O R I G I N A L   A R T I C L E

Serum biomarkers and clinical characteristics of patients with Hodgkin lymphoma

Biomarkeri seruma i kliničke karakteristike bolesnika sa Hočkinovim limfomom

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Abstract

Background/Aim. In classical Hodgkin's lymphoma (cHL) the existing prognostic scoring systems do not include markers that adequately reflect the interaction of malignant Hodgkin and Reed-Sternberg (HRS) cells and tumor environment. The aim of this study was to determine the relationship between serum Galectin-1 (Gal-1) and soluble CD163 (sCD163) and the clinical status of patients with cHL, with special emphasis on the presence of relapse, progression, or resistance to the therapy applied. **Methods**. The research included 79 patients of whom 63 were patients with cHL, and the control group of 16 healthy volunteers. The study group of 63 patients with cHL included a subgroup of newly diagnosed patients without therapy, newly diagnosed patients with therapy, patients with relapse and progression of the disease and primary refractory patients during 2014 and 2015. **Results**. Analysis of the levels of sCD163 and Gal-1 within a group of patients suffering from cHL showed that the values of both molecules were higher in relapsed patients and the subgroup with progressive disease comparing to the subgroup of newly diagnosed patients without therapy or patients with therapy onset. **Conclusion**. Determination of Gal-1 and sCD163 levels is simple and reliable analysis that can contribute to the identification of high-risk patients with cHL and deserves inclusion in current prognostic scoring systems.

Key words:
hodgkin disease; biomarkers, tumor; enzyme-linked immunosorbent assay; treatment outcome; prognosis.

Apstrakt

Uvod/Cilj. Postojeći prognostički skoring sistemi klasičnog Hočkinovog limfoma (cHL)ne obuhvataju markere koji adekvatno reflektuju interakciju malignih Hočkinovih Reed-Sternberg-ovih (HRS) ćelija i tumorskog okruženja. Cilj rada bio je da se utvrdi povezanost nivoa serumskog galektina-1 (Gal-1) i solubilnog CD163 (sCD163) sa kliničkim statusom obolelih od cHL sa posebnim osvrtom na prisustvo relapsa, progresije ili rezistencije na primenjenu terapiju. **Metode.** Istraživanjem je bilo obuhvaćeno 79 ispitanika, od kojih su 63 bili bolesnici sa cHL dok je kontrolnu grupu činilo 16 zdravih dobrovoljaca. Studijska grupa sa 63 bolesnika sa cHL obuhvatala je podgrupe novodijagnostikovanih bolesnika kod kojih nije započeto lečenje, novodijagnostikovane bolesnike kod kojih je započeto lečenje, bolesnike sa relapsom i progresijom bolesti, kao i bolesnika sa primarno refraktornom bolešću tokom 2014. i 2015. godine. **Rezultati.** Analiza nivoa sCD163 i Gal-1 pokazala je da su vrednosti oba molekula kod bolesnika sa cHL bile više kod onih sa relapsom i u podgrupi bolesnika sa progresivnom bolešću, u poređenju sa podgrupom novodijagnostikovanih bolesnika kod kojih nije započeto lečenje ili bolesnika sa započetim lečenjem. **Zaključak.** Određivanje nivoa sCD163 i Gal-1 je jednostavna i pouzdana analiza koja može doprineti identifikaciji bolesnika sa cHL i visokim rizikom i zaslužuje uključivanje u tekući prognostički skoring sistem.

Ključne reči:
hodžkinova bolest; tumorski markeri, biološki; elisa; lečenje, ishod; prognoza.

