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Serum Soluble Interleukin 2 Receptor in Patients with IgA Nephropathy

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ABSTRACT

Serum soluble interleukin 2 receptor (IL-2 R) was determined by the ELISA method in 29 cases of IgA nephropathy and 50 healthy controls. The results showed that the value in IgA nephropathy cases was significantly higher than that in healthy controls. Furthermore, among the cases of IgA nephropathy, the value was significantly higher in the groups with hypertension, elevated serum IgA and depressed creatinine clearance than in that of the corresponding controls. These findings suggest that serum soluble IL-2 R can serve as a prognostic index of IgA nephropathy.

Key words: *Soluble interleukin 2 receptor, IgA nephropathy, ELISA method, Prognostic index*

It is generally assumed that cellular immunity is involved in the development, progression and exacerbation of IgA nephropathy and that lymphokine also plays an important role. Interleukin 2 (IL-2) is known to be a lymphokine, necessary for the proliferation of T cells and its action is induced by binding with a specific cell surface receptor, that is, IL-2 R[9-12]. This IL-2 R is induced and appears on activation of T cells. Determination of serum soluble IL-2 R has recently become possible and a report has been published on its behavior in renal diseases[2]. Much, however, remains to be elucidated with regard to glomerulonephritis. We therefore studied the behavior of serum soluble IL-2 R in other renal diseases, particularly in IgA nephropathy.

SUBJECTS AND METHODS

The subjects were 29 cases of IgA nephropathy, 12 males and 17 females with ages ranging from 18 to 65 years (mean 31.9 ± 12.1 years). The controls were 50 healthy individuals, 31 males and 19 females aged 24 to 52 years (mean 32.4 ± 5.9 years). Serum soluble IL-2 R was determined by using the Cellfree IL-2 R test kit manufactured by T Cell Sciences. This is a sandwich enzyme immunoassay containing two kinds of monoclonal antibodies against different epitopes (Tac epitope and non Tac epitope) on P-55 IL-2 R. Student t-test was employed in the analysis of data.

RESULTS

The value of serum soluble IL-2 R was 381.0 ± 157.8 U/ml in IgA nephropathy cases and 157.4 ± 46.5 U/ml in healthy controls, demonstrating that the value was significantly higher in IgA nephropathy cases than that of the controls ($p<0.001$) (Fig. 1).

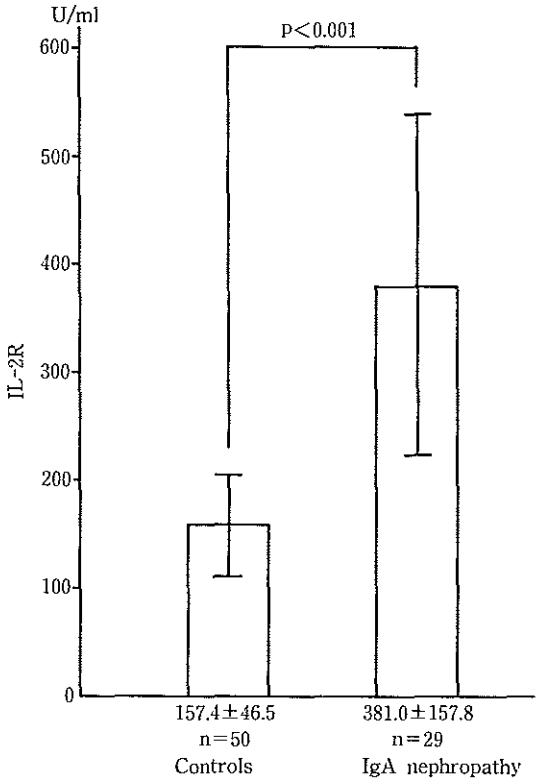

Fig. 1. Serum IL-2 R levels in IgA nephropathy patients and healthy controls
A significant increase was observed in IL-2 R level in IgA nephropathy patients than in healthy controls.

Table 1. Relationship between serum IL-2 R and clinical findings in IgA nephropathy patients

		IL-2R (U/ml)	P Value
Blood pressure	High	527.4 ± 218.9	$p<0.01$
	Normal	334.5 ± 100.6	
Daily urinary protein (g/day)	≧1.0	440.3 ± 236.3	N.S.
	<1.0	354.4 ± 103.8	
Hematuria (/HPF)	≧10	357.7 ± 165.9	N.S.
	<10	395.3 ± 155.8	
Serum IgA (mg/dl)	≧350	451.3 ± 196.9	$p<0.05$
	<350	331.5 ± 103.2	
Creatinine clearance (ml/min)	≧80	318.7 ± 95.1	$p<0.01$
	<80	499.5 ± 188.7	
Mesangial proliferation	Mild	322.5 ± 108.2	N.S.
	Moderate, High	422.4 ± 176.5	($p<0.1$)

IgA nephropathy patients in which recognized hypertension, high serum IgA level, decreased creatinine clearance had a significantly increased IL-2 R level than in those with corresponding normal levels.

