Acta Medica Okayama

Volume 48, *Issue* 4 1994 *Article* 8

AUGUST 1994

Clinical value of soluble interleukin-2 receptor in infectious complications.

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Abstract

In this study, we investigated serum-soluble interleukin-2 receptor (sIL-2r) and neopterin (NPT) levels in five patients with severe postoperative infections. A total of 25 synchronous determinations of sIL-2r and NPT were performed. A marked increase in sIL-2r and NPT levels was observed, and the increase in sIL-2r was significantly correlated to that of NPT which is a marker of macrophage activity. These results suggest that macrophages are involved in the stimulation of sIL-2r release, representing a potentially negative biological effect. The results indicate that sIL-2r may be a useful indicator of the efficacy of antibiotics and of prognosis.

KEYWORDS: soluble interleukin-2 receptor, neopterin, intection

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*PMID: 7817778 [PubMed - indexed for MEDLINE]

ACTA MED OKAYAMA 1994; 48(4): 225-226

— Brief Note —

Clinical Value of Soluble Interleukin-2 Receptor in Infectious Complications

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In this study, we investigated serum-soluble interleukin-2 receptor (sIL-2r) and neopterin (NPT) levels in five patients with severe postoperative infections. A total of 25 synchronous determinations of sIL-2r and NPT were performed. A marked increase in sIL-2r and NPT levels was observed, and the increase in sIL-2r was significantly correlated to that of NPT which is a marker of macrophage activity. These results suggest that macrophages are involved in the stimulation of sIL-2r release, representing a potentially negative biological effect. The results indicate that sIL-2r may be a useful indicator of the efficacy of antibiotics and of prognosis.

Key words: soluble interleukin-2 receptor, neopterin, infection

Macrophages have been shown to play an important role in the immunosuppression associated with infectious complications. *In vitro* results have demonstrated that macrophages are involved in the stimulation of soluble interleukin-2 receptor (sIL-2r) release from activated T-lymphocytes (1). sIL-2r binds with IL-2, thus making less available for binding with IL-2 cell surface receptors (2). However, the biological significance of the increase of sIL-2r is still obscure. Because of the documented role of macrophages in the *in vitro* release of sIL-2r (1), a study was conducted to investigate the relationship between sIL-2r and macrophage activity in patients with severe infections. The macrophage activity was indirectly evaluated using neopterin (NPT), a specific marker of macrophage functions (3, 4).

Patients and Methods

The study included five consecutive patients affected by severe postoperative infectious complications (four men and one women, median age 71 years, range 61-76 years). All the patients were transferred to the intensive care unit (ICU) due to severe pneumonia and peritonitis. Venous blood samples were collected at 8:00 a.m. on 5 consecutive days. No patient was undergoing therapy with steroids and/or other drugs concomitantly which may affect the immune system. In each sample, serum levels of sIL-2r and NPT were simultaneously determined. sIL-2r concentrations were measured with an enzyme immunoassay, using commercially available kits (T Cell Sciences, Cambridge, MA, USA) (1). Serum levels of NPT were detected with high-pressure liquid chromatography (HPLC) (5). The normal levels obtained in our laboratory were: sIL-2r, < 480 U/ml; NPT, $<$ 2.5 pmol/ml. Data are reported as the mean (S.D.), and statistical analysis of variance and determination of the correlation coefficient were determined as appropriate.

Results and Discussion

Table 1 shows that abnormally high serum levels of sIL-2r and of NPT were seen in all five patients and in all 25 determinations. The mechanisms responsible for the increase in sIL-2r in infections need to be further investigated. The results of this study, by showing a positive correlation between sIL-2r and NPT, an indicator of macrophage activity, suggest that sIL-2r release may be at least in part modulated by an enhanced macrophage function. Therefore, this study confirmed *in*

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Table I Serum soluble interleukin-2 receptors (sIL-2r) and neopterin (NPT) levels in patients with severe postoperative infections

Case	Age	(sex)	N	sIL-2r (U/ml)			NPT (pmol/ml)			Coefficient value
				Min.	Max.	Mean ± SD	Min.	Max.	Mean ± SD	
A	61	(M)	5	1680	2690	1996 ± 437	27	39	32.6 ± 5.4	0.863 ($p < 0.060$)
B	69	(F)	5	1660	2510	2020 ± 340	20	50	34.4 ± 12.0	0.984 ($p < 0.003$)
C	76	(M)	5	1750	1980	1860 ± 103	34	46	38.6 ± 4.7.	0.918 ($p < 0.028$)
D	73	(M)	5	1910	5640	3630 ± 1712	86	280	200.6 ± 81.3	0.871 ($p < 0.055$)
E	71	(M)	5	6820	39000	23404 ± 13157	278	1263	733.0 ± 391.7	0.990 ($p < 0.001$)

Abbreviation: N, number of determinations; *p.* probability; Min. minimai; Max, maxinal. Coefficient values of correlation were obtained by simple regression analysis between sIL-2r and NPT levels.

vivo that macrophages influence sIL-2r release from lymphocytes into the blood, as previously demonstrated *in vitro* by Nelson *et al.* (1).

sIL-2r are released by activated normal peripheral blood mononuclear cells and some T- and B-cell lines (6). The details of sIL-2r release and its biological significance are not yet clearly understood, and in particular it has not been established whether the enhanced secretion of sIL-2r simply reflects lymphocyte activation or whether it is due to alterations of IL-2 cell surface receptor expression. There are different theories regarding the mechanism of the release of sIL-2r including: (a) that sIL-2r is produced by alternate mRNA splicing of the IL-2r transcription product, (b) that it is derived by proteolytic cleavage of IL-2r, and (c) that it is coded by a different gene than IL-2 (7).

A concomitant increase in both sIL-2r and NPT blood levels and the corresponding negative prognosis have been described in association with immunodeficiencies such as AIDS (8). If the hypothesis that macrophages are involved in the stimulation of sIL-2r release from activated lymphocytes is true (1), inhibition of macrophages could improve the prognosis in immunosuppressed patients as well as in severe infectious complications. The stimulation of sIL-2r release might represent one of the possible mechanisms through which macrophages suppress IL-2-dependent functions. However, even though sIL-2r have been proven to bind IL-2, it remains to be demonstrated that the increase in sIL-2r levels actually reduces IL-2 availability to IL-2 cell surface receptors on lymphocytes (2).

Previous investigations also show an elevation of sIL-2r serum levels during graft rejection (9). This suggests that an elevation of sIL-2r possesses high sensitivity but no relevant specificity, and that T-cell activation is not restricted to rejection and viral infection but also may be involved in general inflammatory responses to bacterial infection. The present research also demonstrated that elevated sIL-2r showed a continuous decline during effective therapeutic antibiotic treatment. This decline in sIL-2r could reflect a reduction of lymphocyte activity in the more advanced stages of disease. Therefore, blood levels of sIL-2r could assess the efficacy of antibiotics and predict the prognosis of the patient.

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Received March 28, 1994; accepted May 9, 1994.