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ORIGINAL ARTICLE

Magnetic Resonance Imaging (MRI) Findings in Patients with Brain Small Vessel Disease

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ABSTRACT

Background: Cerebral small vessel disease (SVD) affects small perforating arteries, causing both lacunar infarction (LI) and confluent white matter lesions (WML). Small vessel disease or lacunar infarct is one of the major stroke subgroups. Lacunar syndromes may be divided into two groups: the classic group (pure motor hemiplegia, pure sensory stroke, ataxic hemiparesis, dysarthria-clumsy hand syndrome, sensorimotor stroke) and the miscellaneous group, including all other lacunar syndromes. We have evaluated risk factors, clinical syndromes, topography, and laboratory findings of 101 consecutive patients with symptomatic lacunar infarcts diagnosed by magnetic resonance imaging. **Methods:** We analyzed 101 patients with clinical lacunar infarct syndrome who were referred to the neurology department of Qa'em hospital, Mashhad in the northeast of Iran. We assessed clinical features, sex, age, risk factors, radiologic findings and laboratory data of these patients. **Results:** The pure motor hemiparesis (53.5%) constituted the most usual lacunar syndrome. Mean age of the patients was 63.7± 8.5%. Diabetes mellitus was seen in 14 (13.9%) and hypercholesterolemia in 41 (40.6%) of patients. There were significant differences among ataxic-hemiparesis syndrome and hypertriglyceridemia and CVA history. There was a significant difference between miscellaneous syndromes and valve disease history. Also, there was significant correlation between WML and smoking. Thirty percent of the lesions were detected by CT scan. **Conclusion:** Sixty percent of the cases were associated with white matter signal changes. Diabetes mellitus were found in 14% of patients. Hypertriglyceridemia, CVA history and valve disease history were associated with some subgroups, but more investigations should be performed for precise assessment of other risk factors.

INTRODUCTION

Stroke is defined as the sudden occurrence of a focal neurologic deficit, but they may evolve somewhat more slowly over a period of several minutes or hours and occasionally days in thrombotic types. After heart disease and cancer, stroke is the third most common cause of death in the United States (1) and is also the leading cause of disability in adults. The incidence rate of stroke has been increasing during the previous decades which can partly be due to better diagnostic tools, leading to increased detection of less severe strokes (2) Several factors are known to increase the liability to stroke. For ischemic stroke thesefactors can be classified as modifiable and unmodifyable factors. The most important risk factors include older age, male gender, black ethnicity, family history; arterial hypertension, diabetes mellitus, dyslipidemia, heart disease, cigarette smoking,excessive alcohol intake, and body mass index. Increasing age is the most powerful risk factor for stroke (1) Ischemic strokesaccount for approximately 80-85% of all strokes. Ischemic strokes may result from: a) large artery atherosclerotic disease resulting in stenosis or occlusion; b) small vessel or penetrating artery disease (lacunes); c) cardiogenic or artery-to-artery embolism; d) non-atherosclerotic vasculopathies; e) hypercoagulable disorders; and f) infarcts of undetermined causes (3) Cerebral small vessel disease (SVD) affects smallperforating arteries, causing both lacunar infarction (LI) and confluent white matter lesions (WML). Silent brain infarcts and WML are common magnetic resonance imaging (MRI)

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findings in healthy elderly people, but are alsoassociated with increased risk for stroke, cognitive decline and vascular death (3-9)

The term lacune is a pathological one and unfortunately there are few cases in the literature with precise clinicoradiological-pathological correlation; some authors favor the use of the term lacune to describe size and location, without indicating a specific pathology (10). So the term small deep infarcts are preferred.In a recent study, diffusion-weighted magnetic resonance imaging (DWI) showed multiple regions of increased signal intensity in 16% in either a single (6 patients) or different (4 patients) vascular territories, strongly indicating an embolic stroke mechanism (11). LIs due to cholesterolembolism from the aortic arch have also been described (12). In the Barcelona Stroke Registry, 39(11%) of the 3.577 acute stroke patients had an LI (13). MRI is more sensitive to ischemic brain damage than is the CT scan. Softened tissue cannot be seen in CT scan until several days have elapsed. On the other hand, MRI reveals ischemic damage within a few hours, in both white and gray matterand diffusion- weighted MRI techniques do so even earlier. This method has to a large extent replaced conventional angiography, which is reserved for casesin which the diagnosis isin doubt (e.g. suspected angiitis) or when surgical intervention or long-term anticoagulanttherapy is contemplated. Ischemic infarct is hypodense in CT scan and hyposignal in T1w and hypersignal in T2w MRI (14).

