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Case Report

Ictogenesis during sEEG evaluation after acute intracranial hemorrhage☆,☆☆

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ABSTRACT

We present a unique case of a patient with drug-resistant focal epilepsy undergoing stereoelectroencephalography (sEEG) who developed an acute posttraumatic intracranial hemorrhage during monitoring, first detected by changes on sEEG. Our case demonstrates the evolution of electrographic changes at the time of initial hemorrhage to the development of ictal activity. We conducted spectral analysis of the sEEG data to illustrate the transition from an interictal to ictal state. Initially, delta power increased in the region of acute hemorrhage, followed by sustained regional reduction in frequency variability. Our findings provide further information on the development of epileptiform activity in acute hemorrhage.

1. Introduction

Traumatic brain hemorrhage (TBH) can be associated with lifelong functional, cognitive and emotional impairment. The magnitude of tissue damage following trauma is determined by both the primary injury, which is dependent on the kinetic energy at the time of impact, and the secondary injury that accumulates over time due to the response of the brain tissue surrounding the primary injury site [1]. Among different factors that contribute to secondary injury are seizures and hemorrhagic progression of contusion (HPC) [2]. HPC can present as progressive hemorrhagic injury or as delayed intracerebral hematoma 48 h after the trauma. HPC may result in increased seizure burden, although it is unclear if seizures and HPC are corelated or occur independent of each other. Growing evidence suggests that epileptiform transients and seizures are independent predictors of the development of chronic spontaneous seizures (posttraumatic epilepsy; PTE) [3,4]. Therefore, the management of TBH includes monitoring and treatment of HPC and the development of new-onset seizures. Capitalizing on a traumatic HPC following a seizure-related head injury in a patient with drug-resistant focal epilepsy admitted for sEEG monitoring, we demonstrate the temporal evolution of epileptiform activity and the associated spectrographic changes that were localized adjacent to the area of acute hemorrhage. The hemorrhage was noted to be outside of and contralateral to the area eventually determined to be the seizure onset zone (SOZ).

2. Materials and methods

The patient is a 24-year-old right-handed male with epilepsy diagnosed at the age of 3. In his teenage years, he suffered multiple sports-related concussions associated with prolonged loss of consciousness. He presented with multiple seizure semiologies including focal impaired awareness seizures (FIAS). Prior to admission, the patient reported FIAS every 2–3 days, which frequently progressed from focal to bilateral tonic–clonic (BiTC) seizures. The reported semiology includes abrupt onset hypermotor seizures from sleep and episodes of behavioral arrest without manual automatisms lasting a few seconds. His caregiver also described recurrent episodes of prolonged and violent postictal psychosis. His seizures were drug-resistant resulting in a referral for potential epilepsy surgery. He underwent standard phase I investigations including scalp video EEG, MRI, MEG, interictal PET, and ictal SPECT scans that were nonlocalizing. There was no definite lateralization (EEG, semiology, imaging) but the putative localization included prefrontal, premotor, and cingulate networks. Subsequently, he was admitted for sEEG monitoring for better localization of the SOZ as part of a presurgical workup.

Stereo-EEG monitoring was performed using 18 depth electrodes (12–16 contacts per depth electrode, 2 mm contact length, 0.8 mm contact diameter, 1.5 mm intercontact distance; PMT® Corporation,

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Chanhassen, MN) placed throughout the bilateral orbitofrontal, cingulate, temporal, and hippocampal regions. Depth electrode implantation was performed using ROSA® software with subsequent placement assisted by the ROSA® robot (MedTech Surgical Inc., New York, NY). The EEG was sampled at 2048 Hz using the Natus Quantum acquisition system. Preprocessing of EEG included filtering of 60 Hz artifact, using a notch filter, and removal of DC and movement artifact. Power spectral density (PSD) from the right posterior orbitofrontal bipolar electrodes was calculated using FFT (Fast Fourier Transform) and a moving window of 0.5 s with 50% overlap, and the average values per frequency bandwidth were used to create the graphs (Fig. 2). Frequency bandwidths used were delta 1–4 Hz, theta 4–8 Hz, alpha 8–13 Hz, beta 13–30 Hz, and gamma 30–70 Hz. The EEG was visually analyzed and five-minute epochs from each of the described interictal and ictal activities are illustrated in Fig. 1. Finally, the PSD was compared with recordings from the contralateral (left) posterior orbitofrontal electrode that served as a control.

