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Expressions of selected adhesion molecules on peripheral blood leukocytes in patients with aggressive periodontitis

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B Data Collection
C Statistical Analysis
D Data Interpretation
E Manuscript Preparation
F Literature Search
G Funds Collection

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Summary

Introduction: Aggressive forms of periodontitis lead to rapid bone destruction resulting in extensive losses in children's and young adults' dentition. Adhesion molecule deficiency syndrome and abnormalities in the expression of various adhesion molecules on peripheral blood leukocytes can be observed in prepubertal and aggressive periodontitis (AP) patients. The aim of the study was thus to assess the expression of selected cell adhesion molecules (CAMs; CD11a, CD11b, CD11c, CD54, and CD62L) on monocytes, neutrophils, and lymphocytes of the peripheral blood in patients with AP.

Materials and Methods: The study involved 16 patients with AP and a control group of 13 generally healthy subjects with healthy periodontium. CAM expressions were determined by flow cytometry and presented as mean fluorescence intensity (MFI) and percentage of cells showing expression of the assessed adhesion molecules.

Results: Neutrophil CAM expressions in AP patients were comparable with those of the control group. MFI of CD62L on monocytes in AP patients was significantly lower than that of the controls. Lymphocytes showed increased CD11b expression compared with the control group. The percentage of leukocytes showing CAM expression in both groups was similar. Only the percentage of lymphocytes with CD11b in AP patients was significantly higher than in healthy controls.

Conclusions: Because of the evident lack of differences between patients and controls and the great amount of individual dispersion of the results, the above CAMs on peripheral blood leukocytes in generally healthy patients with AP do not seem to be characteristic markers of this disease.

Key words: adhesion molecules • peripheral blood leukocytes • aggressive periodontitis

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INTRODUCTION

Inflammatory infiltration in the gingiva in the course of periodontitis consists mainly of B and T cells and, to a lesser degree, neutrophils (PMNs) and macrophages[16]. Leukocyte migration to the periodontial tissue affected by bacterial infection is regulated by various types of cellular adhesion molecules (CAMs). The initial interactions of leukocytes with the vascular endothelium, defined as "rolling", are selectin mediated[4, 28, 29]. The selectin family contains three proteins, but only L-selectin is expressed on leukocytes[6].

The β2 subfamily integrins are responsible for the adhesion of leukocytes to endothelial cells. The integrins CD11/CD18 are heterodimeric glycoproteins sharing a 95-kDa β subunit (CD18) that is non-covalently associated with various α subunits, CD11a, b, and c (175, 165, and 150 kDa)[26]. Leukocyte adhesion to the vascular endothelium is the result of CD11/CD18 interactions with a suitable ligand on endothelial cells, mainly with CD54 (intercellular adhesion molecule – ICAM-1)[27]. The β2 integrins acquire the ability to bind to ligands upon activation ("inside-out signaling"), leading to integrin clustering and transformation of the β2 integrin family into a population of high affinity[28]. CD11a is responsible for a wide spectrum of leukocyte functions, including T cell-mediated killing, functions of T helper and B lymphocyte responses, natural killing, antibody--dependent cytotoxicity mediated by monocytes and granulocytes, and leukocyte adhesion to endothelial cells, fibroblasts, and epithelial cells[27]. CD11b (CR3) and CD11c (CR4) take part in phagocytosis through IC3b binding; moreover, CD11b enhances the action of natural killer cells. CD11/CD18 are likely to combine directly with lipopolysaccharides (LPS) of the bacterial walls[15, 24, 28, 31]. LPS contributes to the increased expression of the β2 subfamily integrins on PMNs and monocytes[5]. The incubation of PMNs with either fMLP or GM-CSF increases the level of surface CD11b[31]. Many other agonists cause activation of CD11a and CD11b on leukocytes. These are chemoattractants (PAF, IL-8, c5a) and cytokines (TNF-α, IL-1)[10, 28]. However, LPS from *Actinobacillus actinomycetemcomitans* and *Escherichia coli* have no effect on β2 integrin behavior on lymphocytes[5]. Migrating leukocytes alter CD11a expression on the cell surface, it being higher than on nonadherent leukocytes[10]. A deficit of CD11/CD18 has been described as leukocyte adhesion deficiency (LAD)[2, 19]. Patients with LAD syndrome frequently exhibit severe inflammatory changes in the periodontium, referred to as prepubertal periodontitis (PP)[25]. PP occurs in small children with deciduous dentition and is characterized by rapid destruction of the alveolar bone, which leads to premature loss of the deciduous teeth and affects permanent dentition[23, 30]. PP is, however, a rare clinical entity and hence there are very few reports of it.

