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Case Report

Post-operative nonketotic hyperglycemic induced focal motor status epilepticus related to treatment with corticosteroids following standard anterior temporal lobectomy

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1. Introduction

In cases of drug-resistant unilateral mesial temporal lobe epilepsy (MTLE) due to hippocampal sclerosis, standard anterior temporal lobectomy (ATL) may result in seizure freedom in over 65% of cases [1–5]. Complications from standard ATL are relatively uncommon. However, in less than 6% of cases complications could include stroke, subdural hematoma, new neurologic deficits, postoperative infections, and/or cognitive and behavioral changes [5]. The use of post-operative corticosteroids may mitigate post-operative symptoms, e.g., headache, and limit other complications [6–8]. In individuals with diabetes, caution must be employed when using corticosteroids to reduce complications related to elevated blood glucose. One common presentation of nonketotic hyperglycemic states is focal motor status epilepticus or epilepsy partialis continua (EPC) [9–12]. However, post-operative corticosteroid-induced focal motor status epilepticus following standard ATL has been less commonly described. This case report describes a patient with postoperative nonketotic hyperglycemic induced focal motor status epilepticus related to treatment with corticosteroids following standard ATL.

2. Case Report

A 31-year-old right-handed woman presented to the Henry Ford Health System Comprehensive Epilepsy Program with a history of drug-resistant focal epilepsy. Her index seizure was a focal to bilateral tonic–clonic seizure at the age of 15 years old that occurred in the setting of eclampsia. She was placed on a trial of levetiracetam and remained seizure-free until the age of 23 years old when she experienced a focal impaired awareness seizure. Following this seizure, her seizures remained resistant to anti-seizure drug trials of levetiracetam, lamotrigine, clobazam, zonisamide, lacosamide, carbamazepine XR, and perampanel.

Her habitual seizures began with a feeling of nausea or a rising sensation in her abdomen. After this she would lose awareness during which time manual and oral automatisms would occur. Additionally, ictal spitting could be present. On rare occasions her focal seizures could evolve to a bilateral tonic–clonic seizure with versive head movements to the right and left upper extremity tonic posturing.

Her noninvasive diagnostic studies, including inpatient video-EEG monitoring, brain MRI, FDG-PET, and neuropsychology testing, were concordant and implicated an epileptogenic zone within the right temporal lobe (Figs. 1–3). In light of these findings, a right standard ATL was completed (Fig. 4). Her immediate post-operative course was uncomplicated, and she was discharged home on the second post-operative day. At discharge, her anti-seizure medication regimen consisted of lacosamide 200 mg in the morning and 300 mg at bedtime and perampanel 6 mg at bedtime. She was also placed on dexamethasone 4 mg every 6 h with a tapering schedule of 4 mg every 3 days for 12 days followed by 2 mg daily for 3 days before discontinuing this treatment. Her anti-seizure medications were not tapered after surgery, and she initially tolerated treatment with dexamethasone well without adverse reactions.

Then approximately one week following her discharge, she began to experience seizures that were different than her habitual seizures. These new seizures consisted of frequent, brief focal motor seizures characterized by repetitive left hemi-facial contractions without impairment of awareness. She was urgently admitted to Henry Ford Hospital for further evaluation and management. A repeat brain MRI demonstrated postsurgical changes in the right anterior temporal lobe with adjacent increased T2/FLAIR signal along the superior and posterior resection cavity (Fig. 4A–C). Continuous video-EEG monitoring revealed focal motor status epilepticus with seizures arising from the right...
fronto-central region (Figs. 5 and 6). She continued to experience approximately 17 seizures every 6 hours and a loading dose levetiracetam with escalating doses of lacosamide and perampanel were unsuccessful in controlling her seizures.

Review of her laboratory findings revealed markedly elevated blood glucose of 445 mg/dL (range 50–150). Prior to surgery her blood glucose was 136 mg/dL and at discharge from HFH her blood glucose was 113 mg/dL (Table 1). During this admission, she relayed a prior diagnosis of type II diabetes mellitus that resolved following 200-pound weight loss approximately 10 years prior. Upon further review, she also required treatment for gestational diabetes with metformin two years prior to ATL.
With aggressive control of her blood glucose, including a trial of metformin and discontinuation of dexamethasone, her new seizures improved and subsequently resolved. She had no recurrent focal motor seizures after this and she has been free of her habitual seizures for over 3 years.

3. Discussion

In this case, a woman with drug resistant focal epilepsy had concordant noninvasive diagnostic testing that implicated an epileptogenic zone within the right temporal lobe. Following a right standard ATL she experienced a new seizure-type that occurred in the setting of treatment with dexamethasone. She subsequently disclosed a prior diagnosis of type II diabetes mellitus that had previously been managed with weight loss and exercise. After aggressive control of her blood glucose, these new seizures decreased in frequency and resolved. She has remained free of her habitual focal impaired awareness seizures and her postoperative focal motor seizures for over 3 years.

Focal motor status epilepticus or EPC are common and often the presenting sign in nonketotic hyperglycemic states [12,13]. Interestingly, in this case the focal motor seizures arose from the same hemisphere as the resection site. Although this may raise concerns for an independent seizure onset zone or false localization of the hypothesized presurgical epileptogenic zone, one case series of 22 patients with EPC in the setting of hyperglycemia identified a structural lesion in the majority of subjects [13]. In this case, it would be less likely these

Fig. 3. A-B – Preoperative brain MRI (coronal FLAIR sequence); there is atrophy, loss of internal architecture, and increased FLAIR signal within the right mesial temporal structures and hippocampus.

