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Evaluation of the diagnostic and prognostic value of preoperative inflammatory parameters in testicular tumors

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Abstract

Objective: We aimed to investigate neutrophil lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) values can be used as predictors of a tumor marker or disease progression in patients with testicular tumors.

Materials and Methods: A retrospective analysis of 142 patients undergoing orchiectomy in our center was performed. Sixty-six patients with malignant testicular tumor pathology were included in the study group and 14 patients with benign orchiectomy pathology were included in the control group Preoperative inflammatory parameters of both groups were compared.

Results: Mean ages were 30 ± 4 (26, 34 IQR) years in the study group and 30 ± 7 years (23, 41 IQR) in the control group. A total of 66 testiculer tumor patients had a higher neutrophile and NLR compared to the control group (P=0.03, p=0.005, respectively). LnNLR levels [95% CI: 4.90 (1.55, 15.43), P= 0.007] were significantly associated with testicular tumor in logistic regression analysis.

Conclusions: As a result of our study; preoperative NLR can be used as a value that supports other diagnostic methods rather than evaluating the progression of the disease in testicular tumors.

Keywords: Testicular tumor, neutruphyl, platelet, lymphocide, neutrophil lymphocyte ratio, platelet-lymphocyte ratio

1. Introduction

Testicular tumors account for 1% of male solid tumors and 5% of all male tumors [1]. Although it is a rare tumor, it has an important place as it is most commonly seen in young males between 15-35 years old. It is stated that the incidence has increased in the last decade at developing industrial countries. There are basically two histopathological types. One of them is germ cell tumors which cover the 95% of all testicular tumors and the second is sex-cord stromal tumors that constitute the remaining 5%. Germ cell tumors are divided into two subgroups as seminoma and non-seminoma according to the histopathologic characteristics and therapeutic approach.

Testicular dysgenesis (such as cryptorchisism, infertility or subfertility), tumor in the contralateral testis, presence of familial testicular tumor history, to be tall are defined as risk factors in etiopathogenesis [2, 3, 4].

In addition to physical examination and ultrasonography, serum markers which may vary according to the histopathological structure of the tumor are used in the diagnosis.

Cure rates of testicular tumors are satisfactory due to early diagnosis and high sensitivity to chemotherapy and radiotherapy. Inflammatory response has a critical role in every stage of carcinogenesis such as tumor formation, angiogenesis, inhibition of apoptosis and metastasis [5]. Therefore, inflammatory parameters such as CRP and platelet / lymphocyte ratio (PLR) have been investigated in many cancer types in order to detect the changing inflammatory response Various relations have been found between NLR and disease prognosis not only in genitourinary system cancers, but also in other organ tumors such as hepatocellular carcinoma, breast cancer, gastric cancer and pancreatic cancer [6, 7, 8, 9]. Even increased NLR has been reported as a poor prognostic factor for urothelial cancers [10]. There are a limited number of studies in the literature on testicular tumor and inflammatory parameters.

As inflammatory parameters such as neutrophile / lymphocyte ratio (NLR) and platelet / lymphocyte ratio (PLR) are easily accessible from routine whole blood count and they are affordable for diagnosis and prognostic follow-up, they are frequently investigated in solid organ tumors. Therefore, in our retrospective study, we aimed to analyze the effect of preoperative NLR and PLR levels in predicting testicular tumor and tumor prognosis according to pathology results in patients with testicular tumors.

2. Material and Method

After obtaining consent for retrospective screening from the local ethical committee of Koru Ankara Hospital, patients who has undergone orchiectomy between 2011 and 2018 were screened and analyzed retrospectively. A total of 142 patients who has been performed orchiectomy were determined. Of these patients, 68 had malignant testicular tumors. The remaining 74 patients consisted of patients with benign pathologies. Sixty patients with additional malignancy other than testicular tumor such as prostate cancer, those with chronic inflammatory diseases such as brucella-tuberculosis orchitis, active infection or inflammatory disease (e.g.; active connective tissue diseases, HIV, other serious chronic infectious diseases) from benign group were excluded from the study and the remaining 14 patients were identified as the control group. Patients with secondary cancer, metastatic disease, chronic inflammatory disease, active infection and pathologically diagnosed testicular tumors whom medical records could not be achieved or received chemotherapy before orchiectomy from malign group were also excluded from the

Study. Two patients who met the exclusion criteria were excluded from the study and a total of 66 patients were identified as malignancy group.