Aggressive periodontitis (AP), which may appear after 10 years of age, is relatively more frequent. It also occurs with rapid bone destruction, resulting in extensive losses in young adult dentition[13]. Page et al.[22] believe that the adhesion molecule deficiency syndrome involves only children with PP and does not occur in other periodontal diseases. According to other authors, changes in the expressions of various adhesion molecules on peripheral blood leukocytes can also be observed in AP patients[1, 9, 12, 17, 18]. Determination of CAM involvement in the pathogenesis of the respective forms of periodontitis could become an important diagnostic tool to predict the development of the inflammatory process in the periodontium.

Therefore, the aim of this study was to assess the expressions of selected CAMs (CD11a, CD11b, CD11c, CD54 and CD62L) on monocytes, PMNs, and lymphocytes of the peripheral blood of AP patients.

MATERIALS AND METHODS

Sixteen generally healthy subjects with AP (10 women and 6 men), 23–45 years old (mean: 37.5 years), were selected for the study. The control group (C) contained 13 subjects (8 women and 5 men), aged 25–47 years (mean 38.5), with no periodontal lesions. All the subjects in both groups were non-smokers and had not taken any drugs, including antibiotics, for the previous 6 months. Diagnosis was based on clinical and radiological investigations, which allowed detection of characteristic periodontal lesions in molars and/or incisors. Only patients with periodontal pockets (at least 6 mm) found at these teeth in clinical examination and with vertical bony defects in radiological investigation were enrolled. All the subjects gave their informed consent for material collection. The study was approved by the Bioethics Committee of the Medical University of Białystok.

Blood for analysis was collected in the morning hours from the ulnar vein into test tubes containing EDTA-K3 as anticoagulant. The following monoclonal antibodies were used: anti-CD11a, anti--CD11b, anti-CD11c, anti-CD14, anti-CD54, and anti-CD62L, labeled either with fluorescein isothiocyanate or R-phycoerythrin (DakoCytomation, Denmark). Antibody-matched isotypic controls were

used to avoid autofluorescence and non-specific luminescence. Standard techniques of direct fluorescent labeling of whole blood leukocytes were used to assess the expressions of the respective antigens. Ten μl of monoclonal antibodies was added to each 100 μl of blood, and after 15 min of incubation at room temperature in the dark each sample underwent rapid lysis using EPICS Immunology Work Station and ImmunoPrep Reagent System. The samples were gently mixed and examined using a flow cytometer EPICS XL (Coulter, USA) with an argon laser operating at 488 nm. Lymphocytes and granulocytes were gated on a cytogram based on physical properties of the cells (forward scatter, side scatter). Monocytes were identified using anti-CD14 antibodies (Fig. 1).

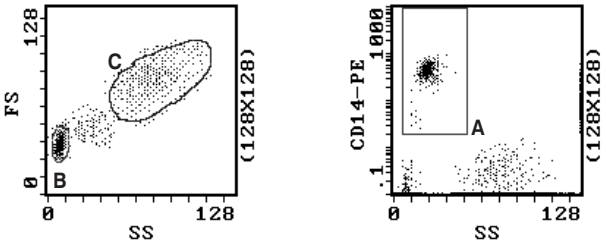

Figure 1. Whole blood flow cytometric analysis. Gate **A** – monocytes (immunogate – CD14+/low SS cells), Gate **B** – lymphocytes (low FS/low SS), Gate **C** – PMNs (high FS/high SS; **B** and **C** are morphological gates). FS – forward scatter, SS – side scatter.

Results were expressed as the percentage of cells showing expression of the assessed adhesion molecules and as mean fluorescence intensity (MFI), indirectly defining the density of the molecules. The percentage of CAM-positive cells was intermediate based on the gate determined by the respective negative control. The gate, including not more than 1% of the negative population, was copied to the histogram containing anti-CAM antibodies. The percentage of cells in the gate was treated as the positive population. The intermediate method was applied to measure the antigen density. Each time, the same quantity of fluorochrom-labeled antibodies was added to the same number of cells (antibodies were added in excess). The quantity of antibodies bound to the cells depends on the number of the respective cell receptors. As the investigations were always performed using the same adjustment of the cytometer (stability of the apparatus was measured by means of DNA-check beads), fluorescence intensity of the sample examined correlates with the number of cell receptors and is best expressed as the mean intensity value. The mathematical procedure is presented by the following formula included in the apparatus' instructions.