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Introduction

Hodgkin's lymphoma (HL) is a lymphoid tumor that accounts for less than 1% of all newly diagnosed neoplasms per year in the world [1]. In the case of classical HL (cHL), the proportion of neoplastic cells in the total tumor mass constitutes only 1%, the remainder being composed of surrounding inflammatory cells, lymphocytes, neutrophils, eosinophils, plasma cells, and other cell types [2]. The composition of tumor environment depends on the histologic subtype of cHL, stage of the disease, and the status of anti-tumor immunity in these patients [3]. Although tissue markers such as p53, high Ki-67 proliferative index and bcl-2, correlate with poor response and short survival of patients with HL, they are not suitable for adequate monitoring of therapeutic response and early detection of relapse [4]. Prognostic scoring systems introduced by German Hodgkin Study Group (GHSG) or Hasenclever scoring system International Prognostic Score (IPS) do not include markers that adequately reflect the interaction of malignant Hodgkin and Reed-Sternberg (HRS) cells and tumor microenvironment [5, 6]. Among the major markers that show the level of tumor immunosuppression in cHL and the ability to identify patients with relapsed/refractory (RR) form of the disease, are Galectin-1 (Gal-1) and soluble CD163 (sCD163). We have attempted to analyze the importance of these molecules in the assessment of the clinical status and responsiveness to therapy in patients treated with standard induction chemotherapy ± radiotherapy, and in RR disease, with salvage chemotherapy with the use of high-dose chemotherapy and autologous hematopoietic stem cell transplantation.

The aim of this study was to determine the relationship between serum Gal-1 and sCD163 and the clinical status of patients with cHL, with special emphasis on the presence of relapse, progression, or resistance to the therapy applied. In line with that objective, the focus was on determining the importance of the simultaneous presence of Gal-1 and sCD163 in the prediction of disease progression, relapse, and refractoriness to treatment in patients with cHL.

Methods

This multicentre prospective study included patients treated at the Clinic of Hematology and Clinical Immunology at the Clinical Center in Niš, the Clinic of Oncology in Niš and the Clinic of Hematology at the Clinical Center of Serbia in Belgrade.

The study included 79 patients. Of this number, 63 were patients with cHL and the control group consisted of 16 healthy volunteers. The study group of patients with cHL included 29 (46.03%) female patients and 34 (53.97%) male patients, at the mean age of 34.89 ± 13.79 years.

The study group of 63 patients with cHL included a subgroup of newly diagnosed patients without therapy (before treatment decision), newly diagnosed patients with therapy, patients with relapse and progression of the disease and primary refractory patients during 2014 and 2015. In the follow-up period two patients died.

The control group included 16 healthy volunteers, at the mean age of 39.75 ± 12.81 years.

The study was performed in line with the Declaration of Helsinki. Study design and its realization were approved by local ethical committees of the institutions where it was implemented.

Diagnosis and determining the clinical status of patients with cHL was done in accordance with the Europen Society for Medical Oncology (ESMO) recommendations. Patients were subjected to evaluation of parameter values covered by the Hasenclever's scoring system, with the resulting poor prognosis parameters serum albumin values < 40 g/L, hemoglobin < 105 g/L, male sex, age > 45, clinical stage IV, leukocytes > 15×10^9/L and < 8% of lymphocytes or in absolute values < 0.6×10^9/L. In accordance with the number of negative scoring points, patients were categorized into groups of 0–5 by International Prognostic Score (IPS), 5 being the situation when the patient had 5 or more of these negative points. Within first-line therapy, patients were treated with adramycin, bleomycin, vinblastine, dacarbazine (ABVD) or escalated doxorubicin, etoposide, cyclophosphamide, procarbazine, prednisone, vincristine, bleomycin (eBEACOPP) polychemotherapy protocol, with the use of radiation therapy for consolidation, or in case of RR disease, salvage dexamethasone, high-dose ara-c-cytarabine, platinum (DHAP) chemotherapy protocol with high-dose chemotherapy and autologous hematopoietic stem cell transplantation.

Concentrations of circulating Gal-1 and CD163 were measured using commercial sandwich enzyme-linked immunosorbent assay (ELISA) in the plasma of patients, which is based on competitive binding of polyclonal antibodies specific of Galectin-1, i.e., CD163, according to the manufacturer's instructions (Quantikine ELISA, R&D Systems, Minneapolis, USA). Concentrations of Gal-1 and CD163 were determined by using standard curves and were expressed in ng/mL. Assay values of Gal-1 and sCD163 in the serum were 0.313–20 ng/mL, and 1.60–100 ng/mL, respectively.

According to the manufacturer, neither for Gal-1 and sCD163 nor for CD163 there was significant cross-reactivity or interference with other proteins.

