Original Article
Mean platelet volume and solitary parathyroid adenoma

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Abstract: Background: Hyperparathyroidism (HPT) is a common endocrine disorder. 85% of patients with primary HPT harbor a single adenoma and cured by excision of the incident gland. Mean platelet volume (MPV) shows the average size of platelets and reflects the platelet production rate and stimulation. We decided to investigate whether MPV would be a useful biomarker in patients with parathyroid adenoma. Materials and Methods: Fourty-four patients with solitary parathyroid adenoma (Adenoma group) and 56 people with normal serum PTH and calcium levels (Control group) were included in the study. The differences in pre-treatment MPV between adenoma group and healthy control group were investigated. The differences between pre-operative and post-operative MPV, PTH, and calcium levels in adenoma group were also analyzed. Results: There was no statistically significant difference between the adenoma group and healthy control group regarding age; gender; smoking status; and white blood cell, hemoglobin, and platelet count (P > 0.05). Post-operative MPV, PTH, and serum calcium levels in patients with solitary parathyroid adenoma (SPA) were found to be significantly lower when compared with pre-operative MPV, PTH, and serum calcium level (P = 0.001). Pre-operative MPV levels in patients with SPA were found to be significantly higher when compared with healthy control group (P = 0.0001). For the diagnosis of SPA, ROC analysis revealed 76.1% sensitivity and 80.4% specificity for a cut-off value of 9.015 fl of MPV whereas positive predictive was 76.1% and negative predictive value was 83.3%. Conclusion: In this study, a significant correlation of MPV level with parathyroid adenoma was found. Therefore, detecting MPV level would be useful for the diagnosis of SPA.

Keywords: Parathyroid, adenoma, MPV, platelet

Introduction

Hyperparathyroidism is a common endocrine disorder with potential complications on the skeletal, renal, neurocognitive and cardiovascular systems [1]. HPT is generally divided into three types: primary, secondary, and tertiary [1-5]. In Europe, primary HPT is now a relatively common disorder that is diagnosed in 0.7% of the general population [2-5]. Primary HPT results from the autonomous overproduction of parathyroid hormone (PTH). A single parathyroid adenoma (SPA) is the cause of disease in approximately 85% of patients, and resection yields a lenghty cure [5, 6].

Mean platelet volume (MPV) is an accurate measure of platelet size which is routinely reported during a complete blood count (CBC) analysis [7-9]. MPV shows the average size of platelets and reflects the platelet production rate and stimulation [10]. In recent years, numerous studies have noted the importance of MPV as a predictor of clinical outcomes in the settings of various diseases, including coronary artery disease, thrombotic disorders, hepatocellular carcinoma, gastric carcinoma and pancreatic adenocarcinoma [6-12]. From this stand-point, we decided to investigate whether MPV would be a useful biomarker in patients with parathyroid adenoma.

Materials and methods

Ethics

This study was approved by the appropriate ethics committee of Adana Numune Research and Training Hospital and has therefore been performed in accordance with the ethical standards in the 1964 Declaration of Helsinki.

Study design and obtaining samples

The present study was a retrospective study. Data collection included patient demographics,

clinico-pathological parameters, and preoperative and postoperative hematological parameters.

As a routine,for blood count analyses, samples were obtained after overnight fasting and between 7:30 AM and 9:00 AM. Pre-operative datas were obtained from the pre-operative results of routine blood tests. Post-operative routine controls performed one and three-months after surgery. Data were obtained from the routine control testswhile the patients serum, TSH, calcium, and parathyroid hormone levels were within normal limits. All blood samples were tested (as a part of their complete blood counts, CBC) using an automated hematology analyzer (Cell-Dyn 3200) (Abbott Diagnostics, Abbot Park, IL, USA) for measurement of MPV. In ourlaboratory, the MPV reference range is determined as 7-11 fl. Pre-operative and post-operative, PTH level, calcium level, phosphate level, lymphocyte count, leukocyte count, neutrophil count, monocyte count, platelet count and MPV in adenoma group were analyzed. The differences in pre-treatment MPV between adenoma group and healthy control group were also investigated.