2.1. Clinical and Laboratory Analysis

NLR was calculated by using preoperative neutrophile and lymphocyte counts in whole blood count. PLR was calculated by using the lymphocyte and platelet counts in the same whole blood count. Preoperative Beta-hCG, alpha-fetoprotein (AFP) and lactate dehydrogenase (LDH) results were obtained and analyzed in all patients. Pathology results were evaluated according to the World Health Organization (WHO) testicular tumor classification [11]. Location side of tumor, pathologic stage, tumor aggressiveness factors existence were recorded. Localised testicular tumor was defined as pT2, N0, M0, and other patients were excluded.

2.2. Statistical Analysis

All collected data were analyzed with SPSS for Mac 25.0 software (SPSS Inc., Chicago, Illionis, United States). P values less than 0.05 were considered statistically significant. All comparison analyzes were performed with non-parametric tests due to limited sample size. While Wilcoxon rank sum test was used for continuous variables, $\chi 2$ test was used for categorical variables during the comparison of characteristics. Results were presented as median and interquartile interval (IQR). Factors that may be effective for testicular tumor malignancy were investigated by using binary logistic regression analysis. 3 independent variables included in regression analysis in multivariate models due to the limited sample size and to avoid over-fitting.

3. Results

Sixty-six patients with localised testicular tumors who has undergone orchiectomy between 2011 and 2018 and also met the study criteria were included in the study as the study group and 14 patients with benign lesions as the control group. The mean age was 30 ± 4 (26, 34 IQR) years in the study group and 30 ± 7 years (23, 41 IQR) in the control group. Orchiectomy lateralities were detected 43 left, 23 right in study groups and 9 left, 5 right in control group. The pathology of 34 of 66 patients in the study group was determined as seminoma (51.51%), 29 as non seminoma (43.93%), one as adenomatoid tumor (1.51%) and two as lymphoma (3.03%) in sex cord stromal tumor. Control group pathologies were determined as atrophic testicles.

The median leukocyte value was determined as 8000 (6540, 9250) / μL, the median neutrophil value was determined as 4735 (3780, 6252) μL, and the median platelet value was determined as 247000 (215750, 304250) μL in the study group. The median NLR value was determined as 2.35 (1.62, 3.65) and the PLR value was determined as 127.7 (101.1, 158.7). The median leukocyte value was determined as 7005 (6340, 9875) / μL, the median neutrophil value was determined as 3760 (3200, 5367) μL, and the median platelet value was determined as 279000 (242750, 371250) μL in the control group. Median NLR was determined as 1.55 (1.02, 2.01) and PLR was determined as 102. 6 (77.6, 193.2) (Table 2). As shown in Table 1, a statistically significant difference was found in median neutrophil counts and NLR rates between the study and control groups.

No statistically significant difference was found in leukocyte, neutrophil and platelet counts, NLR, PLR rates and tumor diameters between the seminoma and non-seminoma patients in the study group (Table 2).

LnLNR [4.90, 95% CI (1.55, 15.43) p = 0.007] was found significantly higher in logistic regression analysis. No statistically significant difference was observed in terms of age, neutrophile and PLR values (Table 3).

No statistically significant difference was observed in testicular tumor size, rete testis invasion, the presence of lenfovascular invasion and NLR, PLR, lymphocyte, neutrophil values. (p = 0.78, p = 0.67, p = 74, respectively)

4. Discussion

In recent years, there are many studies in order to find cheap, easily accessible and practical parameters in clinical use for diagnosis and follow-up of the disease and predicting prognosis in solid organ tumors. The leading parameters are inexpensive and easily accessible parameters such as neutrophil-lymphocyte ratio and platelet-lymphocyte ratio which can be obtained from a simple whole blood count. Since inflammation is closely related to tumor development, angiogenesis, and tumor behavior, there are many studies in the literature about NLR and PLR in liver, stomach, pancreas, and head and neck cancers [6, 7, 8, 9]. Indeed, NLR and PLR rates have become popular in urological cancers and the role of these rates in prostate, kidney, bladder and testicular cancers has been investigated and is investigating [6,8,10]. However, there are not many articles about testicular tumor and inflammatory parameters in the literature. In our study, we investigated whether the NLR and PLR ratios calculated from the preoperative full blood count can be used to diagnose testicular tumors and predict prognosis.

The immune system contributes to the elimination of the formed tumor cells as well as the development and progression of the tumor. The increased number of neutrophiles in circulation is important in tumor progression and angiogenesis. Therefore, increased neutrophile levels can be considered as an indicator of poor prognosis [12]. NLR elevation actually occurs as a result of decreasing lymphocyte levels while neutrophil levels are increasing and causes the suppressed antitumor immune response by decreased lymphocyte levels and resulted with tumor development and progression [13].