In this study, we aimed to update the lessfrequent etiologies causing lacunar infarcts (LIs), to show the sex, and age incidence, to highlight recent advances in risk factors, clinical syndromes, and topography in this subtype of ischemic stroke. The essential goal of this study is to detect theMRI changes in brain small vessel disease in hypertensive patients.

MATERIAL AND METHODS

Research Design and Setting

This study is a descriptive study. All patients with blood hypertensionthat presented with clinicallacunar infarcts referred to Qaem hospital from 11/1383 to 11/1385 were evaluated. For sampling, we used simple sampling method.

Selection Criteria

Inclusion criteria

Hypertensive patients with a history of lacunarstroke, a clinical presentation consistent with one of the lacunar syndrome described by fisher, and MRI evidence of lacunar infarctsthat appeared to be responsible for their symptoms were entered in this study.

Exclusion criteria

Exclusion criteria consist of patients with lacunar infarcts but without hypertension, patients with cortical infarctin MRI, complications of other neurological or psychiatric disorders including drug abuse, depression and hematologic disorders, patients who had clinical syndrome but normal MRI findings, and hemorrhagic CVA or exist of tumor in MRI.

Data Collection

In this study we used a check list to collect data. In this check list we collect all demographic data of patients and the subgroup of the infarct that is report in the result section.

Statistical Analysis

The SPSS© Statistics version 16 (SPSS Inc., Chicago, USA) software is employed for calculation of descriptive statistics, chi- square test. T-test and one - sided variance analysis test for analyzing the statistical data. Diagrams are depicted in MS EXCEL software. For any analyses, P values less than 0.05 were considered statistically significant.

After data collection, these data are described by tables, figures, mid indices, and distribution indices.After that, data were analyzed by chi-square test and t-test. All the above processes are performed by SPSS© Statistics version 17 (SPSS Inc., Chicago, USA) software.

Research Ethics

The written informed consent were obtained from all patients. For the patient's privacy the names of patients were remained private.

RESULTS

In this study there were 101 patients, there were 49 (48.5%) male and 52 (51.5%) female patient (P=0.904). The mean age was 63.7±8.5. The mean age of the male patients was 64.4± 7.7 and of the female patients was 63.1±9.4.

Distribution of age and sex in all types of lacunar infarct has been shown in Table 1.

24 cases of men (44.4%) and 30 cases of women (55.6%) had PMS, but the differences was not significant (P=0.380). we found PSS in 5 men (45.5%) and 6 women (54.5%) that was not significant (P=0.829). Among the patients who suffered from SMS, 3 cases were men (42.9%) and 4 cases were women (57.1%), but this differences was not significant (P=0.756).

Motor deficit was the most common chief complain in patients (47.5%). Other chief complain has been shown in Table 2.

The distribution frequencies of diabetes mellitus and its relation to the five types of infarct are shown in Table 3. In this table diabetes mellitus was more frequent in PMS but there were no significant difference between the other types and diabetes mellitus.

PSS had the highest percent (54.5%) of hypercholesterolemia between the all types but there were no significant difference between them. There was only one patient with hyperuricemia (1%).

The distribution frequencies of TIA history and its relation tothe five types of infarct have been shown in Table 4.

The results showed equal number of positive and negative CVA history in patients who suffered from PMS and

Table 1. Distribution of age and sex and frequencies of lacunar infarct

Subgroup of infarct	Age (year) Mean±SD	Men n (%)	Women n (%)	Total n (%)
Pure motor syndrome	64.2±8.6	24 (29.7)	30 (29.7)	54 (53.5)
Pure sensory syndrome	60.9±7.9	5 (4.9)	6 (5.9)	11 (10.8)
Sensory motor syndrome	63.4±6.2	3 (2.9)	4 (4)	7 (6.9)
AH	64.1±10.2	13 (12.9)	11 (10.9)	24 (23.8)
Miscellaneous	63.4±6.2	4 (4)	1 (1)	5 (5)
Total	63.7±8.5	49 (48.5)	52 (51.5)	101 (100)

Table 2. Distribution of chief complains

Chief complain	N	%
Motor deficit	48	47.5
Memory disorders	12	11.9
Cerebellar symptoms	12	11.9
Sensory loss	11	10.9
Vertigo	8	7.9
Speech disorder	3	3
Miscellaneous	7	6.9
Total	101	100