Statistical methods for data processing and analysis

The study used methods of descriptive statistics and normality of distribution of continuous variables, depending on the size of the sample, was analyzed by using Kolmogorov-Smirnov and Shapiro-Wilk's test.

Comparison of values of continuous variables between two independent groups of patients was performed by Student's t-test, and in the case of deviation of variable distribution from the norm, Mann-Whitney U test was used. Because the distribution of the most variables was not normal, their values are given as medians (Me) and interquartile ranges (IQR, 25th–75th percentile). As the threshold of statistical significance, standard value – $p < 0.05$ was defined.

Testing the significance of differences in values of continuous variables between several independent groups was performed by Kruskal-Wallis test while testing the connection between continuous variables by Spearman's rank correlation coefficient, given that, in these cases, the distribution of the studied variables deviated from normal.

To assess the classification characteristics of the selected variables, i.e., determine their sensitivity and specificity, receiver operating characteristic (ROC) analysis was conducted. Accuracy is measured by the area under the ROC curve (AUC). Statistical data analysis was done by SPSS 15.0 software package.

Results

Comparison of the levels of sCD163 and Gal-1 between the control group with healthy volunteers and patients suffering from cHL showed that the values of sCD163, 77.30 ± 38.80 ng/mL, were higher in the group of the diseased compared to 66.80 ± 16.80 ng/mL in the control group. Gal-1 level in cHL patients amounted to 28.90 ± 2.80 ng/mL, compared to 27.15 ± 1.33 ng/mL in the control group. Compared to the control group, the values of sCD163 and Gal-1 were higher in the group of patients with cHL ($p < 0.05$ and $p < 0.001$, respectively) (Figure 1).

The sensitivity and specificity of sCD163 and Gal-1 was checked by ROC analysis to classify patients suffering from cHL in relation to healthy volunteers. It turned out that the limit values of 78.45 ng/mL of sCD163 can distinguish patients from healthy volunteers with a sensitivity of 49.2% and specificity of 87.5%, AUC = 0.686, 95% confidence intervals (CI) = 0.56–0.80, $p < 0.05$. The same analysis sho-

wed that the value of Gal-1 of 28.45 ng/mL of serum had a sensitivity of 63.5% and specificity of 93.8%, AUC = 0.807, 95% CI = 0.69–0.92, $p < 0.001$. ROC analysis of the sCD163/Gal-1 ratio showed that the value of 2.924 had a sensitivity of 41.3% and specificity of 87.5%, AUC = 0.600, 95% CI = 0.47–0.73, $p > 0.05$. Summarizing the values of sensitivity and specificity for both parameters and their ratio obtained by ROC analysis, it was calculated that the value of Gal-1 higher than 28.45 ng/mL most accurately classified cHL patients, as compared to healthy population.

The clinical status defined the newly diagnosed patients with no treatment started, treated patients as well as the patients in remission, relapse, progression, and resistance.

Accordingly, 4 (6.34%) patients were in relapse, 5 (7.93%) patients showed disease progression and 11 patients had refractoriness to treatment (17.46%). There were 13 (20.6%) newly diagnosed patients, where the analysis of Gal-1 and CD163 was done before deciding on the method of treatment, 12 (19.04%) newly diagnosed ones with the onset of therapy while remission was achieved in 18 (28.57%) patients.

Analysis of the levels of sCD163 and Gal-1 within a group of patients suffering from cHL showed that the values of both molecules were higher in relapsed patients and the subgroup of patients with progressive disease, comparing to the subgroup of patients who were newly diagnosed or with therapy onset (Figure 2).
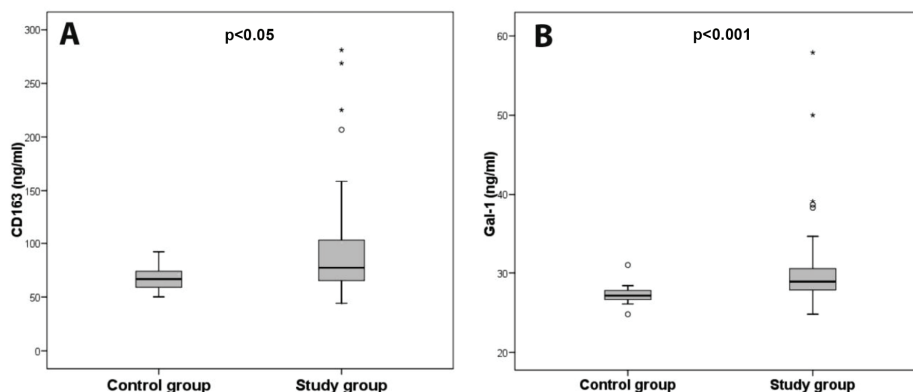

