



Research Article

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## The role of inflammatory markers in the diagnosis of extraperitoneal endometriosis

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### Abstract

This study was concerned with the examination of patients who underwent surgery for subcutaneous endometriosis in our clinic and the relationship between subcutaneous endometriosis and inflammatory markers. Patient demographics and information on history and duration of previous surgery, lesion size, number of lesions, location, recurrence, symptoms, type and number of deliveries, recurrence status, and imaging method were recorded. Laboratory analysis recorded TSH, blood count (Hb), WBC, mean platelet volume (MPV), neutrophil/lymphocyte ratio (NLR), monocyte/platelet ratio (MPR), lymphocyte/monocyte ratio (LMR), platelet/lymphocyte ratio (PLR) and CA -125 values of patients. The study included 28 patients and it was found that the mean age of the patients was 32.67±5.56 years. Five (17.9%) and 18 (64.3%) of the patients complained of a palpable mass and cyclic pain, respectively. Five patients (17.9%) were asymptomatic. Endometriosis associated with the scar line was localized in 18 (64.3%) of the patients. In three (10.7%) of the patients, the endometriosis was localized in the perineal line and in 7 (25%) of the patients in the rectus abdominis. No significant difference was found in the patients' routine laboratory results and inflammatory markers. In the present study, there was no significant association between the levels of inflammatory markers in patients who underwent surgery for subcutaneous endometriosis at different sites and with different symptoms.

**Keywords:** endometriosis, scar line, episiotomy line, abdominal wall, extraperitoneal, inflammatory

### 1. Introduction

Endometriosis is recognized by the presence of endometrial glands and stroma outside the uterine cavity (1). The prevalence of endometriosis is up to 40% of women at reproductive age. Although endometriosis most commonly occurs in the pelvic region, it has also been found in areas outside the pelvis (1). Less common locations include the abdominal wall, cesarean section scar line, and perineal endometriosis associated with episiotomy scarring. It usually occurs after obstetric or gynecologic surgery (2). The incidence of this pathology ranges from 0.04% to 1% for abdominal wall endometriosis (3) and from 0.03% to 0.4% for surgical scar endometriosis (4). Their incidence has increased worldwide due to high cesarean section rates. This particular form of endometriosis has been only partially recognized, and the diagnosis is usually made late. The incidence of the disease increases under the influence of postpartum estrogen exposure and concomitant endometrial inoculation during surgery, variable immunity, chronic inflammation, and local growth factors (5). Nowadays, the first treatment option is surgical excision of subcutaneous endometriosis. Neutrophil/lymphocyte ratio (NLR), lymphocyte/monocyte ratio (LMR), monocyte/platelet ratio (MPR), and platelet/lymphocyte ratio (PLR) in peripheral blood are easy to calculate, inexpensive, and can reveal systemic inflammation. It is believed that these markers can be a prognostic factor for many diseases.

This study focused on the examination of patients who had undergone subcutaneous endometriosis surgery in our clinic and the relationship between subcutaneous endometriosis and inflammatory markers.

### 2. Materials and Methods

The study included patients who underwent surgery for extraperitoneal subcutaneous endometriosis at the Gynecology and Obstetrics Department of Tokat Gaziosmanpaşa University Research and Application Hospital between 2015 and 2021. Prior to the study, approval was obtained from the Clinical Research Ethics Committee of Gaziosmanpaşa University (project number: 21-KAEK-173/05.08.2021). The study was planned as a retrospective study in which 28 patients with extraperitoneal subcutaneous endometriosis were enrolled. Patient data were obtained from hospital records. As for the inclusion criteria, patients who were operated for extraperitoneal endometriosis and whose pathology was endometriosis externa were included in the study. Regarding the exclusion criteria, patients who underwent surgery at an external center and whose data could not be collected were excluded from the study. All patients underwent a physical examination, a detailed medical history, and routine hematologic and biochemical analysis. Patient demographics and information on age, gravid, parity, history and duration of previous surgery, lesion size, number of lesions, location, recurrence, complaints, history of systemic

