RESEARCH ARTICLE

Platelet Indices May be Useful in Discrimination of Benign and Malign Endometrial Lesions, and Early and Advanced Stage Endometrial Cancer

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Abstract

Background: The aim of this study was to investigate the predictive value of white blood cells (WBC), the neutrophil to lymphocyte ratio (NLR), platelet indices including mean platelet volume (MPV), platelet distribution width (PDW), platelet crit (PCT) and platelet to lymphocyte ratio (PLR) in discrimination between benign and malign endometrial lesions, and early and advanced stage endometrial adenocarcinomas. Materials and Methods: Data for 105 patients undergoing total abdominal or vaginal hysterectomy for benign uterine diseases and 114 patients surgically staged for endometrium adenocarcinoma at Ondokuz Mayis University, Department of Gynecology and Obstetrics, between 2008 and 2014, were collected. Parameters were preoperative and postoperative complete blood counts in the week prior to surgery with differentials including WBC, platelet count, platelet indices (MPV, PCT, PDW), NLR and PLR. Pathologic evaluations for both benign and malign endometrium lesions, grade of endometrium adenocarcinoma, tumor stage, presence of lymphovascular space invasion (LVI) were retrospectively analyzed. Results: Regarding definitive factors in discriminating patients with endometrium cancer from those with benign diseases, MPV was significantly increased in the malign group whereas there was a significant decrease in the PDW value compared to the benign group. The best cut-off value in differentiation of the benign and malign groups, malign cases were found to increase over the value of 7.54 for MPV, and under 37.8 for PDW. When definitive factors in discrimination of early stage endometrium cancer from advanced stage disease and LVI in the malign group were evaluated according to the ROC analysis, no significant relation was detected between blood parameters and the stage and the LVI of the disease. Conclusions: MPV and PDW may have predictive value in the discrimination of benign and malign endometrium diseases. Nevertheless, since there have been few reports on this topic, further large-scale prospective studies are necessary.

Keywords: Endometrium cancer - mean platelet volume - platelet distribution width - lymphovascular space invasion

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Introduction

The alterations in the preoperative systemic inflammatory response (SIR) markers including, absolute white blood cells (WBC), platelet count, neutrophil to lymphocyte ratio (NLR) and platelet to lymphocyte ratio (PLR), have been the focus of many investigations in terms of their prognostic and predictive values in several types of benign and malign diseases such as, cardiac-pulmonary diseases, preeclampsia, gynecologic and gastrointestinal malignancies (Ayhan et al., 2006; Kaya et al., 2013; Acmaz et al., 2014; Avci et al., 2014; Kayadibi et al., 2014; Williams et al., 2014; Kokcu et al., 2015; Kurtoglu et al., 2015).

Among these studies, the relationship between the SIR markers and benign and malign diseases of the endometrium has been of little interest. Few studies on this topic reported significant relationships between WBC, NLR and PLR and prognosis of the precancerous and cancerous lesions particularly endometrium adenocarcinoma, which is the most common gynecological cancer in the western world (Doll et al., 2008; Suh et al., 2012; Wang et al., 2013; Acmaz et al., 2014).

In this study we aimed to investigate the values of WBC, NLR, platelet indices including mean platelet volume (MPV), platelet distribution width (PDW) platelet crit (PCT) and PLR in discrimination of the benign endometrial disease and endometrioid endometrial adenocancer and in diffentiation of the early and advanced stage endometrial cancer.

Materials and Methods

The study included 105 patients underwent total abdominal or vaginal hysterectomy for abnormal uterine bleeding and whose pathologic results revealed benign (sixteen endometrial polip without any type hyperplasia, 34 proliferative phase endometrium, 26

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atrophic endometrium, 20 secretory phase endometrium, 9 basal endometrium); and 114 patients surgically staged for endometrioid type endometrial adenocarcinoma at Ondokuz Mayis University, Department of Gynecology and Obstetrics between 2008 and 2014.

Patients were excluded from this study if any of the following were present: second malignancies, precancerous disease such as endometrial hyperplasia with complex atypia, hematological disease, inflammatory disease, recombinant granulocyte colony-stimulating factor use, prior chemotherapy or radiotherapy, incompletely staged surgery, hypertension, diabetes mellitus, metabolic syndrome, nephropathy, renal or hepatic dysfunction, left ventricular dysfunction, valvular heart disease, abnormal thyroid function tests, previous history of local or systemic infection, any medication that is related to patients' inflammatory condition such as corticosteroids and missing preoperative complete blood cell count or complete blood count drawn more than two weeks prior to surgery.