Fig. 1 – A)Values of serum sCD163 in the patients with classical Hodgkin lymphoma (cHL) and the control group; B) Values of Gal-1 in the patients with cHL and the control group. sCD163 – soluble CD163 molecule; Gal-1 – galectin-1.
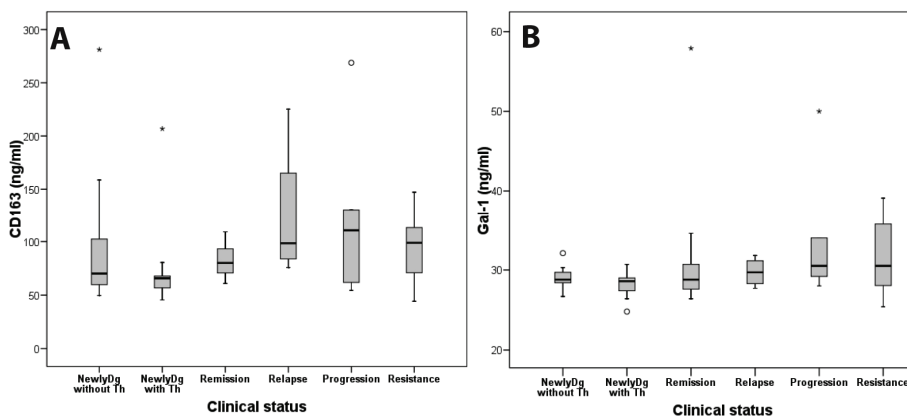

Fig. 2 – A) Values of serum sCD163 in relation to the clinical status of the patients with classical Hodgkin lymphoma (cHL); B) Values of serum Gal-1 in relation to the clinical status of the patients with cHL. sCD163 – soluble CD163 molecule; Gal-1 – galectin-1; Th – therapy.

Thus, in relation to the subgroup of patients with newly diagnosed cHL and therapy onset, the values of sCD163 of 98.50 ± 115.35 ng/mL were significantly higher in the subgroup of patients with relapsed cHL ($p < 0.05$). Comparing to the subgroup of newly diagnosed patients on therapy, sCD163 value was higher in the subgroup of patients who were in remission 80.10 ± 24.10 ng/mL ($p < 0.01$) (Figure 2).

By comparing the value of Gal-1 separately per clinical stages, the highest value of Gal-1 was found in the patients with progression of the disease 30.50 ± 13.40 ng/mL, followed by those with resistance 30.50 ± 10.30 ng/mL] while the lowest values were recorded with the newly diagnosed patients with therapy 28.60 ± 1.70 ng/mL. The values of Gal-1 in the serum were significantly higher in patients with disease progression and resistance ($p < 0.05$), as compared to the newly diagnosed patients with therapy (Figure2).

Although in the disease progression stage the values of sCD163 and Gal-1 were significantly higher than in the newly diagnosed patients with therapy, Kruskal-Wallis test did not show significant differences of their levels between defined clinical statuses. Also, the same test did not show a significant difference of sCD163/Gal-1 ratio between clinical statuses, but by comparing individual values of sCD163/ Gal-1 ratio in the period of treatment (2.32 ± 0.61) in relation to the phase of relapse (3.31 ± 3.98) and remission (2.63 ± 0.83), statistically significant differences were found ($p < 0.05$).

ROC analysis conducted between subgroups of patients according to clinical status showed very good sensitivity and specificity of parameter sCD163 and ratio of sCD163/Gal-1 between the subgroups of the newly diagnosed patients with therapy and the patients in remission as well as between the newly diagnosed patients with therapy and the patients in relapse.

