Journal of the Neurological Sciences 331 (2013) 168–171

Contents lists available at SciVerse ScienceDirect

Journal of the Neurological Sciences

journal homepage: www.elsevier.com/locate/jns

Short communication

Stroke warning syndrome: 18 new cases

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ARTICLE INFO

Article history:
Received 4 April 2013
Received in revised form 17 May 2013
Accepted 20 May 2013
Available online 10 June 2013

Keywords:
Capsular warning syndrome
Intravenous thrombolysis
Pontine warning syndrome
Stroke warning syndrome
Small vessel diseases
Transient ischemic attack

ABSTRACT

Background: Stroke warning syndrome (SWS) is a rare cause of stroke characterized by recurrent and short-lasting episodes of transient focal neurological deficits leading up to infarction. On the basis of clinical findings and neuroimaging, it can be capsular, pontine, or callosal. The aim of this study is to evaluate the prevalence of SWS in patients admitted to our Stroke Unit for an ischemic stroke and to look for the difference in outcome between patients treated or not with systemic thrombolysis by intravenous recombinant tissue plasminogen activator (IV-rtPA).
Methods: Among the 967 patients admitted to our Stroke Unit between April 2008 and January 2013 for ischemic stroke, we identified 18 patients with SWS. Nine patients underwent IV-rtPA (IV Group) and the other 9 (No IV Group) other therapies.
Results: The prevalence of SWS in our population was 1.8%. The most common risk factors were hypertension and dyslipidemia in both groups. A good outcome at 3-month follow-up (modified Rankin Scale 0–2) was found in 3 patients (33%) in IV Group and in 5 patients (55%) in No IV Group.
Conclusion: SWS is an under-recognized syndrome. Intravenous rt-PA treatment seems to have lower efficacy than in other subtypes of strokes, but none of the patients with SWS undergoing treatment presented haemorrhagic transformation or other complications.

1. Introduction

In 1993 Donnan et al. identified for the first time a group of patients that presented "crescendo transient ischemic attacks" characterized by three or more identical episodes occurring within 24 h and affecting face, arm, and leg, without cortical symptoms [1]. A high proportion of these subjects developed subsequent capsular stroke defined as "Capsular Warning Syndrome" (CWS). In the same year, it has been reported a case fitting the clinical criteria for the CWS that progressed to anteromedial pontine infarction [2]. Saposnik et al. coined the term "Pontine Warning Syndrome" (PWS) specifically for those cases in which fluctuating and recurrent stereotyped episodes of pure motor hemiparesis, sensory hemiparesis, sensory motor hemiparesis, or ataxic hemiparesis, with or without dysarthria, result from a pontine infarction, usually localized in anteromedial part of the pons [3]. Recently, Nandhagopal et al. described a "Callosal Warning Syndrome" in a patient with transient, stereotyped symptoms of corpus callosum disconnection, associated with MRI evidence of callosal infarction when the symptoms became persistent [4].

In conclusion, the term "Stroke Warning Syndromes" (SWS) may identified these particular type of stereotyped, crescendo, recurrent, and short-lasting episodes of transient focal neurological deficits leading up to infarction [1–4].

Recently, it was reported [5] that although CWS is rare (1.5% of Transient Ischemic Attack), the risk of early stroke is high and the prognosis is poor.

The pathophysiological mechanisms underlying SWS is not fully understood. A mechanism of lipohyalinosis or microatheromatosis of small cerebral vessels may be postulated [1–8] and some authors suggested an hemodynamic changes in the territory of the penetrating arteries with depolarization affecting adjacent motor pathways [7].

Different treatment modalities have been proposed, including blood pressure therapy [9,10], anticoagulation [1,2,7], double antiplatelet therapy [11,12] and thrombolytic agent [3,8,13–18], without conclusive data.

The aim of this study is to evaluate the prevalence of SWS in patients admitted to our Stroke Unit for an ischemic stroke or TIA and to looking for a difference in outcome between patients treated or not with intravenous recombinant tissue plasminogen activator (IV-rtPA).

2. Patients and methods

From April 2008 to January 2013, we retrospectively reviewed 967 patients admitted to our Stroke Unit because of an ischemic stroke

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http://dx.doi.org/10.1016/j.jns.2013.05.027

and, 198 subjects with TIA to identify patients affected by SWS. One hundred and forty-five subjects underwent IV-rtPA (14.7%).

SWS was defined on the basis of clinical presentation of two or more stereotyped episodes occurring within 48 h of pure motor hemiparesis, sensory hemiparesis, sensory motor hemiparesis, or ataxic hemiparesis, with or without dysarthria.

After the review of history, clinical presentation, vascular risk factors, neuroimaging, and follow-up, we identified 18 patients presenting SWS (1.8% of Stroke Patients). If we considered TIA presentation, 8.3% of patients had a SWS.

