Short Communication

Soluble CD23 in multiple myelomas and related diseases

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ABSTRACT

The serum levels of soluble CD23 (sCD23) were examined in patients with multiple myelomas and related diseases and were compared with levels of sCD23 in healthy, age- and sex-matched controls. The mean levels (95% confidence intervals) of sCD23 in the sera of 40 patients with multiple myelomas, nine patients with myeloma-related diseases (seven primary macroglobulinemia and two chronic lymphatic leukemia) and 30 matched controls were 2.7 (1.9–3.8), 9.9 (5.1–19.2) and 1.5 (1.3–1.7) ng/mL, respectively, showing a significant increase in sCD23 in the circulation of patients with myelomas (P<0.01) and myeloma-related diseases (P<0.001). The potential biologic importance of sCD23 in myelomas and related diseases is discussed.

Key words: interleukin-1α, multiple myelomas, soluble CD23.

INTRODUCTION

CD23, a low-affinity Fce receptor for IgE (FceRII), is found on a variety of human and rodent cells. The role of CD23/FceRII and its soluble products (sCD23; IgE-binding factors) in immunomodulatory functions has been the subject of many recent studies.1-6 It is now recognized that sCD23 has importance in IgE regulation1,2 and that CD23 may influence both antigen presentation to T cells and the differentiation of B cells into immunoglobulin-secreting cells.3 The biological activity of both intact CD23 and/or degradation products (sCD23) appears to extend beyond mere B cell differentiation and may play a role in B cell proliferation and survival.4

An increase in the serum concentration of sCD23 occurs in conditions associated with abnormalities of immunoglobulin production (e.g. autoimmune conditions associated with polyclonal hypergammaglobulinemia, B-chronic lymphatic leukemia and following bone marrow transplantation).5 In view of these findings, in the present study we examined the serum levels of sCD23 in patients with multiple myelomas and related diseases, which may facilitate the understanding of the in vivo activity of sCD23 in humans.

METHODS

Subjects

Forty patients with multiple myelomas, seven with primary macroglobulinemia and two with chronic lymphatic leukemia (age range 28–85 years; M:F = 27:21) were included in the present study. The myeloma patients included three patients with the non-secretory type, two patients with the Bence-Jones type, two with the IgD type, six with the IgA type, 26 with the IgG type and one with the IgA+IgG type. These diagnoses were based on clinical and pathological criteria. Sera were obtained from patients prior to radiotherapy or chemotherapy was initiated and serum samples were stored at −70°C until analyzed. Samples were also obtained from 30 healthy, age- and sex-matched volunteers who served as controls.
Measurement of sCD23, interleukin-1α, IgE, IgG, IgA and IgM

The levels of sCD23 in the sera and culture supernatants were determined as described previously with an ELISA kit (sCD23 enzyme immunoassay (EIA) NICHIRAY; Nichiray, Tokyo, Japan). This kit includes two non-competing monoclonal anti-human CD23 antibodies. Serum interleukin (IL)-1α levels were assessed with the Endogen Human IL-1α ELISA kit (Endogen, Boston, MA, USA). Serum IgE was measured with an IgE EIA kit (MITSUI II; Mitsui-Seiyaku, Tokyo, Japan). Serum samples from patients and controls were mixed on each plate so as to minimize the effects of interplate variability. All samples were coded and were read blind in these assays. Absorbance was measured with an EIA Reader (Model 2550; Bio-Rad, Richmond, CA, USA). Serum IgG, IgA and IgM were determined with a Behring Nephelometer (Behring, Marburg, Germany) according to the manufacturer’s instructions.

Statistical analysis

The data for sCD23 and IgE were logarithmically transformed before statistical analysis and were expressed as geometric means (GM) and 95% confidence intervals (CI). Group means were compared by means of the Student’s paired t-test.

