Clinical research

Platelet mass index is increased in psoriasis. A possible link between psoriasis and atherosclerosis

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Abstract

Introduction: Psoriasis, whose relation with atherosclerosis etc. has long been known, is a chronic inflammatory disease. Besides providing hemostasis, platelets play important roles in inflammatory reactions and immune responses and contribute to endothelial damage, thus leading to atherosclerotic plaque formation. Mean platelet volume (MPV) has been previously reported as a platelet activation marker. Platelet mass index (PMI) is also related to platelet functionality and is thought to be a useful parameter for plaque formation capacity of platelets.
Material and methods: Sex, age, age of onset, disease duration, family history, psoriasis area severity index, nail and joint involvement, platelet count, mean platelet volume, platelet mass index, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) of 320 patients with psoriasis and 200 healthy persons were evaluated.
Results: Mean platelet counts were 277.7 ±73.374 and 265.06 ±59.682 (p = 0.032); MPV values were 8.248 ±1.150 and 7.442 ±1.626 (p < 0.001); and PMI values were 2259 ±545.617 and 1964 ±622.762 (p < 0.001) respectively in the psoriasis and control group. The MPV showed a significant but inverse correlation with hs-CRP (p = 0.047, r = –0.149), and no correlation with ESR (p > 0.05). Platelet count and PMI had a significant and positive correlation with ESR (p < 0.001, r = 0.404 and p < 0.001, r = 0.371), but had no correlation with hs-CRP (p > 0.05).
Conclusions: Higher PMI and MPV values, which mean higher plaque formation capacity and more active platelets, in psoriasis may make psoriasis patients more sensitive to atherosclerotic plaque formation and complications. On the other hand, because of the positive PMI correlation with ESR (MPV had no correlation with ESR and had a negative correlation with CRP), PMI may be a better predictor of inflammation than MPV in psoriasis.

Key words: platelet mass index, atherosclerosis, psoriasis.

Introduction

Psoriasis is a chronic inflammatory disease affecting 2–3% of the world population [1]. Psoriatic patients have been found to have increased concentrations of inflammatory markers such as high-sensitivity C-reactive protein (hs-CRP), interleukin (IL)-6, and tumor necrosis factor α (TNF-α) which reflect an inflammatory status that is the trigger for the development of cardiovascular disease. Thus, while psoriasis is considered primarily as a cutaneous disease, many reports suggest that psoriasis patients have increased risk for occlusive vascular diseases such as atherosclerosis, coronary artery disease and cerebrovascular diseases [1–3].

Besides providing hemostasis, platelets play important roles in inflammatory reactions and immune responses and contribute to endothelial damage, thus leading to atherosclerotic plaque formation or thrombotic complications [4–7]. Platelets also play a crucial role in psoriasis pathogenesis as activated platelets increase migration of leukocytes to skin and release many pro-inflammatory cytokines [2, 3, 5]. Mean platelet volume (MPV) has been previously reported as a platelet activation marker and has been found significantly higher in psoriasis patients [2, 8]. Platelet mass index (PMI) is a new approach and is particularly used in the neonatal intensive care unit (NICU) in order to reduce unnecessary transfusions. Platelet mass index, which can be formulated as "platelet count multiplied by MPV", is related to platelet functionality and is thought to be a useful parameter for plaque formation capacity of platelets. The use of PMI is based on the supposition that "hemostasis is not determined only by platelet count, and in the condition of normal function of platelets and endothelium, the hemostatic efficacy of platelet plug formation may be influenced more by the PMI than by the platelet count. For example, all else being equal, a neonate with a platelet count of 120 × 10^9/l and a MPV of 7 fl would have platelet plug generation hemostatically similar to another neonate with a platelet count of 70 × 10^9/l and an MPV of 12 fl (120 × 7 = 70 × 12)" [9–13]. Additionally, in a recent study it was claimed that PMI may also be a better parameter of inflammation than MPV [11, 14].

Despite the reported role of platelets, as far as we know, PMI has not been studied in psoriasis. In this study, we aimed to evaluate platelet count, MPV, PMI and their relationships with severity of disease, nail and joint involvement, duration of disease and family history.

Material and methods

Three hundred twenty patients followed up in our polyclinic with psoriasis vulgaris and 200 healthy persons were evaluated in the study. Patients with another dermatological disease other than psoriasis, or who have a systemic disease such as hypertension, hyperlipidemia, obesity, diabetes mellitus, cardiac, renal or hepatic disease, active infection, a history of using any drugs in the last one month, smoking and drinking alcohol were not included in the study. On the other hand, healthy individuals with no dermatological diseases or systemic diseases and no history of use of any medication in the last one month were included in the healthy group (control group).