In order to examine the clinical significnance of the high value of serum soluble IL-2 R in IgA nephropathy, a comparative study of clinical findings was carried out (Table 1). In the group accompanied only by hypertension, serum soluble IL-2 R was 527.4 ± 218.9 U/ml which is significantly higher than 334.5 ± 100.6 U/ml observed in the group with normotension ($p<0.01$). A classification was made between the cases with daily total urinaly protein of 1.0 g or more and those less than 1.0 g. However, there was no significant difference between the two groups. Similarly, for hematuria, cases were classified into those with 10 or more cells per hypervisual field and those less than 10 cells, but no significant difference was found between the two groups. The cases were classified into those with serum IgA value of 350 mg/dl or more and those less than 350 mg/dl. The value of serum soluble IL-2 R in the group with serum IgA of 350 mg/dl or more was significantly higher than that of the group with serum IgA of less than 350 mg/dl (451.3 ± 196.9 U/ml, 331.5 ± 103.2 U/ml, respectively, $p<0.05$). Regarding creatinine clearance (Ccr) and grade of histological damage, it was found that serum soluble IL-2 R of the depressed Ccr group of less than 80 ml/min was also significantly higher than that of the normal group with Ccr level 80 ml/min or more (499.5 ± 188.7 U/ml, 318.7 ± 95.1 U/ml, respectively, $p<0.01$). The grade of histological damage was evaluated on the proliferation level of mesangial matrix. Serum soluble IL-2 R in the group whose proliferation level was moderate or more was higher than that of the group with a low proliferation level (422.4 ± 176.5 U/ml, 322.5 ± 108.2 U/ml, respectively, N.S).

DISCUSSION

It is well known that serum soluble IL-2 R increases in T cell leukemia, malignant lymphoma, AIDS, and others[6,8]. Among the renal diseases, its increase has been reported in chronic renal failure and in rejection following renal transplantation[2]. So far, there has been no report of its behavior in IgA nephropathy. We studied, therefore, the behavior of serum soluble IL-2 R in IgA nephropathy. The results showed that the level of serum soluble IL-2 R in IgA nephropathy was significantly higher than that of healthy controls. Furthermore, it was significantly higher in the hypertensive group, elevated IgA group, and depressed Ccr group than that of the normal group. It also seemed to be higher in the group with moderate to high proliferation of mesangial matrix than that of the group with mild proliferation.

As for the etiology of elevated serum soluble IL-2 R in IgA nephropathy, it is still uncertain whether this is attributable to accelerated production in peripheral blood mononuclear cells or whether it is simply due to decreased excretion from the kidneys. Here, it is worth mentioning that Tac (CD 25)$^+$ lymphocyte may be measured to determine the above etiology. However, hypertension, elevated IgA value, depressed Ccr, and proliferation of mesangial matrix have been reported earlier as factors related to progression and exacerbation of IgA nephropathy[1,3,4,5,7]. The demonstration of a significant relationship of these factors to serum soluble IL-2 R suggests that serum soluble IL-2 R may be an index in the progression and exacerbation of IgA nephropathy.

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REFERENCES

1. **Beukhof, J.R., Kardaun, O., Schaafsma, W., Poortema, K., Donker, A.J.M., Hoedemaeker, P.J. and Van Der Hem, G.K.** 1986. Toward individual prognosis of IgA nephropathy. Kidney Int. **29**: 549–556.

2. **Colvin, R.B., Fuller, T.C., MacKeen, L., Kung, P.C. and Ip, S.H.** 1987. Plasma interleukin 2 receptor levels in renal allograft recipients. Clin. Immunol. Immunopathol. **43**: 273–276.
3. **Croker, B.P., Dawson, D.V. and Sanfilippo, F.** 1983. IgA nephropathy: Correlation of clinical and histologic features. Lab. Invest. **48**: 19–24.
4. **D'Amico, G., Barbiano di Belgiojoso, G., Imbasciati, E., Fogazzi, G., Radaelli, L., Ferrario, F., Fellin, G., Ponticelli, C. and Minetti, L.** 1984. Idiopathic IgA mesangial nephropathy: Natural history. Contr. Nephrol. **40**: 208–213.
5. **Droz, D., Kramar, A., Nawar, T. and Noël, L.H.** 1984. Primary IgA nephropathy: Prognostic factors. Contr. Nephrol. **40**: 202–207.
6. **Mackeen, L., Brown, M., Ip, S.H., Kung, P.C., Yasuda, N., Harrington, D., Hinuma, Y., Weisenburger, D., Lai, P. and Purtilo, D.** 1986. Serum interleukin 2 receptor as a marker for active T cell malignancies. Fed. Proc. **45**: 454.
7. **Mustonen, J., Pasternack, A., Helin, H. and Nikkilä, M.** 1985. Clinicopathologic correlations in a series of 143 patients with IgA glomerulonephritis. Am. J. Nephrol. **5**: 150–157.
8. **Nelson, D.L.** 1986. Soluble interleukin-2 receptors: Analysis in normal individuals and in certain disease states. Fed. Proc. **45**: 377.
9. **Robb, R.J., Munck, A. and Smith, K.A.** 1981. T cell growth factor receptors: Quantitation, Specificity, and Biological Relevance. J. Exp. Med. **154**: 1455–1474.
10. **Sharon, M., Klausner, R.D., Cullen, B.R., Chizzonite, R. and Leonard, W.J.** 1986. Novel interleukin-2 receptor subunit detected by cross-linking under high-affinity conditions. Science **234**: 859–863.
11. **Smith, K.A.** 1988. Interleukin-2: Inception, impact, and implications. Science **240**: 1169–1176.
12. **Waldmann, T.A.** 1986. The structure, function and expression of interleukin-2 receptors on normal and malignant lymphocytes. Science **232**: 727–732.