Intracranial hypotension (IH), described for the first time in 1938, can mimic many neurological syndromes by virtue of its presentation, and the condition is frequently misdiagnosed. Any neurosurgical procedure with a risk of CSF leakage puts a patient at a high risk for IH. Even though spontaneous IH is more common, the incidence of IH in the neurocritical care setting is increased by virtue of the increased number of neurosurgical interventions. Whether spontaneous or secondary in etiology, diagnosis of IH usually requires the presence of orthostatic symptoms, including headaches and nausea with low opening CSF pressure. However, typical clinical features in the appropriate clinical context and imaging, even with normal CSF pressure, can indicate IH. In the neurocritical care setting, challenges for accurate semiology include altered sensorium and reduced levels of responsiveness for which many etiologies may exist, including metabolic dysfunction, traumatic brain injury, IH, or nonconvulsive status epilepticus (NCSE). The authors describe 3 patients whose clinical picture and electroencephalography (EEG) findings initially suggested NCSE but who did not respond to treatment with antiepileptic drugs alone. Neuroimaging suggested IH, and subsequent treatment of IH successfully improved the patient’s clinical status. To the authors’ knowledge this paper is the first in the literature that reports a correlation of IH with electrographic findings similar to NCSE as cause and effect. The authors’ hypothesis is that thalamocortical dysfunction causes EEG findings that appear to be similar to those in NCSE but that these conditions do not coexist. The EEG activity is not epileptogenic, and IH results in blocking network pathways producing thalamocortical dysfunction. The authors discuss the hypothesis and pathophysiology of these epileptiform changes in relation to IH. (http://thejns.org/doi/abs/10.3171/2013.7.JNS112308)

**Key Words**
- nonconvulsive status epilepticus
- intracranial hypotension
- epilepsy

Abbreviations used in this paper: AED = antiepileptic drug; EEG = electroencephalography; IH = intracranial hypotension; NCSE = nonconvulsive status epilepticus; SDH = subdural hematoma.

This article contains some figures that are displayed in color online but in black-and-white in the print edition.

**Case Reports**

**Case 1**

A 72-year-old woman was admitted to an outside hospital in November 2009 for a 2-week history of worsening headaches after a fall without loss of consciousness. Magnetic resonance imaging of the brain demonstrated bilateral subdural hematomas (SDHs) that were considered...
unsuitable for surgical treatment. Findings on cerebral angiography were normal. On initial examination, the patient had a left third cranial nerve palsy without any other localizing signs. Her condition deteriorated, and after 1 week she was transferred to our facility. On arrival, she demonstrated bilateral decorticate posturing and required immediate intubation for airway protection. The findings on repeat brain MRI were unchanged. A lumbar puncture in the lateral decubitus position showed an opening CSF pressure of 14 cm H2O. The laboratory results of the CSF sample were unremarkable. Other possible etiologies for her unresponsiveness were also excluded by a comprehensive metabolic workup. Electroencephalography (EEG) showed rhythmic delta and theta activity with superimposed high amplitude 0.5- to 1.5-Hz spike and wave activity in a generalized distribution that appeared to be epileptiform, raising concerns for NCSE (Fig. 1C). The patient was given intravenous fosphenytoin and was monitored on continuous video EEG. Epileptiform discharges persisted despite high therapeutic levels of phenytoin, prompting the addition of valproic acid. The patient’s neurological status and EEG pattern remained unchanged despite high therapeutic levels of fosphenytoin, valproic acid, and the subsequent addition of levetiracetam. Pentobarbital–induced burst suppression was instituted. Two attempts to wean pentobarbital were unsuccessful despite high therapeutic levels of fosphenytoin and valproic acid. Each time, epileptiform discharges concerning for refractory NCSE reappeared.

Findings on a repeat brain MRI study performed after 1 week of admission were initially reported to be unchanged. Reevaluation of the imaging study 2 weeks after the patient’s transfer raised a concern for IH. A review of all neuroimages demonstrated that these changes were present even on the initial scan (Fig. 1A). Spine MRI did not reveal CSF leakage. Two lumbar epidural blood patches were done 3 days apart, the patient was kept in Trendelenberg position, and intravenous fluids were administered. Repeat MRI showed improvement of incisural herniation (Fig. 1B). No changes in the patient’s antiepileptic drug (AED) therapy were made. She was weaned off burst suppression 72 hours after the second epidural blood patch. Continuous EEG showed diffusely slow background with abatement of sharply contoured epileptiform discharges. The other antiepileptic medications were rapidly tapered and discontinued with no recurrence of epileptiform activity. Follow-up EEG 1 week later showed improved amplitude and background activity (Fig. 1D). The patient was discharged 58 days after hospitalization to subacute rehabilitation. On further follow-up by telephone 3 months later, she had regained the ability to independently converse, eat, and participate in physical therapy.