Nine patients undergoing IV-rtPA treatment (IV Group) and the other 9 (No IV Group) were treated with a loading dose of 300 mg of clopidogrel followed by 75 mg/day and daily high-dose atorvastatin (80 mg). Physicians skilled in acute stroke treatment graduated the neurological deficit through the National Institutes of Health Stroke Scale score (NIHSSs) at admission in the Emergency Room, and during the hospitalization in the Stroke Unit. At admission, all patients were subjected to brain CT and CT-angiography of the cervicocranial arteries. In the IV Group, a brain CT or a brain MRI including DWI-ADC sequences was performed from 24 to 48 h after the drug administration. In the No IV Group, a brain MRI including DWI-ADC was performed in case of brain CT negativity. Color-Doppler ultrasound of the extra- and intracranial arteries has been performed at admission and after IV-rtPA. ABCD2 score as index of TIA recurrence was calculated [19] and all patients had electrocardiogram at admission and trans-thoracic echocardiography within 48 h.

Intravenous rt-PA was administered according to the Safe Implementation of Thrombolysis in Stroke-Monitoring protocol [20].

The patients in No IV Group were not treated with intravenous rt-PA because of their arrival after 3 h from symptoms onset, for spontaneous symptoms' resolution or other contraindications to systemic thrombolysis.

All patients were followed up to 3 months after stroke, by modified Rankin Scale (mRS).

All patients gave an informed consent to study participation. All the pertinent guidelines required by our institution for the preparation of retrospective studies have been followed.

3. Results

Demographics, risk factors, clinical history, ABCD2 score, brain CT or MRI results and outcome are summarized in Tables 1 and 2.

The mean age of the patients was 64.6 ± 9.8 years and the most common risk factors were hypertension and dyslipidemia in both groups. No patients had history of previous cardiac arrhythmic events and electrocardiogram showed a sinus rhythm in all patients.

ABCD2 Score evaluated at the moment of the first episodes was 3 in two patients and greater in the others: 89% of patients had a 2 Day Stroke Risk ≥ 4.1%.

In the IV Group all patients had fluctuating symptoms with the same presentation in the same day, a free periods between each episode and a number of episodes ranging from 2 to 4. Four patients were free of symptoms when admitted in the Emergency Room. Dysarthria and pure motor hemiparesis were the prevalent clinical manifestation.

In No IV Group, the number of episodes varied between 2 and 8 and sometime the first episode was the day before. Also in this group dysarthria and pure motor hemiparesis were the prevalent clinical manifestation.

Brain CT was negative for acute intracranial haemorrhage and ischemic lesions in all patients. CT angiography and Color-Doppler ultrasound did not show haemodynamic extra or intracranial stenosis. None of the patients presented cardiac arrhythmia during ECG monitoring, and echocardiography did not show any cardiac embolic sources.

Table 1
Demographics, risk factors, clinical history, and outcome of IV Group.

Patients	Sex/Age (y)	Risk factors	Clinical history	ABCD2 score	Time from beginning of symptoms to IV-rtPA (min)	NIHSSs at beginning IV-rtPA	NIHSSs at discharge	3 months mRS	Site of ischemic lesion (RM and/or TC)
1	M/79	Hy, Dy	2 episodes of right PMH and dysarthria in the same day	5	80	12	9	3	left anteromedial pontine
2	M/72	Hy, Dy, PS	3 episodes of right PMH and dysarthria in the same day	4	105	12	6	3	Left anteromedial pontine
3	F/54	DM	Persistent ophthalmoparesis and 2 episodes of left PMH and dysarthria in the same day	4	170	9	7	3	rigth anteromedial pontine
4	M/65	Hy, Dy PS, IHD, PIS	4 episodes of right PMH and dysarthria in the same day	5	69	7	7	3	left anteromedial pontine
5	F/53	Hy, CS	2 episodes of left MH and SH and dysarthria in the same day	3	30	7	4	1	rigth anteromedial pontine
6	M/55	Hy, Dy	3 episodes of left MH and SH and dysarthria in the same day	4	120	7	7	2	rigth anteromedial pontine
7	M/77	Hy, DM	2 episodes of right MH and SH and dysarthria in the same day	5	130	5	1	0	left capsular
8	M/48	Hy, Dy, CS	3 episodes of right MH and dysarthria in the same day	4	20	12	10	3	left capsular
9	F/76	Hy, Dy, DM	2 episodes of right MH and dysarthria in the same day	6	180	14	11	4	right capsular

CS: current smoker; DM: diabetes mellitus; Dy: dyslipidemia; Hy: hypertension; IHD: ischemic heart disease; IV-rtPA: intravenous thrombolysis by recombinant plasminogen acivator; MH: motor hemiparesis; min: minutes; mRS: modified Rankin scale; NIHSSs: National Institute of Health stroke scale score; PIS: previous ischemic stroke; PMH: pure motor hemiparesis; PS: previous smoker; SH: sensitive hemiparesis; y: years of age.