Stroke Mimics: Experience of a Moroccan Stroke Unit

Naima Chtaou, PhD,*,† Siham Bouchal, PhD,*,† Aouatef E.l. Midaoui, PhD,*,† Zouhayr Souirti, PhD,* Nabil Tachfouti, PhD,† and Mohammed Faouzi Belahsen, PhD*,†

Background: Stroke mimic is a medical condition presenting with acute neurological deficit and simulate real stroke. The objective of this study was to evaluate the frequency and the various etiologies of stroke mimics in our center. *Methods:* We retrospectively reviewed the Thrombolysis Alert registry and we studied the frequency and characteristics of patients with stroke mimic. *Results:* Among 673 patients who were admitted to the emergency department within 4.5 hours for sudden focal neurological deficit suggestive of acute stroke, 105 patients (15.6 %) had a stroke mimic. The mean age of patients with mimics and brain strokes were 66.3 and 64.8, respectively. The mean Onset-to-door time was 136.82 minutes and the mean door-to-imaging time was 32.63 minutes in stroke mimics. Seizure (28.5%) was the most common diagnosis of stroke mimics followed by conversion disorder (25.7%). *Conclusions:* Stroke mimic is frequent and heterogeneous entity that can be difficult to identify. Fortunately, most previous studies show no harmful effects when using thrombolysis in a stroke mimic.

Key Words: Frequency—brain stroke—stroke mimic—thrombolysis alert

Introduction

Brain Stroke is a major cause of mortality and morbidity. In Morocco, the prevalence rate of stroke in all agesis estimated at 292 per 100,000.[1]

The management of ischemic stroke has seen major advances with intravenous thrombolysis (IVT) and endovascular thrombectomy (EVT).

IVT has been the standard treatment for acute ischemic stroke (AIS) patients within 4.5 hours of symptom onset.[2] Thrombolysis with tissue plasminogen activator is the first effective approved therapy for potentially disabling AIS.[3] Recently there is more evidence suggesting that other thrombolytics such as tenecteplase may be even more effective.[4]

EVT is another effective therapy; it reduces the risk of death or dependency in patients with large vessel occlusion if applied within 6 hours. The recently published DAWN and DEFUSE 3 trials have shown that EVT is also beneficial 6-24 hours after the onset of symptoms in selected patients with favorable imaging brain.[3-5]

The diagnosis of acute ischemic stroke is usually easy by carrying out physical evaluation and studying images of the brain, however several disorders, manifested by an acute neurological deficit can mimic AIS.

Stroke mimic term is applied in a clinical evaluation, describing those nonvascular conditions that simulate stroke, namely those presenting with sudden neurological deficit that resembles a stroke but is not related to a vascular cause.

Stroke mimics are a major diagnostic challenge. The aim of this study is to evaluate the relative frequency and the various etiologies of stroke mimics in patients with clinical signs of stroke admitted in our emergency room for "Thrombolysis Alert."

Materials and Methods

We conducted a retrospective study of patients identified in our prospective Thrombolysis Alert registry from January 1, 2015 to July 31, 2018.

From the *Department of Neurology, Hassan II University Teaching Hospital, Fez, Morocco; and †Laboratory of Epidemiology, Clinical Research, and Health Community, Faculty of Medicine and Pharmacy, Sidi Mohammed Ben Abdallah University, Fez, Morocco.

Received August 21, 2019; revision received January 1, 2020; accepted January 3, 2020.

Address for correspondence to Naima Chtaou, PhD, Department of Neurology, Hassan II University Teaching Hospital, Sidi Harazem Road, PO Box 1835, Atlas, Fez, Morocco. E-mail: naimachtaou@gmail.com.