Log region statistics

For log signals, the formulas are:

$$\text{Mean intensity} = \frac{\sum \text{log to lin (channel number)} \times \text{count in the channel}}{\text{area}}$$

$$\text{Log to Lin (N)} = 1.024 \times 10^{[L + D \times (\frac{N}{1024})]}$$

where: L – 1 for four-decade logarithmic amplification, D – number of decades.

MFI values were calculated for the whole population of cells (respectively for monocytes, PMNs, and lymphocytes). Statistical analyses were done using the Mann-Whitney U-test and the SPSS 8.0 PL program. The statistical significance level was set at 0.05.

RESULTS

The MFI values for CD11a, CD11b, CD11c, and CD54 on monocytes of AP patients were comparable with those noted in the control group (Table 1). MFI of CD62L on monocytes of AP patients was significantly reduced compared with controls (2.1±0.7 vs. 3.2±1.3; p=0.02). The expression of all CAMs on PMNs of AP patients resembled that of the control group. Values of the above parameters are presented in Table 2. Mean fluorescence values for CD11a, CD11c, CD54, and CD62L on lymphocytes of patients with AP were similar to those of the controls. The MFI of CD11b on lymphocytes was significantly higher in AP than in control subjects (Table 3).

The percentage of monocytes and PMNs showing the expression of all the CAMs examined did not differ significantly between groups AP and C (Tables 4 and 5). In both groups the percentages of CD11a, CD11c, CD54, and CD62 lymphocytes were similar (Table 6).

Table 1. CAM mean fluorescence intensity (±SD) on peripheral blood monocytes in AP and C patients

	CD11a	CD11b	CD11c	CD62L	CD54
AP	14.9±2.6	18.1±4.7	6.8±2.0	2.1±0.7*	1.8±0.3
C	14.8±3.7	16.0±5.5	7.1±1.9	3.2±1.3	1.7±0.3

* Statistically significant difference between the groups AP and C.

Table 2. CAM mean fluorescence intensity (±SD) on peripheral blood PMNs in AP and C patients

	CD11a	CD11b	CD11c	CD62L	CD54
AP	4.3±0.7	13.5±5.3	2.6±0.7	4.1±2.4	0.7±0.2
C	4.5±1.2	10.4±2.8	3.0±1.2	5.1±2.8	0.7±0.1

Table 3. CAM mean fluorescence intensity (±SD) on peripheral blood lymphocytes in AP and C patients

	CD11a	CD11b	CD11c	CD62L	CD54
AP	7.8±1.6	0.8±0.2*	0.7±0.2	2.6±1.3	0.4±0.1
C	8.0±1.1	0.6±0.1	0.9±0.3	3.0±1.1	0.4±0.1

* Statistically significant difference between groups AP and C.

Table 4. Percentage of peripheral blood monocytes in AP and C subjects showing expression of the assessed CAMs (±SD)

	CD11a	CD11b	CD11c	CD62L	CD54
AP	99.9±0.04	98.9±1.03	98.0±5.5	71.0±21.0	70.3±16.8
C	99.6±1.30	99.1±1.00	98.1±4.8	74.4±19.8	60.7±16.7

Table 5. Percentage of peripheral blood PMNs in AP and C subjects showing expression of the assessed CAMs (±SD)

	CD11a	CD11b	CD11c	CD62L	CD54
AP	99.1±1.1	99.8±0.1	88.7±7.7	82.8±18.6	6.7±6.6
C	98.4±2.7	99.3±1.2	80.4±14.8	80.4±6.7	12.9±27.2

Table 6. Percentage of peripheral blood lymphocytes in AP and C subjects showing expression of the assessed CAMs (±SD)

	CD11a	CD11b	CD11c	CD62L	CD54
AP	95.7±3.0	26.4±7.9*	12.3±5.1	50.5±15.6	3.1±1.9
C	92.6±7.3	15.6±4.5	9.0±7.2	52.0±16.2	2.3±1.8

* Statistically significant difference between groups AP and C.

