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Pineal gland calcification confirmed by CT scan is associated with ischemic stroke

Yaser Moadabi[1,2], Metanat Rezaei[3], Enayatollah Homaei-Rad[4,5], Sima FIlah Arzpeyma[6], Sama Noroozi Guilandehi[3], Sasan Andalib[2,5,7]

[1]Department of Neurology, Poursina Hospital, School of Medicine, Guilan University of Medical Sciences, Rasht, Iran
[2]Neuroscience Research Center, Poursina Hospital, School of Medicine, Guilan University of Medical Science, Rasht, Iran
[3]School of Medicine, Guilan University of Medical Sciences, Rasht, Iran
[4]Social determinants of Health Research Center, Guilan University of Medical Sciences, Rasht, Iran
[5]Guilan Road Trauma Research Center, Guilan University of Medical Sciences, Rasht, Iran
[6]Department of Radiology, Poursina Hospital, School of Medicine, Guilan University of Medical Sciences, Rasht, Iran
[7]Department of Neurosurgery, Poursina Hospital, School of Medicine, Guilan University of Medical Sciences, Rasht, Iran

ABSTRACT

Background. Stroke is the second leading cause of death and the most common debilitating neurological disorder worldwide. The ischemic injury causes inflammation and oxidative stress, and leads to apoptosis, necrosis and activation of autophagal pathways determining final infarct size. Melatonin, a hormone secreted by the pineal gland, is a small molecule that acts as a free radical scavenger, and performs antioxidant activities in several neurodegenerative diseases. Melatonin secretion reduces in aging due to pineal gland calcification and thus the calcification is a representative of reduced melatonin production. In this study, our aim was to evaluate the association of pineal gland calcification and stroke.

Material and methods. An analytical cross sectional single center study was conducted. Pineal gland calcification was assessed by CT scan in 179 patients with ischemic stroke and 177 hospital controls.

Results. The mean age in the control and stroke groups were 58.18 and 61.2 years, respectively. Pineal gland calcification was found in 77.4% of subjects in the control group and 88.8% of the subjects in the stroke group. Pineal gland calcification, alone, was shown to significantly increase the risk of ischemic stroke (P=0.005; OR=2.3; 95% CI=1.2-4.1). Furthermore, after adjustment for diabetes mellitus, hypertension, hyper lipedema, gender, and age, there was still a significant association of pineal gland calcification with ischemic stroke (P=0.04; OR=2.0; 95% CI=1.0-3.9).

Conclusion. The evidence from the present study suggests that pineal gland calcification is associated with ischemic stroke.

Keywords: stroke, ischemic injury, pineal gland calcification, melatonin

INTRODUCTION

Stroke, observed mostly in the old (1), is a leading cause of death. Death and disability due to stroke are major concerns. Ischemic stroke is the most common type of stroke, in contrast to hemorrhagic stroke, which accounts for approximately 10-20% of all strokes (2). Blood pressure, especially systolic blood pressure, is a major risk factor of stroke, as well as diabetes mellitus and hyperlipidemia. Two third of stroke patients show these risk factors, however, others must have other unknown risk factors (3-5).

Corresponding author:
Sasan Andalib
E-mail: andalib@gums.ac.ir

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Inflammatory (6) and mitochondrial (7) pathways are involved in stroke. The ischemic injury causes disruption of blood brain barrier, inflammation, and oxidative stress. Brain cells can attenuate the effects of oxidative stress and are highly susceptible for oxidative damage (8). Reactive Oxygen Species (ROS), as a product of oxidative stress, damages proteins, lipids, and DNA and induces apoptosis, necrosis, and activation of autophagal pathways, which in turn determine final infarct size (9).

The pineal gland is located at the posterior part of the third ventricle. The main responsibility of the pineal gland is to secret melatonin which is a hormone regulating sleep. This small molecule acts as a free radical scavenger with antioxidant activities in many neurodegenerative diseases (10). In addition, melatonin has antioxidant and neuroprotective effects upon cerebral ischemia (11). It has potential benefits in reducing neuronal death in stroke patients through antioxidant treatment (11).

Melatonin serves its protective effect mediated through various pathways. By way of illustration, melatonin can activate nuclear factor-erythroid 2-related factor 2, which is a intracellular oxidative stress manager (12). Moreover, one of the important intracellular events during stroke is oxidative toxicity which increases ca2+ modulated by melatonin.88 Melatonin can also reduce apoptosis and neural cell death through PI3K/Akt cascade (13-15). Melatonin reduces in aging, neurodegenerative diseases, and stroke, which-has been propounded to be caused by pineal calcification (16-19).

Brain ischemia is regulated through multiple signaling pathways result in activation of oxidative stress process, Ca2+ dyshomeostasis, mitochondrial dysfunction, proinflammatory mediators, excitotoxicity and/or programmed neuronal cell death; its actions to improve ischemic long-term behavioral and neuronal deficits, preserving the functional integrity of the blood-brain barrier (BBB) and improving synaptic transmission (20).

Pineal calcification happens when calcified concretions of hydroxyapatite sediment are formed. Computed tomography (CT) is used for evaluation of pineal calcification (21). Pineal calcification and subsequent reduction of melatonin production may predispose individuals to stroke (21). Moreover, therapeutic regimens with melatonin after stroke can reduce injury and improve functional outcomes (22, 23). According to its safety for human and ability to cross the blood-brain-barrier (BBB), it can be a potential novel therapy for ischemic stroke (11). Literature indicates controversial clinical data regarding association of pineal calcifications in various populations. In the present study, we evaluated pineal calcification as a predictor of ischemic stroke in an Iranian population.

