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Role of CT Angiography in Thrombolysis Decision-Making for Patients With Presumed Seizure at Stroke Onset

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Background and Purpose—The presence of seizure at stroke onset is a contraindication for intravenous tissue plasminogen activator treatment. A significant proportion of these patients' deficits are not attributable to Todd's paralysis and could be attributable to reversible ischemia. Currently there are no established methods of differentiating Todd's paralysis from ischemic stroke/early seizure. We sought to determine whether computed tomographic angiography (CTA) can be helpful in differentiating the 2.

Methods—Three hundred and twenty six patients underwent noncontrast CT and CTA for acute stroke at our institution over 3 years (June 2002 to April 2005). Of them, 116 had disabling deficits and presented within 3 hours. We reviewed the clinical data, noncontrast CT, CTA, electroencephalogram and outcome of these patients and identified those who presented with presumed seizure activity at stroke onset (seizure or altered consciousness at stroke onset).

Results—Nine (7.7%) patients had a concern of seizure at stroke onset. Median age 73 years (range, 31 to 85 years), median National Institutes of Health Stroke Scale (NIHSS) score 12 (range, 5 to 29). CTA showed proximal middle cerebral artery occlusion in 2 and distal middle cerebral artery occlusion in 3 patients. All 5 of these patients had evidence of infarction on follow-up (stroke+early seizure group-intracranial occlusion present). Three of these patients received intravenous tissue plasminogen activator because they were deemed to have "ischemic tissue at risk". Four patients had normal CT and CTA studies and recovered completely in 24 hours (Todd's paralysis only group-intracranial occlusion negative).

Conclusion—Seizure at stroke onset was relatively uncommon in a consecutive cohort of acute stroke patients. CTA was a useful modality in differentiating Todd's paralysis from early seizure and ischemia by detection of intracranial occlusion and may contribute to decision-making for thrombolysis. (*Stroke*. 2006;37:000-000.)

Key Word: Todd's paralysis

Seizure occurring in a setting of acute ischemic stroke is a relative contraindication for the use of intravenous tissue plasminogen activator (tPA).¹ This is mainly attributable to the concern that tPA might be given to a patient without stroke. It is difficult clinically to differentiate Todd's paralysis from deficit attributable to ongoing cerebral ischemia. Recent studies of early seizures after stroke report a frequency of 1.3% to 6.2% for acute ischemic stroke.²⁻⁶ No data are available on the frequency of seizure at stroke onset except 1 study which showed that 5.7% experienced single or multiple seizures at the onset of stroke.⁷ It is important to make a rapid diagnosis in the acute setting to decide on thrombolysis in these patients.

We sought to examine this issue and determine whether computed tomographic angiography (CTA) in the acute setting can help to differentiate Todd's paralysis without cerebral ischemia from ischemia with early seizures.

Materials and Methods

All hospitalized patients who underwent noncontrast CT (NCCT) and CTA for a diagnosis of acute stroke within 24 hours of symptom onset over the last 3 years (June 2002 to April 2005) were included in this University of Calgary Institutional Review Board approved study. The clinical data were reviewed and patients with presumed seizure activity at stroke onset were identified. The definition of presumed seizure activity was taken as history of focal seizure with or without secondary generalization or patients with alteration in their consciousness at presentation. Patients with symptoms suggestive of posterior circulation stroke were excluded. Predisposing factors for seizures like metabolic abnormalities and alcohol abuse were also excluded. None of them had a history suggestive of limb shaking transient ischemic attack or hemiballism/hemichorea. The NCCT scans were reviewed and the Alberta Stroke Program Early CT Score (ASPECTS) applied by a 3-reader consensus.^{8,9} Follow-up imaging performed at a minimum of 24 hours after symptom onset were also reviewed. CTA imaging acquisition at our institution has been discussed in detail in a previous study.¹⁰ The presence of intracranial vessel occlusion was identified from the CTA. Clinical

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Clinical Characteristics and Outcome in 9 Patients