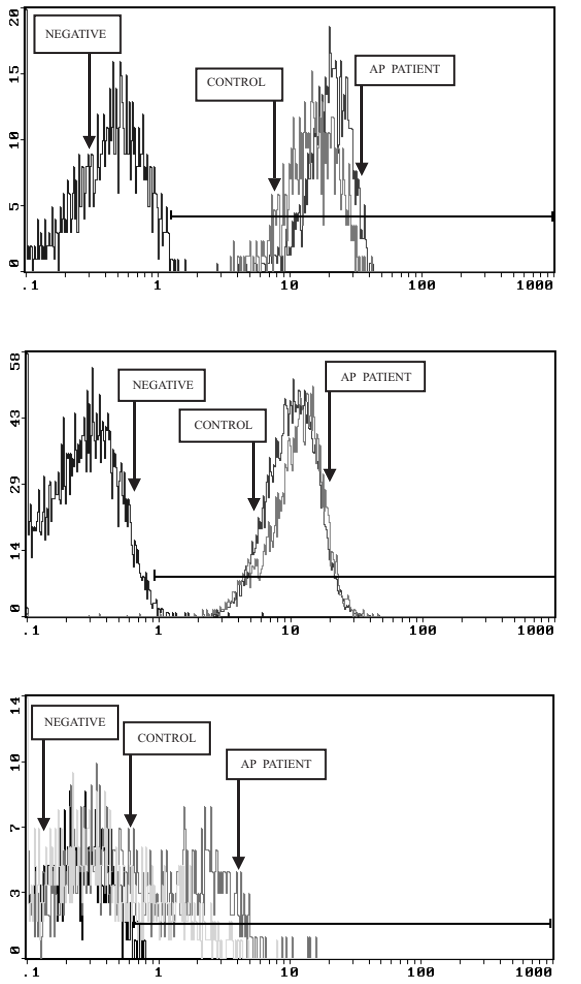

Figure 2. Flow cytometric analysis of CD11b expressions in AP and C patients on: monocytes, PMNs and lymphocytes. Data show one representative case from AP and C groups.

However, the percentage of CD11b lymphocytes in AP patients was higher than in control subjects (26.1±7.9 in AP and 15.6±4.5 in C; p=0.001). To illustrate the study outcome we present representative histograms (Fig. 2 and 3).

DISCUSSION

We found no differences either in CD11a/CD11c expression on leukocytes or in the percentage of CD11a and CD11c leukocytes between groups AP and C. However, we observed a statistically significant increase in the percentage of CD11b lymphocytes and in this receptor expression in AP patients. However, because of the high standard deviation, the difference in CD11b expression on lymphocytes is rather not characteristic. Mouynet et al.[21] did not observe any differences in the percentage of CD11a and CD11b PMNs in the peripheral blood of AP patients nor in CD11a/CD11b expression on PMNs compared with healthy subjects. Watanabe et al.[30] also found no significant differences in the surface expression of CD11b on PMNs in patients with advanced periodontitis (P). However, its expression on PMNs in the fluid from periodontal pockets of P patients was higher than in healthy subjects. According to other authors there is a significant increase in CD11b expression on PMNs in AP patients[1, 9]. Macey et al.[18] believe that PMN isolation procedures can enhance the expression of adhesion molecules so that it is much higher than on whole blood cells. Whole blood was used in the present study and this slight increase in CD11b expression on leukocytes does not seem to result from sample material processing.

Some authors correlate the increased CD11b expression with decreased PMN chemotaxis in AP patients subjects. Elevated CD11b expression may have an effect on the increased PMN adherence, which may lead to a reduction in their spontaneous and directed migration. Therefore, defects of chemotaxis observed in some AP patients are due to PMN overstimulation rather than internal defects[21]. The increased CD11/CD18 expression with simultaneous impair-

