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Relationship between Cognitive Impairment and Serum ALP after Light Acute Ischemic Stroke in the Elderly

Xi Chen[1], Xiaojun Hou[2], Hongjuan Fu[2], Peng Zhang[2], Yueping Huang[2], Ying Shi[2], Jujun Xue[2]*

[1]Department of Laboratory, Heilongjiang Provincial Hospital, Harbin 150036, Heilongjiang Province, China.
[2]Department of Geriatric Neurology, Heilongjiang Provincial Hospital, Harbin 150036, Heilongjiang Province, China.

***Corresponding author:** Jujun Xue, xxuejjun@163.com

Abstract: *Objective:* To analyze the association between cognitive impairment and serum ALP levels in elderly patients who developed light acute ischemic stroke. *Methods:* 100 cases of elderly patients with mild acute ischemic stroke admitted from January 2022 to June 2023 were selected as the study subjects, and were divided into two groups according to whether or not they developed cognitive impairment within six months; those who did not develop cognitive impairment were classified into the control group, with a total of 62 cases, while those who developed cognitive impairment were classified into the case group, with a total of 38 cases. The general data and serum ALP levels of the two groups were compared, and the correlation between serum ALP levels and MoCA scores was analyzed. *Results:* There was no significant difference between the general information of the two groups of patients in the control group and the case group ($P > 0.05$). The serum ALP level of the patients in the case group was higher than that of the control group ($P < 0.05$), and there was a negative correlation between the serum ALP level and the total score of MoCA, the visuospatial and executive scores, and the memory score ($P < 0.05$). *Conclusion:* The serum ALP levels of elderly patients with cognitive impairment after mild acute ischemic stroke were higher than those of elderly patients without cognitive impairment after mild acute ischemic stroke, so the risk of cognitive impairment can be predicted in advance by detecting serum ALP levels.

Keywords: Elderly mild acute ischemic stroke; Cognitive impairment; Serum ALP level

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1. Introduction

Stroke is a very highly prevalent cerebrovascular disease in China, which can be divided into two types, ischemic stroke and hemorrhagic stroke. Statistics show that China has become the country with the highest lifelong risk of stroke. Stroke can cause a variety of functional disorders, such as cognitive impairment, which is experienced by about one-third of all stroke patients and seriously affects the quality of life and even shortens lifespan [1,2]. Post-stroke cognitive impairment is a clinical syndrome that occurs after a stroke event and lasts for six months or more. The increase in the median age at stroke onset and the decrease in stroke mortality rate

in recent years has led to a gradual increase in the prevalence of post-stroke cognitive impairment. So early detection and diagnosis is the key to improving the prognosis, as the burden of cerebrovascular disease and dementia in China is very heavy. Biomarkers with high sensitivity and accuracy should be introduced to predict patients with high risk of post-stroke cognitive impairment in advance to reduce its impact on individuals, families, and even society. ALP (alkaline phosphatase) is a metalloenzyme encoded by a multigene family that dephosphorylates its corresponding substrate and it is commonly used in the diagnosis of liver disease and bone disease. ALP is associated with the prognosis of cardiovascular and peripheral arterial diseases [3]. This study aims to analyze the relationship between cognitive impairment and serum ALP levels in elderly patients with mild acute ischemic stroke. A total of 100 patient cases admitted from January 2022 to June 2023 were included in this study. The details of this study are described in the following section.

2. Information and methods

2.1. Data

One hundred elderly patients with mild acute ischemic stroke were selected as study subjects (admission time: January 2022 to June 2023) based on the criteria and were divided into 62 cases in the control group (no cognitive impairment) and 38 cases in the case group (with cognitive impairment) according to whether or not cognitive impairment had occurred within six months.

The control group consists of 38 men and 24 women with age between 65–79 (70.56 ± 3.35) years. The case group consists of 23 males and 15 females with age between 65–80 (70.32 ± 3.12) years. The gender and age of the two groups were statistically analyzed, yielding a P value > 0.05.

Inclusion criteria:

(1) Meeting the diagnostic criteria of acute ischemic stroke, NIHSS score of 3 or less, and has a new infarct lesion.
(2) Age of 65 years and above.
(3) Normal cognitive function before stroke, good social adaptability, and no history of schizophrenia, depression, anxiety, etc.
(4) Patients or their family members were informed of and agreed to this study.
(5) Complete clinical data.