Table I. Results of patient and control groups

Parameter	Patients (n = 320) (mean ± standard deviation)	Controls (n = 200) (mean ± standard deviation)	P-value
Platelets [×10^3 cell/mm^3]	277.7 ±73.374	265.06 ±59.682	0.032
MPV [fl]	8.248 ±1.150	7.442 ±1.626	< 0.001
PMI	2259 ±545.617	1964 ±622.762	< 0.001

Information such as sex, age, age of onset, disease duration, family history, psoriasis area severity index (PASI), nail and joint involvement, platelet count, MPV, erythrocyte sedimentation rate (ESR) and hs-CRP values of patients were recorded. Blood samples were obtained in the morning and following a 12-hour fast. Platelet counts, MPV, ESR and hs-CRP values were analyzed at the laboratory of our faculty of medicine. Platelet mass index was determined via the formula: platelet count × MPV.

Statistical analysis

Statistical analyses were carried out using the Statistical Package for the Social Sciences for Windows version 18.0 (SPSS, Chicago, IL, USA). Descriptive data are expressed in mean ± SD, number and percentage. Analysis was conducted in compliance with the normal distribution of data. Student's t test was used for comparison of continuous data. The χ^2 test was used to compare categorical data. The relationship between continuous data was assessed by Pearson's correlation test. P-value < 0.05 was accepted as the level of significance.

Results

We evaluated 320 patients with psoriasis vulgaris (154 males, 166 females) and a control group of 200 healthy individuals (male: 111, female: 89) in the study. Median age for men in the group of patients was 35 years (min: 6, max: 77) and for women 30 years (min: 7, max: 79). Median age for men in the control group was 35 years (min: 12, max: 59) and 37 years (min: 16, max: 57) for women in the same group. For the psoriasis group, mean disease duration was 8.73 ±8.446 years (min: 1, max: 56) and median age of onset was 22.5 years (min: 1, max: 73).

Platelet count (p = 0.032), MPV (p < 0.001) and PMI (p < 0.001) were significantly higher in the psoriasis group than the control group (Table I). Platelet count, MPV and PMI showed no significant difference between patients with and without a family history, psoriatic nail disease and psoriatic arthritis (Table II). Platelet count had no

Table II. Results according to family history, nail and joint involvement

Parameter	Family history(+) (*n* = 73) (mean ± standard deviation)	Family history(–) (*n* = 247) (mean ± standard deviation)	Psoriatic nail(+) (*n* = 135) (mean ± standard deviation)	Psoriatic nail(–) (*n* = 185) (mean ± standard deviation)	Psoriatic arthritis(+) (*n* = 17) (mean ± standard deviation)	Psoriatic arthritis(–) (*n* = 303) (mean ± standard deviation)	*P*-value
Platelet [×10^3 cell/mm^3]	268.74 ±66.84	280.34 ±75.12	280.33 ±74.06	275.78 ±73.01	296.71 ±67.55	276.63 ±73.64	0.236/ 0.628/ 0.273
MPV [fl]	8.21 ±1.06	8.25 ±1.17	8.24 ±1.21	8.25 ±1.10	7.918 ±1.202	8.267 ±1.146	0.220/ 0.922/ 0.534
PMI	2190 ±533.90	2279 ±548.44	2276 ±565.59	2246 ±531.75	2339 ±608.52	2.255 ±542.63	0.789/ 0.585/ 0.224

correlation with PASI score, age of onset or disease duration ($p > 0.05$). The MPV had a significant but inverse correlation with PASI score ($p = 0.020$ and $r = –0.130$), and had no correlation with age of onset or disease duration ($p > 0.05$). The PMI had a significant and inverse correlation with age of onset ($p = 0.020$ and $r = –0.130$), but did not show any correlation with PASI score or disease duration ($p > 0.05$) (Table III).

Platelet and PMI had a significant and positive correlation with ESR ($p < 0.001$, $r = 0.404$ and $p < 0.001$, $r = 0.371$), but had no correlation with hs-CRP ($p > 0.05$). On the other hand, MPV showed a significant but inverse correlation with hs-CRP ($p = 0.047$ and $r = –0.149$), and no correlation with ESR ($p > 0.05$) (Table III).

Table III. Correlation of parameters

Parameter		Platelet count	MPV	PMI
Disease duration	*r*	–0.052	–0.024	–0.067
	p	0.350	0.669	0.232
Age of onset	*r*	–0.104	–0.019	–0.130
	p	0.064	0.740	0.020
PASI score	*r*	0.035	–0.130	–0.022
	p	0.528	0.020	0.690
hs-CRP	*r*	0.063	–0.149	–0.019
	p	0.406	0.047	0.805
ESR	*r*	0.404	–0.111	0.371
	p	< 0.001	0.109	< 0.001
MPV	*r*	–0.373		0.153
	p	< 0.001		0.006

Discussion

In addition to their roles in hemostasis, platelets are key mediators in the initiation and maintenance of a chronic proinflammatory and prothrombotic milieu by direct interactions with inflammatory cells and secretion of autocrine and paracrine effector molecules, and as a result contribute to the pathogenesis of many diseases including atherosclerosis, coronary vascular disease, and cerebrovascular disease [4, 15–19].

