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Investigation of The Clinical and Diffusion-Weighted Brain Magnetic Resonance Imaging Findings in The Patients with Repeated Transient Stereotypical Neurological Deficit in Loghman-Hakim Hospital from 2019 to 2020

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ABSTRACT

Background and Aim: Stroke is recognized as the third leading cause of death worldwide and is one of the most important causes of disability in adults. Hence, strategies that can be useful in improving the condition of the patients suffering are constantly investigated. One of these strategies is the precise approach to transient ischemic attacks. Accordingly, this study was done to Determine clinical and brain Magnetic Resonance Imaging findings in patients with repeated stereotypical transient ischemic attack (TIA).

Methods: 36 patients referred to Loghman-e-Hakim Hospital with symptoms of transient stereotypical ischemic attacks within the first 24 hours were enrolled in this study. Patients were followed up for a complete history at the entrance time, and Brain CT was done. Cases with metabolic and toxic causes, existence of non-ischemic evidences in Brain CT, as well as prohibition of MRI were excluded. The information was obtained by the various examinations of clinical presentation, underlying risk factors, as well as the history of medication, and it was entered in a data collection form. MRI (Brain and cervical MRA & Brain MRI) was performed for patients up to 72 hours. EEG was also done on patients with symptoms such as paresthesia or loss of consciousness, or patients suspected of seizure. Finally, the neurologist made the final diagnosis and the data were analyzed by a statistical expert using SPSS version 24.

Results: 36 patients were enrolled in this study. According to the studied clinical symptom, 23 patients (63.8%) had hemiparesis, 5 patients (13.9%) had hemiparesthesia, 20 patients (55.5%) had dysarthria and 23 patients (63.8%) had facial palsy. Among the 36 patients, 20 (55.5%) cases had DWI infarct that 14 (38.8%) cases were lacunar infarct and 6 (16.6%) cases were large infarct. among the 20 patients with infarct, the lacunar infarct of 12 (33.3%) cases were subcortical and 8 (22.2%) cases were cortical. Also, based on investigation of the artery stenosis, 18 patients (50%) had artery stenosis among which, 7 patients (19.4%) had stenosis of small vessels and 11 patients (30.6%) had stenosis of large vessels. According to the results of this study, there is a significant relationship between artery stenosis and infarct in DWI ($P = 0.007$). In addition, there was no significant difference between infarct size and the size of constricted arteries, in terms of DWI ($P = 0.1$).

Conclusion: Most patients with repeated stereotypical TIA have infarct in DWI a thrombotic cause, and anticoagulant drug can be replaced by anticoagulants.

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INTRODUCTION

Stroke is among the leading causes of morbidity, mortality, and disability among both of the developed and developing countries, accounting for approximately 15 million new cases and five million deaths annually [1].

In 2009, the American Heart Association (AHA)/American Stroke Association (ASA) collaboratively presented a new scientific definition for Transient Ischemic Attack (TIA) as follows: "Transient episode of neurological dysfunction caused by the focal cerebral ischemia, spinal cord with no evidence of acute infarction" [2]. Before presenting such new definition, TIA was exclusively and basically defined based on the duration of the symptoms in less than 24 hours along with some typical episodes occurring in less than one hour. The hypothesis regarding the duration of the symptoms was largely based on several studies in which, brain damages were simultaneously visible in more than 50% of the cases evaluated by MRI. Overall, the risk of ischemic stroke after TIA occurrence has been estimated to be about 3 - 4% [3], its incidence would be around 11% after 7 days and 24 - 29% over the next five years [4]. Generally, TIA may last only for a few minutes and often declines prior to the referral of the patient to the medical healthcare centers.

The symptoms of TIA patients are largely similar to those of ischemic stroke patients and include unilateral limb weakness, speech disturbances, sensory symptoms, visual disturbances, and gait difficulties [5].

Neuroimaging is critical in the evaluation of patients with TIA. CT and MRI are the two available options for imaging. Head CT is more widely available and commonly used. Diffusion MRI is the recommended modality to image an ischemic lesion. The presence of a diffusion lesion in a patient with transient neurological symptoms is an indicator of a high risk of recurrent stroke. Perfusion imaging with perfusion MRI or CT perfusion may improve the detection of ischemic lesions. Noninvasive vessel imaging may detect a symptomatic vessel lesion associated with an increased risk of stroke [6].

