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Research Paper

Can Mean Platelet Volume Serve as a Marker for Prostatitis?

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Abstract

Aim: The aim of the study was to compare the yield of mean platelet volume (MPV), total prostate specific antigen (tPSA), free prostate specific antigen (fPSA), f/t PSA ratio and complex prostate specific antigen (cPSA) in patients with prostatitis.

Material and method: The study was designed in the Kayseri Education and Research Hospital. Ninety-six patients with prostatitis were enrolled retrospectively into the study. Laboratory data were obtained from the computerized patient database. We evaluated the correlation between tPSA, fPSa, f/t PSA ratio, cPSA, MPV and extent and aggressiveness of inflammation in the surgical specimens of patients who underwent surgery for benign prostatic hyperplasia (BPH). Inflammation in the prostatic tissues was scored for extent and aggressivity of inflammation using the grading system designed by Irani et al.

Results: The total PSA, fPSa, f/t PSA ratio, cPSA and pre- and post-treatment MPV values of each group did not differ ($p>0.05$) (Table 1). Also there was no correlation between the histopathological grades and the MPV, tPSA, fPSA, f/t PSA ratio and cPSA of patients. However, MPV values significantly decreased after treatment in all grades of prostatitis ($p<0.001$).

Conclusion: MPV values may be used as an inflammation marker in patients with prostatitis.

Key words: MPV, tPSA, fPSA, f/t PSA and, cPSA, chronic prostatitis, BPH.

Introduction

Benign prostatic hyperplasia (BPH) and prostatitis are the most common benign diseases of the prostatic gland. Prostatitis is an inflammatory condition of the prostate and has been divided into four categories according to the National Institutes of Health classification (2). These are Category I: Acute bacterial prostatitis, Category II: Chronic bacterial prostatitis, Category III: Nonbacterial prostatitis, Category IV: Asymptomatic inflammatory prostatitis (This is a histological diagnosis in patients undergoing a prostate biopsy). Histological prostatitis refers to the confirmation of prostate inflammation by microscopic examination. Asymptomatic inflammatory prostatitis is a common pathological finding in patients with BPH. The coexistence of these two diseases is well-known by urologists and pathologists (1, 2, 3, 4, 5).

The Inflammatory injury may contribute to cytokine production by inflammatory cells driving local growth factor production and angiogenesis in the prostatic tissue. This proinflammatory microenvironment is closely related to BPH stromal hyperproliferation and tissue remodeling with a local hypoxia, induced by increased oxygen demands from proliferating cells, which supports chronic inflammation as a source of oxidative stress leading to tissue injury in infiltrated area. Although the pathogenesis of BPH is

not yet fully understood and several mechanisms seem to be involved in its development and progression, recent studies strongly suggest that BPH is an immune inflammatory disease. The T-cell activity and associated autoimmune reaction seems to induce epithelial and stromal cell proliferation (2, 6, 7, 8). Based on the available scientific evidence, it is highly likely that age-dependent weakening of the immune system, coupled with modified hormonal secretion, leads to the deterioration of a postulated population of suppressor cells that actively suppresses the recognition of prostatic antigens; this leads to the gradual infiltration of the prostate by lymphocytes and the subsequent cascade of events that leads to BPH (5).

Platelet volume is an indicator of platelet function and activation. Platelet activity and aggregation capacity can be easily determined by measuring mean platelet volume (MPV). The intensity of systemic inflammation can be viewed as a distinctive factor for classifying conditions associated with large and small-sized circulating platelets. Large platelets have more granules, aggregate more rapidly with collagen, produce higher levels of thromboxane A2 and express more glycoprotein Ib and IIb/IIIa receptors than smaller ones. Platelet activation is a link in the pathophysiology of diseases prone to thrombosis and inflammation. (9-11). Evidence has accumulated suggesting the important role of MPV as a marker of inflammation, disease activity and efficacy of anti-inflammatory treatment in several chronic inflammatory disorders. It seems that the size of circulating platelets is dependent on the intensity of systemic inflammation, with contrasting features of MPV in high and low-grade inflammatory disorders and in the course of anti-inflammatory treatment (11-14). Its relation with many inflammatory disease like ulcerative colitis, Crohn's disease, systemic lupus erythromatosis and rheumatoid arthritis have been studied (11,15,16).

