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Research Article

Histopathological Tumour Component Analysis in Testicular Mixed Germ Cell Tumours: A 10-Year Series

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- Testicular cancer; Non-seminomatous germ cell tumour; Mixed germ cell tumour; Prevalence

Abstract

Objective: In this study, we examined histopathologically the tumour components or combinations of these components and analysed to changes of pathological findings with aging in the patients diagnosed with testicular mixed germ cell tumour (MGCT) in the last 10 years.

Materials and methods: 207 patients who underwent radical inguinal orchiectomy due to testicular cancer between 2010 and 2019 were retrospectively reviewed and 107 cases with MGCT whose data were fully available were included in the study. Age, primary tumour localization, primary tumour size, histopathological components and combinations of these components were analyzed. To compare the change of tumour components with aging, patients were divided into two groups according to patients' age, Group 1 was younger than 25 years of age and group 2 was ≥ 25 years old.

Results: The mean age of the patients was 24.67 ± 4.31 years. Tumour component of MGCT included embryonal carcinoma in 87 patients (81.3%), teratoma in 72 patients (67.3%), yolk sac carcinoma in 66 patients (61.7%), choriocarcinoma in 17 patients (15.9%) and seminoma in 44 patients (41.1%). Current combination of these tumours was analyzed and the most common combination was found as embryonal carcinoma + teratoma + yolk sac carcinoma in 26 patients (24.3%) and the second most common combination was found as embryonal carcinoma + seminoma in 17 patients (15.9%). The incidence of three or more components was significantly higher in group 2 (57.8%) than in group 1 (51.6%) ($p<0.05$). The mean follow-up of the patients was 43.37 months (3-113) and 2 patients died for testicular cancer in follow-up period.

Conclusion: In 10-year series, the most common MGCT component was found as embryonal carcinoma and teratoma, while the most common combination was embryonal carcinoma + teratoma + yolk sac carcinoma. Combination of three or more components in MGCT may be more reported with increasing age (especially over 25 years old).

INTRODUCTION

Testicular cancer represents 5% of urological cancers and more than 90% of testicular cancers are malignant and originate from the germ cells [1]. These germ cell tumours are divided into two main groups: seminomas and non-seminoma germ cell tumours (NSGCTs). NSGCTs represent various groups of neoplasms, including embryonal carcinomas, yolk sac tumours, choriocarcinomas, teratomas as well as mixed germ cell tumours (MGCT) containing the aforementioned types of tumours at varying degrees [2].

MGCTs can include seminomatous and non-seminomatous elements and are classified as NSGCTs. In the literature, the number of studies which evaluate the tumour components of MGCTs is quite low. In this study, we examined the general characteristics of the patients, evaluated histopathologically the tumour components or combinations of these components and analysed to changes of pathological findings with aging in the patients diagnosed with testicular mixed germ cell tumour (MGCT) in the last 10 years.

MATERIALS AND METHODS

Study design

A total of 207 testicular cancer cases that underwent radical inguinal orchiectomy between 2010 and 2019 were retrospectively scanned at our clinic, which was previously a military hospital and is considered as a reference centre for testicular cancer. Of these cases, 133 consisted of NSGCTs. 107 cases with MGCT, whose data were fully available, were enrolled in the study. Age, tumour localization, tumour size, histopathological components and combinations of these components were analyzed in all patients. To compare the change of tumour components with aging, patients were divided into two groups according to patients' age, Group 1 was younger than 25 years of age and group 2 was ≥ 25 years old.

The following patient information was examined: age, primary tumour localisation, primary tumour size and MGCT histopathological components. The histopathological examination of all patients was performed by an uropathologist

experienced in testicular tumours. Tumour component analysis and combinations of all cases were examined.

STATISTICAL ANALYSIS

The data were analysed using PSPP and Microsoft Excel 2010. The statistical methods used to analyse the study data included descriptive analyses (frequency distributions, percentage, average and standard deviation median); the Kruskal–Wallis H test and Mann–Whitney U test to measure the difference between the groups and the chi-square test to reveal the differences between discrete variables. The results were evaluated with a confidence interval of 95% and according to a significance level of $p<0.05$.

RESULTS

MGCT was found in 51.3% of all patients who underwent radical inguinal orchiectomy for testicular cancer between 2010-2019 years and 80.5% of all NSGCTs (Figure 1).