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diseases, type and number of deliveries, recurrence status, and follow-up and imaging were recorded. Laboratory analyzes included TSH, free T4, blood count (hemogram) (Hb), neutrophils, monocytes, lymphocytes, white blood cells (WBC), platelets, MPV, PLR, NLR, LMR, and CA -125 values of patients. A regularly maintained device (Mindray BC-6800, China) was used for complete blood count. A regularly maintained device (Roche Cobas e601, Roche Diagnostics GmbH; Germany) was also used for other tests. In the evaluation, patients were grouped according to their complaint status (asymptomatic, pain, palpable mass) and extra-abdominal and local location (subcutaneous, perineal, rectus-related). Descriptive statistics were performed to obtain data on the general characteristics of the study groups. Continuous variable information is presented as mean±standard deviation and min-max. Differences between groups were examined with Kruskal-Wallis analysis of variance considering parametric conditions. The Bonferroni-corrected Mann-Whitney U test was used for multiple comparisons. Differences were analyzed with the nonparametric test considering the number of subjects in the groups. P values of less than 0.05 were considered statistically significant. Ready-made statistical software was used for calculations (IBM SPSS Statistics 19, SPSS inc, an IBM Co, Somers, NY).

### 3. Results

It was found that the mean age of the patients was 32.67±5.56 years and the parity was 2.32±0.94. Twenty-four (85.7%) of these patients had a cesarean section, 3 (10.7%) had a normal vaginal delivery, and 1 (3.6%) had a previous subcutaneous endometriosis operation with cesarean section. The mean duration after current delivery in these patients was 4.17±1.92 years. The mean lesion diameter was 3.02±1.52 cm<sup>2</sup>. Five (17.9%) and 18 (64.3%) of the patients complained of a palpable mass and cyclic pain, respectively, and 5 patients (17.9%) were asymptomatic. While 18 (64.3%) of the patients had the localization of endometriosis associated with the scar line, 3 (10.7%) of them had the localization of endometriosis with the episiotomy line, and 7 (25%) of them had the

localization of endometriosis with the rectus abdominis. Twenty-seven of the patients (96.4%) were operated for the first time for endometriosis, and 1 patient (3.6%) was operated for recurrence. It was found that 13 (46.4%) of the patients had a history of cesarean section, 7 (25%) had two cesarean sections, 5 (17.9%) had three cesarean sections, and 3 patients (10.7%) had a normal vaginal delivery. Diagnosis was made by ultrasound in 21 (75%) patients, magnetic resonance imaging (MRI) in 2 (7.1%), and computed tomography (CT) and clinical examination in 2 (7.1%) and 3 (10.7%), respectively.

TSH, T4, Hb, Ca-125, neutrophils, lymphocytes, platelets, monocytes, MPR, PLR, NLR, and LMR were calculated in the patients. The laboratory results of the patients are shown in Table 1. Comparison of symptoms (palpable mass, cyclic pain, asymptomatic) and location (under the scar, episiotomy line, rectus-related) and laboratory results were summarized in Table 2 and Table 3. No statistically significant differences were found between inflammatory markers and other laboratory results in the comparisons. It was noted that the patients with excision had no recurrence.

**Table 1.** Laboratory results of the patients

	Laboratory results (n=28)
TSH (mIU/L)	1.87 ±1.39
T4(ng/dL)	1.24 ± 0.24
Neutrophil (10 <sup>2</sup> /μL)	5209.00 ± 3109.95
Lymphocyte (10 <sup>2</sup> /μL)	2263.57 ± 1254.82
Platelet (lakhs/mm <sup>3</sup> )	248232.14 ± 55039.30
WBC (10 <sup>5</sup> /mL)	7.95 ± 3.14
Hb (gr/dl)	12.19 ±1.32
Monocytes (10 <sup>2</sup> /μL)	540.61 ± 143.84
MPV (fL)	9.73 ± 1.34
NLR	2.51 ±1.56
PLR	124.68 ± 49.82
MPR	0.0022 ± 0.0005
LMR	4.25 ± 1.60
Ca-125 (U/mL)	27.96 ± 17.01 (10.13-92.51)

Values are expressed as mean ± standard deviation. TSH: thyroid-stimulating hormone; T4: thyroxine, Hb: blood count, WBC: white-blood cell, MPV: mean platelet volume, MPR: Monosit/platelet, LMR: Lenfosit/monosit, NLR: neutrophil / lymphocyte ratio, PLR: platelet / lymphocyte ratio