In this study we aimed to research the association of MPV and the histopathological activity and aggravation of inflammation in prostatic tissue, as well as any relation between grade of inflammation and total prostate specific antigen (tPSA), free prostate specific antigen (fPSA), f/t PSA ratio and complex prostate specific antigen (cPSA) in patients diagnosed with histological prostatitis according to the surgical specimens.

Material and Method

The study was designed in the Kayseri Education and Research Hospital. Ninety-six surgically treated BPH patients, whose surgical specimens were reported as nodular hyperplasia and chronic prostatitis, were enrolled retrospectively into the study. The patients included in this retrospective analysis were diagnosed with prostatitis on the basis of the mere presence of white blood cell infiltrates in histological specimens taken from surgical specimens. Laboratory data were obtained from the computerized patient database. Samples were analyzed for PSA analyzed by the immuno-inhibition method by an autoanalyser (İmmulite 2000) and platelet size was measured by an automated hematology analyzer (Cell Dyn Ruby) in biochemistry laboratory. We evaluated the correlation and difference between tPSA, fPSa, f/t PSA ratio and cPSA, and pre and post-treatment MPV values according to the extent and aggressiveness of inflammation in the surgical specimens of patients who underwent surgery for benign prostatic hyperplasia (BPH). Histological sections of the prostatic tissues were reviewed in a blinded fashion by a single pathologist. Histological evidence of prostatic inflammation in the prostatic tissues was scored for extent and aggressivity of inflammation using the grading system designed by Irani et al. (1). In this grading system, the extent of inflammation was graded as 0 = no inflammatory cells, 1 = scattered inflammatory cell infiltrate within the stroma without lymphoid nodules, 2 = non-confluent lymphoid nodules and 3 = large inflammatory areas with confluence of infiltrate. Inflammatory aggressiveness was graded as 0 = no contact between inflammatory cells and glandular epithelium (epithelial cells lining acini and ducts), 1 = contact between inflammatory cell infiltrate and glandular epithelium (minimal epithelium dissociation can be observed without disruption), 2 = interstitial inflammatory infiltrate associated with a clear but limited (<25 % of the examined material) glandular epithelium disruption and 3 = glandular epithelium disruption on over 25% of the examined material. We divided the groups into two as low-moderate and high grade.

Blood samples were drawn after an overnight fast from an antecubital vein. MPV was measured in a blood sample collected with ethylene diamine tetra acetic acid (EDTA) as an anticoagulant. The samples were used within one hour to prevent EDTA induced swelling.

Statistical analysis

Data were analyzed using the Statistical Package for Social Sciences version 17.0 (SPSS for Windows 17.0, Inc.,Chicago, IL, USA). The correlation between the extent and aggressiveness scores with tPSA was determined by Spearman correlation analysis. Pearson analysis was used for determining the correlation between histopathological grades and MPV, fPSa, f/t PSA and cPSA. Comparisons of age, serum MPV, tPSA, fPSa, f/t PSA and cPSA according to grades

were performed by Independent Sample t-test. P-values <0.05 were considered as statistically significant. All data were expressed as the mean ± standard deviation (SD).

Results

There were a total of 96 patients diagnosed with prostatitis according to the surgical specimens. Four of them were Grade 3, 49 were Grade 2 and only three were Grade 1. For that reason we divided the groups into two: low-moderate grade (n:52) and high grade (n:44).

