

Decreased serum IL-7 levels in patients with systemic sclerosis

Sirs,

Interleukin-7 (IL-7) was originally defined as a pre-B lymphocyte growth factor and was subsequently found to augment the growth of T lymphocytes. A recent study showed that IL-7 is an anti-fibrogenic factor in pulmonary fibrosis *in vitro*. In this study, we determined the serum levels of IL-7 in patients with SSc.

Forty-three patients with SSc and 28 healthy controls were included in the study. There were 36 female and 7 male SSc patients, with a mean age of 54 ± 13.0 years old. Thirteen cases of diffuse cutaneous SSc and 30 of limited cutaneous SSc were included. We determined the serum levels of IL-7 in patients with SSc by a specific ELISA kit (Biosource, USA), performed by a solid-phase sandwich enzyme immunoassay.

The serum IL-7 levels in patients with SSc were significantly lower than those in the healthy controls ($p < 0.001$, the Mann-Whitney U-test).

The serum levels of IL-7, anti-fibrogenic factor, were down-regulated in SSc, but the clinical symptoms, skin sclerosis or pulmonary fibrosis, did not correlate with serum IL-7 levels.

Systemic sclerosis (SSc) is a generalized connective tissue disease that involves sclerotic changes in the skin and many other organ systems (1). Although the pathogenesis of SSc is still unknown, the basic mechanism appears to involve endothelial cell injury, overproduction of extracellular matrix (ECM), and aberrant immune activation (2). TGF- β is a key mediator of tissue fibrosis in the pathogenesis of SSc (3).

Interleukin-7 (IL-7) was originally defined as a 17.4kDa mature protein (4), a pre-B lymphocyte growth factor and was subsequently found to augment the growth of T lymphocytes (5).

A recent study showed that IL-7 up-regulates Smad7, a major inhibitor of the Smad family, and in parallel significantly reduces TGF- β -induced collagen synthesis in pulmonary fibrosis (PF) *in vitro* (6). Thus TGF- β and IL-7 have opposing effects; TGF- β is a potent fibrogenic factor and IL-7 is an anti-fibrogenic factor.

In this study, we determined the serum levels of IL-7 in patients with SSc.

Forty-three patients who fulfilled the diagnostic criteria for SSc reported by the American College of Rheumatology and 28 healthy controls were included in the study: 36 female and 7 male SSc patients, aged 54.0 ± 13.0 years old. In the age-matched healthy controls, 19 were female and 9 were male. Thirteen cases of diffuse cutaneous SSc (dcSSc) and 30 of limited cutaneous SSc (lcSSc) were included, according to the classification proposed by LeRoy *et al.* (7). Nine cases had anti-topoisomerase I