3. Results

Five typical focal onset seizures, several with progression to BiTC activity, were recorded on sEEG with a common electrographic onset localized to the left anterior to mid-cingulate region. During the fifth seizure, the patient progressed to BiTC activity with review of the video showing violent clonic movements with the right arm and right side of the head making contact with the railing of the bed, despite protective barriers being in place. This clonic activity lasted approximately 20 s. Fifteen hours after this seizure (on day 10 postimplantation), the sEEG revealed new interictal and ictal patterns in the right posterior orbital frontal electrodes that were not part of the previously seen interictal background or ictal pattern with any of his habitual seizures. On further review of the EEG, he was found to have electrographic changes in the electrodes within the right posterior orbitofrontal region (RPOF; Fig. 3), consisting of new-onset rhythmic delta activity (RDA; Fig. 1, T1 and T2) lateralized periodic discharges (LPDs; Fig. 1, T3), intermittent focal seizures, and an interictal–ictal continuum (IIC) pattern (continuous spiking with intermittent evolution to seizure; Fig. 1, T4 and T5). The IIC pattern became sustained at ~18 h after the seizure with associated trauma and continued for approximately 6 h. The postinjury time points at which each epileptiform pattern developed are as follows: RDA within 15 h; LPDs, fluctuating between RDA and intermittent focal seizures at 16–18 h; IIC at 18–24 h, resolution of IIC but continued intermittent focal seizures from 24 to 42 h; and

