Post-Traumatic Status Epilepticus Masquerading as Acute Ischemic Stroke: A Case Report and Literature Review

Dimitrios Panagopoulos
Georgios Markogiannakis
Marios Themistocleous

Corresponding Author: Dimitrios Panagopoulos, e-mail: dimpanayop@gmail.com

Conflict of interest: None

Patient: Male, 7-year-old
Final Diagnosis: Status epilepticus
Symptoms: Local seizure
Medication: —
Clinical Procedure: Computed tomography • magnetic resonance imaging
Specialty: Neurosurgery

Objective: Rare co-existence of disease or pathology
Background: Advanced imaging is one of the main modalities utilized in the diagnostic investigation of a first-time epileptic ictus, as well as in the evaluation of a patient suspected of having an ischemic stroke.
Case Report: We report the case of a 7-year-old boy who was admitted to our hospital because of a depressed skull fracture. Soon after its initial evaluation, he had an episode of generalized tonic-clonic seizures; therefore, a detailed diagnostic work up was scheduled, which raised the diagnostic dilemma of ischemic stroke versus imaging alterations related to status epilepticus. He underwent surgical exploration, and a few days later the repeat MRI verified that the initial signal changes should be attributed to the ictus.

Conclusions: Brain edema, most commonly affecting a cerebral hemisphere in its entirety, is a rare post-ictal imaging finding that is causally related to focal-onset status epilepticus. The aforementioned perfusion changes can aid in the differentiation of ictal-related brain abnormalities from acute ischemic stroke, if regional or more diffuse areas of increased perfusion are shown on MRI. Consequently, MRI should be considered the preferred imaging modality when we are confronted with cases of post-ictal signal changes that could masquerade as acute ischemic stroke.

MeSH Keywords: Brain Edema • Status Epilepticus • Stroke

Abbreviations: MRI – magnetic resonance imaging; CT – computed tomography; EEG – electroencephalography; MRA – magnetic resonance angiography; SE – spin echo; TSE – turbo spin echo; 3D TOF – 3-dimensional time-of-flight; T2W – T2-weighted; FLAIR – fluid-attenuated inversion recovery; DWI – diffusion-weighted imaging; T2FRFSE – fast relaxation fast spin echo; LFF – low-frequency filter; HFF – high-frequency filter; TBI – traumatic brain injury

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Background

Status epilepticus and acute ischemic stroke insult are the 2 most important disorders managed in the neurological emergency department, and they account for about 20% of seizures occurring in the emergency department. They also are the most commonly identifiable entity masquerading as stroke [1,2].

A recent study in a pediatric population cohort concluded that most seizures clinically manifesting as stroke mimics involved an acute neurological illness [3,4].

During an episode of status epilepticus, advanced neuroimaging modalities can help rule out other relevant pathological substrate of neurological origin. Therefore, it is of paramount importance to review the relevant neuroimaging features that could be correlated with status epilepticus. Moreover, abnormal MRI signal characteristics may indicate or even clarify more relevant information regarding the ongoing pathophysiologic basis of status epilepticus [5].

Case Report

We report the case of a 7-year-old boy who fell from a height (approximately 6 feet) with reported immediate loss of consciousness. More precisely, he suffered a fall to the concrete ground after an accidental fall from the balcony of his house. To the best of our knowledge, he was left-handed, and his past medical history and that of his parents was negative. After the event, he was transferred to the emergency department of our hospital, having regained consciousness. The estimated GCS score at the emergency department after his arrival was 13/15 (E: 3, V: 5, M: 5). Based on the mechanism of injury, an initial CT scan was obtained, which revealed a depressed skull fracture in the region of the right temporal bone, with the relevant bone fragments being displaced internally, exceeding the border of the inner surface of the diploe (Figures 1, 2). The patient fulfilled the criteria for surgical exploration and reduction of the bone fragment, as there was an overlying skin laceration (open skull fracture), possibly requiring repair of an underlying dural laceration.