Inclusion criteria

We reviewed the medical records of 44 patients who underwent parathyroid surgery for primary PHT and operated on by a single surgeon (Adenoma group). A diagnosis of primary hyperparathyroidism was based on hypercalcemia and an elevated serum parathyroid hormone level. Those patients who had met the criteria, determined by the NIH consensus panel and those who were symptomatic, were included in the study. Localization of the pathological gland(s) and thyroid tissue were evaluated in all patients pre-operatively by both US and MIBI imaging of the neck. Fifty-six peoples with normal serum PTH and calcium levels were included in the study as a healthy control group (Healthy group).

Exclusion criteria

Patients with suspected parathyroid hyperplasia or multiple endocrine neoplasm syndrome were excluded. The patients with malignancy, solid organ tumor, inflammatory disease, myeloproliferative disorders, diabetes mellitus, hypertension, infection, heart failure, hepatic or renal disorders, taking anticoagulation medicine, abnormal TSH level, and recurrent or permanent hyperparathyroidism were also excluded from the study.

Statistical analyses

Data were analyzed by using the Statistical Package for Social Sciences (SPSS) 20.0 for Windows. Continuous datas were presented as mean ± standard deviation or median (minimum-maximum). The Kruskal-Wallis test, the Mann-Whitney U test and the Wilcoxon test were used to compare the parameters of adenoma group and healthy control group. Pre-operative MPV values were found to be statistically different between groups, and they were analyzed for their diagnostic value in solitary parathyroid adenoma using ROC analysis. Statistical significance was defined as a *P* value < 0.05.

Results

44 (mean age 54 ± 13, m/f = 3/41) patients with SPA underwent to parathyroid surgery. There was no statistically significant difference between the healthy group and adenoma group regarding age; gender; smoking status (*P* > 0.05). We also did not find a statistically significant difference between groups according to white blood cell, hemoglobin, lymphocyte count, leukocyte count, neutrophil count, monocyte count, platelet count (P > 0.05). Additionally, there were no statistically significant difference between pre-operative and post-operative values of above mentioned parameters in adenoma group (P > 0.05).

Post-operative serum calcium levels in patients with SPA were found to be significantly lower when compared with pre-operative serum calcium level. The median pre-operative serum calcium level was 11.4 mmol/l and the median post-operative serum calcium level were 8.8 mmol/l, 9.0 mmol/l, and 9.2 in the post-operative 24 hours, at the first month, and at the thirth month, respectively (*P* = 0.0001) (**Table 1**).

Post-operative serum PTH levels in patients with SPA were found to be significantly lower when compared with pre-operative serum PTH level. The median pre-operative serum PTH level was 202.0 pmol/l and the median post-

Table 1. Comparison of pre-operative and post-operative biochemical parameters

| Parameter | | | | | Wilcoxon test | | | | | |
| | | | | | Preop-Postop1 | | Preop-Postop2 | | Proeop-Postop3 | |
	n	Mean	Median	sd	z	p	z	p	z	p
Preop Ca	44	11.8	11.4	1.1	-5.7	0.0001	-5.8	0.0001	-5.6	0.0001
Postop Ca 1	44	8.8	8.8	.7						
Postop Ca 2	44	8.9	9.0	.7						
Postop Ca 3	42	9.1	9.2	.5						
Preop PTH	44	408.5	202.0	553.7	-5.8	0.0001	-5.8	0.0001	-5.6	0.0001
Postop PTH 1	44	69.5	20.9	272.8						
Postop PTH 2	44	97.6	43.3	242.7						
Postop PTH 3	41	73.8	40.7	141.6						

PTH: parathyroid hormone; Ca: calcium; n: number of patients; Postop 1: value in the post-operative 24 hour; Postop 2: value at the post-operative first month; Postop 3: value at the post-operative 3th month. $P < 0.05$ is considered as statistically significant.

Table 2. Pre-operative MPV levels in patients with SPA were found to be significantly higher when compared with healthy controls

| | | n | Mean | Median | Minimum | Maximum | sd | Mann-Whitney U test | | |
								Mean Rank	U	P
Preop MPV	*Adenoma Group*	44	10.2	10.3	6.8	15.1	1.7	70.17	366.5	0.0001
	Helathy group	56	7.9	7.6	6.0	13.7	1.5	35.04		
Preop PLT	*Adenoma Group*	44	256.1	253.0	78.0	442.0	77.1	45.83	1026.5	0.154
	Helathy group	56	279.8	282.0	166.0	479.0	70.9	54.17		

MPV: Mean platelet volume, PLT: Platelet. $P < 0.05$ is considered as statistically significant.