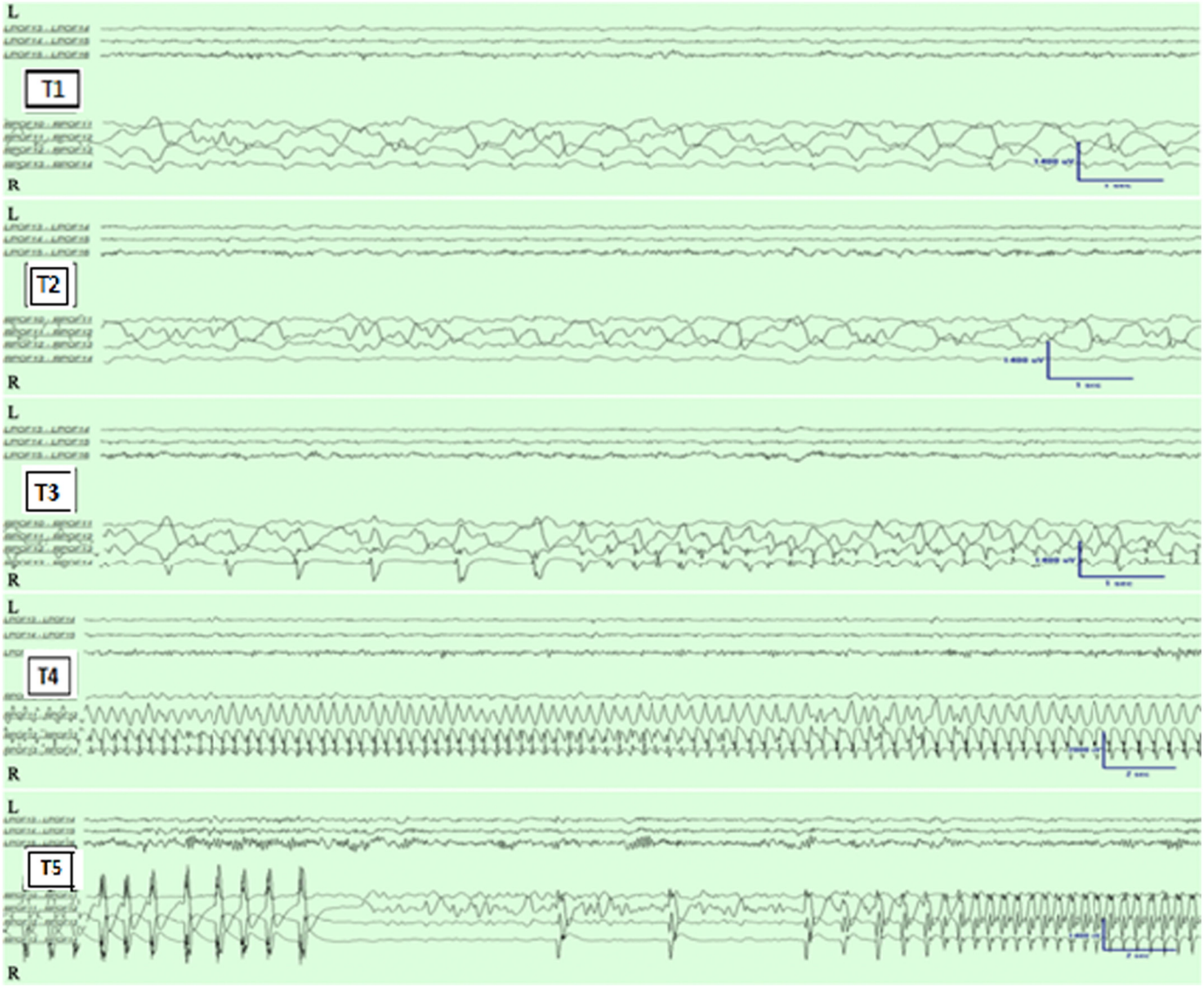

Fig. 1. Stereo-EEG demonstrating evolution over time in a 4 contact regions in the right posterior orbito-frontal region, consisting of new-onset rhythmic delta activity (RDA) (T1; T2), lateralized periodic discharges (LPDs; T3), and interictal–ictal continuum (IIC) pattern and electrographic status epilepticus (T4; T5).