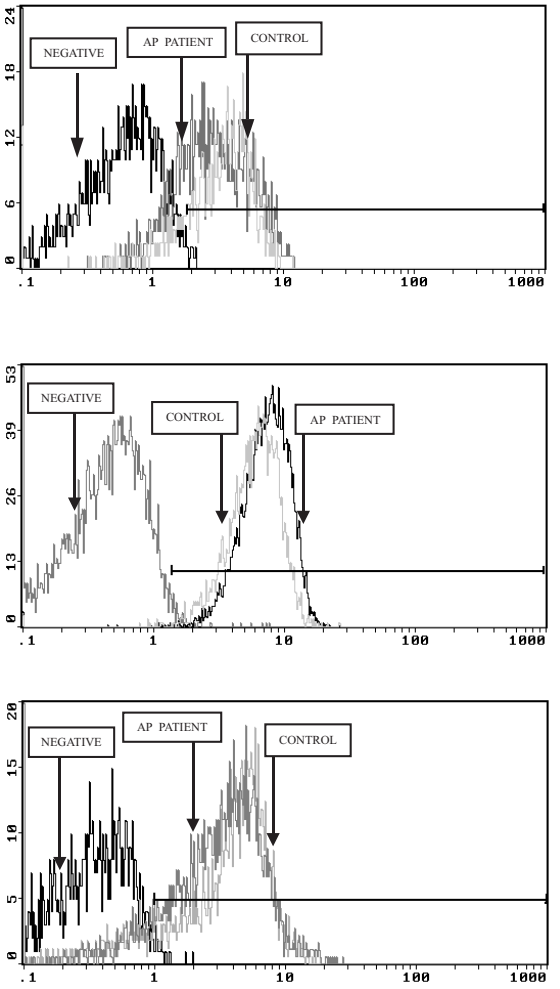

Figure 3. Flow cytometric analysis of CD62L expressions in AP and C patients on: monocytes, PMNs and lymphocytes. Data show one representative case from AP and C groups.

ment of PMN chemotaxis in AP subjects was also reported by Agarwal et al.[1], who associated this fact with the presence of cytokines TNF-α and IL-1β. Increased expression of CD11b/CD18 accompanied by chemotaxis impairment was also noted in patients with PP. Such significant changes in PMN function are a likely result of host response to bacteria invading periodontal tissues and may indicate PMN involvement in the disease pathogenesis[8].

Our observations concerning the percentage of cells with CD11c are consistent with data reported by other authors who found that the percentage of PMNs showing CD11c expression in AP, chronic P, and healthy patients did not differ, being 80 and higher[20].

CD54 belongs to the superfamily of immunoglobulins and is a basic vascular adressin found on endothelial cells, leukocytes, fibroblasts, dendritic cells, and neurons[15]. It is responsible for interactions between cells, especially for the adhesion of leukocytes to the endothelium and their diapedesis. CD54 expression is influenced by cytokines, namely IL-1, TNF, and IFN-γ[27]. In our study, its expression on leukocytes in AP subjects was similar to that in healthy subjects, which allows the assumption that this surface molecule is not involved in periodontal inflammation. However, this has to be confirmed in further research.

CD62L (L-selectin) takes part in the physiological rolling of leukocytes and is rapidly shed from their surface upon activation[14]. Then the β2 integrin-dependent phase of firm adhesion occurs[3]. The shedding of this selectin is increased by IL-8, chemoattractants (PAF, fMLP), and some non-steroidal anti-inflammatory drugs. A decrease in L-selectin shedding, mainly by shedding protease blocking, is caused by tissue inhibitor of metalloproteinase 3, morphine, and hydroxamic acid derivatives[11]. A study on mice with selectin deficiency revealed that L-selectin is responsible for the prolonged presence of PMNs in the capillaries[7]. In our study, L-selectin expression was decreased on all leukocytes from AP patients compared with the control group, although the difference was statistically significant only on monocytes. Other authors also noted a decrease in L-selectin expression on leukocytes[9, 16, 17]. Gainet et al.[9] claim that the reduced expression of this molecule on PMN involves only patients with aggressive destruction of the periodontium and not subjects with mild periodontitis, thus suggesting a relationship between abnormal PMN function and the clinical form of periodontitis. Of interest is the study of Blix et al.[5], who assessed L-selectin level on all types of leukocytes in healthy subjects. They found high expression of this molecule on PMNs, monocytes, and lymphocytes. CD62L expression decreased rapidly on PMNs and monocytes after stimulation by LPS from *A. actinomycetemcomitans*, the bacterium known for its ability to invade periodontal tissues. The reduction in the leukocyte CD62L expression in patients with AP can impair their tethering to the site of inflammation and partly explains individual susceptibility to recurrent severe infections in the periodontium[17]. Krugluger et al.[16] found no differences in the expression of CD62L on peripheral blood PMNs between patients with chronic P and healthy subjects. However, they showed a significant decrease in this parameter on PMNs in gingival crevicular blood, suggesting a significantly reduced selectin-mediated ability to adhere to the inflamed gingival endothelium in chronic P[16].

