Increased Serum Soluble CD23 and Soluble IL-2R Levels in Haematologic Malignancies

Ayþen TÝMURAÐAOÐLU, Ýhsan KARADOÐAN, C. ERDOÐAN, Levent ÜNDAR

Department of Haematology, Akdeniz University School of Medicine, Ankara, TURKEY

ABSTRACT

Serum soluble CD23 (sCD23) and soluble IL-2 receptor (sIL-2R) levels increase not only in disorders with immune system activation, but also in hematological malignancies. They have been used as markers of disease progression and/or the response to therapy in lymphoproliferative disorders (LPD). In this study, we investigated the serum sCD23 and sIL-2R levels of 21 patients with different hematological malignancies [10 LPD, 6 multiple myeloma (MM), and 5 myelodysplastic syndrome (MDS)] before treatment, and compared them with 19 age- and sex- matched healthy subjects. Median sIL-2R levels were found to be significantly elevated in both the overall patient group and each of the subgroups. Median sCD23 levels were significantly higher in the overall patient group and in patients with LPD and MM. A positive correlation was found between sIL-2R and sCD23 levels in LPD. Our preliminary findings suggest that elevated serum levels of these soluble factors are not only markers of LPD but might be also used for other hematologic malignancies, except for MDS. Further studies should be designed to find out if it might be the result of an overactive immune system or not.

Key Words: IL-2R, sCD23, Lymphoproliferative disease, MDS, MM.

Turk J Haematol 1999;16(4):167-169.

INTRODUCTION

Interleukin-2 receptors (IL-2R) are expressed on activated T cells, B cells, and monocytes and its soluble form (sIL-2R) has been known as a T-cell activation marker[1]. Soluble CD23 (sCD23) is another cytokine released from B and T lymphocytes, which has differentiating and proliferating effects on a variety of hemopoietic cells[2]. Serum sCD23 and sIL-2R levels are increased, not only in disorders with immune system activation[3], but also in lymphoproliferative disorders (LPD) [2,4]. They have been used as markers of therapy response and/or disease progression in LPD[5,6].

The objective of this study was to determine the serum sCD23 and sIL-2R levels of patients with different hematological malignancies before treatment, and to compare them with healthy subjects.

MATERIALS and METHODS

Study Population

Twenty one patients, [10 female, 11 male, with a median age of 50 years (range 30-78)], were included in the study. Ten of them had chronic lymphocytic leukemia, Hodgkin's and non-Hodgkin's lymphoma (group I); six patients had multiple myeloma (MM) (group II); and five patients had myelodysplastic syndrome (MDS) (group III). The control group consisted of 19 healthy subjects [9 female, 10 male, median age 43 years (range 30-58)]. All subjects gave their informed consent to participate in the study.

Blood Collection and Methods

The blood samples of the patients were collected at the time of diagnosis, and, at the same time of day, centrifuged at 2500 g at 4°C for 15 minutes. Serum aliquots were stored at -70°C until analysis.

Serum levels of sIL-2R (sIL-2R Immunoenzymometric Assay Kit, Immunotech S.A., France) and sCD23 (Bindazyme™ soluble CD23 EIA Kit MK112, Birmingham, U.K.) were measured by using commercial EIA kits. All determinations were performed in duplicate. Plasma samples of patients and healthy subjects were analyzed in the same run.

Statistical Analysis

Comparisons were performed by the Mann Whitney's Rank-Sum Test "U". A p value below 0.05 was considered significant. Correlation's were examined by using Spearman's Rank Correlation Coefficient.

RESULTS

Median sIL-2R and sCD23 were significantly higher in the overall patient group than in the healthy subjects ($p < 0.0001$ and $p = 0.002$ respectively), and no correlation was found between sIL-2R and sCD23 levels in these groups.

Median sIL-2R levels of each patient group were found to be significantly higher than that of the healthy subjects ($p < 0.001$), but median sCD23 levels were significantly higher in only group I and II ($p = 0.007$ and $p = 0.002$ respectively). Neither sIL-2R nor sCD23 levels showed any difference between each patient group ($p > 0.05$). There was a correlation between sIL-2R and sCD23 levels in only group I ($p = 0.048$, $r = 0.63$). Results are given in Table 1.

DISCUSSION

Increased serum levels of sIL-2R and sCD23 have been documented in LPD, autoimmune disorders, and renal allograft recipients, especially in a rejection episode[7]. The correlation between the disease activity and sIL-2R levels in Hodgkin's and non-Hodgkin's lymphoma, has been previously documented[5,8]. High levels of sIL-2R were also found in chronic myelogenous leukemia in blastic transformation[9] and in high risk MDS patients, with refractory anemia with excess blast, refractory anemia with excess blast in transformation, and chronic myelomonocytic leukemia[10]. Similarly, serum sCD23 levels reflect disease activity in B-cell CLL[6].