Patient Age/Sex	Onset to Diagnosis	Symptoms	Witnessed Seizure/ Altered LOC	NCCT ASPECTS	CTA	Baseline NIHSS	EEG	tPA	Follow-up CT	mRS 3 Months	Final Diagnosis
31/M	1.10	Left-sided weakness	Altered consciousness	10	Normal	11	Normal	No	Normal	0	Seizure
73/F	1.50	Right-sided weakness + aphasia	Focal seizure	10	Normal	12	Left temporal spikes	No	Normal	0	Seizure
85/F	1.05	Right-sided weakness + aphasia	Altered consciousness	7	M1 occlusion	29	Left hemispheric slowing	Yes	Left temporo parietal infarct	3	Stroke
84/M	0.45	Right-sided weakness + aphasia	Focal seizure	10	M2 occlusion	20	Left hemispheric slowing	Yes	Left fronto temporal infarct	1	Stroke
83/F	2.00	Left-sided weakness	Altered consciousness	8	M2 occlusion	6	Right temporal slowing	No	Right temporal infarct	1	Stroke
57/M	1.00	Right-sided weakness	Focal seizure	10	Normal	5	Normal	No	Normal	0	Seizure
75/M	0.30	Right-sided weakness + aphasia	Altered consciousness	10	M2 occlusion	5	Left temporal spikes	No	Left temporal infarct	0	Stroke
48/M	2.45	Right-sided weakness + aphasia	Focal seizure	10	Normal	14	Normal	No	Normal	0	Seizure
35/F	1.00	Right-sided weakness + aphasia	Altered consciousness	10	M1 occlusion	16	Not done	Yes	Left basal ganglionic infarct	0	Stroke

LOC indicates loss of consciousness.

outcome was assessed using the modified Rankin Scale (mRS) during the clinic visit at 3 months. A favorable outcome at 90 days was defined as a mRS of 0 or 1. The electroencephalogram (EEG) done within 24 hours of symptom onset was analyzed and classified into focal slowing, interictal epileptiform abnormalities and electrographic seizures.

Results

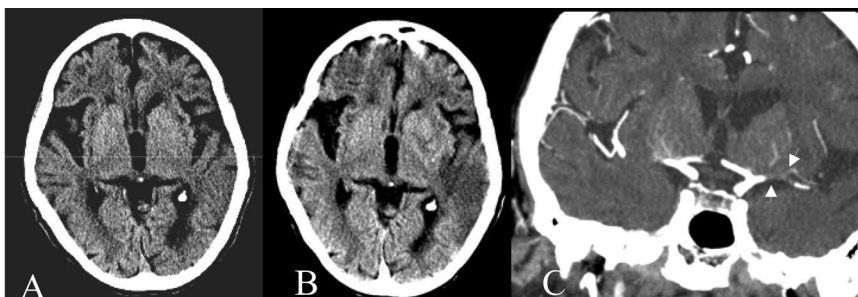
Three hundred and twenty six patients with acute ischemic stroke underwent NCCT and CTA within 24 hours of symptom onset. Of them, 116 had disabling deficits (National Institutes of Health Stroke Scale (NIHSS) ≥ 5) and presented within 3 hours of symptom onset. Nine patients were identified with history of presumed seizure activity at symptom onset. Four patients had witnessed focal motor seizures and 5 had alteration of consciousness with strong suspicion of seizure activity. The clinical, EEG findings and outcome are summarized in the Table. NCCT head showed an ASPECTS of 10 in 7 patients and 7 and 8 in 1 patient each. CTA was normal in 4 patients and showed proximal occlusion of the middle cerebral artery in 2 patients and distal middle cerebral artery branch occlusion in 3 patients. The Figure shows the NCCT, CTA and the follow-up CT of a patient with M1 occlusion. Three of the 5 patients with intracranial occlusion received tPA despite the relative contraindication because there was evidence of ischemia and the deficits were disabling. Two

patients showed rapidly improving deficits and hence were not given thrombolysis. Of the 3 who received tPA, 2 had a favorable outcome (mRS 1) and the 1 had a poor outcome (mRS 3). All 4 patients with normal CT and CTA did not receive tPA and recovered completely with no evidence of infarction on follow-up imaging. The 5 patients with evidence of intracranial occlusion on the CTA had infarcts on the follow-up CT.