Up to a 10% risk of recurrent stroke exists after a TIA, and up to 80% of this risk is preventable with urgent assessment and treatment. Imaging of the brain and intracranial and extracranial blood vessels using CT, CT angiography, carotid Doppler ultrasound, and MRI is an important part of the diagnostic assessment [7].

Accordingly, it is essential to evaluate the hypoglycemia, serum levels of the electrolytes, run coagulation tests; assess the cardiac rhythm by the Electrocardiogram (ECG); determine the Erythrocyte Sedimentation Rate (ESR); and to evaluate the cardiac enzyme levels and lipid profile. In addition, performing the evaluation by the use of the imaging modalities, especially MRI using Diffusion-Weighted Imaging (DWI), will provide the specialists with comprehensive information on the characteristics of brain changes [8-10]. Therefore, the current study was conducted to investigate the clinical outcomes of the patients and findings of imaging (based on MRI using diffusion-weighted sequencing) in the patients who were referred to the hospital presented with transient stereotypical ischemic attacks because MRI is recommended for TIA examination in terms of the National Clinical Guideline for Stroke [2].

METHODS

This study is a routine database study, approved by the University Ethics and Research Committee Shahid Beheshti Medical University with the code of ethics IR.SBMU.RETECH.REC.1397.583 .The aim of this study was to find clinical and radiological findings from patients with the symptoms of repeated transient stereotypical neurological deficit. From the beginning of 2019, 54 patients with these symptoms were referred to a single center for one year. The patients were then examined by a neurologist, and a complete medical history was obtained. Afterward, brain CT was done after ruling out metabolic and toxic causes in the initial tests and ensuring the presence of organic symptoms. The cases with non-ischemic causes (hemorrhagic, tumor, and hematoma) and with contraindication for MRI scan, were excluded from the study, and then, information was obtained from the medical history and physical examination including the clinical presentations (hemifacial paresis, dysarthria, gait disorder, weakness, and numbness of limbs), underlying risk factors (cardiovascular diseases, diabetes, hypertension, hyperlipidemia, and smoking) as well as the history of the medications used (antiplatelets, anticoagulants, as well as those prescribed for blood pressure control, and diabetes) were recorded in the data collection form. Eventually, A total of 36 patients with the symptoms of repeated transient stereotypical neurological deficit in the first 24 hours were included in this descriptive study and patients gave informed consent for entering the study.

Up to 72 hours after the admission, MRI (brain and cervical MRA & brain MRI) was performed for the patients using the Toshiba 1.5 tesla MRI system. Then, the findings of diffusion-weighted imaging were registered in the radiologists' report and the results of ECG and echocardiography including the percentage of Ejection Fraction (EF), the presence of Patent Foramen Ovales (PFO), Myocardial Infarction (MI), arrhythmia, and Atrial Fibrillation (AF) were also recorded by a cardiologist. Moreover, Electroencephalogram (EEG) was done on the patient if there were some positive symptoms such as paresthesia, loss of consciousness, and suspected seizure, and these results were reported by the neurologist and If epileptic discharges were seen on the EEG, a seizure was diagnosed.

In addition, different tests (Complete Blood Count (CBC), C-Reactive Protein (CRP), Erythrocyte Sedimentation Rate (ESR), Low-Density Lipoprotein (LDL), High-Density Lipoprotein (HDL), Total Cholesterol (TC), Triglyceride (TG), glycosylated hemoglobin (HBA1C), and Glucose) were performed on the patients. Patients were excluded from the study if they handed a personal consent and left the hospital prior to performing the diagnostic measures. At last, the final diagnosis was made by the neurologist, and the obtained data were analyzed by the statistician using the SPSS software version 24. Furthermore, minimum, maximum, mean, median and standard deviation indices were used to report the descriptive analysis of the quantitative variables. Frequency and ratio were also used for performing the descriptive analysis of the qualitative variables. Chi-Square and Fisher Exact tests were also used to analyze the qualitative bivariate variables.

RESULTS

A total of 36 patients were included in this study, out of which 19 were female and 17 were male. The data obtained from the statistical analysis are described in following.

In this study, 19 out of 36 patients (52.7%) had hypertension risk and among whom, 15 cases used hypertension medication and 4 cases did not use any hypertension medication. Among the 36 studied patients, 23 (63.8%) cases had hyperlipidemia risk and among whom, 13 patients did not use any drug for hyperlipidemia, and 10 cases used drug for hyperlipidemia. Also, 23 patients (63.8%) had diabetes, among whom, 14 patients used anti-diabetic drugs and 9 patients did not use any anti-diabetic drugs. In terms of investigating the risk factor of ischemic heart disease, 14 patients (38.8%) had ischemic heart disease, and of whom, 8 patients used anti-platelet drug and 6 patients did not use any antiplatelet medication. Also, among the 22 patients (61.1%) who did not have ischemic heart disease, 5 patients used the anti-platelet drugs and 17 did not use the anti-platelet drugs. Moreover, in this study, among the 36 patients, 14 (38.8%) patients were smokers.

