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Short communication

Free thyroxine and TSH interact with secreted protein acidic and rich in cysteine-like 1 in ischemic stroke

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ABSTRACT

The role of the thyroid gland in ischemic stroke pathology is not well understood. As thyroid hormones modulate the extracellular matrix, we explored the possible link between them and secreted protein acidic and rich in cysteine like 1 (SC1) – one of the extracellular matrix molecules.

In the 81 patients with acute ischemic stroke, serum SC1 levels were much higher compared with 30 control subjects: 4.47 vs 2.43 ng/mL ($p < 0.001$). Serum levels of free thyroxine (fT4) were higher in stroke subjects compared to those of controls ($p = 0.03$). In stroke patients, TSH concentration was lower than in the control group ($p = 0.03$). SC1 levels positively correlated with fT4 levels ($p = 0.02$) and negatively with TSH ($p = 0.03$) in stroke patients.

Our results confirmed the association between thyroid hormones and SC1 – extracellular matrix protein.

1. Introduction

Recently, the role of the thyroid gland in the pathophysiology of acute cerebrovascular diseases has been intensively explored. Clinical studies have demonstrated t that thyroid hormones, especially low free triiodothyronine (fT3) are important factors related to ischemic stroke severity and outcome [1,2]. A few studies have also proved the association between TSH (thyroid-stimulating hormone), fT3 and clinical course in subarachnoid hemorrhage [3].

The pathological aspect of thyroid hormones disturbances in acute stroke is not well understood. It is not surprising given the very complex interactions between the thyroid gland and human brain. We know, for a fact, that thyroid hormones participate in brain connectivity by influence on neuronal migration, synaptic plasticity and binding with their receptor on integrin αVß3 which, in turn, affects a large number of extracellular matrix proteins [4]. Secreted protein acidic and rich in cysteine like 1 (SC1) belongs to this family of extracellular matrix molecules presented in the human brain.

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Recently it has been shown that SC1 levels were associated with ischemic stroke severity [5]. It would be interesting if there is a link between thyroid hormones and extracellular matrix (ECM) molecules expression in cerebrovascular disease. Therefore, we investigated the association between TSH, fT3, fT4 (free thyroxine) and SC1 in ischemic stroke patients.

2. Material and methods

We studied ischemic stroke patients consecutively admitted to the Department of Neurology and Cerebrovascular Disorders, within one year of observation. Acute ischemic stroke was defined according to the World Health Organization criteria. We excluded patients with clinical conditions with possible influence on TSH, fT3, fT4 and SC1 levels, such as: a history of thyroid gland disease, recent surgery or trauma, renal insufficiency, malignancy, inflammatory disease, liver failure or recent myocardial infarction. Brain imaging (CT or MRI) was performed routinely within 1 h after admission. Thirty subjects matched for age with confirmed traditional vascular risk factors but without stroke in the history comprised the control group. All study participants gave written, informed consent and the Ethics Committee of our University approved the study.

Baseline characteristics with following variables were recorded: gender, age, history of vascular risk factors and also total cholesterol, HDL cholesterol, triglycerides, white blood cell count (WBC), TSH, fT4, and fT3. Biochemical tests were performed in all patients at the admission. SC1 levels were quantified by commercially available ELISA (Abcam, Cambridge, UK) from blood samples stored at −80 °C until assay.

2.1. *Statistical analysis*

Most of the continuous variables had non-normal distribution; therefore, results are median with interquartile range (IQR). Categorical variables are presented as counts (with percentage). The differences between the study groups were evaluated using Chi-square tests (categorical variables) and Mann–Whitney tests (continuous variables), as appropriate. Because distributions of thyroid gland markers levels appeared to be left-skewed, they were normalized by log-transformation, and we examined associations between SC1 levels and TSH, fT3, fT4 with Pearson correlation analysis. A p-value <0.05 was considered as statistically significant.

3. Results

At the end of the recruitment period, 81 out of 260 acute stroke patients fulfilled inclusion and exclusion criteria and were enrolled in the study. Apart from matching for age the number of women and men was the same in the control and stroke patient groups. Table 1 shows the basic characteristics of the studied population.

In the 81 patients with acute ischemic stroke, serum SC1 levels were much higher compared with 30 control subjects: 4.47 ng/mL (IQR, 3.34–5.16) versus 2.43 ng/mL (IQR, 1.43–3.16) ($p < 0.001$). The TSH and fT4 levels were also significantly different between studied groups. In stroke patients TSH concentration was lower than in the control group: 1.16 μIU/mL (IQR, 0.48–1.85) versus 1.52 μIU/mL (IQR, 0.92–2.61) ($p = 0.03$). Serum levels of fT4 were slightly higher in stroke subjects when compared to the control group 17.6 pg/mL (IQR, 15–19.4) versus 13.8 pg/mL (IQR, 12.68–17.75) ($p = 0.03$).

SC1 levels positively correlated with (logarithmic) fT4 concentration ($r = 0.26$, $p = 0.02$) in stroke patients (Fig. 1A). SC1 levels showed also modest negative correlation with TSH ($r = -0.24$, $p = 0.03$) (Fig. 1B). We did not find any association between fT4 and SC1.

4. Discussion

The present study showed that circulating SC1 levels in patients with acute ischemic stroke were associated with

Table 1 – The basic characteristics of explored population.

Characteristic	Stroke patients ($n = 81$)	Control group ($n = 30$)	p-value
Female sex (n)	32		