It turned out that the limit values of 68.55 ng/mL of sCD163 can distinguish the patients in remission from the newly diagnosed patients with therapy with a sensitivity of 88.9% and specificity of 83.3%, AUC = 0.843, 95% CI = $0.67{-}1.03$, $p < 0.01$. The same analysis showed that the value of sCD163/Gal-1 ratio of 2.36 had a sensitivity of 77.8% and specificity of 75.0%, AUC = 0.772, 95% CI = $0.52{-}0.93$, $p < 0.05$. It turned out that the limit values of

72.00 ng/mL of sCD163 can distinguish the patients in relapse from the newly diagnosed patients with therapy with a sensitivity of 100.0% and specificity of 83.3%, AUC = 0.917, 95% CI = $0.77{-}1.06$, $p < 0.05$. The same analysis showed that the value of sCD163/Gal-1ratio of 2.42 had a sensitivity of 100.0% and specificity of 75.0%, AUC = 0.896, 95% CI = $0.73{-}1.06$, $p < 0.05$.

ROC analysis showed very good sensitivity and specificity of Gal-1 parameter between subgroups of newly diagnosed patients with therapy and patients with disease progression.

It turned out that the limit values of 29.15 ng/mL of Gal-1 can distinguish the patients with cHL proregression from the newly diagnosed patients with therapy with a sensitivity of 80.0% and specificity of 83.3%, AUC = 0.825, 95% CI = $0.60{-}1.05$, $p < 0.05$. Analysis of levels of Gal-1 and sCD163 depending on IPS in patients with cHL showed that their values were highest in cases where IPS = 3. Values of sCD163 at IPS = 3 were statistically significantly higher than IPS = 0, 1, and 4 ($p < 0.05$) as well as than IPS = 2 ($p < 0.01$). Values of Gal-1 at IPS = 3 were statistically significantly higher compared to IPS = 0 ($p < 0.01$) (Table 1).

It should be pointed out that score IPS = 5 was registered only in one patient that was also a newly diagnosed under therapy at the time of taking the biomarker sample which is why a comparison with other groups did not make sense (Table 1).

In order to highlight the difference among the patients based on Hasenclever and Diehl's scoring system, the subgroup with 37 low-risk patients with IPS 3 or less was formed, while 8 patients with IPS 4 and 5 scores were combined into a high-risk subgroup. Level of sCD163 in the group with IPS 0–3 amounted to 75.80 ± 48.70 ng/mL and in the group with IPS 4–5 to 69.60 ± 56.40 ng/mL. Values of Gal-1 in the group with IPS 0-3 amounted to 28.80 ± 2.70 ng/mL and in the group with IPS 4–5 to 29.35 ± 4.90 ng/mL. Comparing the value of sCD163 and Gal-1 among the combined groups did not point to statistically significant difference, although it was evident that the value of sCD163 was higher in the patients with IPS up to 3. The finding that the values of Gal-1 and sCD163 were the highest at IPS = 3, and then fell, can be explained by the fact that in all patients with IPS 4 and 5 therapy was applied.

Table 1

Values of serum sCD163 and Gal-1 in the patients diagnosed with classical Hodgkin lymphoma (cHL) compared to the value of International Prognostic Score (IPS)[6]

IPS score	Patients (number)	sCD163 (ng/mL)	Gal-1 (ng/mL)
0	8	67.25 25.90 (57.53–83.43)	28.05 2.18 (26.82–29.00)
1	5	75.80 37.10 (62.70–99.80)	28.80 4.75 (26.75–31.50)
2	17	66.50 51.00 (61.90–112.90)	28.70 2.45 (27.95–30.40)
3	7	158.70 [abd*c**] 163.70(105.10–268.80)	30.50[a**] 2.70(29.40–32.10)
4	7	77.30 65.70 (45.50–111.20)	29.50 6.00(27.30–33.30)
5	1	61.50	28.90

Values are given as medians (Me) and interquartile ranges (IQR, 25th–75th percentile); sCD163 – soluble CD163 molecule; Gal-1 – golectin-1; * – $p < 0.05$, ** – $p < 0.001$; a – vs IPS = 0, b – vs IPS = 1, c – vs IPS = 2, d – vs IPS = 4.