Among the 36 studied patients, 23 patients (63.8%) had the symptoms of hemiparesis, 5 patients had hemiparesthesia, 20 (55.5%) had dysarthria, and 23 cases (63.8%) had hemifacial paresis.

Herein, among the 36 studied patients, 27 cases (75%) had negative results regarding the risk factor of AF. Also, among these 27 patients, 14 cases had the restricted lesions in the DWI. In addition, out of 36 patients, 9 patients had the risk factor of AF, out of whom 2 patients used the anticoagulant medication. Among these 9 patients, 6 cases had the restricted lesions in the DWI. Moreover, according to MRI results, among 9 patients with AF, 7 patients had subcortical infarct, and 2 patients had cortical infarct. Findings of the Fisher Exact test for the bivariate analysis showed no significant difference between the presence of AF and infarct location on the MRI (P = 0.6). In this study, among the 36 studied patients, 5 patients (13.8%) had positive results in terms of investigating the risk factor of PFO.

Among the 36 patients, infarct (restricted lesion) was observed in DWI of the 20 (55.5%) cases and of these 20 patients, 14 cases (38.8%) had lacunar infarct (less than 15 mm), and 6 cases (16.6%) had large infarct (more than 15 mm). Out of the 20 patients with infarct, 12 patients (33.3%) had subcortical infarct and 8 patients (22.2%) had cortical infarct. Also, in terms of the artery stenosis investigation, 18 patients (50%) had artery stenosis (stenosis more than 50% of vessel diameter), among whom, 7 patients (19.4%) had stenosis of small vessels (Small vessel refers to small end arteries, arterioles, venules, and brain capillaries which are difficult to visualise) as well as 11 patients (30.5%) who had stenosis of large vessels (Large vessel is one of the major arteries of the brain. These large vessels include circle of willis, basilar artery, carotid terminus and middle cerebral artery, anterior cerebral artery and posterior cerebral artery). The findings of this study showed a significant relationship between the artery stenosis and observation of the infarct in DWI (P = 0.007). In terms of investigating the location of artery stenosis, extracranial stenosis was observed in 3 patients (8.3%), intracranial stenosis was observed in 13 patients (36.1%), and both types of stenosis were observed in 2 patients (6.5%). The results of this study indicate no significant difference between the infarct size on MRI and size of the stenosed vessels (P = 0.1). The final diagnosis indicated that 20 patients (55.5%) had ischemic stroke (Ischemic stroke occurs when a vessel supplying blood to the brain is obstructed, and the restricted lesion was observed in DWI), 2 patients (5.5%) had seizure, and 14 patients (38.8%) had TIA.

DISCUSSION

Totally, 36 patients with the symptoms of repeated transient stereotypical neurological deficit within the first 24 hours, and by having no prohibition for MRI, were included in this study. Also, brain MRI, MRA or CT angiography was done for vascular examination up to 72 hours after the admission. Due to the advances in imaging tools and development of DWI sequencing, and based on a new TIA definition, TIA is referred to the transient ischemic attacks occurring within less than one hour caused by the cerebral, spinal cord, or retina ischemia with no evidences of acute infarct in DWI [2].

Among the 36 included patients, 2 (5.5%) cases were finally diagnosed with seizure, and infarct was observed in DWI

sequences of the 20 (55.5%) cases. Accordingly, these patients were finally diagnosed with the ischemic stroke, infarct was not found in 14 (38.8%) cases, and they were finally diagnosed with the TIA. Moreover, there was no difference in the demographic characteristics and cardiovascular risk factors between the two groups with and without the positive DWI findings. None of the patients had cortical symptoms (aphasia, agnosia, apraxia, etc.) and the symptoms included limbs paresis (63.9%), hemifacial paresis (63.9%), and dysarthria (55.6%). Purroy et al. investigated 254 cases of TIA among which, 66 cases had aphasia (cortical symptoms) while among the 254 patients, 62 patients had a TIA re-episode with dysarthria symptom and limbs paresis with no cortical symptoms. Moreover, acute subcortical lesions in DWI were observed in these 62 cases [11].