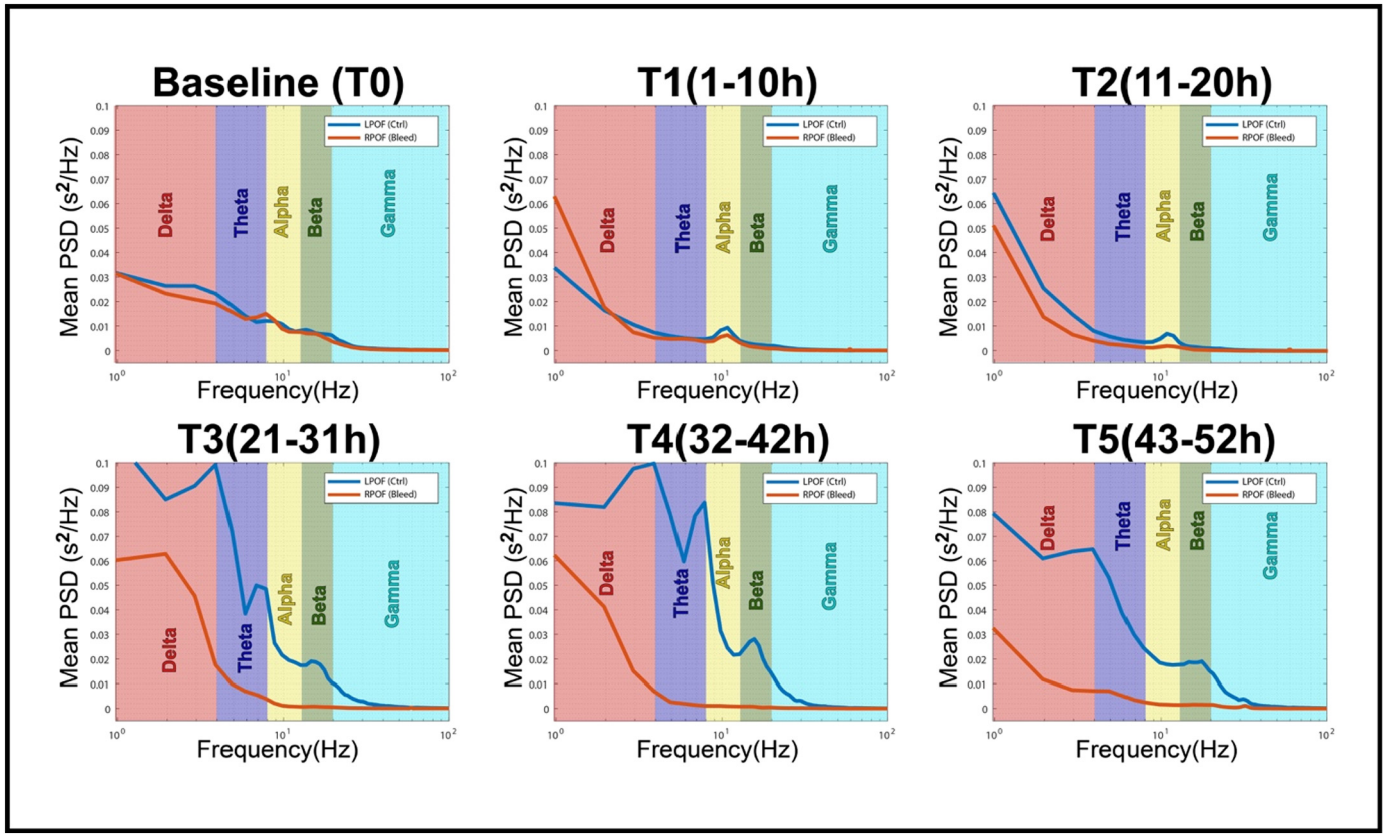

Fig. 2. Power spectral density (PSD) shown for the control region (left posterior orbitofrontal; LPOF) versus the area adjacent to the posttraumatic hemorrhage (right posterior orbitofrontal; RPOF). PSD demonstrates an increase in delta power initially and then a sustained reduction in frequency variability when compared with the internal control electrode symmetrically placed within the contralateral orbitofrontal region.

spontaneous resolution of all epileptiform activity at 42 h. Further, direct cortical stimulation of the (RPOF) electrodes at approximately 48 h postinjury triggered the same atypical ictal pattern seen at 24 h postinjury. Stimulation was performed on RPOF contacts 7–9, 9–11, and 11–13, at both 4 mA and 8 mA stimulation, with a pulse width of 300 ms, 30 Hz pulse frequency, and for a duration of 3 s. The patient had no clinical symptoms with this new-onset interictal and ictal spiking nor during our stimulation procedure. The ictal pattern that developed in the affected leads remained very focal and showed no significant spread.

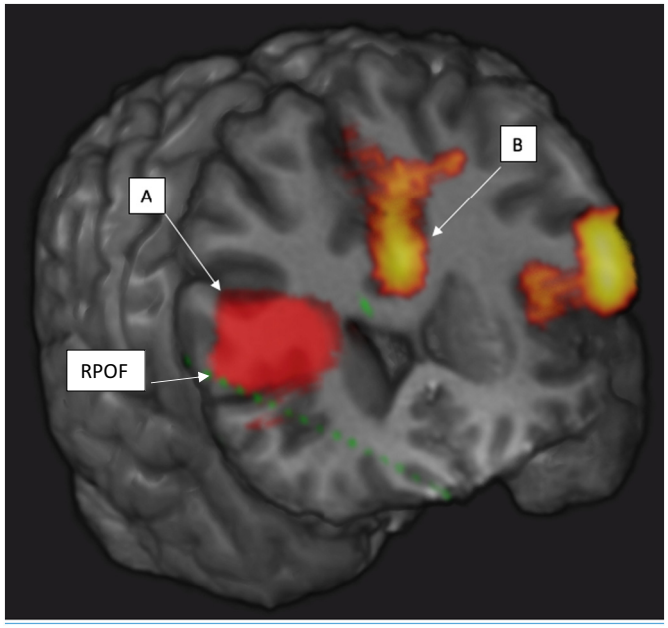

Fig. 3. 2D rendering of hemorrhage and adjacent electrode (A) and ictal SPECT showing seizure onset zone (B) as it was confirmed by sEEG. RPOF = right posterior orbito-frontal.