**Table 2.** Comparison of laboratory values according to symptoms

	Symptom			KW	p
	Asymptomatic (n=5)	Cyclic pain (n=18)	Palpable mass (n=5)		
TSH (mIU/L)	1.1±0,7	2.1±1.47	1.82±1.57	2.882	0.237
T4(ng/dL)	1.39±0.31	1.23±0.24	1.13±0.14	2.263	0.323
Neutrophil (10 <sup>2</sup> /μL)	5320±1536.91	5310.67±3706.11	4732±2049.72	1.536	0.464
Lymphocyte (10 <sup>2</sup> /μL)	2020±761.97	2357.78±1516.29	2168±388.48	0.782	0.676
Platelet (lakhs/mm <sup>3</sup> )	210460±13925.09	258455.56±62942.38	249200±34083.72	5.163	0.076
WBC (10 <sup>5</sup> /mL)	8.07±1.83	7.99±3.68	7.7±2.36	0.798	0.671
Hb (gr/dl)	12.39±0.67	12.2±1.42	11,94±1.64	0.204	0.903
Monocytes (10 <sup>2</sup> /μL)	520±109.77	532.61±154.04	590±151.33	0.791	0.673
MPV (fL)	10.14±1.13	9,53±1.51	10,04±0.75	1.814	0.404
NLR	2.91±1.23	2.48±1.8	2.2±0.93	1.715	0.424
PLR	116.24±42.36	128.92±57.67	117.85±24.37	0.044	0.978
MPR	0.0025±0.0005	0.0005±0.0025	0.0024±0.0004	1.93	0.381
LMR	4.12±1.89	4.41±1.7	3.82±1.01	0.334	0.846
Ca-125 (U/mL)	30.75±13.29	28.91±19.53	21.76±9.7	1.534	0.464

Values are expressed as mean ± standard deviation, KW: Kruskal Wallis Varyans Analysis

**Table 3.** Distribution of laboratory values according to localization

	Localization			KW	p
	Scar line (n=18)	Episiotomy line (n=3)	Associated with rectus abdominis (n=7)		
Tsh (mIU/L)	1.62±0.84	3.84±2.92	1.67±1.3	1.572	0.456
T4(ng/dL)	1.29±0.24	1.34±0.3	1.07±0.16	5.837	0.054
Neutrophil (10 <sup>2</sup> /μL)	5335±2970.49	3286.67±337.24	5708.86±4037.02	3.754	0.153
Lymphocyte (10 <sup>2</sup> /μL)	2087.78±517.82	2050±160.93	2807.14±2420.12	0.059	0.971
Platelet (lakhs/mm <sup>3</sup> )	256322.22±51702.4	208500±43511.49	244457.14±66518.34	1.395	0.498
Wbc (10 <sup>5</sup> /mL)	8.14±3.03	6.03±0.56	8.31±4.04	3.049	0.218
Hb (gr/dl)	12.37±1.31	12.32±1.8	11.67±1.22	2.325	0.313
Monocytes (10 <sup>2</sup> /μL)	527.22±126.81	496.67±112.4	593.86±196.28	0.601	0.740
MPV (fL)	9.68±0.97	10.19±2.01	9.65±1.97	0.121	0.941
NLR	2.74±1.83	1.6±0.09	2.3±0.96	3.924	0.141
PLR	131.88±51.23	101.53±19.09	116.09±55.68	1.523	0.467
MPR	0.0021±0.0005	0.0005±0.0021	0.0025±0.0006	2.386	0.303
LMR	4.14±1.36	4.25±0.84	4.54±2.43	0.134	0.935
Ca-125 (U/mL)	24.55±10.97	41.22±44.51	31.07±12.9	1.426	0.490

Values are expressed as mean ± standard deviation, KW: Kruskal Wallis Varyans Analysis