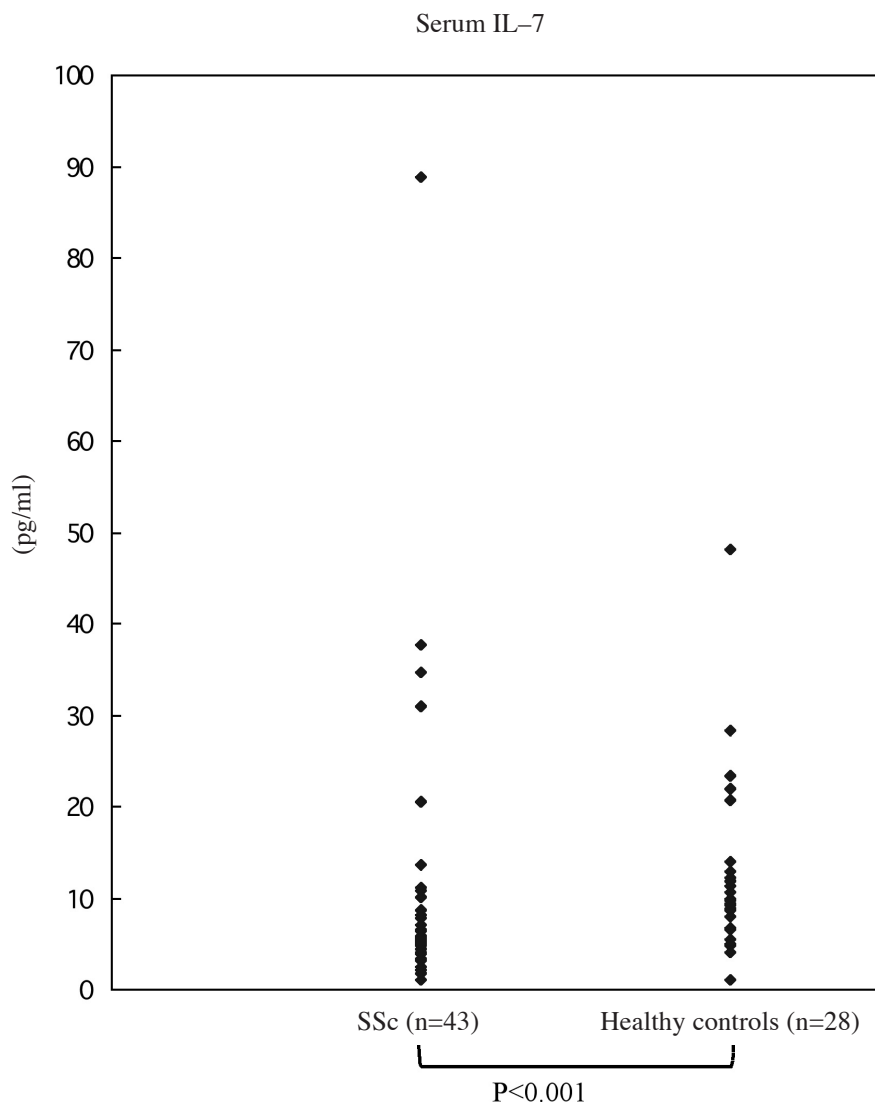


Fig. 1. The serum IL-7 levels in patients with SSc were significantly lower than those in the healthy controls (median 5.4 pg/ml vs. 9.85 pg/ml; 25th-75th percentile 4.25-8.4 pg/ml vs. 6.8-12.45 pg/ml, $p < 0.001$).

antibody, 13 had anti-centromere antibody, 9 had anti-U1-RNP antibody, these SSc-related anti-nuclear antibodies (ANA) were examined by ELISA, and ANA was examined by indirect immunofluorescence tests. In 5 cases ANA was negative.

The serum levels of IL-7 were measured with a specific ELISA kit (Biosource, USA), performed by sandwich ELISA, after clotted venous blood was centrifuged at 3000rpm for 15minutes. Statistical analysis was carried out using the Mann-Whitney U test. P -values < 0.05 were considered significant.

The serum IL-7 levels are shown in Fig. 1. The serum IL-7 levels in patients with SSc were significantly lower than those in the healthy controls (median 5.4 pg/ml vs. 9.85 pg/ml; 25th-75th percentile 4.25-8.4 pg/ml vs. 6.8-12.45 pg/ml, $p < 0.001$). However, there was no significant correlation between serum IL-7 levels and clinical parameters: the age at onset and

the duration of SSc were assessed using the Spearman's rank correlation coefficient. Patients were further classified according to gender, dsSSc or lcSSc, and the presence or absence of digital scars/skin ulcers (16:14.53%), contracture of phalanges (27:4.87%), nailfold bleeding (17:18.49%), pigmentation of skin (6:8.43%), short sublingual frenulum (16:8.67%), oesophageal reflux (15:10.60%), PF (19:17.53%), pulmonary hypertension (9:25.26%), heart (11:26.32%), kidney (2:37.5%) and joint involvement (8:16.33%). These parameters were assessed separately, however there was no statistically significant difference in serum IL-7 levels using the Mann-Whitney U-test.

In particular, the previous report (6) was not consistent with the current result that serum IL-7 levels were not decreased in SSc patients with PF. Nineteen of the 36 patients (53%) were diagnosed as PF by computed tomography, pulmonary func-

tion tests and also examined serum levels of KL-6 (8). Because IL-7 is also produced by various cells, such as thymic stromal cells, keratinocytes (9) and synoviocytes, the serum IL-7 levels may not be proportional to the local or tissue levels. Another report described that serum IL-7 levels were normal in SSc after treatment of high-dose immunosuppressive therapy (10). This discrepancy might be due to the presence of lymphopenia owing to the therapy or the differences in patient population.

In summary, these results suggest that serum levels of IL-7, anti-fibrogenic factor, are down-regulated in SSc, but the clinical symptoms, skin sclerosis or pulmonary fibrosis, are not in parallel with serum IL-7 levels.

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