The patient was explanted after stimulation on hospital day 11. *Postexplantation* CT revealed an area of new-onset hemorrhage in the right posterior orbitofrontal region (Fig. 4A), that was not present on *postimplantation* CT (Fig. 4B). Subsequent 3D reconstructions of the intraparenchymal hemorrhage overlaying the affected sEEG depth electrode (utilizing Curry 7®, Compumedics Neuroscan, 2018) revealed that the four contact areas demonstrating the new-onset epileptiform activity were directly adjacent to the lateral border of the hemorrhage (Fig. 3A). In the following week, multiple CTs of the brain showed evolution in hemorrhage with the development of new adjacent areas of hemorrhage in the anterior mesial frontal region (Fig. 4C). This area of hemorrhage was not present on the initial postexplantation CT and we did not see electrographic changes in this region prior to explantation (Fig. 5). It remains unclear as to the etiology of this second hemorrhage. His hemorrhage was managed conservatively and he recovered completely without any neurological deficits. He underwent an ictal SPECT procedure several months after sEEG monitoring, which provided additional information regarding the SOZ (Fig. 3B); this monitoring also confirmed that there was no irritability of seizures emanating from the region of the hemorrhage. He recently received thermal ablation of the left mesial frontal region including the anterior cingulate gyrus (Fig. 6) and he remains seizure-free several weeks after the procedure.

As the EEG progressed from discrete spikes to LPDs and continuous focal electrographic status epilepticus (Fig. 1), the corresponding

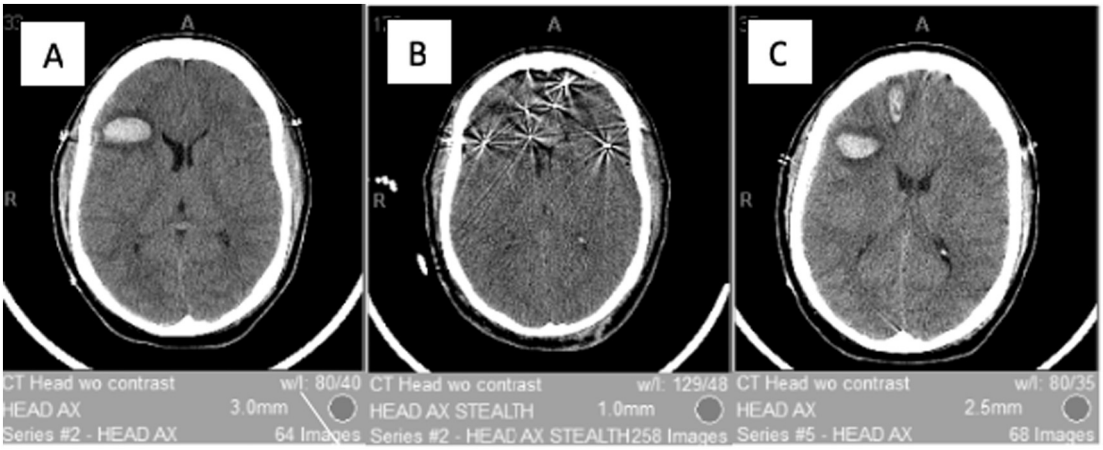

Fig. 4. A. Post*explantation* CT with new onset of right posterior orbitofrontal hemorrhage. B. Post*implantation CT without hemorrhage*. C. Evolution of right POF hemorrhage and subsequent new onset frontal hemorrhage at 2 days post discharge.