Exclusion criteria:

(1) Unable to cooperate with the completion of cognitive function assessment.
(2) Accompanied by other neurological diseases, such as epilepsy, etc.
(3) Accompanied by hematologic diseases, severe cardiopulmonary and renal insufficiency, and malignant tumors.

Diagnostic criteria for acute ischemic stroke [4]:

(1) The results showed acute onset after examination
(2) Symptoms of focal or comprehensive neurological deficits, such as limb weakness, facial numbness, etc.
(3) The presence of signs or symptoms, with the duration of the condition >24 hours
(4) Exclusion of non-vascular causes and cerebral hemorrhage.

Diagnostic criteria for post-stroke cognitive impairment [5]:

(1) Cognitive impairment within six months after stroke.
(2) Emphasizing the causal relationship between stroke and cognitive impairment.
(3) Having the relevance of clinical management, including cognitive impairment due to multiple stroke events.

2.2. Methods

Serum ALP levels of the subjects were tested within two days, at three months, and at six months after the onset of the disease. 5 ml of venous blood was collected from the fasting subjects and centrifuged, then the upper serum layer was analyzed with a fully automated biochemical analyzer.

Cognitive function was assessed within seven days, at three months, and at six months after the onset of the disease. The assessment scales included the mini-mental state examination (MMSE) and the Montreal Cognitive Assessment (MoCA), both of which were in Chinese [6,7]. The critical value of the MMSE scale was set according to the level of literacy, which was illiterate (≤17 points), elementary school (≤20 points), secondary school, and higher education (≤24 points), while the critical value of the MoCA scale was 22 points. The MMSE or MoCA score lower than the critical value indicated the presence of cognitive impairment, whereas a score higher than the critical value indicated the absence of cognitive impairment.

2.3. Observation indexes

(1) Compare the general information of the two groups of patients.
(2) Compare the serum ALP levels of the two groups.
(3) Analyze the correlation between serum ALP levels and cognitive impairment after mild acute ischemic stroke in the elderly.

2.4. Statistical methods

SPSS 25.0 version of the statistical software was used to analyze the data in the text. The count data and the measurement data were expressed by mean ± standard deviation (SD) and [*n* (%)] respectively, in which the former was tested by χ^2 test and the latter was tested by *t*-test. The *P* value < 0.05 indicated that the comparison data were statistically significant.

3. Results

3.1. General information

As shown in **Table 1**, the difference between the general information of the two groups was not obvious when compared, $P > 0.05$.

Table 1. General information of subject groups (mean ± SD)

	Control group	Case group	χ^2/t	*P*
Male/female	38/24	23/15	0.006	0.939
Age (years)	70.56 ± 3.35	70.32 ± 3.12	0.371	0.712
BMI (kg/m^2)	23.25 ± 2.16	23.10 ± 2.21	0.343	0.732
History of hyperlipidemia	11	6	0.064	0.801
History of diabetes	9	4	0.332	0.565
History of hypertension	36	20	0.282	0.595
History of smoking	23	10	1.239	0.266
TG (mmol/L)	1.32 ± 0.26	1.35 ± 0.23	0.611	0.543
TC (mmol/L)	4.51 ± 1.15	4.52 ± 1.20	0.043	0.966
HDL-C (mmol/L)	1.20 ± 0.25	1.18 ± 0.31	0.355	0.723
LDL-C (mmol/L)	3.53 ± 0.75	3.58 ± 0.69	0.347	0.729

3.2. Serum ALP level

As shown in **Table 2**, the serum ALP level of the case group was higher than that of the control group, $P < 0.05$.

Table 2. Serum ALP levels (mean ± SD, U/L)

Group	Case (*n*)	ALP level
Control group	62	76.25 ± 12.31
Case group	38	82.25 ± 10.18
t	-	2.521
P	-	0.013

3.3. Correlation analysis

As shown in **Table 3**, serum ALP level is negatively correlated with the total MoCA score, visuospatial and executive ability scores, and memory scores respectively, $P < 0.05$.