The mean age was 24.67 ± 4.31 (19-41 years). The primary tumour was located in the right testicle in 58.9% and in the left testicle in 41.1% of the patients. The tumour size measured in the scrotal ultrasound performed before orchiectomy was 38.89 ± 17.64 mm. The minimum and maximum tumour sizes measured with scrotal ultrasound were 8 mm and 93 mm, respectively (Table 1).

According to histopathological analysis, 49 cases (45.8%) had two different germ cell tumour components, 46 cases (43%) had three different tumour components, 10 cases (9.3%) had four different tumour components and 2 cases (1.9%) had five different tumour components. Embryonal carcinoma in 87 patients (81.3%), teratoma in 72 patients (67.3%), yolk sac carcinoma in 66 patients (61.7%), choriocarcinoma in 17 patients (15.9%), and seminoma component in 44 patients (41.1%) were found in tumour component analyzes. In the combination of these tumours, the most common combination was found as embryonal carcinoma + teratoma + yolk sac carcinoma in 26 patients (24.3%) and the second most common combination was found as embryonal carcinoma + seminoma in 17 patients (15.9%). The pathological characteristics of the patients are summarized in (Table 2).

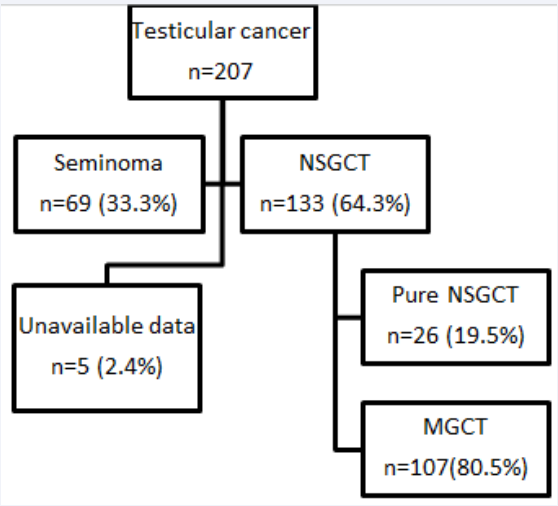

Figure 1 Distribution of testicular cancer cases which have been treated in our clinic for the last 10 years.
NSGCT: Non-seminoma germ cell tumour; MGCT: Mixed germ cell tumour.

Group 1 included 62 patients, while group 2 included 45 patients. In group 1, the diagnostic rate of 2, 3, 4 and 5 components were 48.5%, 43.5%, 6.4% and 1.6%, respectively. In group 2, the diagnostic rate of 2, 3, 4 and 5 components were 42.2%, 42.2%, 13.4% and 2.2%, respectively. The incidence of three or more components was significantly higher in group 2 (57.8%) than in group 1 (51.6%) ($p<0.05$) (Table 2).

The mean follow-up period was 43.37 months (min-max: 3-113), and two patients passed away during this period because of testicular cancer.

DISCUSSION

According to the available literature [3], MGCTs are the second most common testicular germ cell tumours after seminomas and account for 40–45% of all the primary testicular germ cell tumours. While incidence of testicular cancer is increasing worldwide, it has also been observed that, in the last three decades, this increase has been higher for pure seminomas compared with NSGCTs [4-6]. MGCT was found in 51.3% of patients with testicular cancer in our cohort and that was consistent with the literature.

One of the hypotheses in the etiopathogenesis of testicular mixed germ cell tumour is; the differentiation of embryonal carcinoma which have a pluripotent potential to extra-embryonic and embryonic tissues [7]. In hypoxia, a number of vascularization-related factors such as placental-like growth factor and vascular endothelial growth factor are released from embryonal stem cells and embryonal carcinoma cells into the environment [8]. Thus, hypoxia contributes to the development of endothelial precursor cells by stimulating embryonal stem cell / embryonal carcinoma cell exchange. Embryonal carcinoma cells with their pluripotent properties can produce other NSGCTs and MGCTs in the form of teratomas, yolk sacs and choriocarcinomas by somatic differentiation [9]. Similarly seminoma can differentiate and transform embryonal carcinoma and yolk sac tumours into MGCTs [10]. The reason why MGCTs are this common may be linked to the fact that germ cells in the testicles are totipotent and undergo trophoblast or somatic differentiation. In the primary tumours or those that are metastatic, potent types of NSGCT can transform into other NSGCT types [2].