The mean age of the low-moderate grade group was 71.7±7.7 years and that of the high grade group was 69.9±7.8 years. The total PSA, fPSa, f/t PSA ratio, cPSA and pre and post-treatment MPV values of each group did not differ (p>0.05) (Table 1). In addition there was no correlation between histopathological grades and the MPV, tPSA, fPSa, f/t PSA and cPSA of patients (Table 2).

However, MPV values significantly decreased after surgical treatment in both groups (p<0.001) (Table 3).

Table 1. Comparision of mean ages, PSA levels and pre and post-treatment MPV values of patients with prostatitis according to histopathological grades.

	Low-Moderate Grade n:52	High Grade n:44	p
Age	71.7±7.7	69.9±7.8	>0.05
tPSA	8.5±11.5	11.3±14.8	>0.05
fPSA	1.7±1.9	2.2±2.6	>0.05
f/t PSA	0.23±0.11	0.23±0.12	>0.05
cPSA	6.8± 9.2	9.9±12.9	>0.05
MPV before treatment	9.0± 1.3	8.8±1.1	>0.05
MPV after treatment	8.8±1.6	8.2±1.0	>0.05

Table 2. Correlation analysis of histopathological grades and MPV, tPSA, fPSa, f/t PSA and cPSA of patients.

	r(s)	p
tPSA*	0.128	0.108
fPSA	0.104	0.308
f/t PSA	-0.041	0.690
cPSA	0.105	0.303
MPV before treatment	-0.132	0.203
MPV after treatment	-0.235	0.098

* Analyzed by Spearman correlation.

Table 3. MPV values of patients with prostatitis in low- moderate grade and high grade before and after surgical treatment.

	MPV (fL) Before surgical treatment	MPV (fL) After surgical treatment	p
Low- moderate grade (n:52)	9.41±1.48	8.82±1.57	<0.001
High grade (n:44)	8.96±0.99	8.20±1.02	<0.001

Discussion

To our knowledge, prior studies have never analyzed the association between MPV and prostatitis as an inflammation indicator. In this study we evaluated the differences of MPV depending on grades of prostatitis and any correlation between MPV and PSAs. Our study showed that MPV values significantly decreased after surgical treatment in all grades of histological prostatitis, but there was no correlation with the severity of inflammation and MPV.

Prostatic inflammation is a common pathologic finding in BPH patients. Although the pathogenesis of BPH is not yet fully understood and several mechanisms seem to be involved in its development and progression, recent studies strongly suggest that BPH is an immune inflammatory disease. The T-cell activity and associated autoimmune reaction seem to induce epithelial and stromal cell proliferation (2, 5, 6, 7, 8).

Previous studies reported that patients with high serum PSA levels correlate with a high inflammatory aggressiveness score in inflammatory prostatitis (1, 2). In contrast to these studies, Nickel et al. (5) reported no correlation between inflammation pattern, prostate volume and serum PSA levels. Likewise, in our study, there was no correlation between histopathological grades and tPSA, fPSa, f/t PSA ratio and cPSA levels.

MPV is the geometric mean of the transformed log normal platelet volume data in impedance technology systems. In some optical systems MPV is the mode of the measured platelet volume (8, 9, 11, 12,13,14). Prostatitis may alter MPV mainly by affecting thrombopoiesis in bone marrow. Several hormonal and immune agents influence the maturation of thrombopoietin cells and the release of platelets into the circulation. Of these, thrombopoietin, granulocyte - macrophage colony -stimulating factor, (IL)-1, tumor necrosis factor (TNF)-alpha, and IL-6 are important. In stress conditions, a positive correlation among thrombopoietin, ploidy of platelet progenitors, functional activity and high platelet count is more apparent (11,14). The regulation of megakaryocytopoiesis is programmed to meet demands for activated platelets in physiological and pathological conditions, resulting in time-dependent changes of platelet indices. There is an inverse relationship between platelet size

