Increased platelet count in severe peritoneal endometriosis

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Summary

Objective: Platelet count (PC) is higher in chronic inflammatory diseases. The aim of this study was to evaluate the PC in patients with severe pelvic endometriosis. *Materials and Methods:* Patients with advanced stage pelvic endometriosis were retrospectively evaluated in a tertiary center between January 2009 and December 2011. Patients with pelvic endometriosis were divided into two groups; advanced stage peritoneal endometriosis were classified as Group 1 (n = 28). Group 2 consisted of 29 patients which had ovarian endometrioma without clinically apparent peritoneal endometriosis foci. Group 3 included 51 women as control subjects. PC between the groups was tested by Student's t test. The mean values of three groups were analyzed by using one way ANOVA test followed post-hoc test Bonferroni. *Results:* PC in patients with pelvic endometriosis were found to be higher from the control group (290 ± 67 10^9/l; 264 ± 63 10^9/l, respectively; $p = 0.038$). Patients with peritoneal endometriosis (Group 1) had significantly higher PCs compared with the healthy controls (309 ± 65 10^9/l; 264 ± 63 10^9/l; respectively; $p = 0.011$). *Conclusion:* Increased PC in advanced stage pelvic endometriosis may be a sign of increased systemic inflammation. The systemic inflammation may be more apparent in advanced stage peritoneal endometriosis.

Key words: Endometriosis; Inflammation; Platelet count.

Introduction

Endometriosis is defined as presence of endometrial glands and stroma outside the uterine cavity and generally develops within the pelvis. It is a chronic estrogen-dependent disorder. The etiology of this disorder is still unknown. The implantation theory of Sampson, the coelomic metaplasia theory of Mayer, and the induction theory are the classical theories attempting to explain origin of the disease. Combination theory also explains the difference between ovarian and peritoneal endometriosis. Endometriosis lesion has distinctive morphologic appearance; active lesions include vesicles, flat plaques and black coloration [1, 2]. Secretion of various cytokines by endometriotic implants results to activation of inflammatory cells into the peritoneal cavity and leads to a sterile local inflammation of peritoneum [3]. Active endometriotic lesion has metabolic activity, as is suggested by their high concentrations of prostaglandin metabolites. Pain as secondary dysmenorrhea or chronic pelvic pain, is associated with inflammation and anti-inflammatory drugs are used for treatment of pain. Progressive fibrosis occurs and lesion being inactive in the long term [1]. Some researchers suggests that active phase of the disease is associated with systemic subclinical inflammation [4].

Platelets play an important role in thrombosis and hemostasis however they have relevant functions in inflammation. Inflammation is an important stimulant for platelets [5]. The role of platelets in chronic inflammatory diseases has now been convincingly demonstrated. Platelet count (PC) has been reported to be increased in rheumatoid arthritis, ankylosing spondylitis, familial mediterranean fever, and in patients with atherosclerosis which are accompanied with chronic inflammation [6-9].

Like benign chronic disorders, PC has been reported to be increased in solid tumors including gynecologic cancers. Malignant cells produce certain cytokines and growth factors, which are capable of inducing platelet production. Previous studies suggest that elevated platelet count is associated with factors reflecting more aggressive tumor biology, and predicting poor survival in women with such tumors [10, 11].

The aim of present study was to investigate PC in severe pelvic endometriosis especially in patients with severe peritoneal group. To the authors' knowledge, the present study is the first study investigating PC in patients with severe endometriosis.

Materials and Methods

Women with endometriosis which managed and operated at Dicle University School of Medicine, Department of Obstetrics and Gynecology between January 2009 and December 2011 were retrospectively evaluated. Endometriosis was diagnosed by laparoscopy/laparotomy with histological confirmation of the disease. Operative findings and stage of disease consisted of a written report with the use of the revised American Fertility Society classification for Endometriosis [12]. All operations were performed by the four authors (MSE, HES, MES, and AO). Study population consisted of 57 patients with severe pelvic endometriosis that were Stage 3 and/or Stage 4. Patients with minimal or mild stage of endometriosis were not included in the study. Patients with histories of myeloproliferative disorders, presence of acute or chronic inflammatory diseases or history of receiving hormonal therapies

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for the last three months were also not included. After excluding improper subjects from the study, patients with severe pelvic endometriosis were divided into two groups according to the presence of severe peritoneal endometriosis. Patients with peritoneal endometriosis were classified as Group 1 (n = 28) and, patients with ovarian endometrioma without clinically apparent peritoneal endometriosis foci as Group 2 (n = 29).

Control group (Group 3) included 51 women recruited from the patients admitted to outpatient clinic without any gynecological diseases. All the subjects were aged between 18-35 years.

A preoperative automated complete blood count was available for all patients. The following relevant data were retrospectively determined from medical records: age of subjects, hemoglobin, white blood cell counts, PC, presence of Stage 3-4 peritoneal endometriosis or Stage 3-4 ovarian endometrioma. The study protocol was approved by the Medical Ethics Committee of Dicle University.