Wei *et al*. reported that high NLR levels are indicative of poor prognosis, especially in urothelial cancers, renal cell cancers, and bladder cancers in a meta-analysis of 3159 patients on urinary system tumors [14]. Krane *et al*. reported that high NLR levels in patients with bladder tumors in the preoperative period are predictive of extravesical spread and indicative of poor prognosis [15]. Song and colleagues stated that the advance stage of tumor is correlated with high NLR, PLR levels in upper urinary tract urothelial carcinoma [16]. Jang *et al*. stated in their series of 2067 patients that increased preoperative NLR levels are the predictive of poor prognosis and high biochemical recurrence after radical prostatectomy [17].

In addition to all these studies, there are studies in the literature on testicular tumors, albeit in a limited number. There are several proven risk factors for prediction of prognosis for testicular tumors. Tumor size (greater than 4 cm), and rete testis invasion are the poor prognostic indicators for seminomas, whereas

lymphatic and vascular invasion, high proliferation in the tumor (above 70%), and high embryonal carcinoma rate (higher than 40%) are the poor prognostic indicators for non-seminomatous tumors. In a study conducted by Bolat *et al*. on germ cell testicular tumors, it was stated that preoperative NLR cannot be used as a prognostic indicator in germ cell testicular tumors [18]. Gokcen *et al*. [19] reported that preoperative NLR PLR values can be used in the diagnosis of testicular cancer in a series of 39 patients. In our study, we found that there was a statistically significant increase in preoperative NLR values in patients diagnosed with testicular Tumor, but there was no statistically significant difference despite the elevation in PLR values. We did not observe any difference in NLR and PLR between seminoma and nonseminoma tumors in the study group. In our results, it was seen that NLR, PLR ratios have no statistically significance according to the presence of risk factors determined for seminoma and non seminoma testicular tumors. Limitations of our study can be defined as the larger number of cases and control group and inclusion of longer term follow-up.

5. Tables

Table 1: Statistical analysis of demographic and inflammatory parameters in two groups.

	Control group (n=14)	Study group (n=66)	p value
Age (Year, Median IQR)	30 (23, 41)	30 (26, 34)	0.88
Lymphocyte ((/ µL, Median, IQR)	7005 (6340, 9875)	8000 (6540, 9250)	0.52
Neutrophil ((/ µL, Median, IQR)	3760 (3200, 5367)	4735 (3780, 6252)	0.03
Platelet ((/ µL, Median, IQR)	279000(242750, 371250)	247000(215750, 304250)	0.06
NLR (Median, IQR)	1.55 (1.02, 2.01)	2.35 (1.62, 3.65)	0.005
PLR (Median, IQR)	102. 6 (77.6, 193.2)	127.7 (101.1, 158.7)	0.33

IQR: Interquartile range, NLR: Neutrophil-to-lymphocyte ratio, PLN: Platelet-to-lymphocyte ratio

Table 2: Comparison of inflamatuar parameters in study subgroups.

	Seminoma (n=34)	Non-Seminoma (n=32)	p value
Lymphocyte (/ µL, Median, IQR)	7650 (6540, 8880)	8490 (6350, 9785)	0.25
Neutrophil (/ µL, Median, IQR)	4445 (3657, 5767)	5125 (3830, 6952)	0.24
Platelet (/ µL, Median, IQR)	245000 (215750, 307500)	250500 (213000, 298200)	0.84
NLR (Median, IQR)	2.14 (1.56, 3.20)	2.60 (1.74, 3.98)	0.25
PLR (Median, IQR)	128.6 (82.9, 178.0)	126.5 (106.3, 140.3)	0.67
Tumor size (cm, Median, IQR)	3.3 (2.0, 4.6)	3.5 (2.5, 5.2)	0.52

IQR: Interquartile range, NLR: Neutrophil-to-lymphocyte ratio, PLN: Platelet-to-lymphocyte ratio

Table 3: The comparison of parameters between study groups

	Beta coefficient (95%CI)	p value
Age (years, mean±SD)	1.008 (0.94, 1.07)	0.81
Neutrophil (/ µL, median, IQR)	1.000 (1.000, 1.001)	0.09
Ln-NLR (median, IQR)	4.90 (1.55, 15.43)	0.007
PLR (median IQR)	1.002 (0.99, 1.01)	0.73

IQR: Interquartile range, NLR: neutrophil to lymphocyte ratio; PLr: platelet to lymphocyte ratio; LN: log transformed

6. Conclusion

NLR, values for testicular tumors should be considered as values that can be calculated from the results of a routine hemogram in addition to physical examination, Beta hCG, AFP, LDH and ultrasonography tests for diagnosis rather than predicting tumor progression as in other solid organ tumors.

7. Conflict of Interests

None of the contributing authors have any conflicts of interest, including specific financial interests, relationships, and affiliations relevant to the subject matter or materials discussed in the manuscript.

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