Case Report

Reperfusion Seizures: A Manifestation of Cerebral Reperfusion Injury After Administration of Recombinant Tissue Plasminogen Activator for Acute Ischemic Stroke

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Reperfusion injury has been well described in medical literature; cerebral reperfusion injury is commonly seen in association with vascular surgical procedures such as carotid endarterectomies and stent placement procedures. Cerebral reperfusion injury can manifest as blood-brain barrier breakdown, cortical irritability, and epileptic seizures. Seizures induced by cerebral reperfusion have not been documented or reported after thrombolytic therapy for acute ischemic stroke. We report a patient who received intravenous recombinant tissue plasminogen activator within 3 hours of stroke symptom onset and developed the new-onset symptom of continuous, primary motor seizure activity within 20 minutes of recombinant tissue plasminogen activator administration. These epileptic seizures originated in the same area as the acute brain ischemia and occurred during the anticipated period of cerebral reperfusion. In this article we describe a case report and then discuss the pathophysiology and mechanisms that may underlie reperfusion epileptic seizures as a manifestation of cerebral reperfusion injury. **Key Words:** Arrhythmia—cerebral ischemia—epilepsy—plasminogen activators—reperfusion—thrombolytic therapy.

In patients with acute ischemic stroke, timely intervention with thrombolytic agents can potentially induce arterial recanalization, reduce infarct size, and lead to clinical improvement or even complete recovery.

However, recombinant tissue plasminogen activator (rtPA) administration is a double-edged sword and not without potential harmful effects, which may include hemorrhagic complications, direct toxic effects of rtPA on neuronal tissue, and reperfusion-related injury. The toxic effects of tissue plasminogen activator could result directly from enhanced neurotransmission or from immune mobilization, or be triggered by its downstream effector protein, plasmin.[1] In this case report, we will focus on the reperfusion-related injury.

Reperfusion injury can be divided into two categories: hyperperfusion and normoperfusion. The first category, hyperperfusion injury, is well described in medical literature and is commonly seen in association with vascular surgical procedures such as carotid endarterectomies and stent placement procedures. It can manifest as irritability, headache, blood-brain barrier breakdown, and seizures. However, the second category, which is normoperfusion injury, has not been well established and there has been

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no report of epileptic seizures as a result of cerebral reperfusion after thrombolytic therapy for acute ischemic stroke.

We report a patient who received intravenous rtPA within 3 hours of stroke symptom onset and developed the new-onset symptom of continuous, primary motor seizure activity within 20 minutes of rtPA administration. These epileptic seizures originated in the same area as the acute brain ischemia and occurred during the anticipated period of cerebral reperfusion.

Case Report

Sudden stroke symptoms developed in a 78-year-old man who experienced sudden onset of dysphasia and right hemibody weakness. Stroke risk factors included his age, sex, arterial hypertension, and hypercholesteremia. The patient had no history of transient ischemic attacks, stroke-related problems, epileptic seizures, cardiac syncope, or neurologic or cardiologic symptomatology.

The physical examination was normal except for his neurologic findings, which initially included global dysphasia, lethargy, left gaze preference, and weakness of the right face, arm, and leg. The National Institutes of Health Stroke Scale (NIHSS) score was 16. Relevant laboratory data produced normal findings and an emergent noncontrast cranial computerized tomographic head scan revealed entirely negative results. Magnetic resonance imaging/diffusion-weighted imaging was not available at the time.

Intravenous rtPA was administered in a dose and method according to accepted protocols. Near the completion of this infusion, the patient became much more alert and his comprehension was moderately improved. The NIHSS score was 12 when he was transferred to an intensive care department.

Approximately 20 minutes after this infusion was completed, he developed tachycardia, moderate hypertension, unresponsiveness to sensory stimuli, head turning with forced gaze deviation to the right, and intense clonic motor activity of the right arm. Intravenous administration of 2 mg of lorazepam resulted in cessation of seizure activity, return of gaze to the neutral position, and improved alertness. A second noncontrast cranial computerized tomographic head scan revealed, again, negative results.

Approximately 40 minutes after the initial seizure, the patient experienced recurrence of identical seizure activity, which once again resolved with 2 mg of intravenous lorazepam. A stat bedside electroencephalogram (EEG) revealed sharp wave complexes in left parietotemporal leads with superimposed slow wave activity throughout the entire left cerebral hemisphere (Fig 1). The patient then received a loading dose of fos-phenytoin. Relevant laboratory data again revealed normal findings and there was no recurrence of seizure activity. Immediate follow-up EEG after fos-phenytoin infusion revealed slow

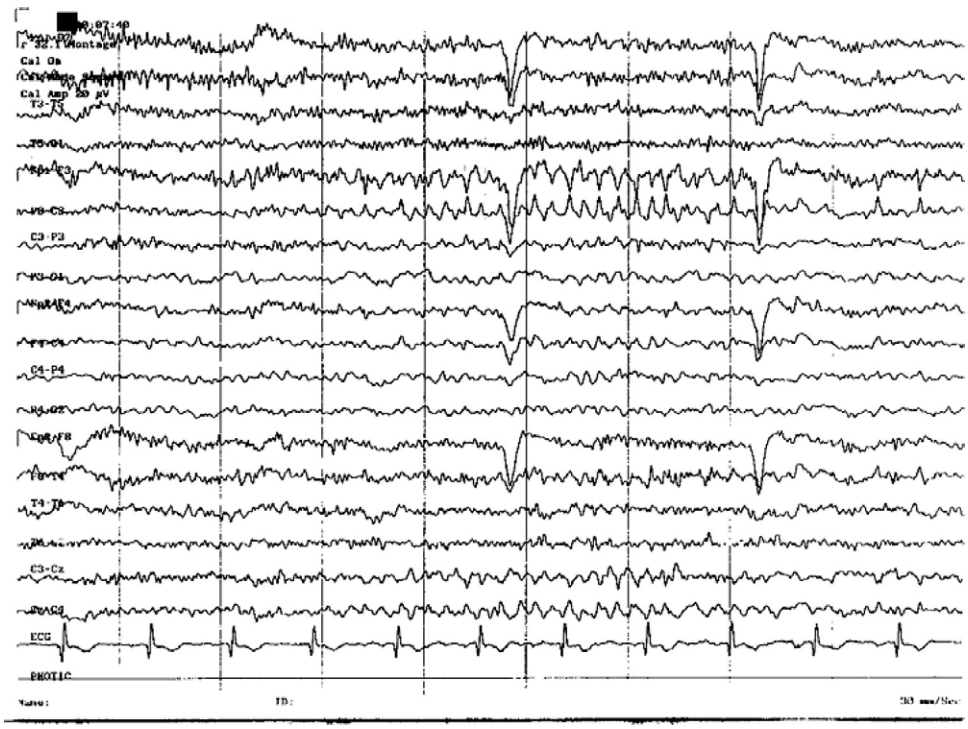

Figure 1. *EEG revealed sharp wave complexes in left parietotemporal leads with superimposed slow wave activity throughout entire left cerebral hemisphere.*