Our results concerning the behavior of selected adhesion molecules demonstrate some discreet deviations. The greatest differences refer to the increased percentage of CD11b on lymphocytes and decreased expres-

sion of CD62L on monocytes in AP patients. As all our patients were in good general health and were not receiving treatment for any chronic diseases, it can be assumed that these slight alterations in the expression of CAMs on leukocytes possibly have the potential to contribute to the development of local inflammatory process in the periodontium, and that is why they may be associated with AP pathogenesis although they have no effect on general health. Thus, CAM expression on leukocytes of the peripheral blood of generally healthy subjects with AP does not seem a characteristic marker of this disease. However, it may help predict the incidence and development of periodontal lesions in patients with recurrent general infections.

REFERENCES

1. Agarwal S., Suzuki J. B., Piesco N. P. and Aichelmann-Reidy M. B. (1994): Neutrophil function in juvenile periodontitis: induction of adherence. Oral Microbiol. Immunol., 9, 262–271.
2. Anderson D. C., Schmalstieg F. C., Amaout M. A., Kohl S., Tosi M. F., Dana N., Buffone G. J., Hughes B. J., Brinkley B. R. and Dickey W. D. (1984): Abnormalities of polymorphonuclear leukocyte function associated with a heritable deficiency of high molecular weight surface glycoproteins (GP138): common relationship to diminished cell adherence. J. Clin. Invest., 74, 536–551.
3. Anderson D. C. and Springer T. A. (1987): Leukocyte adhesion deficiency: an inherited defect in the Mac-1, LFA-1, and p150-95 glycoproteins. Annu. Rev. Med., 38, 175–194.
4. Bevilacqua M. P. and Nelson R. M. (1993): Selectins. J. Clin. Invest., 91, 379–387.
5. Blix I. J., Helgeland K., Kahler H. and Lyberg T. (1999): LPS from *Actinobacillus actinomycetemcomitans* and the expression of beta 2 integrins and L-selectin in an *ex vivo* human whole blood system. Eur. J. Oral. Sci., 107, 14–20.
6. Carlos T. M. and Harlan J. M. (1994): Leukocyte-endothelial adhesion molecules. Blood,84, 2068–2101.
7. Doyle N. A, Bhagwan S. D., Meek B. B., Kutkoski G. J., Steeber D. A., Tedder T. F. and Doerschuk C. M. (1997): Neutrophil margination, sequestration, and emigration in the lungs of L-selectin--deficient mice. J. Clin. Invest., 99, 526–533.
8. Firatli E., Gürel N., Efeoðlu A. and Cebeci I. (1996): Generalized prepubertal periodontitis. J. Clin. Periodontol., 23, 1104–1111.
9. Gainet J., Dang P. M., Chollet-Martin S., Brion M., Sixou M., Hakim J., Goegerot-Pocidalo M. A. and Elbim C. (1999): Neutrophil dysfunctions, IL-8, and soluble L-selectin plasma levels in rapidly progressive versus adult and localized juvenile periodontitis: variations according to disease severity and microbial flora. J. Immunol., 163, 5013–5019.
10. Grisar J., Hahn P., Brosch S., Peterlik M., Smolen J. S. and Pietschmann P. (2001): Phenotypic characteristics of human monocytes undergoing transendothelial migration. Arthritis Res., 3, 127–132.
11. Hafezi-Moghadam A., Thomas K. L., Prorock A. J., Huo Y. and Ley K. (2001): L-selectin shedding regulates leukocyte recruitment. J. Exp. Med., 193, 863–872.
12. Katsuragi K., Takashiba S., Kurihara H. and Murayma Y. (1994): Molecular basis of leukocyte adhesion molecules in early-onset periodontitis patients with decreased CD11b/CD18 expression on leukocytes. J. Periodontol., 65, 949–957.
13. Kinane D. F. and Lappin D. F. (2001): Clinical, pathological and immunological aspects of periodontal disease. Acta Odontol. Scand., 59, 154–160.
14. Kishimoto T. K., Jutila M. A., Berg E. L. and Buther E. C. (1989): Neutrophil Mac-1 and MEL-14 adhesion proteins inversely regulated by chemotactic factors. Science, 245, 1238–1241.