and number; therefore, the total platelet mass, the product of the MPV and platelet count is closely regulated. It has been demonstrated that platelet volume is correlated with platelet function and activation (12, 13). Small platelets have lower functional capabilities than larger ones (13). Evidence has accumulated suggesting the important role of MPV as a marker of inflammation, disease activity and efficacy of anti-inflammatory treatment in several chronic inflammatory disorders. Therefore, MPV has been used as an indicator of platelet function for inflammatory diseases (12, 13, 15). High grade inflammation accompanies a decrease of MPV in rheumatoid arthritis (RA), possibly due to increased consumption of platelets at the sites of rheumatoid inflammation. A reverse shift of MPV results from the suppression of inflammation by disease-modifying and anti -TNF alpha agents (11, 15).

MPV has recently been recognized as an inflammatory marker in various conditions including ulcerative colitis, acute pancreatitis, and myocardial infarction (10-14). There are many studies about the relationship between MPV and some thrombotic and cardiac disorders (11, 16-22). In the literature, the results for infectious diseases seem to be conflicting. While some studies demonstrated a negative correlation between MPV and inflammatory activity, other investigators have reported an association between increased MPV and disease severity. Beyazıt et al. demonstrated that MPV is decreased in acute pancreatitis (23). Zubcevic et al. reported that one of the most reliable indicators of Crohn's disease activity was MPV; however, it was not sensitive enough to distinguish the relationship between moderate and severe disease (24). In chronic inflammatory diseases, such as ulcerative colitis, cystic fibrosis, ankylosing spondylitis, rheumatoid arthritis and Familial Mediterranean Fever (FMF), a decrease in MPV values has been reported (11, 25-28). In addition, the decrease in MPV values was mainly associated with disease activation (25). MPV was found to be decreased in sepsis suggesting a disturbance of platelet production, and altered platelet activity, which probably affected the mortality rate (29), whereas it was found to be increased in acute urinary tract infections (30). Liu S et al. suggest that a decrease in MPV was noted in patients with Crohn's disease compared with healthy controls ($p<0.0001$), but a statistically significant difference was not found between MPV and other inflammatory markers (31). Yuksel et al. reported low levels of MPV to be related to more severe activity in ulcerative colitis patients, postulating that MPV may be equal to other conventional markers as an indicator of disease severity (26). In patients with UC, a low MPV was recorded in those with extraintestinal inflammatory manifestations, suggesting an intense consumption of large platelets (26). Thrombocytosis with an increase in the quantity of low-sized platelets is a frequent feature in both UC and CD. Jaremo et al. demonstrated that a low MPV was associated with active inflammatory disease (32).

At the region of inflammation several hormonal and immune agents, like thrombopoietin, granulocyte-macrophage colony-stimulating factor, interleukin (IL)-1, tumor necrosis factor (TNF)-alpha, and IL-6, influence the maturation of thrombopoietic cells and the release of platelets into the circulation (11, 14). Platelets contain an array of potent proinflammatory substances, and thus they are regarded as mediator cells in inflammation (33). For that reason increased MPV can be the result of an increased proportion of young platelets in the circulation in prostatitis.

Based on these conflicting reports, it seems that both high and low MPVs have diagnostic and prognostic values for different inflammatory conditions (34,35).

In the current study, the main limitation is that neither CRP nor ESR was not recorded or analyzed. This is because, this is a retrospective study and we could not reach all the CRP and ESR data.

In conclusion, the MPVs of patients did not differ between low-moderate and high grade prostatitis and they did not correlate with the grade of prostatitis, like prostate specific antigens in our study. However MPV can be used as an inflammation indicator in patients with histological prostatitis, and cause its levels significantly decrease after surgical treatment.

Author Contributions

Hatice Karaman: Collected the data and wrote the manuscript. Çigdem Karakukcu: Collected the data and made the statistical analysis. Derya Kocer: Collected the data.

Competing Interests

The authors have declared that no competing interest exists.

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