Nonetheless, it is previously reported that platelets have major effects in pathogenesis of psoriasis, and that activated platelets increase migration of leukocytes to skin, thereby increasing release of inflammatory cytokines. Also, platelet activation markers such as MPV, β-thromboglobulin and platelet factor-4 were found to be higher in plasma of psoriasis patients and correlated with PASI score [1–3, 8]. While psoriasis is considered primarily as a cutaneous disease, it is claimed that psoriasis increases the inflammatory load of the patient and causes a state of insulin resistance which results in endothelial cell dysfunction and atherosclerosis. Psoriasis and coronary artery disease have some common underlying immune abnormalities. For example, dysregulation of cytokines, such as IL-1, IL-6 and TNF-α, adhesion molecules, such as intercellular adhesion molecule 1 (ICAM-1) and E-selectin, and angiogenic factors, such as vascular endothelial growth factor (VEGF), has been reported both in psoriasis and coronary artery disease. These cytokines are also associated with platelet activity. For example, IL-6 can cause thrombocytosis and platelet activation, and TNF-α can amplify the inflammatory response induced by platelet activating factor (PAF). We proposed that high platelet count and MPV and PMI levels in psoriasis may be related to these proinflammatory cytokines which have critical effects in psoriasis, coronary artery disease and platelet activities [3, 7, 8].

Platelet mass index is considered as a parameter showing plaque formation capacity of platelets and is primarily used in NICU in order to reduce unnecessary transfusions, which have serious complications [9, 10, 12, 13]. Normally, an inverse

relationship between platelet count and platelet volume with low count and high volume is generally considered to save a balanced PMI and consequently to maintain platelet functions. As well as PMI, MPV related to platelet activity, and larger platelets are found to be more reactive, and are preferentially aggregated after addition of ADP, collagen and thrombin. Platelet activation is also linked to atherosclerosis, increasing plaque formation and plaque vulnerability to rupture [4, 6, 15, 20]. In their previously published study, Bath *et al.* reported higher MPV and higher PMI in patients with renal artery stenosis (RAS), but a similar platelet count as the control group. On the other hand, MPV and platelet count had no correlation in their study. At the end of the study, they claimed that, since large platelets are hyperreactive and platelet mass is the principle determinant of platelet-related hemostasis, the elevated platelet volume and platelet mass may contribute to renal artery atherothrombosis and the development of RAS [20]. In our study, as expected, MPV and platelet count were inversely correlated, but both MPV and platelet count were increased and hence PMI was higher compared with the control group. Since psoriasis is a disease which is expected to be associated with endothelial damage because of its inflammatory nature, we speculated that high platelet count, PMI and MPV may facilitate plaque formation and plaque vulnerability to rupture and finally make psoriasis patients more susceptible to atherothrombotic complications.

Recently, many studies have shown a positive correlation between MPV and inflammation markers and detected higher MPV values in psoriasis patients [2, 8]. These studies also reported a positive correlation of MPV with some disease characteristics of psoriasis such as PASI score, psoriatic arthritis and disease duration [8]. In contrast, some other studies did not reveal any correlation between MPV, inflammation markers and disease characteristics of psoriasis [2]. In our study, we did not find any positive correlation between MPV, hs-CRP, ESR and disease characteristics such as PASI score, disease duration or age of onset, and we found no difference in terms of MPV values between patients with and without a family history, psoriatic nail disease and psoriatic arthritis. On the other hand, PMI had no correlation with hs-CRP, but was significantly and positively correlated with ESR and age of onset. These results suggest that PMI is a better predictor of inflammatory status in psoriasis. The relationship between PMI and age of onset has not been evaluated in previous studies, and the question of why patients with a high PMI are exposed to disease at younger ages is still unanswered. Probably, due to proinflammatory cytokines released from platelets, a high PMI leads to an inflammatory milieu and causes earlier onset of psoriasis. In addition, patients exposed to psoriasis at younger ages may be more likely to have atherothrombotic complications due to longer exposure.