Patients with endometrial carcinoma were staged according to the International Federation of Gynecology and Obstetrics (FIGO) 2009 guidelines which consisted of peritoneal cytology, total abdominal hysterectomy, bilateral salpingo-oophorectomy, systemic pelvic and para-aortic lymphadenectomy (Pecorelli, 2009). Radical hysterectomy was performed when cervical stromal involvement was suspected.

Patients' preoperative and postoperative data, including demographic features, complete blood count in the week prior to surgery with differentials including WBC, platelet count, platelet indices (MPV, PCT, PDW), NLR and PLR; pathologic evaluations for both benign and malign endometrium lesions, grade of endometrioid type endometrium adenocarcinoma, tumor stage, presence of lymphovascular space invasion (LVI) were retrospectively analyzed.

Data analysis was performed by using SPSS for Windows, version 11.5 (SPSS Inc., Chicago, IL, United States). Whether the distributions of continuous variables were normally or not was determined by Kolmogorov Smirnov test. Homogeneity of variances was analyzed by Levene test. Data were shown as mean ± SD or median (min-max), where applicable.

While the mean differences between groups were compared by Student's t test, otherwise, Mann Whitney U test was applied for comparisons of the median values. Nominal data were analyzed by Pearson's Chi-square, Fisher's exact or Likelihood Ratio test, where applicable. While the mean differences among more than two independent groups were evaluated by One-Way ANOVA, otherwise, Kruskal Wallis test was applied for comparisons of the median values.

The optimal cut off point of laboratory measurements to discriminate groups (e.g. malign and benign or cases with LVI or without LVI from each other was evaluated by ROC analysis as giving the maximum sum of sensitivity and specificity for the significant test. Sensitivity, specificity, positive and negative predictive values were also calculated at the best cut-off points.

Determining the best predictor(s) which discriminate malign and benign groups from each other was evaluated by Multiple Logistic Regression analysis. Any variable whose univariable test had a p value <0.25 was accepted as a candidate for the multivariable model along with all variables of known clinical importance. Adjusted odds ratios, 95% confidence intervals and valid statistics also were calculated. A p value less than 0.05 was considered statistically significant.

Results

The study group included 219 women and were divided into two groups; women diagnosed with endometrioid type endometrial cancer and underwent staging laparotomy (malign group, n=114), women underwent laparotomic/laparoscopic or vaginal hysterectomy for benign diseases (benign group, n=105). Demographic and clinicopathologic features are shown in Table 1.

When definitive factors in discriminating patients with endometrium cancer from those with benign diseases, MPV was significantly increased in the malign group whereas there was a significant decrease in PDW value compared to the benign group, so that MPV and PDW were assessed as significant markers in differentiating benign diseases and endometrium cancer according to the receiver operator characteristic (ROC) analysis (AUC: 0.702, 95% CI: 0.633-0.771, p<0.001).

When MPV and PDW were assessed in order to find the best cut-off value in differentiation of the benign and malign groups, malign cases were found to increase over the value of 7.54 for MPV (Odds ratio: 3.736, 95% CI:

Table 1. Demographic and Clinicopathologic Features of Benign and Malign Groups

Features	Benign group (n=105)	Malign group (n=114)	p-value
Age (year)	50.5±7.6	56.4±10.1	<0.001
Gravida	3 (0-9)	3 (0-12)	0.795
Parity	3 (0-9)	3 (0-9)	0.090
HT	27 (25.7%)	51 (44.7%)	0.003
DM	18 (17.1%)	33 (28.9%)	0.039
Hematologic Parameters			
WBC	7150 (1560-28090)	7465 (1540-14000)	0.219
NLR	2.08 (1.02-21.49)	2.11 (1.01-5.55)	0.506
Platelet x103	292 (29.5-366)	294.5 (135-732)	0.745
MPV	7.2 (1.6-14.9)	7.8 (6.2-11.3)	<0.001
PDW	53.1 (22.6-74.5)	48 (6.4-546)	<0.001
PCT	0.22 (0.09-2.28)	0.23 (0.12-0.62)	0.101
PLR	137.9 (12.0-483.1)	129.1 (59.4-418.3)	0.262

*HT:Hypertension; DM: Diabetes Mellitus

Table 2. Comparison of Hematologic Parameters between the Groups with the Early and Advanced Stage Endometrium Cancers

Parameter	Stage I-II (n=99)	Stage III-IV (n=15)	P value
NLR	2.10 (1.01-5.55)	2.13 (1.26-5.40)	0.880
Platelet x103	296 (135-732)	268 (177-385)	0.669
MPV	7.8 (6.2-11.3)	7.9 (6.8-9.0)	0.903
PDW	48.5 (6.4-546)	44.7 (16.3-58.1)	0.502
PCT	0.23 (0.12-0.62)	0.20 (0.15-0.31)	0.312
PLR	135.8 (59.4-418.3)	125.8 (88.5-257.0)	0.675

