Short communication

Stroke warning syndrome: 18 new cases

Rossana Tassi a,⁎, Alfonso Cerase b, Maurizio Acampa a, Paolo D’Andrea a, Francesca Guideri a, Giuseppe Lo Giudice a, Giovanna Marotta a, Sandra Bracco b, Giuseppe Martini a

⁎ Stroke Unit, Department of Neurological and Sensorineural Sciences, Azienda Ospedaliera Universitaria Senese, Policlinico “Santa Maria alle Scotte”, Siena, Italy
b Unit NINT Neuroradiology and Neurointervention, Department of Neurological and Sensorineural Sciences, Azienda Ospedaliera Universitaria Senese, Policlinico “Santa Maria alle Scotte”, Siena, Italy

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A B S T R A C T

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.

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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.
and, 198 subjects with TIA to identify patients affected by SWS. One hundred and forty-five subjects 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.

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 or their arrival after 3 h from symptoms onset, for spontaneous symptoms’ resolution or other contraindications to systemic thrombolysis.

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.

### Table 1

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

<table>
<thead>
<tr>
<th>Patients Sex/Age</th>
<th>Clinical history</th>
<th>ABCD2 Score</th>
<th>Time from beginning of symptoms to IV-rtPA (min)</th>
<th>NIHSSs at beginning of IV-rtPA</th>
<th>NIHSSs at discharge</th>
<th>3 months mRS</th>
</tr>
</thead>
<tbody>
<tr>
<td>IBD</td>
<td>Hy, Dy</td>
<td>2 episodes of right PMH and dysarthria in the same day</td>
<td>5</td>
<td>69</td>
<td>9</td>
<td>7</td>
</tr>
<tr>
<td>Hy, Dy</td>
<td>2 episodes of right PMH and dysarthria in the same day</td>
<td>4</td>
<td>105</td>
<td>6</td>
<td>4</td>
<td>2</td>
</tr>
<tr>
<td>M/53</td>
<td>Dy</td>
<td>2 episodes of left PMH and dysarthria in the same day</td>
<td>4</td>
<td>170</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>M/54</td>
<td>Dy</td>
<td>2 episodes of right PMH and dysarthria in the same day</td>
<td>4</td>
<td>170</td>
<td>7</td>
<td>7</td>
</tr>
<tr>
<td>F/56</td>
<td>Dy</td>
<td>2 episodes of right PMH and dysarthria in the same day</td>
<td>5</td>
<td>69</td>
<td>9</td>
<td>7</td>
</tr>
</tbody>
</table>

IHD: ischemic heart disease; IV-rtPA: intravenous thrombolysis by recombinant plasminogen activator; 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.