but might reflect local environmental factors. The aetiopathogenesis of PSV is unknown, but both genetic and environmental factors are likely to be important. The clinically observed differences between MPA and WG may reflect interaction of varying trigger factors on a heterogeneous genetic background. It should therefore not be assumed that the same triggers operate in all regions of Europe.

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Anti-U3 snRNP antibodies in localised scleroderma

Localised scleroderma (LScl) is a connective tissue disorder usually limited to the skin and subcutaneous tissue, but it sometimes affects the muscle beneath the cutaneous lesions. The absence of Raynaud's phenomenon, acrosclerosis, and internal organ involvement differentiates LScl from systemic sclerosis (SSc).[1] LScl has been reported to be accompanied by a variety of abnormal immune reactions, such as the presence of antinuclear antibody, rheumatoid factor, anti-single-stranded DNA antibody (anti-ssDNA), and antihistone antibody.[2–5]

In our laboratory an indirect immunofluorescent study showed nucleolar staining in the serum samples of some patients with LScl. Although autoantibodies to nucleolar antigens have been well described in patients with SSc,[6 7] these antibodies have not been determined in patients with LScl, and the incidence of anti-U3 snRNP antibodies has not been described previously. In this study we investigated the prevalence of anti-U3 snRNP antibodies using RNA immunoprecipitation,[8] and examined the clinical and laboratory features of patients with LScl. In addition, we examined the serum samples of patients with SSc and control subjects matched for age and sex with the patients with LScl.

We found anti-U3 snRNP antibodies in 2/70 (3%) serum samples from the patients with LScl (fig 1). One of the 28 patients (4%) with linear scleroderma and one of the 20 patients (5%) with morphoea had anti-U3 snRNP antibodies (table 1). This prevalence was smaller than that in patients with SSc,[9] but there was no significant difference. RNA immunoprecipitation using silver staining of the RNA is not as sensitive as other methods—for example, probing with a labelled U3 snRNP probe. Possibly, some anti-U3 snRNP positive serum samples might have been missed. The three patients with SSc and with anti-U3 snRNP antibodies were diagnosed as having diffuse cutaneous SSc, and they tended to be older and have disease of longer duration than patients with LScl; the difference was not significant. In this study the titres of antinucleolar antibodies in the two patients with LScl with anti-U3 snRNP antibodies were 1/320 and 1/640, respectively. The titres of this antibody did not change in a follow up study. A previous study reported that 43/46 patients with SSc and anti-U3 snRNP antibodies produced bright nucleolar staining with titres >1/640.[10] Taken together, the titres of antinucleolar antibodies in patients with LScl were as high as those in SSc. Patients with LScl and with anti-U3 snRNP antibodies did not have sclerodactyly or nailfold bleeding. Raynaud's phenomenon did not occur at any time in the course of their disease. These results suggest that anti-U3 snRNP antibodies occur in patients with LScl as well as in those with SSc.

The patients with LScl and anti-U3 snRNP antibodies tended to be younger, have shorter disease duration, have fewer sclerotic lesions, and have fewer affected areas than those without, but there was no significant difference. We could not find any correlations with clinical manifestations, probably because of the small number of patients. In earlier investigations of systemic sclerosis, anti-U3 snRNP antibodies did not seem to have any distinctive clinical and laboratory correlation. A large group of patients with SSc was assembled and the clinical features of the patients with anti-U3 snRNP antibodies investigated; various clinical associations were reported.[9] A large group of patients with LScl might similarly disclose clinical associations of patients with LScl with anti-U3 snRNP antibodies.

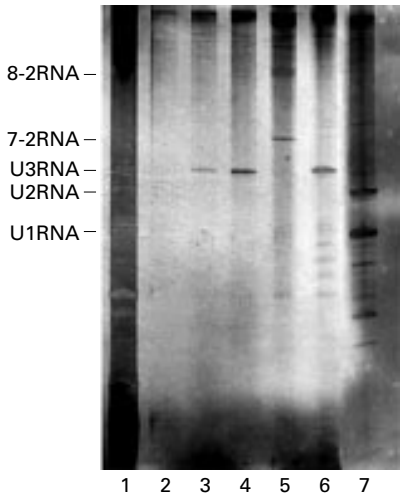

Figure 1 RNA immunoprecipitation. Urea (7 M/10% polyacrylamide gel electrophoresis of phenol-extracted immunoprecipitates from HeLa cell extracts were stained with silver. Total nucleic acids, with 7-2RNA, 8-2RNA, and the U snRNA regions are indicated. Serum samples used for immunoprecipitation included: lane 1, total RNA; lane 2, healthy control serum; lanes 3–4, patients with LScl and with anti-U3 snRNP antibodies; lane 5, patient with SSc and anti-Th/To ribonucleoprotein antibodies; lane 6, patient with SSc and anti-U3 snRNP antibodies; lane 7, patient with systemic lupus erythematosus and anti-Sm antibodies.