In the present study, the restricted lesion was observed in DWI sequences of the 20 patients, and among them, 12 (33.3%) cases had subcortical infarct (4 cases of internal capsule, 4 cases of lenticulostriate, 3 cases of pons, and one case of thalamus) and 8 (22.2%) cases had cortical infarct. Accordingly, in all cases of cortical, the infarct size was less than 15 mm and maybe this was the reason why there was no cortical finding in the examinations. In addition, there was no simultaneous occurrence of cortical and subcortical infarct in any case. In the study by Purroy et al., out of 62 cases with TIA cluster, 7 cases had cortical lesions, 14 cases had subcortical lesions, and 2 cases had lesions in several territories, which show a relationship between subcortical lesions and recurrent TIA episodes [11].

In the current study, among 20 cases with the restricted lesions in the DWI, 14 (38.8%) cases had lacunar infarct, 6 (16.6%) cases had large infarct, and 6 (16.6%) cases had no artery stenosis. Also, 5 (13.8%) cases had stenosis of small vessels, and 9 (25%) cases had stenosis of large vessels; however, no significant relationship was found between the size of stenosed arteries and infarct size in DWI. Moreover, 66.7% of the patients with lacunar infarct had stenosis of large vessels, indicating that, the presence of the stenosis of small or large vessels cannot predict the infarct size.

Villablanca et al., in a study conducted on 45 patients with TIA out of whom 14 cases had the restricted lesions in DWI, found that the cases with positive DWI were more likely to have artery stenosis, which showed no relationship between the size of stenosed arteries and infarct size [12]. In the current study, there was no significant relationship between the presence of AF restricted lesions in DWI and infarct location (cortical and subcortical), while in the study by Purroy et al., the presence of cardiac embolism was the most common cause of cortical restriction [11]. Accordingly, this may be attributed to the fact that, our patients had recurrent stereotypical TIA reducing the probability of cardiac embolism as a cause of TIA. In the present study, artery stenosis was found in the same infarct territory of tract, and simultaneously in 70% of cases with infarct in DWI, whereas there was artery stenosis in 28.5% of the cases with normal DWI, which showed a significant relationship between the artery stenosis and the presence of the restricted lesions in DWI. However, there was no significant relationship between the size of stenosed arteries (small / large), the presence of restricted lesions in DWI, and infarct size (lacunar / large).

In a meta-analysis by Brazzelli et al, a review of 47 articles involving 9,078 stroke patients from 1995 to 2012 showed that in 11 studies there was no association between time and DWI positivity, and in these 11 studies the duration of symptoms was a minor factor [13].

Anticoli et al, in a study conducted on 445 cases with TIA found no corellation between the duration of symptoms and positive or negative DWI, and also showed no relationship between the positive DWI and the risk factors of hypertension, diabetes, smoking, and patients' age. Accordingly, it was also shown that, the risk of long-term stroke recurrence was the same in TIA patients who had positive or negative DWI and received drug treatment, and it was reported that, the positive DWI could not predict the risk of stroke in the future [14]. Hurford et al. (2019), in a study on 633 patients with TIA showed that 13.9% of the cases had the restricted lesions in DWI [15], whereas in the present study, among the 36 studied patients, 20 cases had the restricted lesions in DWI. Accordingly, this higher percentage can be either by accident or by the low number of subjects, or may be because all the cases in our study had recurrent stereotypical TIA within first 24 hours, which has led to the increase in the probability of positive DWI, which mean that, the ischemic stroke has actually occurred as a result of DWI restriction and is presented in the forms of recurrent and stereotypical TIA attacks. Also, there were some limitations in the present study like a small statistical population. Although, the sample size has also been found to be small in other studies that examined the patients with recurrent and stereotypical TIA within the first 24 hours as well, it is suggested to conduct this study during several years.

CONCLUSION

Among the patients who were referred with repeated transient stereotypical neurological deficit within 24 hours, infarct was observed in DIW of 55.5% of the cases, who were finally diagnosed with the ischemic stroke, and 60% of cases had subcortical infarct. Because most patients have a thrombotic cause and a few cases have an embolism, and given the anticoagulant side effects, we may not need to start

anticoagulants abruptly in the emergency room for patients with symptoms of repeated stereotypical TIA and make decisions based on the clinical presentation and MRI manifestations.

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CONFLICT OF INTEREST

The authors declare no conflict of interest in this study.

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