Large Vessel Atherosclerotic Infarction and Lacunar Lesions

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Abstract-

Background and Purpose: Lacunar infarcts are small deep infarcts resulting from an occlusion of a perforating artery, and account for about a quarter of all ischemic strokes. Some new investigations indicate that subcortical lacunar lesions may have a greater chance of causing a progressive cerebral stroke than deep lacunar lesions in future. The goal of this study was to determine the frequency of subcortical and deep lacunar lesions and its association with large vessel atherosclerotic infarction at the Ali-Ibne-Abi Taleb Hospital, Rafsanjan.

Materials and Methods: In a cross-sectional study with consecutive sampling of patients with clinical suspicion of cerebral strokes that were assessed with magnetic resonance imaging (MRI), patients with ischemic strokes were selected. Diagnosis of large vessel atherosclerotic infarction was confirmed with carotid Duplex/Trancranial Doppler sonography. Then patients with lacunar lesions on MRI were assessed about their locations. One hundred and eighty patients were studied. The data were analyzed by SPSS software.

Results: 57.8% of patients were women and 42.2% were men. 58.6% of patients were older than 60 years. 67.8% of patients had deep lacunar lesions, 28.3% had subcortical lacunar lesions, and 3.9% had both. 56.11% had a history of hypertension. In patients with a history of hyperlipidemia, 80.1% had deep lacunar lesions. Frequencies of hypertension and hyperlipidemia were significantly higher among the patients with deep lacunar lesion ($p<0.01$).

Conclusions: There is no association between large vessel atherosclerotic infarction and the site of lacunar lesions. Both hyperlipidemia and hypertension are risk factors for deep lacunar lesions.

Key Words: Cerebral infarction, Thrombotic stroke, Lacunar lesion, Large vessel atherosclerotic disease

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INTRODUCTION

Stroke is a common cause of death in many countries around the world[(1)]. It is also on the top list of neurological diseases due to its high prevalence. Considering its relapse, severity and constant physical and mental complications, stroke is a neurological disease with the highest rate of morbidity[(1)]. Lacunar stroke,

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comprising 25% of all cases, is due to the obstruction of small penetrating branches of the brain, and its risk factors are nearly common with those of large vessel atherosclerotic infarction. In 85% of cases, hypertension, diabetes, or both are involved with the incidence of this condition[1,2]. Some recent studies present that lacunar lesions are not of equal value among individuals and can be categorized according to properties such as patient's age[3,4], electroencephalogram (EEG) changes[5] and location[6]. A study conducted in Japan has shown that lacunar lesions may have prognostic value according to their locations i.e., sub-cortical lacunar lesions are at a higher risk of large vessel atherosclerotic infarction[6]. Another study from Netherland has found that sub-cortical lacunar lesions were more prevalent in patients with subcortical thrombotic stroke[7]. In Hong Kong, sub-cortical lacunar lesions were accompanied with a higher rate of intracranial great vessel stenosis, and therefore a large vessel atherosclerotic infarction is more likely[8]. The purpose of our study was to determine the prevalence of risk factors for lacunar stroke and its association with the large-vessel atherosclerotic infarction.

METHODS

This cross-sectional study with consecutive sampling was carried out in Hazrat-e-Ali Ibn Abi Taleb (AS) University Hospital in Rafsanjan, south of Iran. All patients with the impression of cerebrovascular infarction for the first time, on the basis of clinical findings, were examined by a neurologist and magnetic resonance imaging (MRI) was performed. Those with ischemic stroke were included in the study. In doubtful cases, a brain MRI with contrast medium was performed. Those with a history of head trauma, cerebral infection, migraine, other systemic diseases, or drug consumption (except drugs used to control hyperglycemia, hypertension and hyperlipidemia) were excluded from the study. Among the ischemic cases, those with emboli were also excluded after verification of diagnosis through examinations such as echocardiography (transthoracic and transesophageal), electrocardiogram (ECG), around-the-clock ECG monitoring, and examination by a cardiologist. All the remaining cases underwent Duplex / Transcranial Doppler carotid sonography to confirm large vessel atherosclerotic infarction. Those patients, who had at least a lacunar lesion on MRI, were assessed. The data regarding age and gender, history of high blood pressure, hyperlipidemia, diabetes, smoking, drug abuse and consumption of oral contraceptives (OCP), as well as the location of the lacunar lesion on the basis of MRI findings were gathered through a questionnaire.

A 1.5 Tesla MRI instrument was the imaging tool in this study. Sub-cortical lacunar lesions were defined as linearly arranged groups of rounded, circumscribed lesions just below the cortex at the junction of the gray and white matter with a signal intensity that was identical to that of cerebrospinal fluid (CSF) on images obtained with all pulse sequences. Lacunar lesions in other sites were defined as deep lacunar lesions. A patient was considered to have hypertension or diabetes if the disease was diagnosed by a physician and the patient was being treated by medications for at least one month. Hyperlipidemia was present when diagnosed by a physician and the patient had at least one course of drug therapy in the last six months. The patient was considered a smoker or drug abuser when he / she had a daily routine of the smoking or drug abuse in the last three months or a history of these habits for at least one year. Use of OCP was considered positive if the patient had taken them during the last three months or had previously taken them for at least one year.

SPSS software version-11 was used for data analysis and the results were analyzed using independent T-test; Chi square, and Fisher's exact tests. The meaningful statistical level was set at $p \geq 0.05$.

RESULTS

180 patients (76 men, 104 women) with large vessel atherosclerotic infarction who had lacunar lesions on MRI were studied. Mean age of the patients was 62.5 ± 14 years, and 58.6% of them were over 60 years. There was no significant age difference between 2 genders. Table 1 shows the number of patients in each age group. Most of our patients were in the 6-7 decade of life.