**Case 2**

A 52-year-old woman was admitted in February 2009 for an episode of encephalopathy. More than 10 years prior to this presentation, the patient had undergone ventriculoperitoneal shunt placement for pseudotumor cerebri, which required revisions. She had been diagnosed with persistent

---

**Fig. 1.** Pretreatment (A, E, and I) and posttreatment (B, F, and J) sagittal brain MR images. Clearly significant improvement in brain sagging is shown on the posttreatment images. Pretreatment (C, G, and K) and posttreatment (D, H, and L) EEG findings. The posttreatment findings show dramatic improvement in the high amplitude rhythmical waveform.
IH on brain MRI in 2006 after microvascular decompression for trigeminal neuralgia. Since 2006, she had been hospitalized more than once for mental status changes. At one point, these changes were attributed to seizures, and AED therapy with phenytoin and carbamazepine was initiated. She also suffered sequential bilateral infarctions of the ventrolateral nucleus of the thalamus, which left her with minimal right-sided weakness.

On examination, the patient was stuporous and dysarthric and had increased right hemibody weakness. She was hypoxemic and was subsequently intubated because of worsening mental status. Brain MRI showed features of IH (Fig. 1E). A ventriculoperitoneal shunt valve showed an opening pressure of 8 cm H2O. The remainder of the workup for encephalopathy was unrevealing. Continuous EEG (Fig. 1G) demonstrated sharply contoured activity within the posterior temporal region with poorly organized background rhythm raising concerns for NCSE.

The patient was kept on therapeutic levels of phenytoin and carbamazepine, but we decided against further escalation in antiepileptic treatment given our recent experience with the patient in Case 1. The patient was monitored using continuous video EEG. After a programmable shunt valve set to 18 cm H2O was placed, incisural herniation improved (Fig. 1F), followed by an improvement in epileptiform activity within approximately 24 hours (Fig. 1H). There was significant clinical improvement, allowing for extubation and discharge home.

**Case 3**

This 57-year-old woman was admitted to the neurosurgery service for a left-sided SDH. The patient had a 9-month history of worsening nonpositional headache, nausea, vomiting, visual blurring, and decreased left-sided hearing, all following mild head trauma accompanied by a transient loss of consciousness. On initial examination she was alert, with a mild right-sided pronator drift, but soon she became increasingly unresponsive. Brain MRI showed incisural herniation with a left frontoparietal SDH suggesting IH (Fig. 1I). Spine MRI suggested a CSF leak at the thoracolumbar junction. Continuous EEG showed possible NCSE (Fig. 1K), and the patient was treated with fosphenytoin and valproic acid. The SDH was thought to be the cause of the patient’s declining mental status and seizures; therefore, evacuation of the SDH was performed. This did not lead to any clinical improvement. An intracranial pressure monitor placed at the time indicated persistently low intracranial pressure. Electroencephalography continued to demonstrate alternating slow and rhythmic sharply contoured activity. Since the patient’s condition had failed to improve clinically or electrographically with AED treatment and surgery, a lumbar epidural patch was performed. This treatment resulted in rapid improvement in incisural herniation (Fig. 1J), normalization of EEG within 24 hours (Fig. 1L), and a remarkable turnaround in her clinical condition. A mild right-sided drift was the only residual deficit. The patient was discharged home.

**Discussion**

Even though the diagnostic criteria for NCSE lack consensus, NCSE is frequently recognized in critically ill patients and may be seen in various conditions. Although there is disparity in treatment practices, early treatment is advocated to reduce morbidity and mortality. This case series demonstrates that similar electrographic patterns can be a feature accompanying IH. Our experiences with these 3 cases suggest that when NCSE fails to respond to treatment with AEDs, the diagnosis should be reevaluated. A diagnosis of IH requires diligent clinical assessment and careful review of neuroimaging studies.

It may be argued that our patients did have NCSE and that their improvement resulted from antiepileptic treatment. The patient in Case 1, however, did not improve clinically or electrographically with therapeutic doses of 3 AEDs and 2 courses of pentobarbital with burst-suppression EEG over 3 weeks. Nonconvulsive status epilepticus unresponsive to initial AEDs is more likely to remain refractory to treatment and has a higher mortality. The improvement after treatment for IH included rapid and complete resolution of the epileptiform activity, which would be unlikely if NCSE had been the cause of the patient’s clinical deterioration. The clinical course of the patients in Cases 2 and 3 was much less prolonged; however, in each case, attempts with AEDs failed, and treatment of IH was associated with rapid and nearly complete recovery.

