The Association between Serum Matricellular Protein: Secreted Protein Acidic and Rich in Cysteine-Like 1 Levels and Ischemic Stroke Severity

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Background: The role of matricellular proteins like secreted protein acidic and rich in cysteine-like 1 (SC1) has been shown in important functions in the central nervous system, including the regulation of synaptic stability with upregulation throughout axonal regeneration.The aim of this study was to determine whether SC1 is related to ischemic stroke severity. *Methods:* A total of 132 consecutively recruited patients admitted for acute ischemic stroke were included in this observational prospective study. Stroke severity was evaluated in the National Institutes of Health (NIHSS) scale on hospital admission. *Results:* There was a positive correlation between SC1 levels and NIHSS score (r = .22, *P* = .009). Compared with patients with NIHSS scores lower than 5 at admission, patients with moderate and severe stroke (NIHSS ≥ 6) had significantly higher SC1 levels: 4.84 (2.53-11.58) ng/mL versus 3.31 (1.67-8.95) ng/mL (*P* = .01). SC1 was an independent predictor of stroke severity at admission (adjusted odds ratio =1.25; 95% confidence interval, 1.03-1.97; *P* = .04). *Conclusion:* SC1 levels were independently associated with ischemic stroke severity evaluated by the NIHSS. **Key Words:** Stroke—severity—SC1—matricellular protein.

Introduction

Matricellular proteins in the brain are important in developmental processes, but they are also involved in the support of neuronal integrity. Secreted protein acidic and rich in cysteine-like 1 (SC1) belongs to this family of extracellular matrix molecules. This particle has an impact for synaptic stability and is upregulated during axonal regeneration following brain injury.[1,2] Because experimental studies have also shown that SC1 is expressed after ischemic damage in the brain,[3] we investigated the link between serum SC1 concentration and ischemic stroke severity.

Materials and Methods

We prospectively recruited 132 patients with acute ischemic stroke (characteristics in Table 1) at the Department of Neurology and Cerebrovascular Diseases, Poznan University of Medical Sciences, within 1 year of observation. Stroke was defined according to expert consensus of the American Stroke Association.[4] To rule out other factors possibly affecting SC1 levels, patients were excluded if they had a history of recent surgery or trauma, renal

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Table 1. *Baseline characteristics and comparison between patients with mild and severe stroke*

Characteristic	All	Minor stroke (NIHSS < 5)	Moderate and severe stroke (NIHSS ≥ 6)	*P*
n (%)	132	65 (49%)	67 (51%)	
Female sex, n (%)	57 (43%)	24 (37%)	33 (48%)	NS
Age in years, median (IQR)	67 (59-81)	65.5 (59-74)	70 (58-82)	NS
Atrial fibrillation, n (%)	40 (30.3%)	16 (24.6%)	24 (35.8%)	NS
Hypertension, n (%)	95 (72%)	47 (72.3%)	48 (71.6%)	NS
Diabetes, n (%)	37 (28%)	19 (29.2%)	18 (26.8%)	NS
History of stroke, n (%)	39 (29.5%)	21 (35.3%)	18 (26.8%)	NS
Coronary heart disease, n (%)	49 (37.1%)	23 (35.3%)	26 (38.8%)	NS
Current cigarette smoking, n (%)	28 (22%)	16 (12.1%)	12 (17.9%)	NS
Glucose (mmol/L)	5.8 (5.1-7.9)	5.71 (4.8-7.73)	6.09 (5.2-8.2)	NS
Cholesterol (mg/dL)	190 (153-222)	206 (165-225)	187 (144-218)	.03
Fibrinogen (mg/dL)	382.6 (277-450.7)	400 (327-456)	366 (244-434)	NS
CRP (mg/l)	4.05 (1.45-12.97)	3.3 (1.24-7.1)	7.23 (1.66-20.81)	.005
SC1 (ng/ml)	4.04 (2.26-10.28)	3.31 (1.67-8.95)	4.84 (2.54-11.58)	.01

Abbreviations: CRP, C-reactive protein; IQR, interquartile range; NIHSS, National Institutes of Health Stroke Scale; NS, nonsignificant; SC1, secreted protein acidic and rich in cysteine-like 1.

Data are presented as median with IQRs or number with percentage.

insufficiency, malignancy, inflammatory disease, liver failure, or recent myocardial infarction. Brain imaging was performed routinely within 1 hour after admission. The control group consisted of 30 subjects matched for age with confirmed traditional vascular risk factors but without stroke in the history. The study was approved by the Ethics Committee of Poznan University of Medical Sciences. Informed consent was obtained from all patients.

Baseline characteristics with the following variables were recorded: age, gender, history of vascular risk factors and total cholesterol, fibrinogen, C-reactive protein, and SC1 levels. Biochemical tests were performed in all patients at admission. Stroke severity was quantified using the National Institutes of Health Stroke Scale (NIHSS) at admission. Patients with NIHSS scores lower than 5 were categorized into group 1 (minor stroke), and those with NIHSS scores of 6 or higher (moderate and severe stroke) were classified into group 2.

SC1 levels were quantified by commercially available ELISA (Abcam, Cambridge, United Kingdom).

Statistical Analysis

The results were reported as counts (percentage) for the categorical variables and median (interquartile range [IQR]) for the continuous variables.

Continuous variables were compared using Mann–Whitney tests, and categorical variables were compared using chi-square tests or Fisher's exact tests. Correlations among continuous variables were assessed by the Spearman rank-correlation coefficient. The effect of stroke timing on the serum SC1 level was explored by the post hoc Kruskal–Wallis test.

The relations of SC1 levels with the stroke severity (assessed by NIHSS score) were investigated with the use of logistic regression models. We used univariate and multivariate models adjusted for all significant outcome predictors and reported odds ratios (ORs) and 95% confidence intervals (CIs). All statistical analyses were performed using licensed MedCalc software (Ostend, Belgium).

Results

Finally, 132 patients fulfilled inclusion and exclusion criteria and were enrolled in the study. The baseline characteristics of this population are described in Table 1.

There was a positive correlation between SC1 levels and NIHSS score (r = .22, *P* = .009).

In the 67 patients with moderate and severe stroke, serum SC1 levels were higher compared with those in 76 patients with a mild stroke: 4.84 (IQR, 2.53-11.58) versus 3.31 (IQR, 1.67-8.95) ng/mL (*P* = .01) (Table 1). We also analyzed the concentrations of SC1 with respect to the time between the onset of stroke symptoms and blood sample collection. Time points of 4.5 hours, 6 hours, and more than 6 hours were taken into consideration because of their (4.5 and 6 hours) significance for stroke interventions. In the post hoc Kruskal–Wallis test we did not find significant differences in SC1 levels among these 3 groups (only statistical trend was noticed, *P* = .08). However, SC1 levels were significantly higher in samples collected from patients with stroke symptoms more than 6 hours when compared with samples taken up to 4.5 hours from stroke onset: 4.73 (IQR, 2.17-9.99) versus 3.04 (IQR, 2.00-5.05) ng/mL (*P* = .04) (Fig 1).