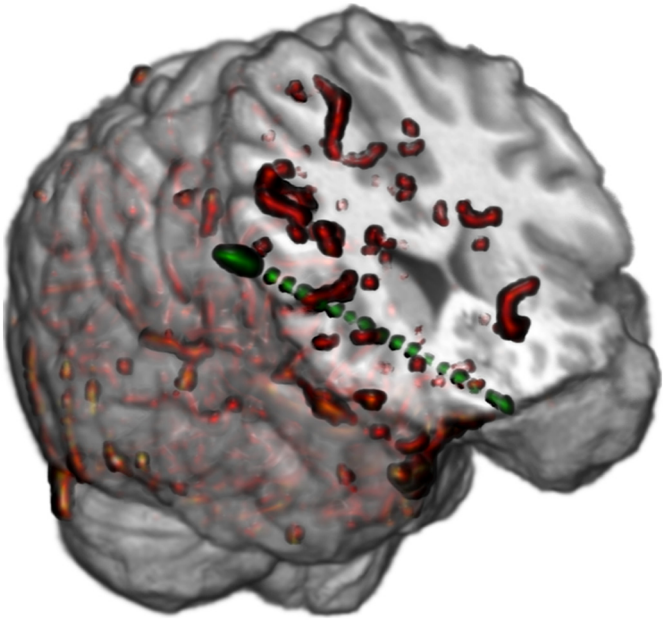

Fig. 5. CTA reconstruction of vessels surrounding the affected RPOF electrode.

changes in PSD were noted (Fig. 2); an initial increase in delta power then a subsequent loss of frequency variability in the involved channels (red) in comparison to the uninvolved channels (blue). In the uninvolved channels, there were mixed frequencies consistent with physiological background activity.

4. Discussion

Early seizures are considered to be predictive of delayed development of posttraumatic epilepsy. There is often a latent period between acute provoked and the development of spontaneous seizures. These late seizures are thought to occur secondary to the process of epileptogenesis, and even a single delayed seizure can be considered proof of epileptogenesis in that particular region [5,6]. Metabolic alterations, namely decreased glucose consumption, are thought to be a key factor in the process of posttraumatic epileptogenesis [7]. Studies have shown that in neurodegenerative diseases, including posttraumatic processes, brain hypometabolism can be an early marker of epileptogenesis [8]. The spectral analysis performed in this case (Fig. 2) revealed a relative increase in delta power initially, consistent with our known understanding of regional hypometabolism, ischemia, and altered neuronal firing during acute hemorrhage [9]. Animal models have shown that seizures themselves can cause oxidative stress and hypometabolism. Therefore, early seizures, as represented in this

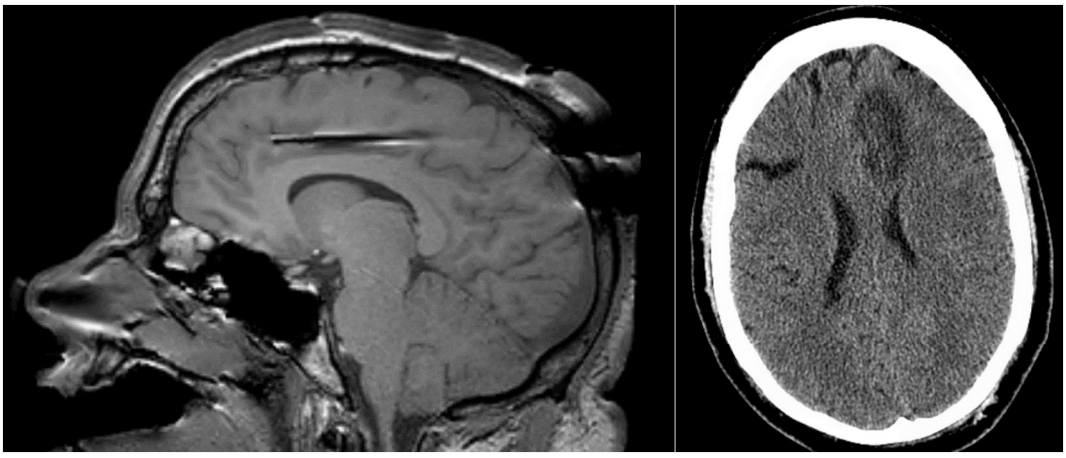

Fig. 6. Laser ablation of the ictal onset zone in the left cingulate and paracingulate region. Left MRI T1 sagittal panel depicts thermal electrode placement. Right panel axial CT depicts the thermally ablated area.