Before moving the patient to the operating theater, he developed first-onset focal-to-bilateral tonic-clonic seizure with upward eye deviation, accompanied by convulsive movement, for approximately 2 min. This was managed by intravenous injection of benzodiazepam (1 mg slow IV injection every 3 min, up to a dose of 7 mg, and no repeat was necessary). Initial arterial blood gas analysis and routine laboratory parameters, including complete blood count, renal and liver function, as well as lactate level, were within the reference range. On gross neurological examination, neither focal neurological deficits, nor other neurological sequelae were depicted. Immediately after the ictus, an EEG recording was made, which revealed the seizure onset to be localized in the right temporal lobe, accompanied by rhythmic alpha activity (Figure 3). Immediately afterward, the patient was sedated and transferred for an emergent MRI-MRA scan. SE and TSE and diffusion sequences were performed in all 3 planes, and a 3D TOF sequence was selected for the angiographic control.

An area characterized by high signal intensity on T2W and FLAIR sequences was revealed in the region of the right temporal lobe, but not in anatomic continuity with the existing...
skull fracture. It was accompanied by edematous appearance of the relevant temporal gyri, with concomitant restriction of diffusion signal intensity, notable on diffusion sequences, a finding compatible with the cytotoxic type of edema. No areas of contusion or intracerebral hemorrhage were detected (Figures 4–6). MRA was performed because there was a possibility that the area with the abnormal signal intensity could be due to a vascular injury, with a relevant ischemic insult, to a branch supplying the aforementioned temporal gyri, provoked by the comminuted bone fragments. The intracranial part of the internal carotid artery, the anterior and middle cerebral arteries bilaterally, as well as their peripheral branches, the posterior cerebral and basal artery, were all inspected, but blood flow was normal, without any evidence of dysplasia, stenosis, or aneurysm (true or traumatic pseudo-aneurysm due to dissection) (Figure 7).

The patient was immediately placed on levetiracetam, an anticonvulsant medication, started at 10 mg/kg twice a day intravenously, which was subsequently increased in increments of 10 mg/kg twice a day in 2-week intervals until the maximum dose of 30 mg/kg twice a day was reached. After the initial diagnostic work up, the patient underwent a limited right subtemporal craniectomy to remove the comminuted bone fragments and ensure the absence of any dural lacerations. A few days after the operation, a repeat EEG was performed on an elective basis, which revealed the same pathological findings. This post-ictal electroencephalography was performed to exclude the possibility of a nonconvulsive status epilepticus. As a second episode of epileptic ictus was recorded, even though the patient was on antiepileptic medication, we decided to gradually increase the dose of the antiepileptic regimen.

Two weeks later, a repeat MRI scan was performed to monitor the evolution of the signal characteristics of the aforementioned area of the temporal lobe. We noted a significant decrease of the pathologic signal intensity region of the right temporal lobe- namely, the high signal intensity on T2 and...
FLAIR sequences, as well as the restriction of the diffusion on DWI images. We detected a few hemorrhagic elements and dural enhancement after intravenous contrast administration, which were compatible with the previous operation for the depressed fracture (Figures 8–10).

One month after the repeat MRI, a new MRI–MRA was performed, which verified the complete disappearance of the abnormal imaging findings depicted on the initial MRI scan. Additionally, an MRA was performed to exclude the slight possibility of the development of a delayed traumatic pseudo-aneurysm, or occlusion of a branch of the intracranial arteries, which could be correlated with the affected temporal region. As the result was negative for pathological findings, this possibility was excluded and no further relevant work up was performed. Regarding the clinical outcome of the patient, although his clinical course was not uneventful, no residual neurological deficit was recognized, he regained full level of consciousness, and no focal neurological deficits were recorded at his discharge or at regular neurological reevaluations.

**Figure 5.** Initial MRI scan, axial T2RFSE, characterized by high signal intensity changes in the region of the right temporal lobe.

**Figure 6.** Initial MRI scan, axial T2 FLAIR, revealing high signal intensity changes in the region of the right temporal lobe.

