Continuous Qualitative Electroencephalography as a Noninvasive Neuromonitor

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Abstract

Intracranial pressure (ICP) monitoring frequently guides key decisions in the management of diseases causing intracranial hypertension. Although typically measured by invasive means, contraindications may leave the clinician with little recourse for dynamic ICP evaluation—particularly when the patient's mental status is compromised. We describe here a healthy 18-year-old woman who subacutely progressed to coma due to diffuse cerebral venous sinus thrombosis. Heparinization precluded the use of invasive ICP monitoring, and electroencephalography (EEG) was used novelly as a surrogate ICP monitor. She responded well to anticoagulation and hyperosmolar therapy guided by qualitative EEG and was later discharged with a nearly normal neurologic examination. She was found to have *Salmonella* bacteremia, heterozygous prothrombin and factor V Leiden mutations, and hemoglobin H disease.

Keywords

intracranial sinus thrombosis, intracranial hypertension, FIRDA, neuromonitoring

Introduction

The inpatient neurologist uses a growing armamentarium to assess for, manage, and treat injury from severe, acute neurologic disease. Multimodal neuromonitoring encompasses older technologies such as ventricular catheterization and jugular venous oxygen saturation measurement alongside newer ones, including direct measurement of brain tissue oxygen tension, thermistor-based measurement of cerebral blood flow, cerebral microdialysis, and near-infrared spectroscopy. Concurrently, novel uses of existing technologies, such as ultrasound and electroencephalography (EEG), are growing and demonstrating their own unique utility.

The neurohospitalist's goal is to mitigate primary neurologic injury while anticipating and preventing secondary injury such as elevated intracranial pressure (ICP). Elevated ICP secondary to a variety of primary injuries may induce poor cerebral perfusion and further brain injury. Although no controlled trial of invasive ICP monitoring has demonstrated benefit,^{1,2} placement of invasive ICP monitoring is recommended in multiple consensus guidelines.^{3,4} Ultimately, the risk of placing an ICP monitor must be weighed against the risk of managing a patient without invasive ICP devices. In many cases, a noninvasive monitor of ICP is needed in order to guide therapy while minimizing the risks of diagnostic and therapeutic interventions.

Case Report

A healthy 19-year-old woman of Filipino heritage with no significant medical history was found unconscious and drooling. Her friend reported that she was normal 5 hours earlier but that she had complained of progressive, intermittent holoccephalic headache, nausea, and blurry vision for the past month. She had undergone maxillary root canal for a small dental abscess 2 days prior to presentation but had not otherwise felt ill. She took no medications, including hormonal contraception. Emergency medical services reported a Glasgow Coma Scale of 5 on their initial assessment. At the local hospital, she was found to be febrile to 39.8°C and tachycardic with leukocytosis, elevated lactate, and microcytic anemia. She was HIV negative. Lumbar puncture was remarkable only for an

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Figure 1. Magnetic resonance (MR) imaging of the brain at the time of admission (left) and after 7 days of treatment with heparin infusion (right) demonstrates superior sagittal, bilateral transverse, and straight sinus thrombosis with subsequent recanalization. A, Axial susceptibility-weighted imaging, (B) axial postcontrast sequences, and (C) sagittal MR venogram (MRV).

opening pressure in excess of 40 mm Hg. Magnetic resonance imaging revealed diffuse cerebral venous sinus thrombosis (CVST) of the superior and inferior sagittal, straight, and sigmoid sinuses bilaterally, mildly dilated temporal ventricular horns, as well as a small acute infarct of the corpus callosum (Figure 1). Computed tomography (CT) angiography of the head and neck incidentally revealed pulmonary embolism, and further CT imaging revealed a splenic infarct of undetermined age. Intravenous heparin infusion was initiated prior to transfer to a large university hospital.

On initial examination, eyes were open spontaneously, and the patient was unable to track or regard the examiner. Brain stem reflexes were intact with reactive pupils, and marked optic disc edema was present bilaterally. She exhibited flexor posturing. Electroencephalography was obtained to evaluate for nonconvulsive status epilepticus and initially showed

continuous, symmetric, frontally predominant delta activity. The etiology of her ongoing coma was attributed to intracranial hypertension secondary to diffuse venous thrombosis. Invasive monitoring of ICP was relatively contraindicated due to anticoagulation; the risks of temporarily stopping anticoagulation with possible worsening thrombosis were felt to exceed the risk of empiric treatment of elevated ICP without invasive monitoring.

The patient's EEG initially showed continuous frontally predominant rhythmic delta activity, which became intermittent within minutes of administering mannitol (Figure 2). This EEG finding was reproducible with subsequent hyperosmolar treatment. Based on this observation, EEG was used as a surrogate noninvasive monitor of cerebral dysfunction due to elevated ICP. The patient was treated with 30 mL boluses of 23.4% saline approximately every 6 hours or when increasing frequency of frontal rhythmic delta activity suggested increasing ICP. As thrombosis resolved, the requirement for hyperosmolar therapy diminished, and the EEG background progressively improved (Figure 2). Within 48 hours of initiating hyperosmolar therapy, her EEG normalized alongside improving mental status, and she was extubated. At that time, left ophthalmoparesis was noted. Over the ensuing days, she additionally developed left ptosis, a right abducens nerve palsy, and numbness in an upper right trigeminal distribution. Repeat magnetic resonance venogram showed no cavernous sinus thrombosis but was suggestive of venous congestion (Figure 1). The cranial neuropathies resolved over the course of weeks.

One of 2 blood culture samples drawn on presentation grew *Salmonella* species, for which she was treated with a course of ceftriaxone. A peripheral blood smear revealed hypochromia, microcytosis, and Heinz bodies. Hemoglobin electrophoresis showed hemoglobin H disease. Further testing revealed heterozygosity for both factor V Leiden and prothrombin G20210A mutations. She was discharged on warfarin and experienced a full recovery.