RESULTS

Figure 1 shows the serum levels of sCD23 in patients with multiple myelomas and related diseases (GM (95% CI): 3.2 (2.2–4.5) ng/mL; n = 49) and the results were almost double when compared with those in healthy, age- and sex-matched controls (GM (95% CI): 1.5 (1.3–1.7) ng/mL; n = 30), the difference being statistically significant (P < 0.01). Such an increase was observed in most patients, including ones with chronic lymphatic leukemia, primary macroglobulinemia, non-secretory type myelomas, Bence-Jones type myelomas, IgD type myelomas and IgG type myelomas, the GM of sCD23 levels in these patient groups being 8.2, 10.3, 5.5, 7.4, 7.9 and 2.5 ng/mL, respectively. The serum levels of sCD23 did not differ statistically between patients with IgA type myelomas and controls. Consequently, 12 of 49 patients and none of 30 controls exhibited serum levels of sCD23 >5 ng/mL. The mean (95% CI) IL-1α concentration in sera from patients was 23 (3–49) pg/mL.

In contrast to the results obtained for sCD23, the serum levels of IgE were significantly decreased in patients with multiple myelomas and related diseases (GM (95% CI): 24 (17–34) IU/mL; n = 49), when compared with levels in controls (GM (95% CI): 107 (69–166) IU/mL; n = 30; P < 0.001). As shown in Fig. 2, such a decrease was observed in patients with primary...
macroglobulinemia, non-secretory type myelomas, IgA type myelomas and IgG type myelomas, the GM of the IgE levels in these patients being 20, 10, 23 and 23 IU/mL, respectively. Decreased serum levels of other types of immunoglobulins were also observed in patients with primary macroglobulinemia and patients with all types of multiple myeloma compared with controls, with the exception of serum levels of IgM in a patient with IgA + IgG type myeloma (Table 1).

**DISCUSSION**

Mean serum levels of sCD23 have been shown to be elevated in a variety of disease states. With regard to patients with multiple myelomas, the results of the present study agree with the preliminary findings reported by Sarfati and co-workers. Beguin et al. have also studied the serum sCD23 levels and have reported no increase in patients with multiple myelomas; however, the results in myeloma patients in the study of Beguin et al. showed a large standard deviation when compared with results from normal individuals (1.1±1.4 vs 0.9±0.4 u/mL, mean ± standard deviation). As shown in Fig. 1, the serum levels of sCD23 were not statistically different between patients with IgA type myelomas and controls; however, the analysis with regard to this was lacking in the report of Beguin et al.

As serum sCD23 levels have been reported to be related to peripheral blood B cell counts in immunodeficient patients with hypogammaglobulinemia and...
varying B cell numbers, the increased sCD23 levels in our patients with multiple myelomas and related diseases seemed to be due to cells of a B cell origin. The expression of CD23 on cells is closely associated with natural killer (NK) cell function and strong NK cell activity has been reported in patients with multiple myelomas. Alternatively, these lines of evidence may also be related to the elevation of sCD23 seen in myeloma patients.

The observation by Liu et al. that a high dose of 25 kDa sCD23 of more than 5 ng/mL protected germinal center B cells from apoptosis in the presence of 5 U/mL of IL-1α is quite interesting. The mean concentration of IL-1α in the patients in the present study (23 pg/mL) approximately corresponds to 5 U/mL according to the manufacturers of the human IL-1α ELISA kit. The serum level of sCD23 was less than 5 ng/mL in most patients; however, whether the large amounts of sCD23 that accumulate around cells of a B cell origin can influence myeloma and related cells remains open to discussion.

In a previous study on sCD23 focusing on childhood atopy with high IgE levels, we demonstrated a wide deviation and overlapping of sCD23 levels with those in non-atopic controls. However, a difference in the molecular weight pattern of sCD23 in atopic and non-atopic sera has been reported and a dose-dependent inhibitory effect of 16 kDa sCD23 was demonstrated in an in vitro IgE production assay using B cells from patients with chronic lymphocytic leukemia. Because most patients with multiple myelomas and related diseases were hypogammaglobulinemic and had low serum IgE levels, the correlation between serum IgE and sCD23 was difficult to interpret. A study on the serum size profile of increased sCD23 may help to clarify the biologic role of sCD23 in patients with multiple myelomas and related diseases.

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REFERENCES