Values of serum sCD163 and Gal-1 in the classical Hodgkin lymphoma (cHL) patients in relation to applied therapeutic modalities

Therapy (Th) modalities	n	sCD163 (ng/mL)	Gal-1 (ng/mL)
One Th line	40	70.60	28.80
(ABVD or eBEACOPP as first line)		31.45(61.60–93.05)	2.75(27.52–30.27)
Two and more Th lines	23	91.90	29.50
(DHAP, ESHAP, ICE, Brentuximab)		41.00(70.20–111.20)	6.00(28.00–34.00)
Salvage Th, HDT and ASCT	15	100.70**	31.80**
		43.00 (80.80 – 123.80)	10.00(28.20–38.20)
Salvage Th	48	70.60	28.75
		31.45 (61.60–93.05)	2.67(27.60–30.27)

Values are given as medians (Me) and interquartile ranges (IQR, 25th–75th percentile).
** – $p < 0.01$ *vs* salvage Th.
sCD163 – soluble CD163 molecule; Gal-1 – galectin-1.
HDT– high dose chemotherapy; ASCT– autologous stem cell transplantation.
ABVD – adriamycin, bleomycin, vinblastine, dacarbazine; eBEACOPP – escalated doxorubicin, etoposide, cyclophosphamide, procarbazine, prednisone, vincristine, bleomycin; DHAP – dexamethasone, high-dose ara-c-cytarabine, platinum; ESHAP – etoposide, methylprednisolone, cytarabine & cisplatin.

Spearman's correlation coefficient for IPS and sCD163 amounted to 0.20, and for IPS and Gal-1 0.35, which shows that both markers correlate positively with IPS, but that only IPS and Gal-1 ($\rho = 0.35$, $p < 0.05$) had a statistically significant correlation of an average intensity. On the basis of the earlier identified elevated levels of sCD163 and Gal-1 in the patients with cHL and disease progression, further analysis focused on the relationship between their values based on the applied therapy. After the initial application of ABVD protocol in the treatment, relapse occurred in 4 patients, progression during treatment in 5 patients and primary refractory disease in 7 patients. Primary refractoriness to eBEACOPP was recorded only in two cases. DHAP protocol was administered as a second-line therapy in 13 patients, and most often continued after ABVD in 4 patients in relapse and two with progression during ABVD treatment. Etoposide, methylprednisolone, cytarabine & cisplatin (ESHAP) protocol was in the second line of treatment given to one patient. The largest number of transplant patients was from the group of 9 primarily refractory patients, 3 patients were in relapse, and only one patient had disease progression.

It was observed that in the patients who received two or more therapeutic modalities, values of sCD163 and Gal-1 were elevated, but not statistically significantly, compared to the patients with one line of treatment (Table 2). Values of sCD163 and Gal-1 were higher in the patients who underwent transplantation than in those who did not, at the level of statistical significance of $p < 0.05$ (Table 2). The value of Gal-1 and sCD163 was measured after transplantation.

Transplantation was not applied in all patients because of the lack of complete and/or partial remission (CR/PR), chemosensitive relapse (CSR), and chemoresistant disease (HD).

Discussion

The basis of this study is the importance of Gal-1 and sCD163 to identify patients with cHL compared to reactive states as well as their significance in the assessment of the disease phase of patients. There is unequivocal evidence of the links of both Gal-1 and sCD163 with the processes of immune suppression in cHL.

M2a-type macrophages are the most common in advanced tumor stages, which is associated with the progression of malignant disease and correlates with primary and secondary failure of therapy [7, 8].

Presence of M2 macrophages correlates with levels of sCD163, making this protein considered to be their reliable serum marker [9]. Antiinflammatory function of M2 macrophages is reflected in the secretion of immunosuppressive cytokines (transforming growth factor-β), transforming growth factor beta (TGF-β1), and IL-10, which further induce T helper cells type 2 (Th2) differentiation, favoring the development of T-regulatory (Treg) lymphocytes promoting the growth of tumors by inhibition of anti-tumor immune response [10].