Discussion

Certain populations inevitably have relative contraindications to invasive ICP monitoring, such as therapeutic anticoagulation and coagulopathy, prompting ongoing efforts to develop noninvasive measures of ICP. Several noninvasive modalities have been posited and validated to varying degrees, including transcranial Doppler ultrasound, tympanic membrane displacement, and measurement of optic nerve sheath diameter. Of note, none of the aforementioned noninvasive techniques is capable of continuous monitoring, instead providing serial snapshots in time. Furthermore, each reflects mechanical changes due to elevated ICP, as opposed to assessing brain function directly.

Continuous EEG monitoring has long been used to monitor adequacy of electrical suppression in the treatment of status epilepticus and to detect subclinical seizures in critically ill populations. Due to its complexity, qualitative EEG is often

Figure 2. Initial electroencephalography (EEG) showed continuous frontal predominant monomorphic 2-Hz delta activity (A). Electroencephalography changed in response to hyperosmolar therapy with mannitol and 23.4% hypertonic saline, evolving over minutes into frontal intermittent rhythmic delta activity (FIRDA) superimposed on a disorganized, low-amplitude background with admixture of theta, delta, and beta frequencies (B). The underlying background EEG showed gradual improvement in background organization and complexity with eventual development of a rudimentary posterior rhythm of 6 to 8 Hz (C). Gradual improvement in EEG occurred alongside gradual improvement in her neurologic examination.

distilled into a number of useful quantitative parameters to simplify analysis and facilitate rapid decision-making. Such quantitative EEG is used not only in anesthesia and intraoperative settings but also in the early detection of ischemia, where EEG changes reflect early cortical dysfunction from a variety of causes including delayed ischemia after subarachnoid hemorrhage. Beyond a measure of seizure activity, EEG should be appreciated as a direct monitor of cerebral function.

Continuous EEG may also reflect ICP, presumably by way of diminished cerebral perfusion and relative ischemia, resulting in diffuse cortical dysfunction. Unlike many other noninvasive measures, EEG is particularly attractive as a bedside, real-time, continuous, functional neuromonitor. Little literature exists on the use of qualitative EEG specifically as a surrogate metric of ICP. However, the relationship between specific quantitative EEG measures and ICP has been explored in small studies using EEG metrics calculated from simplified montages, such as power spectrum analysis, entropy, and bispectral index. Power spectrum analysis from a simplified montage, for example, may be used to calculate an index of delta frequency power and regularity, which in one study correlated well with ICP as measured by lumbar puncture.⁵ This observation is consistent with prior observations that EEG frequency decreases proportionally with decreasing cerebral blood flow, as first described in transient carotid occlusion during endarterectomy.⁶ Quantitative EEG measures are beyond the scope of this report but would be of interest in future investigations. For example, spectral analysis could potentially demonstrate episodic increases in delta activity.

The EEG pattern in this case may be labeled frontal intermittent rhythmic delta activity (FIRDA) and is nonspecific. In its initial description by Cobb, intermittent rhythmic delta activity was associated with elevated ICP and damage to deep, midline cerebral structures.^{7,8} Indeed, one study posited that intermittent rhythmic delta activity is a “transmitted pattern” arising from lesioned deep, midline structures, which furthermore may correlate with localized mass effect from third ventriculomegaly.⁹ In an early observational studies of 100 patients with FIRDA, the predominant underlying etiology was space-occupying lesions; many—but not all—participants also exhibited clinical evidence of elevated ICP.¹⁰ However, no study has examined qualitative EEG patterns specifically with respect to elevated ICP, and the association remains controversial.

More recent studies of adults and children with FIRDA suggest the pattern is nonspecific and associated much more commonly with toxic-metabolic encephalopathy, as well as structural brain lesions; elevated ICP probably is associated with FIRDA as classically thought, though relatively infrequently.^{8,11-13} The present case demonstrates a compelling temporal correlation between administration of hyperosmolar therapy and resolution of FIRDA. Thus, it is possible that FIRDA is the electrographic manifestation of diffuse cerebral dysfunction due to elevated ICP. It is also possible that

impaired venous drainage from deep, midline structures generated an abnormal “transmitted rhythm,” which may be more congruent with classical descriptions of FIRDA.

This patient’s CVST manifested in many ways as a textbook presentation. Her symptoms, and their evolution, illustrate neuroanatomic–phenotypic correlations of CVST—with headache and blurry vision from early sagittal thrombosis evolving into coma from straight sinus thrombosis. She was also subjected to several well-described precipitants of CVST, including systemic infection, anemia, and thrombophilia.¹⁴ Double heterozygosity for both factor V Leiden and prothrombin G20210A mutations has a substantially higher risk of venous thromboembolism than those with either mutation alone.¹⁵ Hemoglobin H disease, a moderate to severe α -thalassemia, does not itself induce thrombophilia, although it causes anemia and may predispose to systemic infection, both of which are strongly associated with CVST.¹⁴

Conclusion

The EEG finding of FIRDA ultimately served as a surrogate measure of ICP in this case and therefore informed the duration of hyperosmolar therapy. Secondary neurologic injury was effectively mitigated in the acute setting, allowing treatment of the patient’s primary insult with anticoagulation. Qualitative EEG is useful in monitoring sedation, ischemia, and seizure activity. Furthermore, it may be interpreted in a broader sense as a continuous, direct, functional measure of neurologic status in a variety of settings including intracranial hypertension.

Authors’ Note

This study was approved by the institutional review board of University of California, San Francisco (#149359). The patient consented to the publication of this manuscript.

Declaration of Conflicting Interests

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