case, can further cultivate epileptogenesis and create a positive feedback loop for the development of delayed onset epilepsy [7]. Given that the IIC pattern and seizure activity resolved spontaneously in our case, it remains to be determined if this area of injury evolves into a sustained epileptogenic focus. Additionally, there is a lack of published data to suggest that the patient's long-standing drug-resistant nonlesional epilepsy would put him at higher risk of developing a new ictal focus following acute hemorrhage compared with the general population. Further, his routine EEG studies prior to sEEG implantation did not show interictal abnormalities suggestive of a diffuse hypoexcitable state, like those found in the genetic generalized epilepsies. While his SOZ is presumed to be hypoexcitable, areas lying outside of this area are presumed to be comprised of normal functioning brain parenchyma.

In cases of acute injury (e.g., trauma), prophylactic anti-seizure drugs are given to decrease the change of immediate posttraumatic seizures [10]. However, subclinical seizures, as seen in our patient, likely continue to go unnoticed and may play a strong role in the development of posttraumatic epilepsy [5]. The use of intracranial depth electrodes has expanded beyond seizure localization in patients with epilepsy. In addition to other multi-modal monitoring techniques, depth electrodes have been used in assessing the cerebral physiologic effects of seizures after acute brain injury [11–13]. Previous studies incorporating simultaneous monitoring of EEG from the surface of the scalp, and subdural strip electrodes placed around the traumatic hemorrhagic contusions showed higher prevalence of epileptiform activities (including seizures and spikes) that may be undersampled with scalp recordings. Further, cortical spreading depression and infra-slow activity that can contribute to excitotoxicity activity and can be associated with subclinical seizures, are typically only detectable with intracranial recordings. With increasing evidence that ongoing uncontrolled seizures in patients with acute brain injury have worse functional and cognitive outcomes, and the fact that seizures in acute brain injury are often not detectable by scalp EEG, better detection of these clinically silent seizures becomes imperative [11,12,14]. Intracortical EEG provides a better signal-to-noise ratio, increased detection of seizures and localized recording from affected neuronal tissues [12]. The risks of depth electrode implementation in this realm are similar to the risks associated with the use of sEEG electrodes in the surgical workup of drug-resistant focal epilepsy. Hemorrhagic complications are the most prevalent risk with sEEG, with a pooled risk of approximately 1%. Other complications include infection, cerebral abscess being most common, hardware-related complications, and permanent neurologic deficit [15].

This case demonstrates a unique situation of intracerebral hematoma development 10 days after sEEG electrode implantation. Given that the patient was already implanted with depth electrodes, the electrographic changes on sEEG were evaluated in the context of a known time course following the initial insult. The evolution noted on both sEEG and spectral density analyses provides further insight into the physiology of new-onset seizures and how they might contribute to the development of posttraumatic epilepsy.

5. Conclusion

In this study, we document the electrographic changes in the human brain in response to acute traumatic brain hemorrhage as detected by sEEG electrodes. We hypothesize that the hemorrhage described in this case was multifactorial. It is likely that the violent tonic head movements noted during seizure five caused significant shear stress in the right frontal brain regions. While this scenario would not normally cause hemorrhage, shear strain in the area of the affected implanted electrode likely resulted in small vessel damage adjacent to the electrode. Our findings reinforce prior studies showing that acute intracranial hemorrhage can result in new-onset epileptiform activity that can be present despite the absence of neurological deficits. This may have implications regarding prophylactic anti-seizure drug therapy and extension of intracranial monitoring of perilesional brain tissue in cases of hemorrhage where otherwise small focal seizures would not be left unnoticed and untreated based on current evidence from clinical practice [10]. Patients with epilepsy are prone to traumatic falls that can produce TBI and intracranial hemorrhage. This case study highlights that in patients with epilepsy, a TBH can provoke seizures in regions outside the putative SOZ, and that new epileptiform activity in areas outside of the suspected SOZ should raise the suspicion for the interval development of a second lesion including intracranial hemorrhage. Moreover, seizures resulting in head trauma over the course of invasive EEG monitoring may increase the risk of acute posttraumatic hemorrhage.

