Diagnostic Puzzle of Acute Ischemic Stroke Mimics – Seizure Versus Post-Stroke Recrudescence: A Case Report

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Patient: Female, 65-year-old
Final Diagnosis: Post-seizure Todd’s phenomenon
Symptoms: Combativeness and aggressiveness • confusion • worsening weakness of the right upper and lower limbs
Medication: —
Clinical Procedure: Brain imaging: NCCT • CTA • CTP • MRI
Specialty: Neurology • Radiology

Objective: Challenging differential diagnosis
Background: Focal seizure with impaired awareness, post-seizure Todd’s phenomenon, and post-stroke recrudescence can all present with focal neurological deficits, mimicking stroke. As acute ischemic stroke mimics, they are distractors in the emergency setting where management is time-sensitive both for seizure and stroke. Nevertheless, a timely diagnosis can be made with exploration of the clinical features supported by investigation such as computerized tomographic perfusion.

Case Report: Our patient was a 65-year-old woman who was known hypertensive, with type 2 diabetes mellitus, and previous intracerebral hemorrhage with minimal right-sided residual deficits, but still able to ambulate independently. She was brought to the Emergency Department because 1 hour prior to presentation, she had sudden worsening of weakness of the right limbs, aphasia, aggression, and confusion. An initial impression of repeat acute stroke, focal seizure with impaired awareness, Todd’s phenomenon, and post-stroke recrudescence was considered. While CT angiography was suggestive of left middle cerebral artery occlusion, CT perfusion revealed extensive hypoperfusion patterns beyond the region of the occlusion, thus suggesting a different etiology from acute ischemic stroke. In view of her previous left hemispheric lesion coupled with the presentation, our working diagnosis was seizure with Todd’s phenomenon, and she was started on an anti-epileptic drug. Her condition returned to baseline within 24 h of admission and was subsequently discharged.

Conclusions: Our case demonstrates that adequate elucidation of clinical features in conjunction with CT perfusion, as a dual-purpose tool, can aid the diagnosis of both stroke mimics and acute ischemic stroke in the Emergency Department where rapid treatment is essential.

Keywords: Stroke • Stroke Mimics • Seizure • Todd’s Phenomenon • Post-Stroke Recrudescence • Computed Tomographic Perfusion

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Background

Focal seizure with impaired awareness is the “alteration in awareness” for any portion of focal seizure, which can range from motor to non-motor features [1]. Focal seizure is the most common form of seizure associated with stroke [2] and is the most frequent presentation of unprovoked seizures and epilepsy in adults [3]. Post-seizure Todd’s phenomenon refers to the various neurologic and psychiatric symptoms following a seizure, which is not limited to motor weakness (Todd’s paralysis) [4]. Post-stroke recrudescence is the re-emergence of previous stroke-related neurological deficits in the presence of metabolic and/or infectious derangements [5]. Focal seizure with impaired awareness, post-seizure Todd’s phenomenon, and post-stroke recrudescence are stroke mimics that can present with focal neurological deficits. Thus, they can be challenging distractors, especially in the Emergency Department, where decision making is time-sensitive for the management of seizures and acute ischemic stroke (AIS). However, they can be distinguished with adequate elucidation of the clinical features supported by appropriate investigation such as CT perfusion.

Case Report

Our patient was a 65-year-old woman with hypertension, type 2 diabetes mellitus, requiring minimal support for her activities of daily living, and pre-morbid modified Rankin score of 2; unable to perform all previous activities but able to look after own affairs without assistance. One hour prior to presentation, she developed sudden worsening of weakness of the right arm and leg after she had an unwitnessed fall in the bathroom. Her spouse’s attention was drawn by the sound and found her on the floor, confused with inability to stand up as a result of worsened weakness on the right side. She could neither express nor understand spoken words or signs. Subsequently, she became combative and aggressive. No loss of consciousness, incontinence, or bleeding from the mouth was reported. There was no previous history of seizures. About a year prior to this presentation, she developed left intraparenchymal hemorrhage secondary to arteriovenous malformation (AVM) and underwent hematoma evacuation and embolization of the AVM with residual right-sided weakness and mild expressive aphasia.

Examination revealed a confused woman, talking irrationally and unable to understand spoken communication. Vital signs were stable. She moved her eyes in all directions, had no gaze preference, blinked to confrontation, had mild right facial asymmetry, flexor contracture of right arm, and power of zero in the right arm and leg. She was able to move her left limbs spontaneously. Tone and reflexes were increased on the right limbs.

After history-taking and rapid physical examination, we considered the following differentials: acute stroke, focal seizure with impaired awareness, post seizure Todd’s phenomenon, and post-stroke recrudescence.

Serum glucose was 7.8 mmol/L and other metabolic/electrolytes work-up were essentially normal. Non-contrast CT revealed a large region of encephalomalacia and gliosis of the left fronto-temporal lobes (Figure 1). CT angiography demonstrating occlusion of the left M2 branch of the middle cerebral artery (white arrow) (Figure 2).

Figure 1. Non-contrast CT showing encephalomalacia and gliosis of the left fronto-temporal lobes (white arrow).