15. Kopeć-Szlęzak J. (1998): CD54 (ICAM-1) adhesion molecule expression on leukocytes [Ekspresja cząsteczki adhezyjnej CD54 (ICAM-1) na leukocytach]. Acta Hematol. Pol., 29, 4–9.
16. Krugluger W., Nell A., Solar P., Matejka M. and Boltz-Nitulescu G. (1995): Influence of sE-selectin and L-selectin on the regulation of cell migration during chronic periodontitis. J. Periodontal. Res., 30, 198–203.
17. Macey M. G., McCarthy D. A., Howells G. L., Curtis M. A., King G. and Newland A. C. (1998): Multiparameter flow cytometric analysis of polymorphonuclear leucocytes in whole blood from patients with adult rapidly progressive periodontitis reveals low expression of the adhesion molecule L-selectin (CD62L). Cytometry, 34, 152–158.
18. Macey M. G., McCarthy D. A, Vordermeier S., Newland A. C. and Brown K. A. (1995): Effects of cell purification methods on CD11b and L-selectin expression as well as the adherence and activation of leukocytes. J. Immunol. Methods, 181, 211–219.
19. Matysiak W. (1995): Circulatory adhesion molecules: their importance in diagnostics and prognostics [Krążące cząsteczki adhezyjne: znaczenie diagnostyczno-rokownicze]. Postepy Med. Wewn., 10, 367–374.
20. Mouynet P., Genetet N., Picot C., Apiou J., Nicolas P. and Michel J. F. (1995): Expression of the α-subunit of CR4 (CD11c) by peripheral blood and crevicular fluid neutrophils. Eur. J. Oral. Sci., 103, 413–415.
21. Mouynet P., Picot C., Nicolas P., Geneted B., Apiou J., Genetet N. and Michel J. F. (1995): *Ex vivo* studies of polymorphonuclear neutrophils from patients with early-onset periodontitis (III). CR3 and LFA-1 expression by peripheral blood and gingival crevicular polymorphonuclear neutrophils. J. Clin. Periodontol., 22, 110–117.
22. Page R. C., Beatty P. and Waldrop T. C. (1987): Molecular basis for the functional abnormality in neutrophils from patient with generalized prepubertal periodontitis. J. Periodontal. Res., 22, 182–183.
23. Page R. C., Bowen T., Altman L., Vandesteen E., Ochs H., Mackenzie P., Osterberg S., Engel L. D. and Williams B. L. (1983): Prepubertal periodontitis. I. Definition of a clinical disease entity. J. Periodontol., 54, 257–271.
24. Ramos O. F., Kai C., Yefenof E. and Klein E. (1988): The elevated natural killer sensitivity of targets carrying surface-attached C3 fragments require the availability of the iC3b receptor (CR3) on the effectors. J. Immunol., 140, 1239–1243.
25. Ranney R. R. (1991): Diagnosis of periodontal diseases. Adv. Dent. Res., 5, 21–36.
26. Sanchez-Madrid F., Nagy J. A., Robbins E., Simon P. and Springer T. A. (1983): A human leukocyte differentiation antigen family with distinct α-subunits and a common β-subunit; the lymphocyte function-associated antigen (LFA-1), the C3bi complement receptor (OKM1/Mac-1)and the p150,95 molecule. J. Exp. Med., 158, 1785–1803.
27. Springer T. A. (1990): Adhesion receptors of the immune system. Nature, 346, 425–434.
28. Vignola A. M., Gjomarkaj M., Arnoux B. and Bousquet J. (1998): Monocytes. J. Allergy Clin. Immunol., 101, 149–152.
29. Waldrop T. C., Anderson D. C., Hallomon W. W., Schmalstieg F. C. and Jacobs R. L. (1987): Periodontal manifestations of the heritable Mac-1, LFA-1 deficiency syndrome. Clinical, histophatologic and molecular characteristics. J. Periodontol., 58, 400–416.
30. Watanabe K., Blew B., Scherer M., Burke J., Koh G., Block C., Ramakrishnan V. and Frommel T. O. (1997): CD11b mRNA expression in neutrophils isolated from peripheral blood and gingival crevicular fluid. J. Clin. Periodontol., 24, 814–822.
31. Witko-Sarsat V., Rieu P., Descamps-Latscha B., Lesavre P. and Halbwachs-Mecarelli L. (2000): Neutrophils: molecules, functions and pathophysiological aspects. Lab. Invest., 80, 617–653.