Table 3. Distribution of diabetes mellitus in different subgroups of infarct

Subgroup of infarct	Non diabetic	Diabetic	P value
Pure motor syndrome			
Yes	48 (88.9)	6 (11.1)	0.391
No	39 (83)	8 (17)	
Pure sensory syndrome			
Yes	9 (81.8)	2 (18.2)	1.000
No	78 (86.7)	12 (13.3)	
Sensory motor syndrome			
Yes	6 (85.7)	1 (14.3)	1.000
No	81 (86.2)	13 (13.8)	
AH			
Yes	20 (83.3)	4 (16.7)	0.906
No	67 (87)	10 (13)	
Miscellaneous			
Yes	4 (80)	1 (20)	1.000
No	83 (86.5)	13 (13.5)	
Total	87 (86.1)	14 (13.9)	

Table 4. Distribution of TIA history in different subgroups of infarct

Subgroup of infarct	Without TIA	With TIA	P value
Pure motor syndrome			
Yes	45 (83.3)	9 (16.7)	0.962
No	39 (83)	8 (17)	
Pure sensory syndrome			
Yes	8 (72.7)	3 (27.3)	0.579
No	76 (84.4)	14 (15.6)	
Sensory motor syndrome			
Yes	7 (100)	0 (0)	0.477
No	77 (81.9)	17 (18.1)	
AH			
Yes	21 (87.5)	3 (12.5)	0.736
No	63 (81.8)	14 (18.2)	
Miscellaneous			
Yes	3 (60)	2 (40)	0.419
No	81 (84.4)	15 (15.6)	
Total	84 (83.3)	17 (16.8)	

AH, but none of the patients who were affected by PSS, AH, and miscellaneous have positive history of CVA. Differences between these subgroups were not significant except the patients with AH that showed significant difference between patients with positive and negative history of CVA (P=0.012).

In patients with PMS, 9 patients had positive and 9 patients had negative history of myocardial infarction (MI) (P=0.745). None of the patients who were in miscellaneous subgroup have positive history of MI (P=0.639). Positive history of MI were seen in 2 patients with PSS, 1 cases of SMS and 6 cases of AH, but there were no significant difference between them (P=1.000,1.000, and 0.292 respectively).

The distribution frequencies of valve disease history and its relation to the five subgroupsof infarct were shown in Table 5.

The distribution of all lacune number that was detected in MRI has been shown in Figure 1.

The distribution of lacune number between male and female has been shown in Figure 2. There was no significant differences between male and female in number of lacunes (P=0.638, 0.632, and 0.876 in 1, 2, and more than 2 lacunes respectively).

The most common location of lacunes was internal capsule (61 cases). Location of lacunes in 32 cases (59.3%) of patients with PMS was basal ganglia (P=0.000). In patients with PMS, the differences between persons with lacune in paraventricular area and persons without lacune in paraventricular area was significant (P=0.005). We found significant

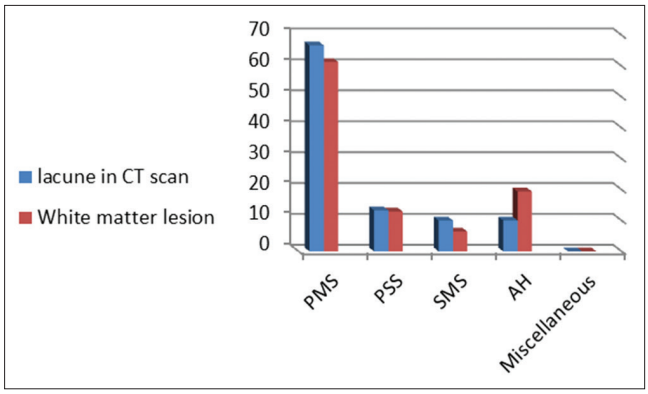

Figure 1. Distribution of lacunar number in different subgroups of infarct

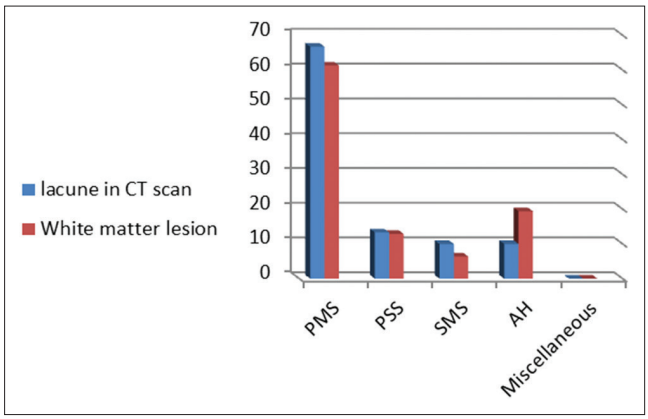

Figure 2. Distribution of lacune number between male and female

Table 5. Distribution of valvular heart disease history in different subgroups of infarct