**Figure 7.** Initial MR 3D TOF, not depicting any gross vascular abnormality.

**Figure 8.** MRI scan 2 weeks later, axial diffusion imaging, depicting significant decrease of restriction of the diffusion in the region of the right temporal lobe.
Discussion

The widespread use of MRI in patients with status epilepticus is helpful in the determination of relevant alterations in brain parenchyma frequently encountered in this subgroup of patients [6,7]. Abnormal brain MRI signal intensities that are correlated with seizure in their topography, and there is no strict correlation between their anatomical distribution and the specific, underlying, subtype of epilepsy. Additionally, their extent, signal, and morphological parameters are quite variable [6,8]. Although the vast majority of relevant data are based on anecdotal case reports or small patient series, it seems that the most commonly encountered neuroimaging abnormalities related to status epilepticus are unilateral changes affecting the entire cerebral hemisphere [9–11]. This is in contrast to our case, in which the pathological signal alteration was restricted to a specific part of the temporal lobe, which was most probably the epileptogenic zone. According to published studies, the typical pattern of signal abnormalities in these patients includes hyperintense signal intensities on T2WIs with restricted diffusion, a finding that is compatible with the hypothesis that the diffusion of water molecules in vivo is limited [6,7,9]. This evidence strongly supports the concept that the underlying pathophysiologic substrate is the development of cytotoxic edema, not vasogenic edema. Some patients that were included in previous studies and examined with MRA demonstrated increased arterial circulation in the affected hemisphere, which could be explained as a compensatory response to the relative hypermetabolic state provoked by the epileptic ictus [6]. Our angiographic results differ from the relevant published series, perhaps due to the relatively restricted area of the temporal lobe affected by the injury, so it seems that the possible hyperdynamic circulation provoked by that ictus was unable to create angiographic changes detectable by MRA. A wide variety of imaging modalities have shown that focal-onset seizures are associated with increased energy consumption from the affected brain and an associated significant increase in regional cerebral blood flow [6,12,13]. When the compensatory brain autoregulation mechanisms are

It is widely accepted that brain damage induced by seizure activity remains a diagnosis of exclusion, as other causes of symptomatic seizures should be excluded before such a diagnosis is verified. Ischemic stroke is one of these, although we abandoned it as a diagnostic possibility for various reasons. First of all, the signal alterations at MRI were not restricted to a brain region that was nourished by and correlated with a specific, anatomically specified vascular distribution. This is supported by the fact that MRA did not verify any signs of cerebral artery occlusion or other form of disruption, as well as the reversibility of the abnormal signal intensities on the repeat MRI scan.

This report aimed to elucidate the underlying pathophysiological mechanism of brain injury in our patient, which was strongly correlated with the episode of status epilepticus. According to published studies, the typical pattern of signal abnormalities in these patients includes hyperintense signal intensities on T2WIs with restricted diffusion, a finding that is compatible with the hypothesis that the diffusion of water molecules in vivo is limited [6,7,9]. This evidence strongly supports the concept that the underlying pathophysiologic substrate is the development of cytotoxic edema, not vasogenic edema. Some patients that were included in previous studies and examined with MRA demonstrated increased arterial circulation in the affected hemisphere, which could be explained as a compensatory response to the relative hypermetabolic state provoked by the epileptic ictus [6]. Our angiographic results differ from the relevant published series, perhaps due to the relatively restricted area of the temporal lobe affected by the injury, so it seems that the possible hyperdynamic circulation provoked by that ictus was unable to create angiographic changes detectable by MRA. A wide variety of imaging modalities have shown that focal-onset seizures are associated with increased energy consumption from the affected brain and an associated significant increase in regional cerebral blood flow [6,12,13]. When the compensatory brain autoregulation mechanisms are
unable to withstand the elevated metabolic brain demands, local glucose metabolic pathways turn from aerobic to anaerobic, and metabolic decompensation begins [6,14].