Subcortical and deep lacunar lesion were diagnosed in 51 (28.3%) and 122 (67.8%) of patients, respectively, and both were 3.9%. There was no significant relationship between large-vessel atherosclerotic infarction and the location of lacunar lesions (Chi-square test). Table 2 shows the frequency of hyperlipidemia (HLP), hypertension (HTN), diabetes, smoking, opioid consumption, and OCP usage in all patients according to the location of lacunar lesions. Frequencies of HTN and HLP were significantly higher among patients with deep lacunar lesion than patients the subcortical lacunar group ($p<0.01$) while frequencies of diabetes, smoking, opioid consumption, and OCP usage were not different between the 2 groups.

DISCUSSION

Considering the improvement of diagnostic methods such as MRI in neurologic diseases especially in the field of lacunar lesions, remarkable evolutions have been turning up during the recent years. New clinical studies show that lacunar lesions are variously different in many viewpoints such as clinical symptoms, pathogenesis and their location. They are also of different prognostic value[1,9,10].

Although the assessments have already shown that all types of lacunar lesions are at a higher risk for thrombotic stroke[2,6,10,11], some studies indicate that subcortical lacunar lesions are more important. In a study by Adachi et al, it was shown that on the basis of cerebral imaging findings, these patients with subcortical lacunar lesions have a higher chance for a progressive infarction, and it seems that in those cases large cerebral vessels are affected[6]. Also, a study on small subcortical cerebral infarctions in Hong Kong revealed that 16.9% of patients had their large intracranial vessels affected and in 4.2% large extracranial vessels were involved. These findings indicate the probability of a higher rate of constriction of large cerebral vessels in small subcortical lesions[8]. A study by van Den Boom et al.[7] on subcortical lacunar lesions reveals that these lesions, unlike Virchow-Robin spaces which are seen in deep regions of the brain as normal variations, may have prognostic value in large ischemic lesions. In our study, the frequency of deep lacunar lesions (67.8%) was higher than other lesions, but there was no significant relationship between large vessel atherosclerotic infarction and the location of the lacunar lesion. Also in Switzerland, lacunar lesions showed a higher prevalence of thrombotic stroke, regardless of their locations[12]. Ohara et al.[10] from Japan demonstrates that in some cases of deep lacunar lesions there exists an intra- and extra-cranial vessel constriction, although it is mild (less than 25%) and has no relation with the location of lacunar lesion. The fact that in our study, like the two studies mentioned above, there was no relation between the location of the lacunar lesion and large vessel cerebral infarction indicates that

Table 1. *Distribution of age groups among patients*

Age groups	Absolute frequency	Relative frequency (%)
20-29 years	4	2.2
30-39 years	11	6.1
40-49 years	27	15
50-59 years	32	17.8
60-69 years	49	27.2
70-79 years	45	25
80 years or more	12	6.7
All age groups	180	100

Table 2. *Frequency of cerebrovascular risk factors*

Risk factor	Subcortical (N=51)	Deep (N=122)	Both (N=7)	All (N=180)	p-value
Hypertension	38 (74.5%)	59 (48.36%)	4 (57.14%)	101 (56.11%)	0.006
Diabetes	8 (15.68%)	26 (21.31%)	3 (42.85%)	37 (20.55%)	0.23
Hyperlipidemia	7 (13.72%)	46 (37.70%)	4 (57.14%)	57 (31.66%)	0.0028
Smoking	14 (27.45%)	19 (15.57%)	2 (14.28%)	35 (19.44%)	0.18
Opioid consumption	13 (25.50%)	18 (14.75%)	2 (28.57%)	33 (18.33%)	0.19
OCP	10 (19.60%)	16 (13.11%)	1 (14.28%)	27 (15%)	0.55

at least in some cases there is a similar pathogenesis for deep and subcortical lacunar lesions and this may lead to an increased probability of large vessel infarctions. However, this effect may vary in different cases. Another chance is that our research methodology has had ruled in such a defintion. Since the present study is a cross-sectional one, evidently it would be more valuable to design a study for follow-up of patients with subcortical or deep lesions to see if they will proceed to enlarge cerebrovascular infarction.

Many studies similar to ours showed a higher prevalence of deep lacunar lesions compared to subcortical ones[2,11,13]. In this study, the highest prevalence of large vessel atherosclerotic infarction (58.8%) was found at about the age of 60 years that matches many other studies[1,4]. Most cases of large vessel atherosclerotic infarction occur at old ages that match the pathogenesis of stroke, because atherosclerosis, as the most important cause of large vessel atherosclerotic infarction, is more common at older ages[1]. In this study, we also realized that hypertension, with a prevalence rate of 56.11%, is still on the top list of risk factors for thrombotic stroke. In this study, hypertension and hyperlipidemia were significantly more prevalent in cases with deep lacunar lesions than in cases with subcortical lesions ($P<0.01$). Besides hypertension and diabetes which increase the incidence of deep lacunar lesions in many studies[4,9,14], hyperlipidemia also seems to be a risk factor of deep lacunar lesions. These risk factors specifically act through involving small penetrating vessels[1,13].

It seems that we should look for the role of other factors in subcortical lacunar lesions as some recent studies indicate the role of large cerebral vessel stenosis and other mechanisms like brain emboli and CADASIL syndromes[6,7,12] in the incidence of subcortical lacunar lesions that requires further assessment. Therefore, the results of this study suggest that there is no association between thrombotic stroke and the site of lacunar lesions.

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