It could also be argued that SDHs resulted in true epileptogenic discharges; however, surgery in the patient in Case 3 did not improve the electrographic discharges or the clinical condition. After treatment of the IH, the electrographic epileptiform discharges dissipated and the patient clinically improved. We hypothesize that incisural herniation from IH may lead to dysfunction in thalamocortical pathways. Electrographically, this manifests as epileptiform discharges on EEG and clinically it can cause myoclonus-like movements. The clinician may be falsely led to believe that this clinical presentation (accompanied by the aforementioned EEG changes) is NCSE. Thalamic lesions from other etiologies have been hypothesized as a potential etiology of stimulus-induced rhythmic, periodic, or ictal discharges. We did not observe obvious signs of thalamic dysfunction in our patients. We believe that the thalamic infarcts in Case 2 and the hippocampal and pontine infarcts in Case 1 were probably a result of incisural herniation, causing compromise in the blood supply in those regions. Our hypothesis needs to be further tested. The relationship between IH and epileptiform discharges could be better understood by using animal models.

Clinical findings in IH are extremely vague and lead to frequent delay in diagnosis as in the patient in our first case who exhibited a normal CSF opening pressure. Our experience highlights that normal CSF pressure does not exclude IH. A high degree of suspicion is required to identify this condition early and initiate appropriate measures.

Brain MRI is critical in the early diagnosis of IH (Table 1). Characteristic brain MRI changes can be best remembered by the mnemonic “SEEPS” for Subdural fluid collections, pachymeningeal Enhancement, Engorgement of venous structures, Pituitary hyperemia, and Sagging of the brain.

The imaging spectrum of IH on MRI is wide.
earliest or mild sign is distension of the dural sinuses. Brainstem herniation is seen as a later severe sign. Other features include diffuse continuous linear pachymeningeal enhancement without nodularity both above and below the tentorium, reduced distance between the pons and the mammillary body due to the descent of the mammillary body, crowding of posterior fossa due to brainstem descent, bilateral or unilateral subdural fluid collection, pituitary enlargement, descent of cerebellar tonsils, effacement of the prepontine cistern and interpeduncular cistern, inferior displacement of the optic chiasm, sagging of the tuber cinereum, inferior displacement of splenium, slit-like ventricles, descent of the fastigium of the fourth ventricle, and decreased ventricular size.

Although brain MRI is the diagnostic modality of choice, other imaging techniques, such as radioisotope cisternography, CT myelography, and plain-film myelography, will help to localize the etiology and plan the treatment strategy including administration of an epidural blood patch. The various brain imaging abnormalities described by other authors in the literature are helpful. Careful interpretation of images is required as there are instances in which subdural fluid collection due to IH was misdiagnosed as a neurological problem and was evacuated, resulting in bad outcome. Nonetheless, there are instances in which cerebellar descent due to IH has been misdiagnosed as Chairi malformation.

Conclusions

Intracranial hypotension may present with clinical and electrographic activity including mental status changes and epileptiform discharges mimicking NCSE. The worst possible outcome in IH can be coma, respiratory depression, and even death. When antiepileptic therapy for NCSE is not effective in patients treated neurosurgically (especially procedures putting them at risk for CSF leakage), appropriate imaging should be performed and carefully examined for the classic findings of IH, and if present, treatment should be undertaken. Normal CSF pressure does not rule out IH, and misdiagnosis may result in increased morbidity and mortality.

Disclosure

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author contributions to the study and manuscript preparation include the following. Conception and design: all authors. Acquisition of data: Hedna, Kumar, Miller, Bidari, Salardini, Waters, Hella, Valenstein. Analysis and interpretation of data: Eisenschenk, Hedna, Kumar, Bidari, Waters, Hella, Valenstein. Drafting the article: Hedna, Kumar, Waters, Hella, Valenstein. Critically revising the article: all authors. Reviewed submitted version of manuscript: all authors. Approved the final version of the manuscript on behalf of all authors: Eisenschenk. Statistical analysis: Hedna, Kumar. Administrative/technical/material support: Hedna, Kumar. Study supervision: Hedna, Kumar.

References


Manuscript submitted December 13, 2011. Accepted July 30, 2013. Please include this information when citing this paper: published online August 23, 2013; DOI: 10.3171/2013.7.JNS112308.

Address correspondence to: Stephan Eisenschenk, M.D., Department of Neurology, University of Florida College of Medicine, P.O. Box 100236, Gainesville, FL 32610. Email: stephan.eisenschenk@neurology.ufl.edu.