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Original research article

Evaluation of simple blood counts as inflammation markers for brain tumor patients

Yasar Dagistan [a,*], Emine Dagistan [b], Veli Citisli [c]

[a] Abant Izzet Baysal University Hospital, Department of Neurosurgery, Bolu, Turkey
[b] Abant Izzet Baysal University Hospital, Department of Radiology, Bolu, Turkey
[c] Pamukkale University Hospital, Department of Neurosurgery, Denizli, Turkey

ARTICLE INFO

Article history:
Received 30 April 2015
Accepted 7 March 2016
Available online 19 March 2016

Keywords:
Brain tumor
Metastasis
Mean platelet volume
Red cell distribution width
Inflammation

ABSTRACT

Aims: Hemogram parameters in routine blood panels have been proposed as inflammation markers. These parameters, especially the red cell distribution width (RDW) and mean platelet volume (MPV), were evaluated as surrogate inflammatory markers in brain tumor patients. We aimed to observe RDW and MPV values of tumor patients and compare to those in healthy population.

Methods: We recorded white blood cell count, neutrophil count, lymphocyte count, hemoglobin, hematocrit, RDW, platelet count, and MPV of the study group at the time of diagnosis and compared to those of the control subjects.

Results: The RDW was significantly elevated in study group compared to that of the control subjects ($p = 0.001$). The MPV was significantly lower in study group than that of the control group ($p = 0.01$).

Conclusion: Decreased MPV and increased RDW were both associated with brain tumor. However, prospective studies with larger sample sizes are needed to support the results and expose MPV and RDW variations between metastatic and primary brain tumors.

1. Introduction

The inflammatory response plays a crucial role in neoplastic diseases and closely correlates with tumor progression and metastasis [1–3]. The severity of inflammation serves as an important indicator of tumor progression and survival among patients with cancer [2,4,5]. Additionally, inflammatory molecules have been shown to be overexpressed by tumor cells [6].

The hemogram parameters in routine blood panels have been proposed as markers of inflammation [7]. The size variability of erythrocytes has been reported in terms of the red cell distribution width (RDW) value in hemogram assays, with higher RDW meaning higher variability. The RDW levels are elevated in iron deficiency anemia. Elevation in RDW has also been associated with inflammatory conditions [7–10].

Platelets are the smallest product of bone marrow in the blood stream, and they have a crucial role in hemostasis and inflammation. They are involved in the inflammatory

* *Corresponding author at*: Abant Izzet Baysal University Hospital, Department of Neurosurgery, 14280 Bolu, Turkey. Tel.: +90 3742534656; fax: +90 3742534615.
E-mail address: dagistanyasar@hotmail.com (Y. Dagistan).

http://dx.doi.org/10.1016/j.pjnns.2016.03.002

Table 1 – Characteristics and data of patients in the brain tumor and control groups.

		Brain tumor group	Control group	p
Gender	Men (n)	27	26	0.83
	Women (n)	21	22	
		Median (Min–Max)[a]		
Age (years)		40.5 (13–71)	43 (32–51)	0.38
Lymphocyte count (k/mm^3)		2 (0.7–3.8)	2.1 (1.5–3.7)	0.24
Neutrophil/lymphocyte ratio (%)		2.4 (1.1–7.5)	2 (0.6–3.5)	0.11
Hemoglobin (g/dL)		14.4 (10.2–16.4)	14.6 (12.3–17.5)	0.30
Hematocrit (%)		43 (30–50)	44 (36.5–53)	0.77
Mean corpuscular volume (fL)		86 (63–94)	87 (73–98)	0.09
Mean platelet volume (fL)		8.2 (6.3–10.5)	8.9 (6–10)	**0.01**
		Mean ± standard deviation[b]		
White blood cell count (k/mm^3)		7.5 ± 2	7.1 ± 1.6	0.30
Neutrophil count (k/mm^3)		4.5 ± 1.6	4.3 ± 1.3	0.28
Red cell distribution width (%)		15.5 ± 1.7	14.4 ± 1.2	**0.001**
Platelet count (k/mm^3)		255 ± 84	256 ± 49	0.95

[a]Mann–Whitney *U* test.
[b]Independent sample *t*-test.

processes with proinflammatory molecules they secrete [11]. The surrogate marker of platelet activation and production is the mean platelet volume (MPV). Various studies have shown a relationship between the MPV and inflammatory diseases [12–14]. Another inflammatory marker derived from a routine blood count test is the neutrophil to lymphocyte ratio (NLCR). NLCR has been reported as a predictive marker of outcomes in patients treated for various cancers, such as, colorectal adenocarcinoma [2], renal cancer [4], hepatocellular carcinoma (HCC) [15], cancer of esophagogastric junction [16], and lung cancer [17]. In a recent study, the preoperative NLCR corresponded to glial brain tumor grading [18].

In the present retrospective study, these simple inflammatory markers were evaluated in patients with brain tumors and compared with those in the healthy population. These laboratory parameters were also compared within brain tumors of either metastatic or primary etiology, as the radiological imaging of brain masses usually cannot differentiate metastatic or primary tumors [19–21].