Figure 2. CT angiography demonstrating occlusion of the left M2 branch of the middle cerebral artery (white arrow).
angiography showed focal occlusion of the anterior superior left M2 branch of the middle cerebral artery, abutting the anterior aspect of the aforementioned encephalomalacia (Figure 2). CT perfusion (RAPID software) showed core of 0 ml and penumbra of 47 ml, that extended to the contralateral right frontal region (Figure 3A). The arterial input and venous output functions placement and curves were good. Furthermore, cerebral blood volume (CBV) and cerebral blood flow (CBF) were decreased, and mean transit time (MTT) and time to drain (TTD) were increased (Figure 3B-3E and Videos 1-4). These perfusion maps were noted to be widespread beyond the region of the suggested vascular occlusion seen on the CT angiography.

The working diagnosis was narrowed down to post-seizure Todd’s phenomenon, thus prompting commencement of an anti-epileptic drug (AED). Confusion, aggression, and weakness of the right arm and leg resolved to baseline within 8 h. Magnetic resonance imaging (MRI) done 10 h later did not reveal any restricted diffusion (Figure 4A, 4B). She was discharged home 24 h after admission on AED. At 2- and 4-month follow-up visits, she remained stable.

**Discussion**

Studies have shown that seizure is the most common stroke mimic [6-8]. The Framingham heart study [2] revealed that...
early or late seizures present in approximately 5% of acute ischemic stroke and over 70% are focal at onset. A Minnesota study [3] that spanned about 5 decades showed that 60% of new cases of epilepsy and unprovoked seizures manifested with focal seizures. Presence of cardiovascular risk factors and positive findings of hemiparesis, aphasia, dysarthria, gaze preference, facial palsy, hemianopia, visuospatial dysfunction, and extensor planter response point to acute ischemic stroke [6,8]. On the other hand, seizures at onset and isolated sensory loss with no objective deficit may suggest seizures [6,8]. Our patient had a combination of these features. Hence, it was difficult to make a clear diagnosis of either acute ischemic stroke or seizure based on the clinical features alone. Post-stroke recrudescence may occur with ‘deconditioning’ and can display an exacerbation of previous deficits. Topcuoglu et al [5] found that post-stroke recrudescence was more common in women and most resolved in about 24 h. However, risk factors for this disorder, such as

Figure 3. (A) RAPID map which demonstrates absent core, penumbra of 47 ml and extension to the contralateral hemisphere. (B, C) Cortical-subcortical decreased CBV and CBF maps demonstrating post-ictal hypoperfusion patterns (CBV – cerebral blood volume. CBF – cerebral blood flow). (D, E) Widespread increased MTT and TTD maps demonstrating post-ictal hypoperfusion patterns (MTT – mean transit time. TTD – time to drain).

Video 1. Extensive left hemispheric cortical-subcortical decreased CBV.

Video 2. Extensive left hemispheric cortical-subcortical decreased CBF.
metabolic derangement, electrolyte imbalance, and infection, were absent in our patient.

Diffusion-weighted imaging (DWI) with apparent diffusion coefficient (ADC) are the most sensitive techniques to diagnose acute ischemic stroke. This is routinely unavailable in the acute setting. CT angiography finding was inconclusive due to prior AVM repair. CT perfusion is useful in AIS to estimate the ischemic core and penumbra, which is restricted to the region of vascular occlusion seen on the CT angiography. However, studies have also demonstrated the diagnostic utility of CT perfusion in stroke mimics, especially seizure [9,10]. Although electroencephalography may help with the diagnosis of seizure, this is not practical in the emergency setting. Findings in CT perfusion range from hyperperfusion and hypoperfusion to normoperfusion, which generally correspond to ictal and post-ictal stages of seizure, respectively [9,11]. In the ictal phase of seizure, activation of the neurons leads to

Figure 4. (A, B) DWI and ADC sequences which showed hypo- and hyper-intensities, respectively, in the left fronto-temporal areas, not in keeping with restricted diffusion to suggest an acute infarct (white arrows) (DWI – diffuse weighted imaging, ADC – apparent diffusion coefficient).
increased perfusion [11], while neuronal inhibition has been observed in the post-ictal phase; thus, hypoperfusion is seen [12]. These changes on perfusion maps are not restricted to a vascular territory as would be expected for an ischemic lesion, with a good interobserver agreement (K=0.60) for these patterns [10]. To emphasize the vascular pathological mechanism behind post-ictal hypoperfusion, Gaxiola-Valdez et al, utilizing arterial spin labeling MRI sequence, reported vasoconstriction and hypoperfusion within 90 min after seizure in 80% of their cohorts [13]. Furthermore, electrical activities as demonstrated by EEG from the focus of the seizure may persist for most adults up to 120 min and may last maximally for 420 min [14]. The switch from ictal hyperperfusion to post-ictal hypoperfusion has been demonstrated by single-photon emission computed tomography to be 60-120 s [15]. The pathophysiologic of post-seizure Todd’s phenomenon can be explained by neuronal electrophysiologic exhaustion due to post-ictal hyperpolarization with resultant neuronal inhibition, ultimately leading to hypoperfusion [16]. Our patient presented with features of hypoperfusion to alert us to a possible post-ictal state suggesting post-ictal Todd’s phenomenon – widespread cortical-subcortical hypoperfusion.

Conclusions

CT perfusion may be useful in the acute setting to help distinguish between stroke and some stroke mimics. In our case, the patient’s clinical presentation together with widespread hypoperfusion seen on the CT perfusion assisted in the rapid diagnosis and appropriate management, which in turn led to a good outcome.

Declaration of Figures’ Authenticity

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