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A new marker in inflammatory etiopathogenesis of Bell's palsy: Immature granulocyte

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Abstract

Aim: Bell's palsy (BP) pathogenesis is not fully understood, but is generally idiopathic. Studies investigating the etiopathogenesis of BP suggest have implicated factors such as inflammation, viral infection, microvascular dysfunction, and exposure to acute cold. The purpose of this study was to reveal the effectiveness of immature granulocyte (IG) as an inflammatory marker in the etiopathogenesis of BP.

Materials and Methods: The retrospective study was performed September 2019 and January 2021. Thirty-three patients presenting to the our Ear, Nose, and Throat Clinic diagnosed with BP were included in the study. A control group consisting of 50 individuals with similar age and gender distributions to the patient group and presenting for routine examinations was also established. Immature granulocyte count (IGC), and immature granulocyte percentage (IG%) values were calculated from complete blood count (CBC) data.

Results: No significant difference was determined between the two groups in terms of age or gender ($p > 0.05$). IGC values found to differ significantly between the patient and control groups ($p=0.004$). No significant differences were observed in the IG% ($p=0.061$).

Conclusion: Inflammation is one of the main theories in the context of BP. Higher IGC being determined in patients with BP compared to the healthy control group supports the idea of the role of inflammation in the etiopathogenesis.

Introduction

Bell's palsy (BP), also known as idiopathic peripheral facial paralysis, is seen in 15-30 out of every 100,000 individuals. It can cause symptoms such as unilateral facial muscle weakness, epiphora, decreased sense of taste, earache, and hypersensitivity to sound [1]. Unilateral facial muscle paralysis is the most common form, at a rate of 60-75% [1, 2]. BP can be seen at any age and in both genders, and generally heals completely [1, 3]. The pathogenesis is not fully understood, but is generally idiopathic [2]. Studies investigating the etiopathogenesis of BP suggest have implicated factors such as inflammation, viral infection, microvascular dysfunction, and exposure to acute cold [2, 4]. Inflammation may play an important role in BP. The response to steroid therapy is significant in showing that inflammation plays a role in the etiopathogenesis of BP [3]. Edema forms in the fallopian canal, and particularly in the labyrinthine segment, as a result of inflammation [1]. The peripheral myelin sheath of the facial nerve can also be affected in association with inflammation [3].

The neutrophil-lymphocyte ratio (NLR), platelet-lymphocyte ratio (PLR), and systemic immune-inflammation index (SII) (platelet × neutrophil / lymphocyte) can be calculated from the peripheral blood count [1]. Studies have shown that the NLR, PLR, and SII can be used as inflammatory markers [3]. Various studies have also examined the relationship between BP and hematological parameters such as NLR, PLR, and SII [2, 3].

Immature granulocyte (IG) cells are found in peripheral blood under physiological conditions [5]. The immature granulocyte count (IGC) is a parameter showing increased bone marrow activation in peripheral blood [6]. The immature granulocyte percentage (IG%) is a novel inflammatory marker easily obtained with automated hematology analyzers at complete blood count (CBC). Studies have shown that the IG% increases earlier than traditional parameters such as C-reactive protein (CRP) and leukocyte count in inflammatory states such as infection and sepsis [5]. The

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purpose of this study was to reveal the effectiveness of IG as an inflammatory marker in the etiopathogenesis of BP.

Materials and Methods

Approval for this retrospective study was granted by the Kastamonu University Clinical Research Ethics Committee (no:2020-KAEK-143-36, date:11.02.2021). Thirty-three patients presenting to the Kastamonu Training and Research Hospital Ear, Nose, and Throat Clinic between September 2019 and January 2021 and diagnosed with BP were included in the study. A control group consisting of 50 individuals with similar age and gender distributions to the patient group and presenting for routine examinations was also established. Patients who had undergone infection within the previous week, patients aged under 18, pregnant women, with diseases or malignancies capable of altering CBC parameters and inflammatory markers, with congenital or central facial paralysis, with Ramsey-Hunt syndrome, with active otological disease or histories of otological surgery, or with parotid gland disease, traumatic patients, and patients with missing CBC data were excluded.

Data for laboratory tests, and patients' ages and genders were obtained from the hospital Laboratory Information System. CBC parameters at time of presentation and before the receipt of any treatment were calculated using an automated hematology analyzer (XN-1000-Hematology-analyzer-Sysmex Corporation, Japan). White blood cell (WBC), platelet distribution width (PDW), mean platelet volume (MPV), neutrophil count (NEUTC), eosinophil count (EOC), basophil count (BASOC), neutrophil percentage (NEUT%), lymphocyte percentage (LYMPH%), monocyte percentage (MONO%), eosinophil percentage (EO%), basophil percentage (BASO%), IGC, and IG% values were calculated from CBC data. NLR, PLR, and SII values were calculated using the relevant formulae. The data obtained were then compared between the two groups. The normal reference values for these parameters are as follows: WBC (3,5-10,5)x103/μL, PDW (8.29-25) fL, MPV (7-10.3) fL, NEUTC (1.7-7)x10^3/μL, EOC (0.05-0.5)x10^3/μL, BASOC (0-0.3)x10^3/μL, IGC (0-0.03)x10^3/μL.