Disclosures

None.

Ethical statement

This material has not been published in whole or in part elsewhere. The manuscript is not currently being considered for publication in another journal. All authors have been actively involved in work leading to the manuscript. This is a retrospective case report and the patient's identity is concealed.

References

[1] Prins M, Greco T, Alexander D, Giza CC. The pathophysiology of traumatic brain injury at a glance. Dis Model Mech 2013;6:1307–15.
[2] Kurland D, Hong C, Aarabi B, Gerzanich V, Simard JM. Hemorrhagic progression of a contusion after traumatic brain injury: a review. J Neurotrauma 2012;29:19–31.
[3] Vespa PM, Nuwer MR, Nenov V, Ronne-Engstrom E, Hovda DA, Bergsneider M, et al. Increased incidence and impact of nonconvulsive and convulsive seizures after traumatic brain injury as detected by continuous electroencephalographic monitoring. J Neurosurg 1999;91:750–60.
[4] Kim JA, Boyle EJ, Wu AC, Cole AJ, Staley KJ, Zafar S, et al. Epileptiform activity in traumatic brain injury predicts post-traumatic epilepsy. Ann Neurol 2018;83:858–62.
[5] Herman ST. Epilepsy after brain insult: targeting epileptogenesis. Neurology 2002; 59:S21–6.
[6] Angeleri F, Majkowski J, Cacchio G, Sobieszek A, D'Acunto S, Gesuita R, et al. Posttraumatic epilepsy risk factors: one-year prospective study after head injury. Epilepsia 1999;40:1222–30.
[7] Malkov A, Ivanov AI, Buldakova S, Waseem T, Popova I, Zilberter M, et al. Seizure-induced reduction in glucose utilization promotes brain hypometabolism during epileptogenesis. Neurobiol Dis 2018;116:28–38.
[8] Zilberter Y, Zilberter M. The vicious circle of hypometabolism in neurodegenerative diseases: Ways and mechanisms of metabolic correction. J Neurosci Res 2017;95: 2217–35.
[9] Qureshi AI, Mendelow AD, Hanley DF. Intracerebral haemorrhage. Lancet 2009;373: 1632–44.
[10] Chang BS, Lowenstein DH. Quality Standards Subcommittee of the American Academy of N. Practice parameter: antiepileptic drug prophylaxis in severe traumatic brain injury: report of the Quality Standards Subcommittee of the American Academy of Neurology. Neurology 2003;60:10–6.
[11] Waziri A, Claassen J, Stuart RM, Arif H, Schmidt JM, Mayer SA, et al. Intracortical electroencephalography in acute brain injury. Ann Neurol 2009;66:366–77.
[12] Claassen J, Perotte A, Albers D, Kleinberg S, Schmidt JM, Tu B, et al. Nonconvulsive seizures after subarachnoid hemorrhage: Multimodal detection and outcomes. Ann Neurol 2013;74:53–64.
[13] Mikell CB, Dyster TG, Claassen J. Invasive seizure monitoring in the critically-Ill brain injury patient: Current practices and a review of the literature. Seizure 2016;41: 201–5.
[14] De Marchis GM, Pugin D, Meyers E, Velasquez A, Suwatcharangkoon S, Park S, et al. Seizure burden in subarachnoid hemorrhage associated with functional and cognitive outcome. Neurology 2016;86:253–60.
[15] Mullin JP, Shriver M, Alomar S, Najm I, Bulacio J, Chauvel P, et al. Is SEEG safe? A systematic review and meta-analysis of stereo-electroencephalography-related complications. Epilepsia 2016;57:386–401.