In the present study, the overall patient group and each group showed high serum sIL-2R levels which were consistent with previous studies, and these results suggest that the elevation of serum sIL-2R levels are not specific to LPD. Although serum sCD23 levels were found to be increased in the overall patient group, group I and group II,

Table 1. Serum sCD23 and sIL-2R levels in patients and control group

	Overall patient group (n = 21)	Group I (n = 10)	Group II (n = 6)	Group III (n = 5)	Control group (n = 19)
sCD23(g/L) median (range)	10.1 (0-21.2)*	10.6 (0-21.2)*	10.5 (5.6-16.4)*	3.0 (2.3-8.4)**	5.1 (0-8.7)
sIL-2R (pM) median (range)	180.5 (42-423)*	153.5 (42-423)*	246 (84-316)*	134 (79-362)*	60 (28.5-100)

*p 0.002 **p > 0.05

it was found to be lower in MDS patients in this study; but it was not significant. Low levels of sCD23 in MDS patients might be due to the heterogeneity of MDS and the small number of patients included in the study. Klouche and his colleagues reported low levels of sCD23 in Ig G MM patients[11]; myeloma patients did not express the same immunoglobulin in our study and this might be the cause for the different results. Since serum sCD23 and sIL-2R levels correlated with each other only in LPD ($p = 0.048$, $r = 0.63$), it might be suggested that elevated serum levels of these cytokines were dependent upon each other in LPD. Increased serum levels and a positive correlation between sIL-2R and sCD23 in LPD may be due to the high tumor burden which expresses these receptors and releases them.

Since IL-2R and CD23 are mostly expressed on activated T cells and B cells, and they have a differentiating and proliferating effect on a variety of hemopoietic cell lines, including T and B cells, high serum levels of these receptors in a variety of hematological malignancies may be due to excessive immune response against malignant cells. But soluble forms of IL-2R are capable of binding; IL-2[12] and sCD23 have multifunctional effects and sustain the growth of hemopoietic cells[13]; therefore, increased levels of these soluble receptors may cause disease progression by preventing the immunoregulatory effects of IL-2 and promoting the growth of malignant cells. Further investigations are required to disclose the mechanisms of elevation and the effects of increased serum levels of these soluble factors in a variety of hematological malignancies.

REFERENCES

1. Rubin LA, Nelson DL. The soluble interleukin-2 receptor: Biology, function, and clinical application. Ann Intern Med 1990;113:619-27.
2. Sarfati M, Fournier S, Wu CY, Delespesse G. Expression, regulation and function of human Fc RIII (CD23) antigen. Immunol Res 1992;11:260-72.
3. Bansal AS, Ollier W, Marsh MN, Pumphrey RSH, Wilson PB. Variations in serum CD23 in conditions with either enhanced humoral or cell- mediated immunity. Immunology 1993;79:285-9.
4. Pavlidis NA, Manoussaki MN, Germanidis GS, Moutsopoulos HM. Serum soluble interleukin-2 receptors in B-cell lymphoproliferative malignancies. Medic Pediatr Oncol 1992;20:26-31.
5. Ambrosetti A, Nadali G, Vinante F, Carlini S, Veneri D, Todeschini G, Morosato I. Serum levels of soluble interleukin-2 receptor in Hodgkin's Disease. Cancer 1993;72:201-6.
6. Reinisch M, Willheim M, Hilgarth M, Gasche C, Mader R, Szepfalusi S, Steger G, Berger R, Lechner K, Nitulescu BG, Schwarzmeier JD. Soluble CD23 reliably reflects disease activity in B-cell chronic lymphocytic leukemia. J Clin Oncol 1994;12:2146-52.
7. Beksaç M, Dalva K, Gönenç F, Dalva I, Garibo¤lu S, Batur N, Çetin S. Soluble CD23 and interleukin-2 receptor levels in renal allograft recipients. Transplant Proc 1993;25:2145-7.
8. Stasi R, Conforti M, Poeta DG, Simone DM, Coppetelli U, Tribalto M, Cantonetti M, Perrotti A, Vendetti A, Papa G. Soluble factor levels in the initial staging of high-grade non Hodgkin's lymphomas. Haematologia 1992;77:518-21.
9. Motoi T, Uchiyama T, Hori T, Itoh K, Uchino H, Ueda R. Elevated serum soluble interleukin-2 receptor (Tac Antigen) levels in chronic myelogenous leukemia patients with blastic crisis. Blood 1989;74: 1052-7.
10. Zwierzina H, Herold M, Schöllenberger S, Geissler D, Schmalzl F. Detection of soluble IL-2 receptor in the serum of patients with myelodysplastic syndromes: induction under therapy with GM-CSF. Br j Haematol 1991;79:438-43.
11. Klouche M, Wilhelm D, Kirchner H. Cytokines, immunoglobulins, and IgG subclasses in patients with IgG plasmacytomas. Immun Infekt 1994;22:149-51.
12. Rubin L, Kurman C, Frtz M, Biddison W, Boutin B, Yarchoan R, Nelson D. Soluble interleukin 2 reseptors are released from activated human lymphoid cells in vitro. J Immunol 1985;135:3172-7.
13. White LJ, Ozanne BW, Graber P, Aubry Jp, Bonnefoy JY, Cushley W. Inhibition of apoptosis in human pre-B cell line by CD23 is mediated via a novel receptor. Blood 1997;99:234-43.

Address for Correspondence:

Ayþen TÝMURAÐAOÐLU MD

Akdeniz University, School of Medicine
07070, Antalya, TURKEY