT is the most common malignant tumor in young men. In this study, we investigated the clinical and pathological characteristics and survival data of young Turkish patients with TGCT. When the tumor localization was evaluated in all patients, it was observed that tumors were equally located in both testes but more frequently in the left testis in patients with seminoma. These findings are consistent with another study (Tan et al., 2011). In terms of histopathological type distribution, it was observed that the majority of the patients (67.8%) had mixed non-seminomatous germ cell tumors. In their study, Park and Purdue found that the majority of their patients had seminoma (Purdue et al., 2005; Park et al., 2008). In many other studies, however, the majority of the cases had mixed non-seminomatous germ cell tumors as in our study (Dieckmann et al., 2004; Eble et al., 2004; Bray et al., 2006; Jemal et al., 2010). When the distribution of the patients according to stage were evaluated, it was seen that a vast majority of the patients were at an early stage and only 22.9% of them were at an advanced stage at the time of diagnosis. These findings are consistent with the findings of previous studies (Bosl et al., 1997; Dieckmann et al., 2004; Eble et al., 2004; Chia et al., 2010).

TGCT is highly responsive to chemotherapy. A great majority of the patients included in the ourstudy achieved a complete response with treatment. Only a minority of the patients (13.5%) relapsed. Previous studies reported a relapse rate ranging between 6% and 14% (Einhorn et al., 1989; Bajarin et al., 1993; Horwich et al., 1997; Saxman

et al. 1998; de Wit et al., 2001; Bokemeyer et al., 2004; Kondagunta et al., 2005; Culine et al., 2007; Grimison et al., 2010). Our study is similar to these studies in terms of relapse rat es. It is notable that the majority of the patients who relapsed had seminoma. Among patients with advanced stage disease, 27.3% achieved a complete response following chemotherapy. This rate was 46% in the study by Motzer et al. (2007) 33% in the study by Daugaard et al. (2010) and 60% in the study by Hinton et al. (2003). The lower complete response rate observed in our study may be explained by the fact that a high proportion of the patients receiving treatment consisted of the patients in the poor-risk group. The response to chemotherapy was also similar in patients who received salvage chemotherapy.

When the overall survival of the patients was analyzed, it was found that the 2-year survival rate was over 90% for all patients; this rate was 70% in Stage III disease. Overall survival rate decreased with advancing stage and this was statistically significant. These findings are similar to the findings from previous studies (Bosl et al., 1997; Dieckmann et al., 2004; Kondagunta et al., 2005; Culine et al., 2007). However, no significant association was found between histopathological type and overall survival.

The most important limitations of this study are that there were more censored data due to the low number of patients who died and that the 5-year overall survival rates for stages were notachieved since the follow-up was not long enough. Therefore, we calculated the 2-year overall survival rates for stages.

In conclusion, in young Turkish patients with TGCT, good results are obtained with appropriate treatment. Most patients are treated with chemotherapy and the prognosis of the disease is good even in the advanced stage. However, larger-scale studies with longer follow-up are needed to reliably obtain long-term survival data of these patients.

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