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Prognostic value of ABO blood group in patients with nonseminomatous testicular cancer who treated with autologous stem cell transplantation

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ABSTRACT

Aim: Even though ABO blood group surface antigens are expressed in red blood cells, they can be observed in many normal and pathologic cells. Relationship between ABO blood groups and progression and prognosis of cancer has been mainly demonstrated in gastric and pancreatic cancer. However there is no study in current literature about its relation with testicular cancer. The aim of this study is to demonstrate the prognostic value of the ABO blood group in nonseminomatous testicular cancer patients who treated with high dose chemotherapy and autologous stem cell transplantation.

Material and method: 64 patients who diagnosed as non-seminomatous testicular cancer and treated with HDC and OSCT in Gulhane Medical Oncology Clinic between January 2011 and December 2016 were enrolled to the study. Patients' age, TNM stage, chemotherapy protocols and blood group characteristics were obtained retrospectively.

Results: The mean age of patients was 31.4 (18–61) years. Blood groups of patients' were as follows: A blood group 19 (29.7%), B blood group 7 (10.9%), O blood group 34 (53.1%), AB blood group 4 (6.3%). Rh was negative in 3 patients (4.7%) and Rh positive in 61 patients (95.3%). 1-year progression-free survival (PFS) was 72.5% and 2-year PFS was 68.4%. 1-year overall survival (OS) was 82% and 2-years OS was 72%. While 1-year and 2-year OS was 88.2% and 84.4% in O blood group individuals, respectively, it was 75.6% and 59.5% in all other blood types, respectively. Although the OS was superior in individuals with O blood group, the difference was not reached the statistically significance ($p = 0.071$). When O blood group was compared with other blood groups in terms of PFS, 1 year PFS was 79.1% in O blood group and 65.2% in the all other blood groups ($p = 0.19$).

Conclusion: OS and PFS were superior in O blood group than other blood groups, however the difference was not reached statistical significance. In the literature, there is no study that focused on the relationship between stem cell transplantation and blood groups. ABO blood groups are the phenotype of a person's genotype and may reflect differences in the individual's immune mechanisms. However, due to small number of cases and heterogeneity of the group, the results and the strength of the study may have affected negatively. So, the prognostic importance of ABO blood groups can be shown with multi-center studies that performed with larger number of cases.

1. Introduction

Although it is 1% common among all cancers, testicular cancers are the most common solid malignancies in males between the ages of 15 and 35.[1] Germ cell tumors constitute 95% of testicular cancers. Germ cell tumors are classified as benign seminomas and nonseminomatous germ cell tumors. Testicular cancers are the

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most successfully treatable solid tumors through new treatment modalities that starting and ongoing since the 1970s.[2] Even though the initial treatment for testicular cancer is radical orchiectomy, treatment is planned according to the stage of disease, histology or other risk factors. The 5-year survival rate with platinum-based combination chemotherapy in testicular cancer is 95%.[1] Even if patient has extensive organ metastasis and/or high serum tumor markers, cure could be obtained by cisplatin-based combination chemotherapy. Despite this good response rate, additional treatments may be needed in patients with relapsed and/or refractory to first line therapy.[3–6] Relapse usually develops in the first 2 years after first line therapy. There is no standard chemotherapy or high dose chemotherapy modality is existing for the patients with relapsed/refractory germ cell testicular carcinoma. For patients who do not respond to standard combined chemotherapy or relapsed, complete remission can be achieved with high dose chemotherapy (HDC) and autologous stem cell transplantation (OSCT).[1] However, there is no predictive factor for which group of patients will benefit from HDC and OSCT.

Even though ABO blood group surface antigens are expressed in red blood cells, they can be observed in many normal and pathologic cells. Many studies that conducted with ABO antigens shown that it has been associated with most types of cancer.[7–12] Relationship between ABO blood groups and cancer survival rate has been demonstrated in many cancers such as pancreas, colon, lung and esophageal cancer.[7–11] However there is no study in current literature about its relation with testicular cancer.

The aim of this study is to demonstrate the prognostic value of the ABO blood group in nonseminomatous testicular cancer patients who treated with HDC and OSCT.

2. Material and method

2.1. Patient selection

Patients' files of Gulhane Medical Oncology Clinic in between January 2011 and December 2016 were scanned retrospectively and 64 patients who diagnosed as non-seminomatous testicular cancer and treated with HDC and OSCT were enrolled to the study. Data such as patients' ages, stages of diseases, prior chemotherapy protocols, and chemotherapy cure cycles, responses to chemotherapies, radiotherapy histories, metastasectomy histories, relapse or refractor situations, and blood groups were obtained retrospectively from the patients' files. HDC protocols of all patients were as follows: ifosfamide 12 g/m^2 (divided into 1–6 days), carboplatin 1200 mg/m^2 (divided into 1–6 days), etoposide 1200 mg/m^2 (divided into 1–6 days) and stem cell reinfusion was performed on day 8.[13]

2.2. Response criteria and statistical analysis

World Health Organization and National Cancer Institute—CTC (version 2.0) criteria were used for assessment of treatment response. The period between the ASCT and first relapse, progression, death from any cause, or the last date at which the patients were drop out from follow-up was named as Progression-free survival (PFS). Overall survival (OS) was determined as the period between the date of ASCT performed and either the time of death from any cause or the last date at which patients were censored. Either Pearson's Chi square test or Fisher's test (for categorical variables) were used in assessment of relationship between ABO blood type and clinical/laboratory variables. Kaplan–Meier method and the log-rank test were used for univariate survival analysis. A two-tailed $P < 0.05$ was accepted significant. SPSS 22.0 (SPSS Inc., Chicago, IL, USA- The statistical software package) was used for statistical calculations.