While seminomas are more common in fourth decade, non-seminomatous tumours show a peak incidence in the third decade [11,12]. MGCTs have the same clinical characteristics as the non-seminomatous tumours they contain. If the embryonic carcinoma is dominant, the mean age is 28 and if the seminoma is dominant, it is 33 [13]. In our study, mean age for MGCTs was 24.7, which was consistent with the literature.

According to sources of pathological evaluations, the most common MGCT combinations are embryonal carcinoma + teratoma, embryonal carcinoma + seminoma, embryonal carcinoma + yolk sac tumour + teratoma, embryonal carcinoma

Table 1: Patient demographics and pathologic data (n=107).

Characteristic		n	%
Age (years)	Mean±SD	24.67±4.31	
Site of tumour	Right testicle	63	58.9
	Left testicle	44	41.1
Tumour size (mm)	Median	34	
	Mean±SD	38.89±17.64	
Histopathology	EC	81	81.3
	T	72	67.3
	YSC	66	61.7
	CC	17	15.9
	S	44	41.1

Abbreviations: USG: Ultrasonography; EC: Embryonal Carcinoma; T: Teratoma; YSC: Yolk Salk Carcinoma; CC: Chorio Carcinoma, S: Seminoma

Table 2: Combination and incidence of mixed germ cell tumours according to histopathological components.

	Two types (n)				Three types (n)				Four types (n)				Five types (n)			
		G1	G2	T		G1	G2	T		G1	G2	T		G1	G2	T
T	EC/S	11	6	17	EC/T/YSC	19	7	26	EC/T/YSC/S	2	5	7	EC/T/YSC/CC/S	1	1	2
	EC/T	5	6	11	EC/YSC/CC	2	4	6	EC/T/YSC/CC	2	1	3				
	EC/YSC	5	2	7	EC/T/S	1	4	5								
	T/YSC	4	2	6	T/YSC/S	1	2	3								
	YSC/S	1	2	3	T/CC/YSC	1	1	2								
	T/S	3	1	4	EC/T/CC	1	-	1								
	T/CC	1	-	1	T/CC/S	1	-	1								
					EC/YSC/S	-	1	1								
					EC/CC/S	1	-	1								
		30	19	49		27	19	46		4	6	10		1	1	2

Abbreviations: EC: Embryonal Carcinoma; T: Teratoma, YSC: Yolk Salk Carcinoma, CC: ChorioCarcinoma, S: Seminoma; G1: Group 1; G2: Group 2; T: Total

+ teratoma + choriocarcinoma, embryonal carcinoma + teratoma + seminoma and teratoma + seminoma [14,15]. In a study conducted in 2009, it was reported that the most common MGCT combinations are embryonal carcinomas with or without seminoma, teratomas with or without seminoma and the combinations of these two [16]. In the present study, it was observed in parallel with the literature that the most common components were embryonal carcinoma, teratoma, yolk sac carcinoma and seminoma. In agreement with the literature, the present study also showed that the combination of embryonal carcinoma + teratoma + yolk sac carcinoma is the most common combination [17,18].

In the literature, only one study reported histological component analysis results of MGCTs [19]. In this study, 1097 MGCT cases were evaluated; 688 cases (62.7%) had two different germ cell tumour components, 300 cases (27.3%) had three different germ cell tumour components, 101 cases (9.2%) had four different germ cell tumour components and 8 cases (0.7%) had five different germ cell tumour components. According to histopathological analysis of our study, 49 cases (45.8%) included two different germ cell tumour components, 46 cases (43%) had three different tumour components, 10 cases (9.3%) had four different tumour components and 2 cases (1.9%) had five different germ cell tumour components. When compared to our study; MGCTs which contained two different germ cell tumour components have been reported most frequently, although different rates have been found. Similarly, the total rate of MGCTs which contained four and five different tumour components appears to account for about 10% of all MGCTs. However, our study shows that the rate of having three or more tumor components at the age of 25 and over increases significantly in patients with MGCT. We think that this result may be explained by the fact that MGCTs have pluripotent properties and have the ability to transform into other NSGCTs over time.

CONCLUSION

Testicular mixed germ cell tumour components and their combinations are extremely important in the diagnosis and treatment of the patients. In our study; the most common MGCT component was found as embryonal carcinoma and teratoma, while the most common combination was embryonal carcinoma + teratoma + yolk sac carcinoma. Combination of three or more components in MGCT may be more reported with increasing age (especially over 25 years old) (Figure 1) (Tables 1,2).

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