DWI is a commonly used MRI sequence for evaluation of acute ischemic stroke, and is sensitive in the detection of small and early infarcts. Conventional MRI sequences (T1WI and T2WI) may not demonstrate an infarct for 6 h, and small infarcts may be hard to appreciate on CT for days, especially without the benefit of prior imaging. Within minutes of arterial occlusion, diffusion-weighted imaging demonstrates increased DWI signal; after 6 h, high T2 signals will be detected, initially more easily seen on FLAIR than on conventional fast spin echo T2. In the subacute period, which is 10–15 days, DWI remains elevated due to persistent high T2/FLAIR signal (T2 shine-through). The time evolution of the imaging findings of MRI reduce the diagnostic possibility of the offending lesion being an ischemic stroke.

Consequently, certain MRI sequences from the time period immediately related to the ictus can detect subtle differences between pathological substrates that are exacerbating brain consumption of energy storages, with a relevant cortical hyperperfusion, versus when neuronal cortical activity is markedly reduced due to depletion of metabolic storage [3]. Most reports in children with seizure activity that must be differentiated from stroke were in the setting of an acute neurological illness [3,15]. The imaging characteristics may alter in the time course of the disease, ranging from initial hyperperfusion signaling characteristics to mainly vasogenic extracellular edema, and even to cytotoxic edema [16]. Recently published research shows a wide spectrum of transient peri-ictal MRI signal changes that encompass a group of reversible brain pathologies, which include signal abnormalities on T2 W and FLAIR sequences, as well as vasogenic and cytotoxic edema on DWI and hyperintense areas on FLAIR or T2W images [3,17].

In the present case, abnormal signal intensity of the right temporal lobe showed cytotoxic edema due to status epilepticus; this location was not contiguous with the depressed skull fracture, but the brain contusion (or concussion) definitely affected the status epilepticus, probably due to the so-called remote effect.

Many animal models of TBI are available for studies on mechanisms and experimental treatments of this phenomenon. Immediate- and early-onset seizures have been described in many of these models with focal or mixed type (both gray and white matter damage) injury. These animals develop hippocampal alterations that are described in detail in status epilepticus-induced spontaneous seizure models and human post-traumatic epilepsy [18].

Several animal models have been developed that reproduce aspects of human TBI, including focal contusion, petechial intraparenchymal and subarachnoid hemorrhages, tissue tears, and traumatic (diffuse) axonal injury. The most commonly reported sequelae are blood–brain-barrier disruption, white matter damage, neuronal loss, gliosis, altered cerebral metabolism, altered cerebral blood flow, and altered brain electrical activity. The damage appears most severe in the ipsilateral cortex, hippocampus, and thalamus [19].

The natural history of the consequences of TBI include several phases: primary injury, evolution of primary injury, secondary injury, and regeneration [20,21]. Primary injury by definition occurs at the moment of TBI and is accompanied by massive disturbance of the cellular ion homeostasis, release of excitatory neurotransmitters, and exacerbation of excitotoxicity. Secondary injury occurs within the hours and days after the primary injury, and is considered to be an indirect result of the insult. It includes a complex spectrum of molecular changes and cellular processes, which may be, partially or completely, involved in post-traumatic epileptiform activity. It may be a clinical equivalent of the remote effect, in which the seizure onset zone is remote from the region of the primary brain insult, and the epileptiform discharges are provoked by secondary changes associated with the primary brain injury.

Conclusions

Focal status epilepticus can cause unilateral brain edema, and in our case, the distribution of the edematous abnormality was restricted in the vicinity of the epileptogenic zone. Based on MRI findings, cytotoxic edema seems to be an important contributing factor in the evolution of the underlying brain insult. The uniqueness of our case is the absence of a definite anatomic or other pathologic substrate (e.g., viral encephalitis, metabolic encephalopathy, and ischemic stroke) that could explain the development of the epileptic ictus. The depressed skull fracture, although occurring on the same side as the seizure onset activity, was neither correlated with a cerebral contusion nor an arterial injury, so the existence of an anatomic substrate that was the offending lesion, causing the epileptic ictus, is lacking. The differential diagnosis between acute ischemic stroke and cytotoxic edema attributable to seizure activity was challenging, necessitating the performance of MRA and subsequent MRI to resolve this diagnostic dilemma.

Conflict of interest

None.
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