2.3. Ethical approval

The local ethics committee application was performed for the study. The study was performed in accordance with the Declaration of Helsinki and the institutional guidelines of the local ethics committee.

3. Results

The mean age of 64 patients included in the study was 31.4 (18–61) years. Blood groups of patients' were as follows: A blood group 19 (29.7%), B blood group 7 (10.9%), O blood group 34 (53.1%), AB blood group 4 (6.3%). Rh was negative in 3 patients (4.7%) and Rh positive in 61 patients (95.3%) (Table 1).

Responses of patients' were as follows: Complete response was in 34 (53.1%) patients, partial response was in 7 (10.9%) patients, stable disease was in 3 (4.7%) patients, progression was in 20 (31.3%) patients.

The PFS was 20 months and did not reach the median. 1-year PFS was 72.5% and 2-year PFS was 68.4% (Fig. 1).

The OS was 18 months and the median did not reach the overall survival time. 1-year OS was 82% and 2-years OS was 72% (Fig. 2).

1-year and 2-year OS data according to blood groups are presented in (Fig. 3).

While 1-year and 2-year OS was 88.2% and 84.4% in O blood group individuals, respectively, it was 75.6% and 59.5% in all other blood types, respectively. Although the OS was superior in individuals with O blood group, the difference was not reached the statistically significance ($p = 0.071$).

When O blood group was compared with other blood groups in terms of PFS, 1 year PFS was 79.1% in O blood group and 65.2% in the all other blood groups ($p = 0.19$) (Fig. 4).

4. Discussion

In our study, we investigated whether there was a significant relationship between PFS and OS according to ABO blood groups. Our study was the first in the literature that investigating the effects of ABO blood groups on survival of patients with testicular cancer. So, it was evaluated by comparing it with studies conducted in other cancer types. In a study that performed with 2036 invasive breast cancer patients to assess the relationship between ABO blood group and survival and risk factors, it has been demonstrated that there was no relationship between ABO blood groups and survival or risk factors.[14]

In another study that conducted with 3172 renal cell carcinoma patients that evaluated effects of ABO blood groups on recurrence free survival (RFS), disease-specific survival (CSS), and total survival (OS), it has been shown that there was no significant relationship between blood group and RFS ($p = 0.921$), CSS ($p = 0.808$) and OS ($p = 0.990$).[15] Likewise, in our study, we have been revealed that there was no significant relationship between blood group and PFS and OS in nonseminomatous testicular cancer patients.

Table 1
Descriptives.

Mean Age	31.4 (18–61)	
	n	%
A Blood group	19	29.7
B Blood group	7	10.9
O Blood group	34	53.1
AB Blood group	4	6.3
Rh Positive	61	95.3
Rh Negative	3	4.7

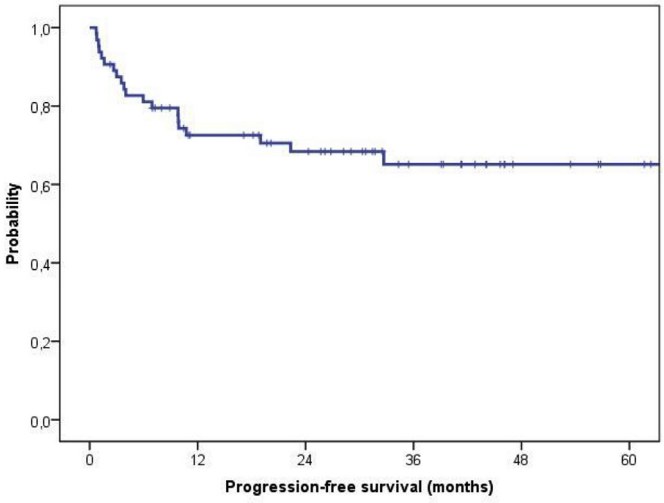

Fig. 1. Progression free survival (proportion) over time (months).