Table 3. Comparison of Hematologic Parameters between the Malign Groups with Positive and Negative Lymphovascular Space Invasion

Parameter	LVI negative (n=100)	LVI positive (n=14)	p-value
NLR	2.13 (1.01-5.55)	1.97 (1.26-5.4)	0.714
Platelet x103	292.5 (135-732)	303 (189-385)	0.710
MPV	7.8 (6.2-11.3)	7.9 (7.0-11.2)	0.429
PDW	48.9 (6.4-546)	30.9 (16.3-63.6)	0.463
PCT	0.23 (0.12-0.62)	0.24 (0.15-0.31)	0.452
PLR	131.1 (59.4-418.3)	127.9 (65.0-257.0)	0.836

LVI: Lymphovascular invasion

1.865-7.486, p <0.001) and under 37.75 for PDW (Odds ratio: 41.725, 95 CI: 5.426-320.868, p <0.001).

None of the examined hematological parameters showed a significant difference between the groups with early and advanced stage endometrium cancer and the malign groups with positive and negative lymphovascular space invasion (LVI) (Table 2 and Table 3).

Discussion

Since the association between cancer and inflammation was first discovered, there have been several studies on this topic (O'keefe et al., 2002; McMilan et al., 2003; Cho et al., 2009; Feng et al., 2014). Although the mechanism remains unclear, neutrophils, lymphocytes and platelets have been shown to contribute tumor growth and invasion with various cytokines, growth factors and local mediators (Karpatkin et al., 1981; Bhatti et al., 2010; Cho et al., 2012; Kwon et al., 2012). Endometrium cancer has been less investigated from this viewpoint among gynecologic cancers. We aimed to find out the predictive value of the preoperative alterations of the complete blood count parameters in the discrimination of the benign and malign endometrium diseases and differentiation of early and advanced stage endometrial cancer.

There have been few studies investigating the complete blood count parameters in order to find out their value in the discrimination of benign, precancerous and malign diseases of the ovary, cervix and endometrium. In one of these studies, platelet count was found to be higher and lymphocytes were to be lower in the malign ovarian cancer group when compared to the benign group (den Ouden et al., 1997). Another study showed significantly higher neutrophilia in patients with cervical cancer than those with preinvasive cancer (Tavares-Murta et al., 2010). The only study investigating the relationship between the endometrial benign, precancerous and malign diseases and blood count alterations found that, WBC, platelet count, NLR and PLR were higher in the patients with endometrium cancer than that of the benign group. WBC was also found to be significantly higher in the malign group when compared to the patients with precancerous diseases (Acmaz et al., 2014). In the line with this study, we searched the value of the blood count parameters in discrimination of the benign and malign disease of the endometrium but as distinct from them, to the best of our knowledge we investigated platelet indices for the first time and found MPV and PDW to have significant cut-off values in the discrimination of the benign and malign cases, whereas there was no significant alteration in other parameters (Table 1).

The predictive value of the preoperative complete blood count parameters in the staging of the endometrium cancer has been also investigated. In one of these studies, preoperative inflammatory markers were evaluated in terms of relationship between cervical stromal involvement which is an important parameter in staging endometrium cancer. As a result, elevated NLR and PLR were found to be significantly related to cervical stromal involvement (Wang et al., 2013). In the present study, we assesed the predictive value of the preoperative blood count parameters in discrimination of the early and advanced stage disease but no significant relationship with any of them was found (Table 2).

The association between preoperative blood count parameters and lymphovascular space invasion and lymph node metastasis in different types of cancer has been an other novel investigation topic in this field (Bhatti et al., 2010; Kwon et al., 2012). One of the relevant studies evaluated the predictive value of the preoperative systemic inflammatory response (SIR) markers including complete blood count with differential WBC counts, CRP, fibrinogen and albumin for lymph node metastasis in comparison with serum CA-125 in patients with endometrial cancer. They reported that although there was a significant relationship between preoperative NLR, PLR and lymphovascular space invasion, SIR markers didn't appear to have more effect than CA-125 in prediction of LVI (Suh et al., 2012). In contrast, we didn't find a significant relation between complete blood parameters and lymphovascular space invasion (Table 3).

The major limitation of the present study is the small percentage of the advanced stage endometrium cancer when compared to the early stage group.

In conclusion, this report shows, for the first time, the predictive value of MPV and PDW in the discrimination of benign and malign endometrial pathologies diseases. On the other hand, blood count parameters including WBC, NLR, PLR, platelet number and indices were not found to be significant in the discrimination of the patients in terms of the LVI and the stage of the disease. Since there have been few reports on this topic, it may be difficult to comment the present findings, therefore, further large-scale prospective studies are warranted.

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