Statistical analyses were performed on Statistical Package for Social Sciences 18.0 for Windows software (SPSS Inc., Chicago, IL, USA). Descriptive statistics for the data obtained were expressed as number and % for categorical variables and as median (minimum, maximum) values for numerical variables. The Mann Whitney U test was used for comparisons between the control and BP groups since the results were not normally distributed. The chi-square test was applied to investigate whether there was any difference in terms of age and gender between the two groups. Receiver Operating Characteristic (ROC) analysis and Youden's index were used to determine Area Under the Curve (AUC), cut-off, sensitivity, and specificity values. p values < 0.05 were regarded as statistically significant.

Results

Thirty-three patients with BP, 18 men and 15 women, with a median age of 48.5 (18-71) years, and a 50-member control group, 26 men and 24 women, with a median age of 39 (27-60) years, were included in the study. No significant difference was determined between the two groups in terms of age or gender ($p > 0.05$) (Table 1).

Table 1. Patients' age and gender distribution.

		BP group	Control group	p value
Age		48 (18-66)	40.5 (29-60)	0.135
Gender	Male	18	26	0.976
	Female	15	24	

BP: Bell's palsy

Table 2. Comparison of BP and control groups.

	Control group	BP group	p value
	median (IQR)		
WBC	6.94(5.69;7.94)	8.73(6.87;10.83)	< 0.001
NEUTC	3.57(2.84;4.18)	5.14(3.94;7.84)	< 0.001
EOC	0.15(0.10;0.25)	0.09(0.05;0.21)	0.014
BASOC	0.05(0.04;0.06)	0.04(0.02;0.06)	0.027
NEUT%	51.95(47.2;57.8)	63.2(54.7;73.7)	< 0.001
LYMPH%	36.6(32.2;43.1)	28.7(19.9;34.9)	< 0.001
MONO%	7.25(6.78;8.90)	6.5(5.2;8.3)	0.005
EO%	2.65(1.48;3.73)	1.1(0.45;2.50)	0.001
BASO%	0.7(0.6;0.83)	0.4(0.3;0.6)	< 0.001
IGC	0.02(0.01,0.03)	0.03(0.01;0.05)	0.004
IG%	0.3(0.20;0.40)	0.4(0.20;0.55)	0.061
NLR	1.42(1.11;1.78)	2.21(1.59;3.70)	< 0.001
PLR	110.5(95.1;129)	104.8(80.6;153.9)	0.894
SII	389(270;510)	566.4(447;955)	< 0.001
PDW	11.9(10.9;13.5)	11.4(10.3;12.4)	0.015
MPV	10.3(9.8;11.1)	10.0(9.4;10.5)	0.030

BP: Bell's palsy; WBC: white blood cell; NEUTC: neutrophil count; EOC: eosinophil count; BASOC: basophil count; NEUT%: neutrophil percentage; LYMPH%: lymphocyte percentage; MONO%: monocyte percentage; EO%: eosinophil percentage; BASO%: basophil percentage; IGC: immature granulocyte count; IG%: immature granulocyte percentage; NLR: neutrophil to lymphocyte ratio; PLR: platelet to lymphocyte ratio; SII: systemic immune-inflammation index; PDW: platelet distribution width; MPV: mean platelet volüme

Laboratory findings of the patient and control groups are shown in Table 2.

At ROC analysis, WBC count at a cut-off value of 8.52 differentiated the patient and control groups with 54% sensitivity and 86% specificity ($p < 0.001$). NEUTC at a cut-off value of 4.42 differentiated the two groups with 72% sensitivity and 84% specificity ($p < 0.001$). NEUT% at a cut-off value of 62.1 differentiated the two groups with 54% sensitivity and 90% specificity ($p < 0.001$). IGC at a cut-off value of 0.035 differentiated the two groups with 45% sensitivity and 84% specificity ($p=0.018$). NLR at a cut-off value of 1.78 differentiated the two groups with 66% sensitivity and 78% specificity ($p < 0.001$). SII at a cut-off value of 441 differentiated the two groups with 81% sensitivity and 66% specificity ($p < 0.001$) (Figure 1).

Discussion

The lengthy intracranial course of the facial nerve and the anatomical proximity of the facial canal to the temporal

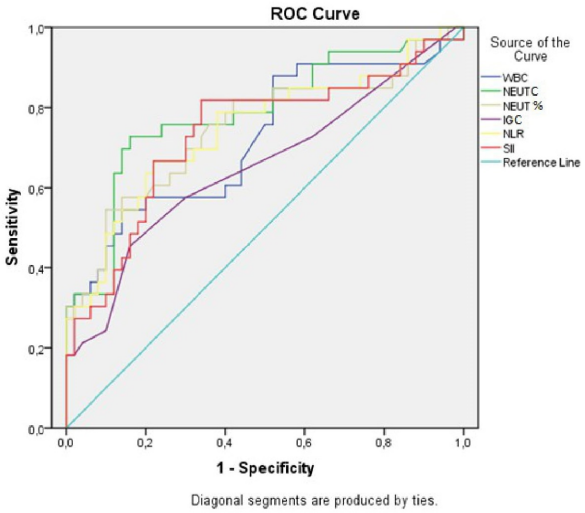

Figure 1. The graph of the ROC analysis.