The findings of high levels of sCD163 primarily in the patients with disease progression as well as in relapse phase, where these levels were statistically significantly higher compared to patients whose treatment has just begun is in line with the information referred to above. These results support the impact of immunosuppression on the deterioration of the clinical course of the disease in cHL patients, which can be observed through a high level of sCD163 in the patients who were treated with a large number of chemotherapy lines and in the subgroup of patients undergoing transplantation.

The lowest values of sCD163 among the investigated cases were recorded in the subgroup of newly diagnosed patients who started chemotherapy. A possible explanation of these findings lies in the fact that chemotherapy, together with the elimination of malignant cells, modifies the population of infiltrating cells in HL by killing Treg lymphocytes and monocytes of type M2, thus reducing tumor immunosuppression [9, 11].

Galectin-1 belongs to a group of proteins with an affinity for binding carbohydrates which is in large quantities produced by HRS cells. Immunosuppressive function of Gal-

1 is reflected in the inhibition of secretion of IL-2, interferon-γ [IFN-γ and tumor necrosis factor α (TNFα)] with the induction of the immunosuppressive IL-10 creation. Furthermore, it selectively kills Th17 cells, influences the polarization of Th1 response in the direction of Th2 response, by initiating Th1 cell apoptosis [10]. Therefore, Gal-1 is considered to be an indicator of immunosuppression, caused by the malignant HRS cells and the indicator of absence of Th1 anti-tumor immune response [12].

Clinical studies have shown that elevated Gal-1 is associated with a shorter period and leads to progression in patients with cHL [13].

Findings regarding our patients are in line with literature data, because the values of Gal-1 were significantly higher in subgroups of relapsing, refractory patients who had to receive more therapeutic lines and undergo autologous hematopoietic stem cell transplantation.

Low levels of Gal-1 in the patients with chemotherapy in our study are most likely the result of reduction in the HRS cells under the influence of therapy. Such a drop in the level of Gal-1 during treatment compared to the level before therapy is recorded in the work of Plattel et al. [14].

However, the values of Gal-1 and sCD163 can also be elevated to normal cells and grow with age [15]. These findings may partly explain the high levels of these molecules in healthy volunteers who made up the control group in this study. Our study has for the first time identified limit values by which it is possible to reliably distinguish reactive states from the active form of cHL.

Over the past decade, a large number of prognostic systems have been developed in order to identify high-risk patients with HL. Despite some shortcomings, IPS is today still used in risk stratification at the initial presentation of advanced stages of HL [6]. However, this system does not contain markers that accurately reflect the state of immuno-suppression and tumor microenvironment that play a significant role in the evolution and prognosis of HL. By comparing the levels of sCD163 and Gal-1 with the IPS system scores in our study, two important findings were obtained. In spite of the influence of the administered therapy, it was found that the levels of sCD163 and Gal-1 correlated with the IPS score, but that only IPS and Gal-1, had statistically significant correlation of an average intensity.

These findings open up the possibility of correction of IPS system by incorporating these simple serum molecules, which could eliminate its shortcomings, especially in the domain of R/R forms of cHL.

Conclusion

The values of Gal-1 > 28.45 ng/mL and levels of sCD163 > 78.45 ng/mL exclude reactive states and they can be considered as reliable values found in variants of cHL.

High values of sCD163 and Gal-1 are characteristics of the patients with relapsing and/or refractory variant of cHL, requiring the use of salvage chemotherapy with high-dose chemotherapy and hematopoietic stem cell transplantation, while serum concentrations of these proteins were the lowest during chemotherapy in the newly diagnosed patients.

Applied therapy in the patients with cHL affects the values of Gal-1 and CD163, but research has pointed to a positive correlation among IPS score and values of CD163 and Gal-1 which is statistically significant in the case of Gal-1 and IPS score relationship.

Determination of Gal-1 and sCD163 levels is simple and reliable analysis that can contribute to the identification of high-risk patients with cHL and deserves inclusion in current prognostic scoring systems.

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