Table 3. Comparison of preoperative and postoperative parameters in patients with solitary parathyroid adenoma

| Parameter | Patients with solitary parathyroid adenoma | | | | | Wilcoxon Test | |
	n	Mean	Median	Minimum	Maximum	sd	z	P
Preop PLT	44	256.1	253.0	78.0	442.0	77.1	-0.362	0.717
Postop PLT	44	251.6	246.0	141.0	410.0	66.5		
Preop MPV	44	10.2	10.3	6.8	15.1	1.7	-3.3	0.001
Postop MPV	44	9.3	9.3	6.2	12.5	1.6		

MPV: Mean platelet volume, PLT: Platelet. $P < 0.05$ is considered as statistically significant.

operative serum PTH levels were 20.9 pmol/l, 43.3 pmol/l, and 40.7 pmol/l in the post-operative 24 hours, at the first month, and at the thirth month, respectively ($P = 0.0001$) (**Table 1**).

Pre-operative the mean MPV levels in patients with SPA were found to be significantly higher when compared with healthy controls (10.2 fl versus 7.9 fl, $P = 0.0001$) (**Table 2**). After surgical treatment of SPA patients, a significant decrease in the mean MPV level was seen (10.2 fl versus 9.3 fl, $P = 0.001$) (**Table 3**). The post-operative MPV levels of SPA patients and healthy controls were found to be comparable ($P > 0.05$). Additionally, when we made a sub-group analysis, we found that pre-operative MPV levels were higher in both minimally invasive surgery and classical bilateraly neck exploration groups than healthy subjects ($P = 0.0001$) (**Table 4**).

For the diagnosis of SPA, ROC analysis revealed 76.1% sensitivity and 80.4% specificity for a cut-off value of 9.015 fl of MPV whereas positive predictive value was 76.1% and negative predictive value was 83.3% (**Figure 1**).

Discussion

Hyperparathyroidism is a common endocrine disorder with potential complications on organ systems [1]. Eighty-five percent of patients with pHPT harbor a single adenoma and cured by excision of the incident gland [1-3]. Over the last 25 years, much has been learnt about the

Table 4. Preoperative MPV levels when subgroups compared

		n	Mean	Median	Minimum	Maximum	sd	Mean Rank	H	P	Comparison of two groups
Preop MPV	1-Classical Operation	20	10.8	11.0	7.9	15.1	1.6	78.10	38.6	0.0001	3-1
	2-Minimaly Invasive Operation	24	9.7	10.0	6.8	12.2	1.6	63.56			3-2
	3-Healthy Control	56	7.9	7.6	6.0	13.7	1.5	35.04			
Preop PLT	1-Classical Operation	20	262.2	247.0	114.0	406.0	83.6	46.93	2.1	0.352	-
	2-Minimaly Invasive Operation	24	251.1	255.5	78.0	442.0	72.7	44.92			
	3-Healthy Control	56	279.8	282.0	166.0	479.0	70.9	54.17			

MPV: Mean platelet volume, PLT: Platelet. $P < 0.05$ is considered as statistically significant.
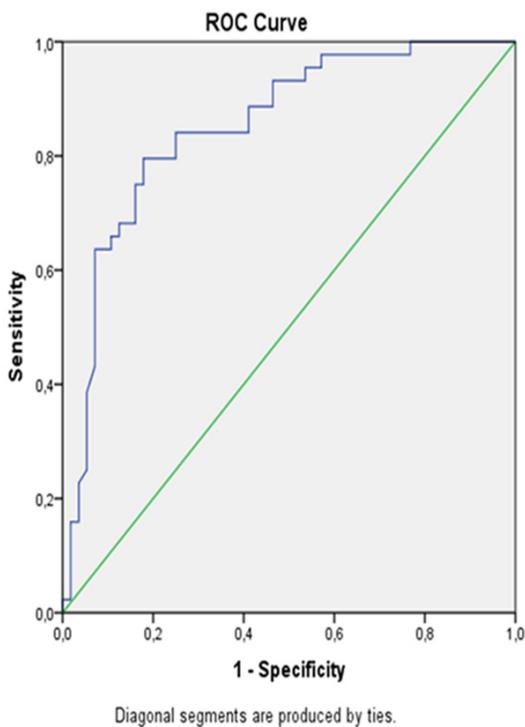