Subgroup of infarct	Negative VHD history	Positive VHD history	P value
Pure Motor Syndrome			
Yes	51 (94.4)	3 (5.6)	1.000
No	44 (93.6)	3 (6.4)	
Pure Sensory Syndrome			
Yes	10 (90.9)	1 (9.1)	1.000
No	85 (94.4)	5 (5.6)	
Sensory Motor Syndrome			
Yes	7 (100)	0 (0)	1.000
No	88 (93.6)	6 (6.4)	
AH			
Yes	24 (100)	0 (0)	0.359
No	71 (92.2)	6 (7.8)	
Miscellaneous			
Yes	3 (60)	2 (40)	0.019
No	92 (95.8)	4 (4.2)	
Total	95 (94.1)	6 (5.9)	

differences in patients with PSS between who had lacune in internal capsule and who had no lacunes in internal capsule

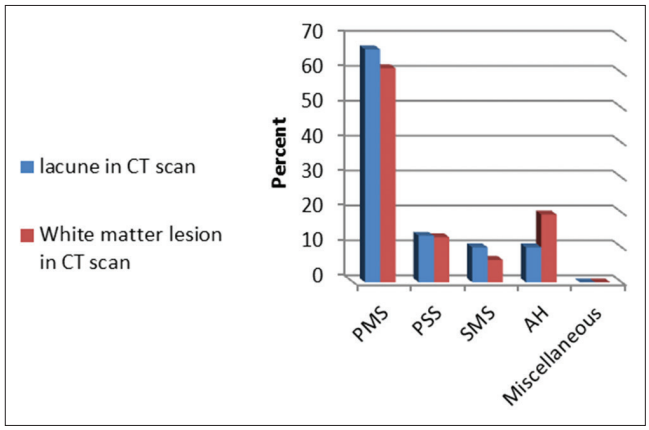

Figure 3. Distribution of lacunes and white matter lesion in CT scan in each subgroup of infarct

Table 6. Distribution of age and sex according to WML

Sex	n	%	Mean age (year)± SD
Men	28	46.7	66.6±8.6
Women	32	53.3	63.6±9.9
Total	60	100	64.9±9.4

(P=0.004). Also there was same result in patients with SMS (P=0.03). These lacunes were in pons in 12 patients (50%) with AH.

Results showed significant difference between patients with lacune in basal ganglia and patients without lacune in basal ganglia in AH subgroup (P=0.011).

We found white matter lesion (WML) in brain MRI of 48.4% of patients with PMS. 10% of patients with PSS, 8.3% of SMS, 28.3% of AH, and 5% of miscellaneous subgroup had WML in MRI, but we found no significant differences between them (P=0.211, 1.000, 0.703, 0.128 respectively. Because of few sample in miscellaneous subgroup, we didn't have p value for it).

The distribution of lacunes and white matter lesion in CT scan in each subgroup of infarct has been shown in Figure 3.

According to distribution of WML in brain CT scan and brain MRI, motor deficit (45%) and memory disorders(20%) were the most frequent chief complaints.

Distribution of age and sex according to WML has been shown in Table 6. The differences were not significant statistically (P=0.653).

DISCUSSION

In this study, there were 101 patients that PMS was the most frequent syndrome. The clinical pictures were including PMS (54 cases), PSS (11 cases), AH (24 cases), SMS (7 cases), and miscellaneous syndrome (5 cases). The miscellaneous group included PMS plus 6th-nerve palsy (2case),-Claude syndrome (1 cases), and cerebellar hemiataxia and dissociated sensory loss (2 cases). There were 49 (48.5%) male and 52 (51.5%) female. There were no significant differences in incidence of lacunar syndromes between male and female. The mean age was 63.7. For assessment the distribution of age, we used the kolmogorov-smirnov goodness

of fit test and the distribution of the age was normal with a S.D= 8.5 year. The mean age of the male patients was 64.4 ±7.7 (they were in range of 41-80) and of the female patients was 63.1± 9.4 y (they were in range of 40-83). Although in most other studies (15), lacunar infarct was more frequent in males, in this study, it was more frequent in females, but there was no significant difference between them.