#### 4. Discussion

Abdominal wall endometriosis is a form of endometriosis characterized by a painful or painless lump in the previous incision scar. It is most commonly seen after cesarean section, laparotomy, and hysterectomy. It can also be observed after gynecologic laparoscopic surgery (2, 4). In the literature, case series of scar endometriosis after episiotomy have been reported rarely (6). In our study, 64.3% of patients were found to have endometriosis associated with the scar line, 10.7% had endometriosis associated with the episiotomy line, and 25% had endometriosis associated with the rectus abdominis. The time between surgery and diagnosis of endometriosis varied from 3 months to 20 years, and the mean age at diagnosis was 35 years (7). In the present study, the mean age at diagnosis was found to be 32.6 years, and the time to diagnosis and surgery after surgery in our study was 4.17 years. Concurrent pelvic lesion was not observed in the patients. Tatli et al. in their series of 14 cases also reported that there was no concurrent pelvic lesion (7). Sumathy et al. in their series of 16 cases found that 18.9% of patients had concurrent endometriosis (8). Most patients had symptoms of cyclic pain associated with menstruation at the surgical incision site (4). Occasionally, a palpable mass may be found without pain. These symptoms must be a warning for scar endometriosis. In our study, 17.9% of patients had a palpable mass, 64.3% of them had cyclic pain complaints, and 17.9% of them were asymptomatic. A noninvasive examination is beneficial to differentiate the mass from surrounding tissues in terms of location, size, density, and homogeneity. Ultrasonography is a practical, accessible, reliable, and inexpensive method (9). On ultrasound, the appearance of a vascularized, hypochoic, heterogeneous solid lesion is a supportive finding for scar endometriosis. If there is doubt about the diagnosis, CT and MRI can be used. In the present study, 75% of patients were diagnosed by ultrasound, 7.1% by MRI, and 7.1% and 10.7% by CT and clinical examination, respectively. Fine needle aspiration cytology (FNAC) is a simple, convenient, and cost-effective method that can be used in cases with uncertain diagnosis (10).

However, the use of this method is controversial. It is argued that this technique increases the risk of developing new endometriotic implants at the administration site and the risk of injury to internal organs (incisional hernia is the differential diagnosis of endometrioma) (11). The final diagnosis is made by histopathologic evaluation after complete excision. In our study, the final histopathologic diagnosis was compatible with the provisional diagnosis in all patients. The recognized most appropriate treatment model is wide surgical excision, which provides the final diagnosis and treatment simultaneously. In wide surgical excision, it is important to operate at least 1 cm from the margin of the lesion (12). The recurrence rate is very low for excisions with appropriate surgical margins. Yela et al. reported a high recurrence rate of 36.1% in patients with positive surgical margins (13). Because of the likelihood of recurrence, it is necessary to monitor patients after surgery. If recurrence is detected, surgical resection must be repeated. None of the patients in our series had a recurrence of the disease. Only 1 patient had previously been operated on at another center and was operated on again at our center. Our patients had no recurrence. It was assumed that the reason was resection of at least 1 cm of endometriosis. It was found that the mean value of Ca-125 was within normal limits. Its use in patients was not found to be beneficial. To the best of our knowledge, this is the first study to investigate the systemic inflammatory markers MPR, NLR, LMR, and PLR in subcutaneous endometriosis. MPR, NLR, LMR, and PLR are systemic inflammatory markers associated with various diseases such as coronary artery disease, peripheral vascular disease, rheumatologic disease, gastrointestinal tract disease, and malignancy (14,15). In the literature, some authors suggest that NLR may be a prognostic factor for many diseases. Endometriosis is a chronic inflammatory disease associated with findings such as dysmenorrhea, dyspareunia, and chronic pain. In their study of 467 patients with endometrioma, Tokmak et al. reported that NLR and Ca-125 levels were correlated and higher than other patients with benign ovarian cysts (16). In another clinical study, Cho et al. found that

NLR levels were higher in 231 patients with endometriosis compared with the other group with benign ovarian cysts and the control group (17). While Kim et al. performed laparoscopic endometrioma surgery in 419 patients and found no association between NLR and endometrioma (18), Yavuzcan et al. reported no association between PLR and NLR and endometriosis in 33 patients who underwent endometriosis surgery (19). While the retrospective and sectional nature of the study and the limited number of patients are the weaknesses of the study, the facts that inflammatory markers were studied for the first time in the subcutaneous endometriosis series and that it includes results from the only tertiary hospital in the region are the strengths of the work.

When evaluating masses near the incision site in patients with a history of surgery, cyclic pain that increases with menstruation should be especially investigated, and endometriosis should always be considered. It is necessary to reduce the possibility of recurrence by performing a comprehensive surgical excision in these cases. Our study showed that there was no significant association between MPR, NLR, LMR and PLR values in patients operated for subcutaneous endometriosis at different sites and with different symptoms. There is a need for studies with larger patient populations to determine the role of these markers in subcutaneous endometriosis.

#### Conflict of interest

The authors have no conflict of interest.

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None to declare.

#### Authors' contributions

Concept: S.G., Design: S.G., N.G., Data Collection or Processing: S.G., Analysis or Interpretation: S.G., Literature Search: S.G., N.G., Writing: S.G., N.G.

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