Discussion

We found that CT angiography is useful in discriminating paralysis attributable to seizure alone versus paralysis attributable to ongoing ischemia. Eight percent of all emergency CT angiogram cases with acute focal neurological deficits were referred because of presumed seizure with acute presentation to the emergency department. The presence of an intracranial occlusion identified all 5 patients who experienced infarction on follow-up imaging. In patients with normal CT and CTA the recovery was complete and follow-up CT was normal, suggesting that they had Todd's paralysis alone attributable to seizure.

Seizure at stroke onset is still considered a relative contraindication for thrombolysis.^{1,11} This is based on the fear of risking treatment in a patient with Todd's paralysis. Todd's paralysis is a condition characterized by brief period of partial or com-



A, CT scan at baseline of 85-year-old woman with right hemiparesis and aphasia (NIHSS 29) shows left insula, M2 and M3 hypodensity (ASPECTS 7). B, Follow-up 24-hour scan shows infarct in the left temporal and parietal region. C, CTA shows left M1 occlusion (arrow).

plete paralysis with or without aphasia after a seizure. It usually subsides in 48 hours. All the patients in our series presented with disabling right- or left-sided weakness with or without aphasia. In a setting of history of focal seizures or patient in altered consciousness in an anterior circulation stroke, it is important to differentiate postictal Todd's paralysis alone from early ischemia with seizure. The exact frequency of seizure at stroke onset is not known. The study by Shinton et al showed a frequency of 5.7% with single or recurrent seizures at stroke onset.⁷ Intravenous tPA given within 3 hours of symptom onset is a proven effective therapy for acute ischemic stroke. Seizure at stroke onset hinders the option of thrombolytic treatment; hence, an investigation that can help to differentiate Todd's paralysis from deficit attributable to early ischemia is necessary in the decision-making.

CTA is quickly gaining widespread use for triaging acute stroke patients. It has become widely available because of new generation spiral CT scanners and only takes 10 additional minutes to perform to diagnose intracranial occlusion. CTA offers information on the vascular status^{12,13} and extent of parenchymal ischemic injury with the CTA source imaging information.^{10,14} Studies have shown its role in selection of patients for thrombolytic therapy, and its diagnostic accuracy is in good agreement with the angiographic findings.¹² It appears ideally suited to assist in this clinical scenario. EEG is a sensitive neurodiagnostic tool in the detection of acute cerebral ischemia and epileptic activity, but its specificity is low.¹⁵ Focal slowing and epileptiform activity can occur in both ischemia and seizures; hence, it does not help in the differentiation of these entities as was seen in our patients. Specific EEG findings of seizure still do not distinguish seizure with Todd's paralysis versus ischemic seizures. Multimodal MRI techniques may also be useful in this setting by providing information regarding presence of ischemia (diffusion-weighted imaging) as well as perfusion information or status of intracranial vessels (magnetic resonance angiography). One would anticipate similar differences between Todd's paralysis alone versus early seizure with ischemia. One challenge in treating patients with seizure and stroke relates to an acceleration of ischemia which may hasten evolution to infarction attributable to increased cerebral glucose metabolic demand caused by excessive neuronal activity from seizures. This could lead to extension of infarction and worse outcome as shown in a positron emission tomography study.^{16,17} This rapid evolution to infarction may limit thrombolysis benefit unless treatment can be given early.

In conclusion, seizure at stroke onset is an uncommon clinical scenario facing clinicians in the emergency room. CTA is useful in differentiating patients with Todd's paraly-

sis alone from those with early seizure and stroke. Thrombolysis could be carefully contemplated in patients with stroke and presumed seizure and intracranial occlusion, but more safety data may be required.

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