MATERIAL AND METHODS

An analytical cross-sectional single center study was conducted in order to study the potential role of pineal gland calcification in ischemic between 2017 and 2018. Ischemic stroke patients (n=179) were recruited from Poursina hospital of Guilan University of Medical Sciences. Diagnosis was made using Brain CT scan imaging. Hospital controls (n=177) with head trauma, without neurological and neurosurgical complications were also recruited. We collected subjects with 50-70 years of age.

Demographic characteristics of the subjects (age and gender) were collected, in addition to data on history of hypertension, diabetes mellitus, and hyperlipidemia. Pineal calcification was diagnosed using Brain CT scan. Association of pineal calcification was calculated by logistic regression analysis using STATA SE V.1. Odds ratio (OR) along with 95% confidence interval (95% CI) were also calculated.

RESULTS

The mean±SD of age was 61.23±5.5 and 58.18±5.5 years in the case and control groups, respectively (P=0.001). There was a significant difference in pineal calcification, gender, diabetes mellitus, hypertension, and hyperlipidemia between the case and control groups (Table 1).

TABLE 1. *Univariate logistic regression analysis of various parameters involved in stroke*

Parameter	Case N(%)	Control N(%)	P value	OR	95% CI
Pineal calcification	159(89%)	137(77%)	0.005	2.3	1.2-4.1
Diabetes Mellitus	63(35%)	33(18%)	0.001	2.3	1.4-3.8
Hypertension	125(70%)	53(30%)	0.001	5.4	3.4-8.5
Hyperlipidemia	46(25%)	18(10%)	0.001	3	1.6-5.5
Gender (Female)	85(47%)	70(39%)	0.13	0.7	0.4-1.1
Age	-	-	0.001	1.1	1.0-1.1

TABLE 2. *Multivariate logistic regression analysis of various parameters involved in stroke*

Parameter	P value	OR	95% CI
Pineal calcification	0.04	2.0	1.0-3.9
Diabetes Mellitus	0.32	1.3	0.7-2.3
Hypertension	0.001	5.4	2.3-6.2
Hyperlipidemia	0.09	3	0.9-3.5
Gender	0.85	0.9	0.6-1.5
Age	0.001	2	1.0-1.1

Table 2 illustrates multivariate logistic regression parameters involved in stroke. After adjustment for diabetes mellitus, hypertension, hyper lipedema, gender, and age, there was a significant association between pineal calcification and stroke (P=0.04).

DISCUSSION

Stroke is one of the most common life-threatening neurological disorders and a leading cause of disability (24). It mostly affects the elderly causing a significant burden to their family (25). Melatonin has antioxidant activities useful against ischemic injuries. It has been used against as a therapeutic agent ischemic brain injury (20). In the present study, we studied association of pineal calcification and ischemic stroke in an Iranian population.

Our study showed that 77 % of the hospital control group had pineal calcification. Daghighi et al. (26) reported that 71% of patients with trauma had pineal calcification in their brain CT scan. Moreover, Yalcin et al. (27) studied 12,000 Turkish patients without any pathologic lesion and reported pineal calcification in 71.6% of the subjects.

We found that gender was not associated with ischemic stroke in the studied population. However, age, hypertension, and hyperlipidemia were demonstrated to have an association with ischemic stroke. In our investigation, pineal calcification, alone, was shown to significantly increase the risk of ischemic stroke. Furthermore, after adjustment for diabetes mellitus, hypertension, hyper lipedema, gender, and age, there was still a significant association of pineal gland calcification with ischemic stroke.

Our finding was in agreement with those of Kitkhuandee et al. (21) studying association of pineal calcification and symptomatic cerebral infarction in 620 Thai patients. In their study, by univariate logistic regression was used and age of more than 50 years, hypertension, diabetes, dyslipidemia, and pineal calcification were significantly related to cerebral infarction. Moreover, pineal calcification as a risk factor of cerebral infarction showed an adjusted OR of 1.35 (95% CI=1.05-1.72).

Kitkhuandee et al. (28) investigated 1071 Brain CT scans of patients with symptomatic intracerebral hemorrhage and evaluated the association of and pineal calcification and the disease. Intracerebral hemorrhage and pineal calcification were observed in 77 (7.2%) and 689 (64.3%) of Thai patients, respectively. The authors pointed out that pineal calcification is a significant risk factor of intracerebral hemorrhage (OR=2.36; 95% CI=1.22-4.54). Moreover, age of more than 50 years, hypertension, and diabetes, were found to be associated with the disease.

On the other hand, Del Brutto et al. (29) tested the hypothesis of the association of pineal calcification and stroke in a population-based study in Ecuador. Pineal calcification was found in 61% versus 54% of individuals with and without stroke, respectively. After adjustment for age, sex and cardiovascular health, no association was observed between any evidence (p=0.916) or severity (p=0.740) of pineal calcification and the disease.

CONCLUSION

Altogether, the evidence from the present study suggests that pineal calcification is associated with stroke and has a predictive value in this regard. Therefore, we suggest that clinicians attend to the imaging evidence of pineal calcification in CT scans. Further investigation is required to assess the predictive role of pineal calcification size and severity of ischemic injury.

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