2. Material and methods

2.1. Subjects

The use of the data in this retrospective study was approved by our hospital. Patients with brain tumor visited outpatient clinics of our institution were enrolled to the study as study group. Both primary and metastatic newly diagnosed brain tumor cases that not received any treatment were included to the study. None of the participants in study group were receiving medications that may probably affect hemogram parameters. Hemogram of the tumor patients have been obtained at the time of diagnosis before administration of corticosteroid therapy. The control group was selected from patients who visited the hospital's out patient clinics for routine checkups. Of the 48 brain tumor patients, 28 had primary brain tumors, and 20 had metastatic tumors. For the 28 primary tumor patients, 20 had glioblastoma multiforme (grade 4), 6 had anaplastic astrocytoma (grade 3), and 2 had diffuse astrocytoma (grade 2). The control group was selected from patients who visited the hospital's outpatient clinics for routine checkups. None of the subjects in the study and control groups had a history of chronic use of maintenance medicines. The characteristics and laboratory data of the study population are summarized in Tables 1 and 2. No significant difference was seen between the study and control groups in terms of age ($p = 0.38$) or gender ($p = 0.83$).

2.2. Blood panel

The laboratory data of the brain tumor patients were recorded before surgery from database of our institution. The white blood cell count (WBC), neutrophil count (neu), lymphocyte count (lym), hemoglobin (Hb), hematocrit (Htc), RDW, platelet count (PLT), and MPV of the participants were obtained from the hospital's medical database. Venous blood samples were collected in sterile standard tubes containing constant amounts of ethylene diamine tetraacetic acid as an anticoagulant. The laboratory assessment was conducted within several minutes after the blood samples were obtained. The LH 780 automatic analyzer (Beckman Coulter, Inc., Brea, CA, USA) was used for complete blood count analyses. Original kits of the producer were used in these measurements.

2.3. Statistical analysis

All data recorded were assessed with SPSS software (SPSS 15.0; SPSS Inc., Chicago, IL, USA). The independent samples *t*-test was used for normally distributed variables and the Mann–Whitney *U* test was used for non-homogeneously distributed parameters. The primary brain tumor, metastatic brain tumor, and control groups were compared with an ANOVA test. The results of the statistics were expressed as either mean ± SD or median (min–max). Statistical significance was set as p value of lower than 0.05.

3. Results

This retrospective study examined 48 patients with brain tumors (primary and metastatic) and 48 healthy control

Table 2 – Characteristics and data of primary and metastatic brain tumor patients.

		Primary brain tumor group	Metastatic tumor group	p
Gender	Men (n)	14	13	0.30
	Women (n)	14	7	
		Mean ± standard deviation[a]		
Age (years)		42 ± 16	38 ± 16.2	0.38
White blood cell count (k/mm^3)		7.5 ± 2.1	7.4 ± 2	0.77
Neutrophil count (k/mm^3)		4.6 ± 1.7	4.6 ± 1.6	0.89
Lymphocyte count (k/mm^3)		2 ± 0.6	2.1 ± 0.4	0.71
Neutrophil/lymphocyte ratio (%)		2.4 ± 1.3	2.2 ± 0.8	0.56
Hemoglobin (g/dL)		14.1 ± 1.7	14 ± 1.8	0.63
Hematocrit (%)		42.7 ± 5.2	42.2 ± 5.2	0.72
Mean corpuscular volume (fL)		83.5 ± 7.9	85 ± 6.1	0.47
Red cell distribution width (%)		15.4 ± 1.5	15.5 ± 1.9	0.82
Platelet count (k/mm^3)		262 ± 92	244 ± 71	0.48
Mean platelet volume (fL)		8.2 ± 1.2	8 ± 1	0.49

[a]Independent samples t-test.

subjects. The characteristics and laboratory data of the study population are summarized in Tables 1 and 2. No significant difference was seen between the study and control groups in terms of age ($p = 0.38$) or gender ($p = 0.83$). For the blood panel, no difference was seen between the study and control groups for the WBC, neu, lym, NLCR, Hb, Htc, mean corpuscular volume, or PLT ($p > 0.05$ for all). However, the mean RDW value of the study group was significantly elevated compared to that of the control subjects ($p = 0.001$). In addition, the MPV of the study group was significantly lower than that of the control group ($p = 0.01$).

The patients in the study group were further analyzed. Of these patients, 28 had primary brain tumors and 20 had metastatic lesions. General characteristics and laboratory parameters of the patients with primary and metastatic tumors are presented in Table 2. These parameters showed no difference between primary and metastatic brain tumor patients.

4. Discussion

This study showed that the RDW was higher and the MPV was lower in patients with brain tumors than they were in healthy subjects. Although the literature reported an increase in the NLCR in neoplasms, the present study lacked such an association. The possible mechanism for the reduction in the MPV could be that the inflammatory burden interferes with megakaryopoiesis in bone marrow, resulting in the production of smaller platelets. Another explanation could be that the involvement of the larger, active platelets in the inflammatory microstructure and the remaining smaller, inactive platelets cause a reduction in the MPV. Similarly, the elevation in the RDW can be explained by the inflammatory situation causing the bone marrow to produce red blood cells of different size. Inflammatory molecules may alter the use of iron in bone marrow, consequently, causing an increase in the RDW.

