Secreted Protein Acidic and Rich in Cysteine, a new biomarker of localized scleroderma

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Background

What's SPARC?

- Secreted Protein Acidic and Rich in Cysteine
- Multifunctional secreted glycoprotein found in the extracellular matrix
- SPARC is expressed only at sites of tissue remodeling and wound repair
- SPARC gene overexpression by cultured dermal fibroblasts from the patients with SSc (Zhou et al. Arthritis Rheum 2002)
- Attenuation of collagen production with siRNA of SPARC in cultured fibroblasts from the patients with SSc (Zhou et al. Arthritis Rheum 2006)
- Increased plasma concentrations of SPARC and Thrombospondin-1 in SSc. SPARC concentration was greater in limited SSc compared with controls, however, it was not elevated in diffuse SSc (Macko et al. J Rheumatol 2002)
- SPARC concentrations of patients with localized scleroderma and the other collagen disease were not assessed.

About Scleroderma

- An autoimmune disorder
- Fibrosis of the skin and internal organs
- Pathogenesis: inflammation, autoimmune attack, vascular damage, activation of fibroblasts and abnormal accumulation of extracellular matrix
- classification:
 - systemic sclerosis (diffuse or limited cutaneous SSc)
 - localized scleroderma (LSC) (morphea, linear scleroderma, generalized morphea)

Objective

To examine whether serum concentrations of SPARC are elevated in systemic or localized scleroderma

Results

Serum concentrations of SPARC in LSC were extremely increased

Conclusion

- Serum concentrations of SPARC in LSC were extremely increased among scleroderma
- Serum concentrations of SPARC in Scleroderma and DM were significantly higher than those of normal controls
- LSC patients with elevated SPARC levels showed greater number of lesions, larger BSA of lesions and higher titer of anti-ssDNA antibodies
- Serum SPARC levels may serve as a useful maker for the severity of LSC

Serum SPARC in GM were significantly higher than linear scleroderma

Serum SPARC in SSc and DM were significantly higher than normal controls

Correlation of serum SPARC levels with clinical and serological features in patients with LSC

	Patients with elevated SPARC levels (n=7)	Patients with non-elevated SPARC levels (n=8)
Sex (male : female)	0 : 7	6 : 2
Age of onset (years)	24.8±12.8	19.5±12.3
Duration of disease (years)	9.2±5.9	4.6±1.9
Number of skin lesion	5.7±2.1*	1.5±0.6
BSA of skin lesion (%)	4±2.3*	1
anti-ssDNA Ab (mg/ml)	48.7±53.9*	4±0.29
sIL2R (mg/ml)	299±34.8	448±196.7
PAP (mg/ml)	0.84±0.09	1.6±0.6

Relative expression levels of SPARC mRNA in the skin tissues

SPARC Protein expression in the skin tissue of LSC (IHC)

Comparison of the expression levels of SPARC mRNA and protein in the skin tissue and serum

ID	relative expression of SPARC mRNA	protein expression of SPARC (IHC)	serum concentration of SPARC
LSC1	0.32	++	21.6
LSC2	0.53	++	22.8
LSC3	0.78	++	25.9
LSC4	0.07	++	12.7
LSC5	0.24	+	0.7
LSC6	1.84	+	11.0
LSC7	0.13	++	7.1
dcSSc1	0.46	ND	0.8
dcSSc2	0.13	ND	0.8
dcSSc3	0.17	+	0.7
dcSSc4	0.11	++	0.8
dcSSc5	0.27	++	0.8
dcSSc6	0.59	ND	0.8
lcSSc1	0.06	ND	0.9
lcSSc2	0.30	+	0.5
lcSSc3	0.18	+	0.2
lcSSc4	1.29	+	0.7
lcSSc5	1.87	ND	0.9
lcSSc6	0.12	ND	0.2
lcSSc7	0.04	+	0.7
lcSSc8	0.25	+	0.5
lcSSc9	0.16	+	1.0
lcSSc10	0.78	++	0.8
lcSSc11	0.34	+	0.4
lcSSc12	0.22	+	0.1
NS1	0.30	+	ND
NS2	0.00	+	ND
NS3	0.14	+	ND
NS4	0.00	+	ND
NS5	0.01	+	ND
NS6	0.04	+	ND
NS7	0.00	-	ND
NS8	0.21	-	ND
NS9	0.01	+	ND

COI Disclosure Information

MINA TSURUTA
I have no financial relationships to disclose.