PMS were the most frequent syndrome in this study (53.5%) which resembles the other studies (16). AH syndrome was the 2nd common syndrome (23.8%) and this also meets with the other studies.Diabetes mellitus was more frequent in PMS but there were no significant difference between diabetes mellitus and the lacunar subgroups. Diabetes mellitus was seen in 17% of patients in Baumgartner's study (13) PSS had the highest percent (54.5%) of hypercholesterolemia between the all subgroups, but also like diabetes mellitus there were no significant differences between them. There were 15 (14.9%) patients that had triglyceridimia, and triglyceridemia had a significant relation with AH syndrome with. But there were no significant differences between triglyceridemia and the other subgroups of infarct. Although we did not find any significant difference between triglyceridemia and PSS and SMS syndromes, hyperlipidemia has been reported as a risk factor for lacunar infarcts in many studies (15)

Cigarette smoking was more frequent in PMS. There were 28 (27.7%) patients with smoking history but there were no significant differences between it and the subgroups of infarcts. Baumgartner et al (21) reported cigarette smoking in 51%. In contrast with our study, Bessonet al. and spolveri obtained significant differences (15, 23). TIA history was more frequent in PMS but there were no significant differences between it and the all subgroups of infarcts. Our study showed TIA history in 16.8% of all patients. This rate was 10% in Baumgartner et al (13)

There were 14 (13.9%) patients that had positive history of CVA. CVA history had a significant relation with AH syndrome. 29.2% of AH subgroup had positive CVA history. There were no significant differences between CVA history and the other subgroups of infarct. This suggests that AH syndrome may have a common pathogenesis with CVA and it maybe a result of emboli process. AH syndrome had highest percent (25%) of MI history between the all subgroups but also like diabetes there were no significant differences between them.

There were 2 (40%) patients that had history of valvular heart disease. Valvular heart disease history had a significant relation with miscellaneous syndrome, but because of few sample, this relation may be wrong (only 5 patients had miscellaneous lacunar infarct). There were no significant differences between valve disease history and the other subgroups of infarct. As it is mentioned, lacunar infarct was most commonly multiple, and more than 75% of lacunar infarcts had two or more than two lacunas. This finding is similar to other studies (1, 14). Single lacuna,two lacunas and more than two lacunas were more frequent in PMS (60%, 48.8%, and 58.6% respectively). This finding is probably because PMS was the most frequent syndrome.

We studied the relation between sex and the number of lacunas. There were no significant relation between sex and number of lacunas. This result also was similar to other studies (5). Internal capsule and basal ganglion were the most common locations in this study that were affected. There were a significant difference between PMS and locations include internal capsule and basal ganglion. PMS had also a significant difference to semi oval areas. These findings are similar to the literature (13, 17). Thalamus was the most common location that affected in PSS subgroup in this study. There were a significant difference between PSS and areas include thalamus and internal capsule. This finding also correlates well with literatures (18) Thalamus and internal capsule were the most common locations of lacunas in SMS subgroup patients. There were also a significant difference among this areas and SMS. Pons and internal capsule areas were the most common locations of lacunas in AH subgroup patients. There were a significant differences between pons, internal capsule and basal ganglia and AH.

CT scan detected lacunes in 30 patients (29.7%). This is slightly lower than what the many studies mentioned it (17). CT scan detected white matter changes in 31 patients (30.7%) that were lower than what has been mentioned in many other studies (12, 16). These two findings may be as a result of different CT scan protocols or programs used in Iran compared with other radiologic centers. In present study, 18% of all patients had MI history. This rate was lower than Arauz et al. They reported MI history in 32% of patients (15) White matter lesion was seen in 60 (59.4%) of all patients. Motor deficit (45%) and memory disorders (20%) were the most common chief complaint in patients that had WMLs. There was a significant difference among cigarette smoking and WML, but there were no significant difference between it and the other risk factors.

CONCLUSION

In conclusion, Triglyceridemia, CVA history and valve disease history were associated with some subgroups but more investigations should be done for precise assessment of other risk factors.

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AUTHORS CONTRIBUTION

All the authors contributed in this study equally.

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