1052-3057/$ - see front matter

https://doi.org/10.1016/j.jstrokecerebrovasdis.2020.104651

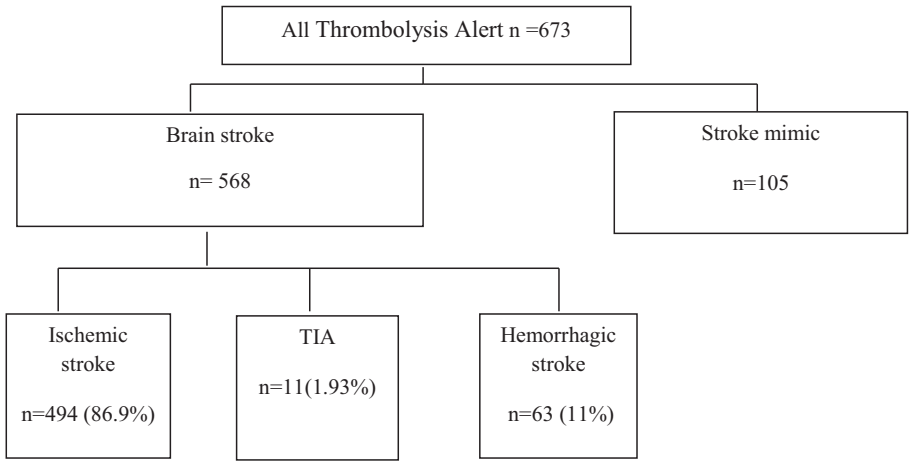

Figure 1. *The distribution in different stroke categories.*

The study included all patients aged over 18 years admitted to the emergency department for sudden focal neurological deficit suggestive of acute stroke within 4.5 hours, for whom a Thrombolysis Alert has been triggered. In some cases, the Thrombolysis Alert was maintained over 4.5 hours for a possible Thrombectomy without IVT.

In Thrombolysis Alert protocol, the neurologist performed a rapid neurological evaluation by using the National Institutes of Health Stroke Scale (NIHSS) and decided or not to maintain Thrombolysis Alert. If Thrombolysis Alert protocol was maintained, emergency brain computed tomography (CT) scan was acquired including brain nonenhancement CT and CT angiography (CTA). In rare cases, magnetic resonance imaging (MRI) was performed especially when it was difficult to precise the delay of the stroke. Emergency blood tests will be also performed including complete blood count, prothrombin time, blood sugar, and kidneys function.

Once the diagnosis of ischemic stroke is retained, the neurologist verifies the inclusion and exclusion criteria for IVT before deciding to start intravenous administration of rt-PA or Tenecteplase.

Patients for whom a Thrombolysis Alert was triggered and among whom imaging did not show an acute stroke were considered to be a stroke mimics.

Our study was approved by the Institutional Review Board of Hassan II University Teaching Hospital of Fez.

All statistical analyses were performed with SPSS software version 20 (SPSS Inc., Armonk, New York).

Results

This study included 673 patients consulted for suspected stroke; the mean age was 65 (19-110). In total, 51.6% (347) were females and 48.4% (326) were males.

The definition of stroke mimic cases for our center was those in which the final diagnosis was a disorder other than brain stroke. Of all participants, 105 patients (15.6 %) had a stroke mimic and final diagnosis of ischemic stroke was made for 494 (86.9%), only 11patients (1.93%) had a transient ischemic attack (TIA) (Fig 1).

In both groups (stroke mimic and brain stroke), the ratio of women was more than the men; the proportion of female patients in the stroke mimic group was 2.1 higher than the other group (53.3 versus 51.2%). Chi-square test showed no significant relationship between sex and early diagnosis of mimic or brain stroke.

The mean age of patients with mimics and brain strokes were 66.3 and 64.8, respectively. There was no significant difference in the mean age of these groups. Patients over 65 years of age in stroke mimic group accounted for 41.9% of cases.

The mean Onset-to-door time (ODT) was 126.38 minutes in brain stroke versus 136.82 minutes in stroke mimic; the majority of patients were admitted within a period of less than 3 hours (180 minutes) in both groups.

Almost all patients had brain CT, MRI was performed just for 14 patients especially for the situation of wake up stroke. The mean door-to-imaging time was 28.71 $\pm$ 21.56 minutes in brain stroke group and 32.63 $\pm$ 20.36 minutes in mimic stroke, there was not statistically any significant difference between these groups.

Patients admitted on weekends accounted for 22% of cases for brain stroke group and 15% for stroke mimic. The comparison between the average ODT of the patients admitted on weekends and that of the patients admitted outside the weekends in both group did not show any significant statistical difference.

The mean NIHSS for brain stroke was 11.6 $\pm$ 5.6 versus 8.6 $\pm$ 3.9 for stroke mimics (Table 1), and statistically there was no significant difference.

Of all 494 ischemic stroke patients, 132 were thrombolysed, with a frequency of 26.7% (132 of 494). The thrombolysis rate all over Thrombolysis Alert group was 19.6% (132 of 673). Seizures were the first most common diagnosis as stroke mimic (n = 35, 28.5%) following by hysterical attacks (n = 29, 25.7%) and hypoglycemia (n = 16, 15.2%), respectively (Table 2).