In conclusion, high PMI, which is a determinant of plaque formation capacity of platelets, and high MPV, which means more reactive platelets, predispose psoriasis patients to atherothrombotic complications. To reduce this predisposition, antiplatelet therapy is recommended in many diseases such as diabetes mellitus and obesity due to the effects of antiplatelet therapy reducing the risk of cardiovascular disease, not only by inhibiting platelet activation and aggregation, but also by limiting local and systemic inflammatory responses [15]. Therefore, it may be beneficial to use prophylactic antiplatelet therapy in psoriasis to reduce the cardiovascular disease risk. On the other hand, we did not find any positive correlation between MPV, hs-CRP and ESR. However, PMI was significantly and positively correlated with ESR and may be a better predictor than MPV of the inflammatory status in psoriasis. To our best knowledge, PMI has not been evaluated previously in psoriasis patients. Further work is needed to better understand the use of PMI in psoriasis.

Conflict of interest

The author declares no conflict of interest.

References

1. Aykol C, Mevlitoğlu I, Özdemir M, Unal M. Evalution of clinical and sociodemograpic features of patients with psoriasis in the Konya region. Turk J Dermatol 2011; 5: 71-4.
2. Unal M, Küçük A, Ürün Ünal G, et al. Mean platelet volume, neutrophil to lyphocyte ratio and platelet to lymphocyte ratio in psoriasis. Turk Derm 2015; 49: 112-6.
3. Chandrashekar L, Rajappa M, Revathy G, et al. Is enhanced platelet activation the missing link leading to increased cardiovascular risk in psoriasis? Clin Chim Acta 2015; 446: 181-5.
4. Nording HM, Seizer P, Langer HF. Platelets in inflammation and atherogenesis. Front Immunol 2015; 6: 98.
5. Kaser A, Brandacher G, Steurer W, et al. Interleukin-6 stimulates thrombopoiesis through thrombopoietin: role in inflammatory thrombocytosis. Blood 2001; 98: 2720-5.
6. Katoh N. Platelets as versatile regulators of cutaneous inflammation. J Dermatol Sci 2009; 53: 89-95.
7. Boehncke WH, Boehncke S, Tobin AM, Kirby B. The 'psoriatic march': a concept of how severe psoriasis may drive cardiovascular comorbidity. Exp Dermatol 2011; 20: 303-7.
8. Canpolat F, Akpinar H, Eskioğlu F. Mean platelet volume in psoriasis and psoriatic arthritis. Clin Rheumatol 2010; 29: 325-8.
9. Zisk JL, Mackley A, Clearly G, Chang E, Christensen RD, Paul DA. Transfusing neonates based on platelet count vs. platelet mass: a randomized feasibility-pilot study. Platelets 2014; 25: 513-6.

10. Kahvecioglu D, Erdeve O, Alan S, et al. The impact of evaluating platelet transfusion need by platelet mass index on reducing the unnecessary transfusions in newborns. J Matern Fetal Neonatal Med 2014; 27: 1787-9.
11. Okur N, Buyuktiryaki M, Uras N, et al. Platelet mass index in very preterm infants: can it be used as a parameter for neonatal morbidities? J Matern Fetal Neonatal Med 2016; 29: 3218-22.
12. Gerday E, Baer VL, Lambert DK, et al. Testing platelet mass versus platelet count to guide platelet transfusions in the neonatal intensive care unit. Transfusion 2009; 49: 2034-9.
13. Christensen RD. Platelet transfusion in the neonatal intensive care unit: benefits, risks, alternatives. Neonatology 2011; 100: 311-8.
14. Korkmaz L, Baştuğ O, Ozdemir A, et al. The efficacy of propranolol in retinopathy of prematurity and its correlation with the platelet mass index. Curr Eye Res 2016 in press.
15. Müller KA, Chatterjee M, Rath D, Geisler T. Platelets, inflammation and anti-inflammatory effects of antiplatelet drugs in ACS and CAD. Thromb Haemost 2015; 114: 498-518.
16. Park BJ, Shim JY, Lee HR, Jung DH, Lee JH, Lee YJ. The relationship of platelet count, mean platelet volume with metabolic syndrome according to the criteria of the American Association of Clinical Endocrinologists: a focus on gender differences. Platelets 2012; 23: 45-50.
17. Jesri A, Okonofua EC, Egan BM. Platelet and white blood cell counts are elevated in patients with the metabolic syndrome. J Clin Hypertens (Greenwich) 2005; 7: 705-11; quiz 712-3.
18. Ed Rainger G, Chimen M, Harrison MJ, et al. The role of platelets in the recruitment of leukocytes during vascular disease. Platelets 2015; 26: 507-20.
19. Wagner DD, Burger PC. Platelets in inflammation and thrombosis. Arterioscler Thromb Vasc Biol 2003; 23: 2131-7.
20. Bath PM, Missouris CG, Buckenham T, MacGregor GA. Increased platelet volume and platelet mass in patients with atherosclerotic renal artery stenosis. Clin Sci (Lond) 1994; 87: 253-7.