bone result in the nerve being easily affected by diseases such as infection, trauma, and tumor, and inflammatory events. Although the etiopathogenesis is not yet fully understood, viral, inflammatory, and immune system mechanisms play the most important role in the etiopathogenesis of BP [2]. Yılmaz et al. reported significantly higher levels of inflammatory cytokines such as IL-6, IL-8, and TNF-alpha in BP patients compared to a control group [7]. Edema developing in association with inflammation secondary to viral infections can also easily damage the facial nerve, with its anatomically narrow canal. The fact that BP generally resolves completely suggests a close association with inflammation and edema.

NLR, an inexpensive and easily calculated systemic inflammatory marker, is used in the diagnosis of several inflammatory diseases [2]. Bucak et al. investigated 54 patients with BP and a 45-member control group and observed significantly higher NEUTC and NLR values in the BP group [8]. In another study of 54 children with BP, Kim et al. reported significant elevation in NLR and PLR values in the patient group compared to a 39-member control group [9]. A different study showing higher NLR in patients with BP determined that a high NLR value was positively correlated with House-Brackmann (HB) grading and was associated with poor prognosis [10]. In Oya et al.'s study of patients with BP, NLR values were significantly elevated in the patient group, while PLR values were not [11]. Consistent with the previous literature, NLR in the present study was significantly higher in the BP group compared to the control group. PLR values were higher in the control group, although the difference was not statistically significant.

Other hematological parameters exhibiting statistically significant elevation in the BP group compared to the control group in this study were WBC, NEUTC, EOC, BASOC, NEUT%, LYMPH%, MONO%, EO%, BASO%, SII, PDW, and MPV. Of these parameters, WBC, NEUT, LYMPH, and MONO have been used as inflammatory markers in conditions such as infection, autoinflammatory disease, and cancer with inflammatory components [12]. EOC elevation may occur in allergies, infections, autoimmune conditions, and malignancies [4]. EO and BASO counts have been shown to rise in allergic inflammation [13]. In a study of 88 patients with BP and 50 healthy controls, Kınar et al. reported elevation in the novel inflammatory index SII in the BP group [3]. MPV demonstrates platelet function and activation and can be used as an inflammatory marker [12]. Inflammation increases platelet breakdown. PDW values reflecting a change in platelet dimensions associated with platelet breakdown can also rise [14]. The increase in these parameters in the present study also supports the role of inflammation in the etiopathogenesis of BP.]Other hematological parameters exhibiting statistically significant elevation in the BP group compared to the control group in this study were WBC, NEUTC, EOC, BASOC, NEUT%, LYMPH%, MONO%, EO%, BASO%, SII, PDW, and MPV. Of these parameters, WBC, NEUT, LYMPH, and MONO have been used as inflammatory markers in conditions such as infection, autoinflammatory disease, and cancer with inflammatory components [12]. EOC elevation may occur in allergies, infections, autoimmune conditions, and malignancies [4]. EO and BASO counts have been shown to rise in allergic inflammation [13]. In a study of 88 patients with BP and 50 healthy controls, Kınar et al. reported elevation in the novel inflammatory index SII in the BP group [3]. MPV demonstrates platelet function and activation and can be used as an inflammatory marker [12]. Inflammation increases platelet breakdown. PDW values reflecting a change in platelet dimensions associated with platelet breakdown can also rise [14]. The increase in these parameters in the present study also supports the role of inflammation in the etiopathogenesis of BP. Technical improvements in automated hematology analyzers in recent years have made it possible to determine IG percentages and counts. Various studies have shown that IG can be used as an effective inflammatory marker [6]. To the best of our knowledge, no studies have investigated increases in IGC in BP. Karakulak et al. observed significant elevation in IG% in patients with acute pancreatitis exhibiting a severe course [5]. Another study of patients with acute appendicitis reported that IG was quite specific for diagnosis and an important parameter in predicting complicated cases [6]. Similarly in the present study, IGC was significantly higher in the patients with BP than in the healthy controls (p=0.004). ROC analysis produced significant results for IGC ((AUC 95%) = 0.654 (0.528-0.779)) value.

To the best of our knowledge, this is the first study to investigate IGC to support the role of inflammation in the etiopathogenesis of BP. The principal limitation of this study is that due to the low patient number it was not possible to examine the relationship between BP grading or prognosis and hematological parameters. However, the purpose of this study was to reveal the role of the IGC in the inflammatory etiopathogenesis of BP, and a statistically significant result on that subject was obtained.

Conclusion

Inflammation is one of the main theories in the context of BP. Higher IGC being determined in patients with BP

compared to the healthy control group supports the idea of the role of inflammation in the etiopathogenesis. IG, a novel and inexpensive marker that can be easily determined from CBC, can be used in the diagnosis of BP. Further, more extensive studies might now usefully examine the effect of IG in the prognosis of BP.

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