Table 1. *Epidemiological, clinical, and etiological features of the brain stroke and stroke mimics patients*

	Brain stroke	Stroke mimic
Sex		
Males%	48.8	46.7
Females%	51.2	53.3
Age (years)		
Mean	64.8	66.3
Median	65	68
ODT(min)		
Mean	126.38 ± 73.68	136.82 ± 74.34
Median	120	135
≤180	425 (74.8%)	96 (91.4%)
181-270	109 (19.1%)	8 (7.6%)
>270	34 (0.05%)	1 (0.9%)
NIHSS		
Mean	11.6 ± 5.6	8.6 ± 3.9
0-4	113 (19.9%)	27 (25.7 %)
5-15	380 (66.9%)	68 (64.7%)
≥16	75 (13.2%)	10 (9.5%)
CT image	558	105
MRI	14	0
DIT (min)		
Mean	28.71 ± 21.56	32.63 ± 20.36
Median	22	25
Thombolysis IV	132 (23.2%)	0
Thrombectomy	11(1.9%)	0
Weekend		
Yes	125 (22%)	15 (14.2%)
No	443 (77.9%)	90 (85.7%)

Abbreviations: DIT, door-to-imaging time; NIHSS, National Institutes of Health Stroke Scale; ODT, onset-to-door time.

Table 2. *Relative frequency distribution of different diagnoses for brain stroke mimics*

Diagnosis	Number (Percentage)
Seizure	35 (28.5%)
Hysterical attacks	29 (25.7%)
Hypoglycemia	16 (15.2%)
Brain tumors	10 (9.5%)
Brain metastasis	4 (3.8%)
Encephalitis	2 (1.9%)
Subdural hematoma	2 (1.9%)
Hyperglycemia	2 (1.9%)
Toxic	2 (1.9%)
Vestibulopathy	1 (0.9%)
Syncope	1 (0.9%)
Cavernoma	1 (0.9%)

Discussion

In this retrospective and descriptive study of 673 patients consulted for suspected stroke and seen for Thrombolysis Alert in the ED of Hassan II University Teaching Hospital of Fez (Morocco), 105 patients (15.6 %) had a stroke mimics.

There was harmony between the stroke mimic prevalence identified in our study and that reported by Hosseininezhad et al; 1985 patients with primary diagnosis of brain stroke, referring to the emergency room were studied and 14.9% had stroke mimics.[6]

On the other hand, we found that some studies reported high prevalence of stroke mimics, 30% was the prevalence of stroke mimics in the Merino et al study.[7] In Suggi et al study, 226 patients were admitted for suspected stroke/TIA and 64 patients (28.3%) had confirmed stroke mimics.[8]

In the present study, we found that the average ODT for both stroke mimic patients and brain stroke patients was longer but the average door-to-imaging time was better, 32.63 minutes for stroke mimic patients and 28.71 minutes for brain stroke patients. In previous study conducted in our department,[9] over a period of 2 years (from January 1, 2015 to December 31, 2016); the ODT for all Thrombolysis Alert was also elongated (125.59 minutes). Unfortunately, until now we did not succeed to reduce this delay because to the persistence of the same constraints especially that of medical transportation, which is almost absent for our stroke patients. Only a minority (3.5%) arrived by ambulance.[9]

There are several etiologies revealed by acute onset focal neurological signs, which later found to be noncerebrovascular diseases (Fig. 2).[10] The stroke-mimics identified in our study were similar to previous reports.[11-13] Epilepsy was the most common etiology in our study as in most published studies about stroke mimics.[11-13]

The explanation of the high rate of epilepsy in stroke mimic studies is that, after an epileptic seizure some people can experience a transient focal neurological deficit which can be misdiagnosed as stroke notably if no convulsion are reported. These postictal negative symptoms are not restricted to motor symptoms, others deficits can be observed like aphasia, gaze palsy, and sensory disturbance.[14] Postictal paresis of an arm or leg, also called Todd's palsy, the symptoms could persist for several hours and be considered as stroke symptoms.[15] These transient symptoms are due to cortical neuronal exhaustion following hypoxia or energy depletion because of an underlying predisposing lesion.[16] Imaging has an important contribution for the differential diagnosis. In postictal negative symptoms, brain MRI diffusion-weighted imaging is negative or shows transient changes without a clear vascular topography.[14] Also, CTA is usually unremarkable without evidence of vessel occlusion in this situation.[14] CT perfusion in AIS has become an important adjunct, along with CTA to conventional no enhancement CT brain. It effectively identifies salvageable ischemic brain tissue (penumbra) from irreversible infarction (ischemic core). Perfusion imaging abnormalities have also been reported to be useful in differentiating stroke mimics from AIS.[17] A case-control study of 133 patients confirmed that the value of volume perfusion CT scan differentiate ictal stroke mimics with hyperperfusion from acute ischemic stroke but volume perfusion CT cannot distinguish postictal patients with a normal perfusion or a cortical-subcortical hypoperfusion from acute ischemic stroke patients.[18]