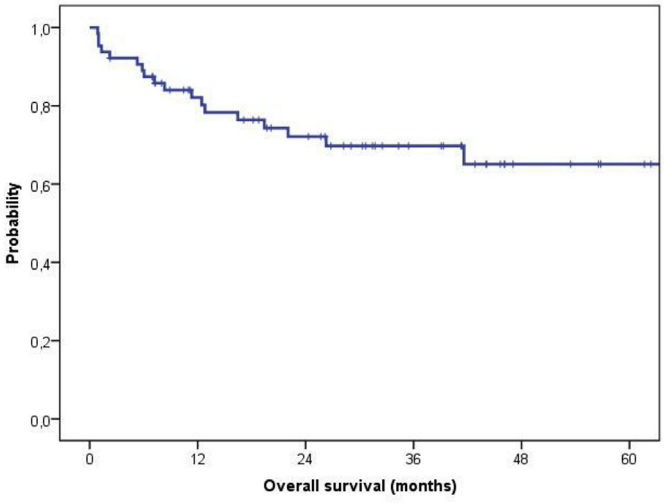

Fig. 2. Overall survival (proportion) over time (months).

Although there was no correlation was founded in our study, a significant relationship between ABO blood group and OS and PFS was shown in many studies in the literature. In a study with 627 pancreatic cancer patients that published by *Rahbari* et al., it has been shown that O blood group was a favorable prognostic factor (hazard ratio [HR] = 0.78, P = 0.037).[16] And also, it has been reported that O blood type was related with longer RFS (p = 0.04) and longer CSS (p = 0.02) among patients with urothelial carcinoma of the bladder undergoing radical cystectomy.[17] Additionally, Ya-Jun Li et al. have been reported that extra nodal natural killer/t cell lymphoma patients with non-O blood group have shorter PFS (p < 0.001) and shorter OS (p = 0.001) than patients with O blood group.[18] In another study that administered with 1601 curatively resected non-small cell lung cancer patients, *Li* et al. have been demonstrated that patients with O and B blood type have longer OS and disease-free survival (DFS).[19] In our study, although the blood group was superior to the other blood groups in terms of OS, it was not reached statistical significance (p = 0.071).

Despite our patients were consisted of heterogeneous subgroups with different chemotherapy sensitivity and relapse/refractory patients, we included these patients in a standardized

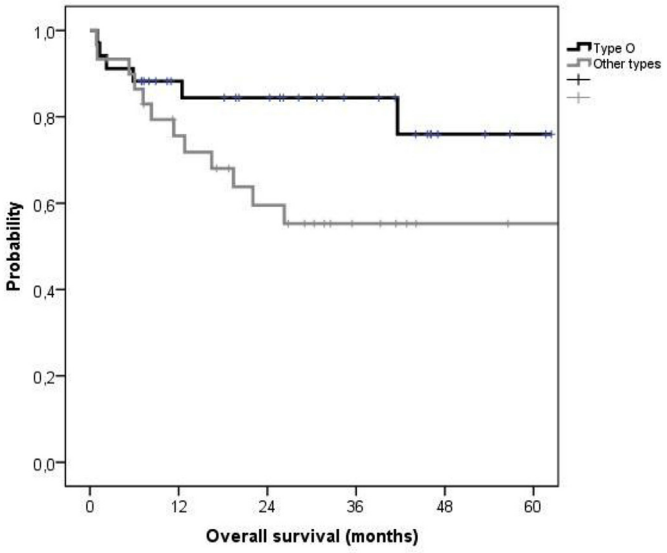

Fig. 3. Overall survival (proportion) according to blood types.

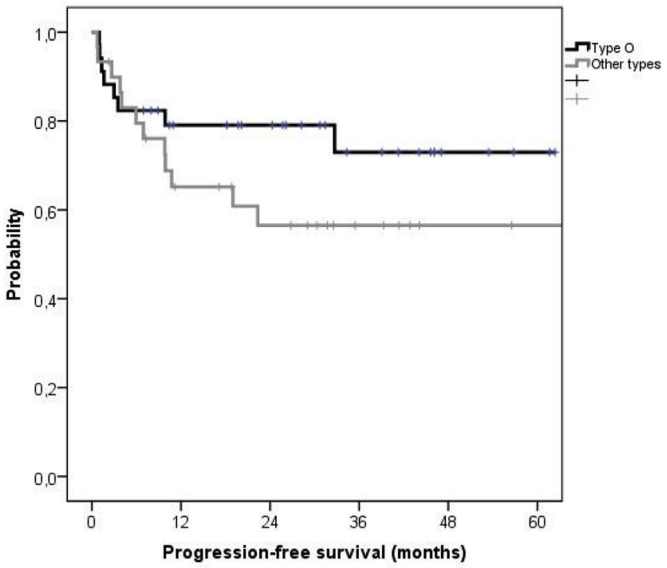

Fig. 4. Progression free survival (proportion) compared to O and Non-O blood types.

group as homogeneous nonseminomatous testicular cancer patients who received 2 cycles of chemotherapy prior to HDC and OSCT. So, we believe that this was another limitation of our study to achieve statistical significance.

5. Conclusion

As a conclusion, OS and PFS were superior in O blood group than other blood groups, however the difference was not reached statistical significance. In the literature, there is no study that focused on the relationship between stem cell transplantation and blood groups. ABO blood groups are the phenotype of a person's genotype and may reflect differences in the individual's immune mechanisms. However, due to small number of cases and heterogeneity of the group, the results and the strength of the study may have affected negatively. We believe that the prognostic importance of ABO blood groups can be shown with multi-centered studies that

performed with larger number of cases.

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