Table 1 Frequencies of antibodies to U3 small nuclear ribonucleoprotein (snRNP), detected by immunoprecipitation, in patients with localised scleroderma (LScl), systemic sclerosis (SSc), and control subjects

	Anti-U3 snRNP antibodies (%)
Patients with LScl	2/70 (3)
GM	0/22 (0)
LS	1/28 (4)
M	1/20 (5)
Patients with SSc	3/30 (10)
Control subjects	0/40 (0)

LScl = localised scleroderma; GM = generalised morphoea; LS = linear scleroderma; M = morphoea; SSc = systemic sclerosis.

Previous studies have shown that anti-U3 snRNP antibodies rarely coexist with other autoantibodies.[9] Okano *et al* reported that each distinctive serum antibody is associated with its own unique combination of clinical features.[9] In our study antihistone antibodies or anti-ssDNA did not coexist with anti-U3 snRNP antibodies, and no other autoantibodies were detected by RNA immunoprecipitation. LScl may be a heterogeneous condition with diverse autoantibodies, and these antibodies may have a mutually exclusive status.

In conclusion, we showed for the first time that anti-U3 snRNP antibodies are found in patients with LScl by RNA immunoprecipitation. We found no correlations between clinical and laboratory manifestations in the present study. Our study suggests that the presence of anti-U3 snRNP antibodies is one of the serological abnormalities in LScl. A study of more patients may assist in showing a distinctive association between anti-U3 snRNP antibodies and the clinical and laboratory features of patients with LScl.

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Telomerase activity in peripheral blood mononuclear cells from patients with SLE

Telomerase is a reverse transcriptase that adds the telomeric sequence to the terminal of chromosomes, prevents shortening of telomere, and maintains the complete telomeric structure.[1] It has been recently reported that an increase in telomerase activity is associated with the activation of lymphocytes,[2–7] and, in general, much attention has been paid to the role of telomerase in immunopathology. Katayama *et al* reported the telomerase activity in patients with systemic lupus erythematosus (SLE).[8] They analysed 17 patients with SLE, and the telomerase activity in peripheral mononuclear cells was increased to 64.7%. Thus, in this study, we divided patients with SLE into treated and untreated groups, and measured the telomerase activity of peripheral mononuclear cells.

Thirteen patients with SLE (1 man, 12 women) with a mean (SD) age of 30.7 (6.5) years (range 19–61) were enrolled in this study. All patients fulfilled the 1997 revised American Rheumatism Association criteria. As a control group, 10 normal volunteers, six women aged 19–41 and four men aged 30–37, were also included in the study. After informed consent had been obtained, 10 ml of peripheral blood was taken and heparinised. The mononuclear cell fraction was isolated from 10 ml of heparinised peripheral blood by Ficoll-Paque (Sigma Inc, St Louis, USA) density gradient centrifugation. A sample of 1.0×10^6 mononuclear cells was analysed by the TRAP assay method. The TRAP assay was performed with a TRAPeze telomerase detection kit produced by the Intergen Company (Purchase, NY, USA). The level of telomerase activity was expressed by a ratio of the entire TRAP ladders to an internal control band.

Table 1 shows the telomerase activity level data and clinical data used for determining the SLE Disease Activity Index (SLEDAI). Significant differences (p=0.006) were detected in the telomerase activity level between the control group, untreated SLE group, and treated SLE group by Kruskal-Wallis test with a significance level of 5%. For multiple comparisons the Mann-Whitney U test was used to evaluate intergroup differences after lowering the significance level using Bonferroni's technique. The p value was 0.002 between the control group and untreated SLE group, 0.005 between the untreated SLE group and treated SLE group, and 0.118 between the control group and treated SLE group. Compared with other groups, telomerase activity was significantly higher in the SLE untreated group. The Spearman rank correlation test with a significance level of 5% showed a significant positive relationship between telomerase activity and SLEDAI in the SLE group with a correlation coefficient of 0.872 and p value of 0.003. The relation between telomerase activity and clinical data in SLEDAI was also analysed using the Spearman rank correlation test with a significance level of 5% in the SLE group. The correlation coefficient and p value were −0.614 and 0.033 between telomerase activity and white blood cell count, −0.715 and 0.013 between telomerase activity and serum complement activity, and 0.637 and 0.027 between telomerase activity and serum IgG level, respectively, with a significance level of 5%. However, the relation between telomerase activity and other clinical data was not significant in the SLE group. Telomerase activity was measured before and after treatment and changes in the activity level were analysed.