Conversion disorder or functional neurological symptom disorder was adopted by the DSM-V (Diagnostic and Statistical Manual of Mental Disorders, 5th Edition), replacing the term psychogenic with functional.[19]

Previous physical disability, exposure to other disabled subjects and extreme psychological anxiety are the principle risk factors of conversion disorder.[20] The diagnosis of conversion disorder as a stroke mimic can be difficult. Looking for the "Hoover sign," can help to distinguish organic from functional weakness of the leg, extension of the paretic leg can be felt when the contralateral leg is flexed against resistance.[20]

Functional weakness is characterized by its variability in severity overtime, discordant performance between assessments, especially during the same examination. The symptoms disappeared with distraction and increased with attention.[19]

Hypoglycemia is well-known stroke mimic, commonly manifests with acute mental status changes and autonomic symptoms but also with focal neurological deficits such as hemiplegia and aphasia.[21] In patients presenting with acute hemiparesis, the diagnosis of hypoglycemia needs to be considered and a blood glucose test performed. When rapidly recognized, hypoglycemia is easily correctable, and patients often quickly improve.

The conditions most frequently mimicking beside seizures, conversion disorder, and metabolic disorders are brain tumor (Fig. 2), migraine, syncope, and others disorders but the proportion of each etiology varied between studies.[8-15]

None of the stroke mimic patients had an MRI because this exam was not available in an emergency for the majority of our Thrombolysis Alert patients. A careful anamnesis, neurological evaluation and blood tests, absence of early ischemic changes on conventional nonenhancement CT brain, and normal CTA were the primary instruments to identify stroke mimic patients in our study.

In Hand et al study, the authors concluded that NIHSS was useful in distinguishing mimic from stroke.[22] In their study, a low NIHSS predicted a mimic but 19% of brain attacks with an NIHSS >10 were attributable to a mimic.[22] In our present study there was not statistically any significant difference between NIHSS brain and stroke mimics groups.

Significant proportion of patients (9%-30%) presenting with acute neurologic symptoms are stroke mimics, and about 15% of these patients receive IVT.[23] Thrombolysis with Tenecteplase or Alteplase seems to be safe in this condition.[24,25] The symptomatic intracranial hemorrhage rate in this population has been reported around 1.0%.[26] However, it is important to perform all necessary diagnostic methods (clinical assessment, brain imaging, and other tests) to reduce the risk of unnecessary therapy in such cases. Khan et al proposed an algorithm with a scoring system to help identify stroke mimics.[23] Several variables have been used in this scoring included age; presence or not of stroke risk factors; presence of medical history of migraine, epilepsy or psychiatric illness. For patient with a high score (>5), the authors recommend to perform a rapid-sequence MRI to exclude a stroke mimic.[23]

		
A 70 year old man; right ischemic stroke in 2014. Presents left hemicorporal seizures with post-critical left hemiparesis. NIHSS: 6 Cerebral CT (delay 1h20): sequellar lesion making retain vascular epilepsy	A 55 year old woman; History of diabetes treated with insulin. Presented to the emergency room with a right hemiplegia, dysarthria and right facial paralysis. NIHSS: 12 Glucose test: 0.3g/dl; immediate recovery after injection of intravenous glucose. Cerebral CT(delay: 2 hours): normal	A 60 year old man with left hemiparesis. NIHSS: 5 Cerebral CT (delay: 3 hours): cerebral metastasis

Figure 2. *Examples of stroke mimic situations. Abbreviations: NIHSS, National Institutes of Health Stroke Scale.*

Conclusions

The present study showed that a great interest should be given for stroke mimic. Evaluation strategies need to be improved to be able to distinguish ischemic stroke from stroke mimic and to help the decision making when patients with suspected acute stroke are being considered for acute interventions such as IVT.

Conflict of Interest

None.

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