Statistical analysis

Statistical analysis was performed by SPSS statistical software (SPSS for windows 15.0, Inc., Chicago, IL, USA). Data were presented as mean ± standard deviation. Differences between the two groups were tested by Student's t test. The mean values of three groups were compared by using one way ANOVA test followed post-hoc test Bonferroni. A *p* value less than 0.05 was accepted as statistically significant.

Results

Patients with pelvic endometriosis (290 ± 67 10^9/l m^3) had significantly higher PC compared with the control group (264 ± 63 10^9/l) ($p = 0.038$). Mean diameter of endometrioma cyst were 6.18 ± 1.96 cm (min-max, 3-11) in Group 2. Hematological parameters are shown in Table 1.

PCs also were compared according to coexistency of peritoneal endometriosis. The mean PC was significantly higher in Group 1 (severe peritoneal endometriosis) when compared with Group 3 (control subjects) (309 ± 65 10^9/l and 264 ±63 10^9/l; respectively; $p = 0.011$). No significant difference was found in PC between peritoneal endometriosis group and the ovarian endometrioma subjects (Table 2).

Table 1. — *The comparisons of age and hematological parameters between endometriosis and control groups.*

Variable	GR1+ GR2 ($\bar{x}$ ± SD)	GR3 ($\bar{x}$ ± SD)	*p*
Age (years)	29,6±4,13	28.2±5.3	0.342
Platelet count (-10^9/l)	290±67	264±63	0.038*
Hemoglobin (g/dl)	12.8±0.8	12.8±0.9	0,755
White blood cell (x10^9/l)	8,3±1,6	7,9±1,6	0,151

($\bar{x}$ ± SD) = Mean ± standard deviation.
* = Statistically significant.

Table 2. — *The comparison of age and platelet count among three groups.*

Variable	Group 1 ($\bar{x}$ ± SD)	Group 2 ($\bar{x}$ ± SD)	Group 3 ($\bar{x}$ ± SD)	*p*	Bonferroni, *p*
Age (years)	29.7±4.2	29.4±4.1	28.2±5.3	0.291^{NS}	-
PC (10^9/l)	309±65	272±64	264±63	0.011*	0.091 (Groups 1 vs 2) 0.010** (Groups 1 vs 3) 1.000 (Groups 2 vs 3)

($\bar{x}$ ± SD) = Mean ± standard deviation
PC = Platelet count
NS = not significant
* = The mean values of three groups were analyzed by using one way ANOVA test followed by Bonferroni post-hoc test
** = The differences between Group 1 - Group 3 were found significant by Bonferroni post-hoc test.

Discussion

Endometriosis is associated with increased inflammatory activity. Patients with endometriosis had higher rates of autoimmune inflammatory diseases, allergies, and asthma, when compared with the general female population [13]. Elevated peritoneal fluid inflammatory markers have been observed in the literature. Pelvic pain related to endometriosis, is relieved by anti-inflammatory drugs, supporting thus the contribution of chronic inflammation in the pathogenesis of this disease [1, 4].

Agic *et al.* [4] reviewed the literature and found a number of studies related to increased number of activated macrophages in peritoneal fluid of women with endometriosis and that secrete various local products, such as growth factors and cytokines. Levels of many cytokines in the peritoneal fluid of women with endometriosis have been found to be increased, thus implicating that these cytokines might be important for the progression of endometriosis. Furthermore, it has been reported that the levels of various cytokines also increased in the serum of patients with endometriosis and this suggested that there was an association of subclinical inflammation in patients with endometriosis. Although many studies showed increased inflammatory cytokine levels, there were also some researchers that found no difference in levels of inflammatory markers in endometriosis [4]. The differences in various studies may be due to that endometriosis lesions are sometimes inactive; estrogen status of the patients may differ at the time of the study, difference etiopathogenesis of ovarian or pelvic endometriosis and the severity of the disease. In this study, PC was significantly higher in severe pelvic endometriosis and in severe peritoneal endometriosis group compared to control. The authors suggest that further studies to investigate inflammation in advanced endometriosis must examine peritoneal endometriosis and ovarian endometrioma groups separately. Inflammatory markers (IL-6, TNF-α), especially have been found in higher concentrations in severe endometriosis groups [4, 14]. In this study the authors investigated the PC in severe endometriosis patients and despite different etiopathogenesis of the ovarian and peritoneal endometriosis, they cal-

culated PC separately in Stage 3-4 ovarian endometrioma group (without clinically apparent peritoneal endometriosis foci) and Stage 3-4 peritoneal endometriosis.

In conclusion, the authors found significantly increased PC in severe peritoneal endometriosis group when compared with the control subjects and this finding may be a sign of increased systemic inflammation. Increased PC in patients with severe peritoneal endometriosis may be related to chronic inflammation that in long term may cause some negative health consequences such as atherosclerosis.

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