SLEDAI decreased in all patients after treatment. Wilcoxon signed rank test with a significance level of 5% showed a significant decrease in telomerase activity (p=0.043) after treatment.

The treatment reduced the telomerase activity in peripheral mononuclear cells. We could not confirm whether the cause was due to the steroids or the reduction of disease activity. However, because the telomerase activity of peripheral mononuclear cells was correlated with SLEDAI, the peripheral blood telomerase activity may be useful in the evaluation of disease activity and in judging the therapeutic effects in SLE.

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Table 1 Telomerase activity and clinical laboratory parameters and SLE disease activity index (SLEDAI)

Patient No	*Age*	*Sex*	*Telomerase activity*	*WBC*	*Lymph.*	*Plt. (×10³)*	*CH_{50}*	*IC (C1q)*	*dsDNA*	*u-prot.*	*ANA*	*IgG*	*IgA*	*IgM*	*SLEDAI*	*Symptom*	*Treatment (prednisolone)*
1	23	M	1.96	2700	800	158.0	31.2	1.5	5	(−)	640	14.69	3.05	0.53	10	2,4,5,6,8	None
			0.00	6500	1200	211.0	37.0	1.9	5	(−)	1280	—	—	—	2	None	20 mg/day
2	36	F	0.76	2900	900	48.0	23.6	9.3	165	(1+)	1280	12.82	1.68	0.65	12	2,4,8	None
			0.00	5800	1700	243.0	29.2	—	72	(−)	—	—	—	—	2	None	30 mg/day
3	28	F	0.82	3700	1000	226.0	31.6	1.5	77	(±)	640	18.98	3.89	1.98	10	2,5,8	None
			0.78	8000	700	253.0	28.1	1.5	32	(±)	1280	—	—	—	2	None	20 mg/day
4	61	F	0.47	3600	400	201.0	15.0	34.5	83	(±)	5120	31.37	3.44	0.76	16	2,3,4,5,8	None
			0.29	5800	600	200.0	34.8	9.9	12	(−)	5120	—	—	—	0	None	30 mg/day
5	19	F	0.85	4520	920	311.0	27.2	1.9	13	(3+)	320	15.60	3.54	2.24	21	1,2,4,5,8	None
			0.28	16130	1130	327.0	30.0	1.5	5	(1+)	40	6.44	1.84	1.79	0	None	30 mg/day
6	24	F	0.25	8700	1400	149.0	34.2	1.5	185	(2+)	5120	11.34	3.33	0.90	2	None	50 mg/day
7	53	F	0.40	5600	1200	13.0	36.2	1.5	5	(2+)	160	18.24	6.00	0.79	1	None	60 mg/day
8	39	F	0.05	6800	1300	248.0	35.6	1.9	5	(−)	40	9.80	2.09	0.55	0	None	15 mg/day
9	41	F	0.18	12400	400	247.0	47.6	1.6	5	(1+)	640	13.13	2.73	0.51	0	None	20 mg/day
10	36	F	0.06	7900	1400	209.0	41.0	1.5	12	(−)	80	11.89	1.71	0.88	0	None	5 mg/day
11	56	F	0.04	7900	1200	219.0	41.5	1.5	5	(1+)	40	12.19	4.17	0.66	0	None	10 mg/day
12	39	F	0.10	5600	600	134.0	34.2	1.5	7	(3+)	640	7.65	2.32	0.38	0	None	20 mg/day
13	36	F	0.58	9000	1100	138.0	24.0	1.5	21	(2+)	320	16.53	3.55	1.39	4	7	30 mg/day

WBC = white blood cell count (/μl); Lymph. = lymphocyte count (/μl); Plt. = platelet count ($\times10^3$/μl); CH_{50} = serum complement activity (U/ml); IC (C1q) = serum immune complex level with a C1q solid phase method (μg/ml),;dsDNA = anti-double stranded DNA antibody level (IU/ml); u-prot. = urine protein analysis with a test paper method; ANA = antinuclear antibody (titre); IgG = immunoglobulin G level (g/l), IgA = immunoglobulin A level (g/l); IgM = immunoglobulin M level (g/l); SLEDAI = SLE disease activity index.
Symptom: 1 = central nervous system lupus; 2 = arthritis; 3 = myositis; 4 = nephritis; 5 = new rash; 6 = alopecia; 7 = serositis; 8 = fever.