Figure 1. For the diagnosis of SPA, ROC analysis revealed 76.1% sensitivity and 80.4% specificity for a cut-off value of 9.015 fL of MPV whereas positive predictive value was 76.1% and negative predictive value was 83.3%.

molecular mechanisms of benign and malign tumours. The molecular basis of parathyroid adenoma is no exception [13]. In other words parathyroid adenoma is benign tumour and its molecular mecanism is still not well known. Platelets have an important effect on tumor progression and metastasis. From this stand point, we decided to investigate the correlation between parathyroid adenoma and MPV in this study.

Platelets are the cellular orchestrators of primary hemostasis. Blood platelets are discoid anucleate cellular fragments originating from the cytoplasm of megakaryocytes. In 1882, Bizzozero introduced the term "blood plates" and documented their importance in blood coagulation and in the formation of thrombus [14, 15]. About a century later, researchers were demonstrated that platelethas different functions other than thrombosis such as secreating growth factors, to help damaged tissue recovery, managing inflammation and alert the immune cells [7-15]. The tumor cells and their microenvironment is increasingly recognized as a key regulator of tumour growth. In the 19th century. Gasic et al., described an interesting association between number of platelets and metastatic potential of cancer [16]. Today it is well-known that, platelets are the major serum source of many pro-angiogenic proteins in the circulation of patients with tumour [17]. The is also a known association between platelets and immune system. In 1999, Nieswandt et al., were reported that the main contribution of platelets to tumour growth and metastasis seems to consist in protection of tumor cells from NK cell lysis [18].

Even if the platelets have an effect on tumour progression, there might be an association between parathyroid adenoma and platelet functions. In our study, MPV level was higher in patients with parathyroid adenoma than healthy controls ($P = 0.0001$). MPV is the platelet activity marker that is most commonly used to evaluate inflammatory processes and malignancies. Platelets with larger MPV are thought to have granules containing more mediators and thus play a bigger role in tumour development and progress [18-24]. MPV also shows the activity of platelets. Larger platelets have more reactivity than smaller ones [19].

The correlation between MPV and tumour progression was analyzed in different types of can-

cers [20-25]. Karateke et al. reported that MPV, PDW, and PCT to be correlated with the severity of endometrial pathology with the highest values in endometrial cancer [25]. Baldane et al. studied on the association between thyroid papillary carcinomas and MPV. They reported that thyroid papillary carsinomas had higher MPV levels than beningn goiter patients and controls and in the same research the MPV levels decreased after surgical treatment [20]. It was an interesting result for us, because also in our study we found that in all cases pre-operative MPV levels decreased to normal ranges after the parathyroid adenoma excised (P = 0.0001). Additionally, when we were considered the post-operative MPV levels, there were not a statistically significant difference between healthy controls and patients who underwent successfull parathyroid surgery. In another study, Eryılmaz A et al. concluded that MPV may be used as a new marker in the diagnosis of head and neck cancers [23].

Recently Yilmaz H. showed that subjects with PHPT lead to have increased platelet activation [26]. Smilarly, in our study, post-operative serum calcium and parathyroid hormone levels were decreased to normal ranges after operation in all cases which were correlated with MPV. For the diagnosis of SPA, ROC analysis revealed 76.1% sensitivity and 80.4% specificity for a cut-off value of 9.015 fL of MPV whereas positive predictive value was 76.1% and negative predictive value was 83.3%.

We found a significant correlation between MPV and parathyroid adenoma in this study and believe that this will provide useful information in the diagnosis of SPA and evaluating the success of the operation. The main limitation of our study is the low number of cases. Although this study was showed the relationship between MPV and parathyroid adenoma, the specific mechanisms of the relationship needs further studies.

Disclosure of conflict of interest

None.

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