Table 3. Correlation analysis of serum ALP level and MoCA score

MoCA variable	R	*P*
Total score	-0.359	0.011
Visuospatial and executive ability	-0.380	0.006
Memory	-0.329	0.023
Naming	-0.158	0.291
Language	-0.225	0.123
Attention	-0.185	0.201
Orientation	-0.045	0.749
Abstraction	-0.116	0.425

4. Discussion

Stroke is a very typical cerebrovascular disease with a high prevalence in the elderly that can lead to balance disorders, cognitive disorders, vascular dementia, and other adverse manifestations. The etiology of the disease is unknown but studies have suggested that it is related to structural changes in small blood vessels, microembolism, hypoperfusion, or metabolic disorders [8]. Stroke lesions can cause cognitive disorders such as ischemic alterations in both deep gray matter and subcortical white matter. The ischemic alterations cut off the frontal-subcortical circuit, which causes a decrease in the normal speed of information processing, frontal lobe attention, and executive function. This will lead to dementia and vascular cognitive impairment if the disease continues to progress, affecting the subsequent quality of life. Previous studies have suggested that vascular calcification is prevalent in all stages of human pathology and physiology and that it is an uncontrollable and passive process. However, recent studies have found that the pathological basis of vascular calcification is a transitional stage that triggers atherosclerosis, which is a common pathological manifestation of chronic kidney disease and cardiovascular disease that can be regulated and controlled [9]. Moreover, vascular calcification decreases vascular elasticity and increases vascular stiffness and the risk of atherosclerosis and vascular rupture. So the degree and location of vascular calcification can serve as an early warning for stroke and cardiovascular disease. Post-stroke cognitive impairment has its characteristics, such as fluctuating course, patchy cognitive

deficits, and so on, which can be prevented and cured. Currently, cognitive function is often used in clinical screening and assessment, while the diagnosis is mainly based on clinical manifestations, neuroimaging, and neuropsychological assessment. Sensitive, accurate, and reliable biomarkers should be introduced to identify patients at high risk of developing post-stroke cognitive impairment to reduce its negative impact [10].

ALP is a metalloenzyme encoded by a multigene family that is mainly found in bone, liver, and kidney. ALP increases the incidence of cardiovascular and cerebrovascular diseases through vascular calcification and vascular endothelial dysfunction in response to inflammatory factors. ALP is divided into two types according to tissue expression, the first is tissue-specific alkaline phosphatases (ALPs) expressed in the intestine, placenta, and germ cells, while the other is tissue-nonspecific alkaline phosphatases (TNAPs), which are expressed in tissues such as the liver, kidneys, and bones. TNAPs account for more than 90% of the total circulating ALP, which is expressed in neuronal cells, endothelial cells, and neuronal synapses of the brain [11,12]. Relevant studies have indicated that circulating ALP levels can predict the prognosis of cerebral infarction [12]. So in this study, 100 elderly patients with mild acute ischemic stroke were selected as research subjects and divided according to the occurrence of cognitive impairment into the control group (without cognitive impairment) and the case group (with cognitive impairment). The data showed that the differences in the general conditions of the two groups were not obvious, but the serum ALP levels of patients in the case group were higher than those of the patients in the control group. There was a negative correlation between the ALP level of the patients in the case group and their MoCA total score, visuospatial and executive scores, and memory scores. This suggests that there is a correlation between serum ALP level and cognitive deficits in the post-stroke period which can be used as a biomarker for early identification of high-risk cases of cognitive deficits in post-stroke periods.

As for the mechanism of vascular calcification, it works by promoting calcification in vivo and inhibiting calcification at the same time [13]. These two systems interact with each other, so when ALP is elevated, the balance between these two systems is disrupted. When ALP is overexpressed, it increases the rate of hardening of the blood vessels, which causes atherosclerosis and cerebral ischemic changes. These changes can lead to mild manifestations of vascular cognitive impairment and dementia.

As for the inflammatory mechanism, serum ALP levels will be raised similar to C-reactive protein when the body is subjected to inflammatory infections, thus triggering endothelial dysfunction and vascular damage. Cerebrovascular pathological changes of the collagen deposition mechanism have many types. Such as in periventricular venous collagenous disease, ALP will induce collagen deposition that increases the thickness of the venous and microvascular wall, triggering chronic ischemia of brain tissue [14].

In summary, it is shown that cognitive impairment is a common manifestation after a stroke. Hence assessing the risk coefficient of cognitive impairment in advance and adopting certain interventions can actively reduce its incidence and impact. The present study found that there is a correlation between the level of ALP and cognitive impairment after mild acute ischemic stroke in the elderly. The level of ALP in patients with cognitive impairment is significantly elevated, which suggests that it is possible to predict the incidence and severity of cognitive impairment through the detection of the serum ALP level in advance. Thus, a targeted therapeutic plan can be formulated in advance to improve the clinical prognosis positively.

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Disclosure statement

The authors declare no conflict of interest.

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