The studies comparing MPV in patients with malignancies had differing results. Karaman et al. found a significant difference in the MPV of patients with pancreas adenocarcinoma than that of patients with pancreatic neuroendocrine tumor; however the age and mean Hb levels were also different between the study groups [22]. Kılınçalp et al. reported higher MPV levels in preoperative gastric cancer patients compared to healthy subjects [23]. Similarly, a study from South Korea evaluated MPV in HCC patients and reported an elevation in the MPV for the patients in comparison to the control subjects [24]. On the other hand, Aksoy et al. found the MPV and PLT values of solid tumor patients with bone marrow metastasis to be significantly decreased compared to the MPV and PLT values of healthy subjects [25]. The present study found decreased MPV values in the brain tumor patients compared to the controls; however, the PLT was not statistically different between the groups.

There could be several explanations for decreased MPV in brain tumor patients. IL-6 has been reported to be elevated in various types of cancers [26,27] and it is also associated with platelet production in bone marrow [28]. Increased levels of IL-6 may interfere with platelet production, causing the creation of smaller platelets and, thus, leading to a decrease in MPV [29]. Another speculation could be considered for the MPV decrease in brain tumor patients. Tumors cause inflammation because of the various cytokines produced by tumor cells [30] and active platelets, which tend to be larger than rested platelets, are involved in inflammatory processes. The use of the larger, active platelets may cause a reduction in systemic MPV value because of the remaining smaller platelets. Feng et al. [31] demonstrated that platelets secrete and account for circulating CD40 ligand, chemokine (C-X-C motif) ligand 5, chemokine (C-C motif) ligand 5, and epidermal growth factor by detecting mRNA expression in platelets and megakaryocytes and measuring cytokine levels in the platelet culture supernatants, prion protein-derived sera, and murine immune thrombocytopenic purpura model. They suggested that the measurement of platelet-specific cytokines would allow inferences concerning physiology and pathophysiology in quantitative platelet disorders.

Seretis et al. [32] studied RDW levels of breast cancer patients and found that the RDW was higher in the patients than it was in the controls. Elevated RDW has also been associated with poor prognoses in multiple myeloma [33] and lung cancer [34]. As the RDW increases in inflammatory status [10], and cancer is an inflammatory condition, one can theorize that the RDW will elevate in brain tumors. Our results agreed

with this expectation. Additionally, previous studies [35,36] have shown that high RDW and low Hb levels are significant, independent predictors of poor survival in cancer patients and, therefore, might be relevant prognostic factors in these patients. In contrast, Riedl et al. [35] suggested that several red blood cell parameters of the hemogram, including Hb levels, might not contribute to improved risk stratification of cancer-associated venous thromboembolism.

Zadora et al. [18] found that glioblastoma patients had the highest preoperative value of NLCR. An elevated preoperative NLCR may also result from the peritumoral infiltration of macrophages, which associates with an increase in cytokine levels, such as levels of tumor necrosis factor-alpha (TNF-a), interleukin 6, and interleukin 8 [37]. Both Glasgow prognostic score GPS and NLCR are associated with tumor invasion and the rate of combined CBD resection. Wu et al. [1] demonstrated that GPS had a stronger association with clinic pathological factors than NLCR did. As GPS is easy to measure before starting treatment, they proposed it could be a useful tool for the stratification of gallbladder carcinoma patients. Bambury et al. [38] suggested that in the future creation of prognostic risk scores for glioblastoma multiforme, NLCR should be considered an initial candidate variable given its ease of measurement. Although an association has been seen between inflammation and NLCR [15], the present study failed to show such an association in brain tumor patients.

All hematologic parameters, including MPV and RDW, were similar in patients with either primary or metastatic brain tumors. This finding suggests that any malign neoplasm causes similar amounts of inflammatory burden. However, our cohort with primary or metastatic brain tumor was relatively small. Larger sample sizes should show significant differences between primary and metastatic processes.

The results of the present study were difficult to interpret due to the retrospective design and small sample size. Another limitation was the single center design of the work. A fourth limitation could be that we have not compared postoperative hemogram parameters to preoperative data. However, to the best of our knowledge, this study was the first in the literature to study MPV and RDW in brain tumor patients.

5. Conclusion

The decreased MPV and increased RDW of brain tumor patients show the usefulness of simple blood panels as inflammation indicators in these patients. However, prospective studies with larger sample sizes are needed to support our results and to expose MPV and RDW variations between metastatic and primary brain tumors.

Conflict of interest

None declared.

Acknowledgement and financial support

None declared.

Ethics

The work described in this article has been carried out in accordance with The Code of Ethics of the World Medical Association (Declaration of Helsinki) for experiments involving humans; Uniform Requirements for manuscripts submitted to Biomedical journals.

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