Fig. 4. A-C – Post-operative brain MRI (A – coronal magnetization-prepared rapid gradient-echo (MP-RAGE), B – axial MP-RAGE, C – sagittal MP-RAGE); there are post-surgical changes in the right temporal lobe without obvious structural abnormalities within the adjacent right frontal and temporal lobes.
seizures were due to perioperative focal seizure aggravation in the frontal neocortex with asymptomatic glucose elevation. Rather, in the setting of a structural abnormality, hyperglycemia from treatment with dexamethasone could have contributed to the onset of postoperative focal motor status epilepticus.

Early seizure recurrence after epilepsy surgery may suggest failure to adequately resect or disconnect the epileptogenic zone [14]. However, the seizures in this case were markedly different than her preoperative seizure semiology. Additionally, early studies reviewing criteria for localizing an epileptogenic focus reported focal functional deficits.
provided beneficial nonconflicting confirmatory information [15]. In this regard, FDG-PET could be useful in the epilepsy presurgical evaluation. A review of epilepsy networks by Spencer in 2002 noted hypometabolism on FDG-PET is a consistent finding in MTLE and its absence should raise doubt to accurate localization of an epileptic network within the medial temporal structures [16]. Therefore, if there was no hypometabolism within the right temporal lobe on FDG-PET, consideration should be given to an epileptic network outside of this region. This was not the case in this patient where FDG-PET demonstrated hypometabolism within the right temporal lobe.

A recent prospective study evaluated the utility of inpatient video-EEG monitoring in people with suspected MTLE associated with unilateral MTS [17]. In this study, there was no difference in seizure outcome after surgery between the groups who had video-EEG monitoring and those who did not. The authors suggested it could be safe to recommend epilepsy surgery without inpatient video-EEG monitoring in people with MTLE with unilateral MRI signs of MTS, clinical semiology consistent with MTLE, no suspicion of nonepileptic events, and adequate outpatient EEGs with lateralized interictal epileptiform activity to MTS [17]. The patient in this case demonstrated many of these characteristics, and this would strengthen the hypothesis of right MTLE as opposed to an epileptic network within the right frontocentral region.

Despite the concordant noninvasive diagnostic testing implicating an epileptogenic zone within the right mesial temporal lobe, “secondary epileptogenesis” could produce an independent, de novo, epileptogenic focus. However, this phenomenon has not been described in the hyperacute post-operative period [14]. In fact, secondary epileptogenesis is believed to be a phenomenon that occurs often over 12 months after epilepsy surgery [14].

Therefore, in light of a preoperative seizure semiology consistent with mesial temporal lobe seizures, unilateral right MTS on structural brain MRI, the presence of right temporal lobe hypometabolism on FDG-PET, and markedly different seizure semiology between pre- and post-operative seizures, a diagnosis of right MTLE is favored over an overlooked epileptic network within the right frontocentral sulcus. Furthermore, the improvement in her seizure frequency after blood glucose control would suggest the new seizures in this case were most likely related to elevated blood glucose from treatment with dexamethasone.

Overall, complications from epilepsy surgery, and particularly ATL, are relatively uncommon. Previous studies have estimated complication rates around 6–10% in all surgical cases, and more recent studies have suggested the complication rates may be significantly lower at high-volume, compared to low-volume, epilepsy surgical centers [3–5,7,8].

However, a recent review of CMS Part B data and the National Surgical Quality Improvement Program (NSQIP) database, reported complications in nearly 18% of surgical cases [7]. Complications were more common in older individuals, male gender, those with higher American Society of Anesthesiologists (ASA) classification, and in those people with a pre-existing bleeding disorder [7]. The most common complication was a return to the operating room (primarily for hemorrhage), but complications ranged from death and cardiac arrest to septic shock and deep vein thrombosis [7].

Table 1

<table>
<thead>
<tr>
<th>Date</th>
<th>Serum glucose</th>
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<tbody>
<tr>
<td>3 months prior to surgery</td>
<td>136 mg/dL (range 50–140)</td>
</tr>
<tr>
<td>Day of surgery</td>
<td>176 mg/dL (range 50–140)</td>
</tr>
<tr>
<td>2 weeks post right standard ATL</td>
<td>445 mg/dL (range 50–140)</td>
</tr>
<tr>
<td>3 weeks post right standard ATL after treatment</td>
<td>113 mg/dL (range 50–140)</td>
</tr>
<tr>
<td>6 months post right standard ATL (treatment with metformin)</td>
<td>106 mg/dL (range 60–99)</td>
</tr>
<tr>
<td>30 months post right standard ATL (treatment with metformin)</td>
<td>121 mg/dL (range 60–99)</td>
</tr>
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Treatment with corticosteroids following ATL dates back to the 1960’s [6]. The use of corticosteroids may reduce cerebral edema and other perioperative complications. However, the use of corticosteroids in people with diabetes mellitus may result in elevated blood glucose and serum osmolality. In cases of nonketotic hyperglycemic states, seizures, and specifically focal motor seizures, may be common and a presenting feature [9–12]. The mechanism behind seizures due to elevated blood glucose and serum osmolality is poorly understood, but some studies have suggested glucose is a “pro-convulsant,” [12]. Interestingly, 20 people had comorbid diabetes mellitus, and an additional 35 were receiving chronic steroids [7]. Six of the 20 people with comorbid diabetes experienced complications, while ten out of thirty-five people with chronic steroid use also had a complication [7]. There was no report of focal motor status epilepticus or EPC in this database review [7].

Conclusions

This case demonstrates a previously unreported potential complication following an ATL. Overall, complications after ATL are relatively rare, and corticosteroids may mitigate some postoperative complications. In people undergoing epilepsy surgery, corticosteroids should be used cautiously in people with comorbid diabetes mellitus to avoid nonketotic hyperglycemic states. Aggressive blood glucose control in the postoperative period may reduce surgical complications and the potential for post-operative corticosteroid-induced focal motor status epilepticus.

References