Epilepsy & Behavior Reports 21 (2023) 100577

Contents lists available at ScienceDirect

Epilepsy & Behavior Reports

journal homepage: www.elsevier.com/locate/ebcr

Case Report

Anorexia and the hippocampus: A case report

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ARTICLE INFO

Article history:
Received 4 October 2022
Revised 30 November 2022
Accepted 10 December 2022
Available online 12 December 2022

Keywords:
Anorexia
Hippocampus
Eating disorder
Epilepsy
Temporal Lobe
Appetite

ABSTRACT

Eating disorders have been shown to be associated with epilepsy, typically associated with the temporal lobe and usually of non-dominant hemisphere origin. We report the case of a 56-year-old woman with drug resistant epilepsy, localized to the dominant left hippocampus. She experienced an increasing frequency of seizures over a two-year period associated with loss of appetite and substantial weight loss independent of antiseizure medication changes. Extensive workup eliminated gastrointestinal and paraneoplastic etiologies. There was no history of psychiatric illness, including anorexia nervosa. Pre-surgical workup showed mesial temporal sclerosis on MRI and video-EEG was consistent with ipsilateral medial temporal seizure onset. The patient underwent laser interstitial ablation of the left amygdala and hippocampus, which resulted in a cessation of seizures. Within 24 h of the laser ablation, her appetite returned to normal and, within 8 months she regained 26 lbs. To our knowledge, this is the first case report of a patient with dominant temporal lobe epilepsy with anorexia that was temporally associated with escalating seizure frequency and stopped with treatment and cessation of seizures, suggesting a causal and pathogenic relationship.

Introduction

Eating disorders have been shown to be associated with epilepsy, typically associated with the temporal lobe and usually related to non-dominant hemisphere origin [1,2]. However, the precise relationship between seizure frequency and seizure localization is unclear from prior reports [3–6]. (See Table 1).

The hippocampus, typically involved in most cases of temporal lobe epilepsy, may play a crucial role in feeding behavior in addition to its role in memory and spatial localization [7]. Multiple studies in rodents have demonstrated hippocampal dysfunction altering feeding behavior. This is thought to be due to impairments of mental representation from memory loss and the hippocampus' active role in feeding behavior, such as reward-place memory [7,8].

We describe the case of a patient with progressive nausea and anorexia associated with an increase in seizure frequency, independent of antiseizure medication (ASM) changes. There was an immediate reversal of nausea and appetite loss after laser ablation of the left (dominant) hippocampus in addition to seizure cessation.

Case report

A 56-year-old woman with a history of focal epilepsy was followed over 20 years at our institution. Focal seizures, initially without altered awareness, started at age 23. Inpatient video/EEG monitoring with medication reduction in 2000 demonstrated two focal seizures with retained awareness and an ictal EEG discharge over the left temporal region. MRI of the brain showed left mesial temporal sclerosis with atrophy and abnormal T2 signal of the hippocampus. The only epilepsy risk factor described was childhood febrile seizures. Her adult seizures began with an indescribable "weird feeling" over her entire body, associated with anxiety and nausea, then, rarely, progressed to seizures with impaired awareness. Her seizures lasted for less than a minute and produced post-seizure language dysfunction with paraphasic errors. With changes in ASMs, seizures were controlled and she had multiple years of seizure freedom from 2000 to 2016.

In 2016, with no obvious cause, her seizures began to increase. Initially, she did not have impaired awareness, but, by 2018, her seizures included impaired awareness and occurred on average 8

Abbreviations: EEG, electroencephalogram; MRI, Magnetic resonance imaging; ASM, Anti-Seizure Medication; lbs., pounds; GI, Gastroenterology; FSIQ, Full-Scale Intelligence Quotient; PET, positron emission tomography; LITT, Laser Interstitial Thermal Therapy.

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https://doi.org/10.1016/j.ebr.2022.100577
2589-9864/

Table 1
Case reports (patient profiles) of eating disorders associated with epilepsy in the literature.

Study	Pt #	Age, gender	Seizure focus	EEG findings	Weight change	Appetite change	Body self-image	Neuro-psychopathology	Etiology or Risk Factors	Medication or Treatment
Signer et al., 1990	1	36, F	Right temporal lobe	Generalized spike and wave pattern superimposed on a slow background frequency, with right frontal and mid-temporal foci.	Loss	Loss	Impaired	Psychotic symptoms (agitation, overactivity, extroverted behavior, thought disorder)	TBI, ICH, frontotemporal lobectomy	Valproic acid, carbamazepine, benztropine, fluphenazine, and conjugated estrogens.
Signer et al., 1990	2	25, F	Left frontotemporal region	Intermittent sharp 5 to 7 cycles/*sec* slow waves and irregular 3 to 4 cycles/*sec* slow waves in the left frontotemporal region.	Loss	Loss	Impaired	Major depressive disorder with suicide attempts, auditory hallucinations.	Family history of epilepsy. CT head normal.	Phenytoin, Carbamazepine and Valproic acid.
Signer et al., 1990	3	28, AD	Right temporal lobe	Diffuse paroxysmal activity.	Loss	None	Impaired	Depression with suicidal ideation, Bulimia	Ischemic stroke	Neuroleptics, Tricyclic antidepressants. Carbamazepine and Lithium.
Tachibana et al., 1989	4	13, F	Right occipital	Frequent spike discharges localized in the right occipital are and a remarkable slowing of the background activity.	Loss	Loss	Impaired	None	CT head general atrophy	Valproic acid and Clonazepam.
Rott, Brian.,1991	5	33, F	Left temporal lobe	Burst of theta slow waves in the left temporal lobe	Loss	Binge eating	Impaired	Bulimia nervosa, alcohol abuse	MRI brain showed lesion in the left temporal lobe in the region of the HIP.	Carbamazepine

times per month despite trials of multiple different ASMs (Table 2). Repeat MRI showed unchanged left mesial temporal sclerosis. Further workup did not reveal any obvious cause for the progressive increase in seizures. In May 2018, her weight was 165 lbs. (BMI 27.5). The patient was taking topiramate at the time of her maximum weight. However, topiramate was discontinued in June 2018 before she started to lose a significant amount of weight. Over the next year, she had lost 43 lbs. and was referred to gastroenterology, with a negative extensive workup including a CT of the abdomen and upper-GI endoscopy. The gastroenterologist believed nausea and appetite loss were seizure related.

The patient also had a history of being diagnosed with breast cancer and underwent a lumpectomy, chemotherapy, and radiotherapy in 2014. Paraneoplastic workup was negative in May of 2019. Depression and anxiety office screening tests over a 6-year period were also negative. Full pre-surgical neuropsychological tests showed a full-scale intelligence quotient (FSIQ) of 104 with a decline in verbal memory and executive problems, compared to 2013. The neuropsychological testing did not reveal psychiatric illness in any of the evaluations. She underwent repeat video/EEG monitoring in January 2019 where an episode of non-convulsive status lasting 15 min was associated with clear left temporal ictal discharges. A brain positron emission tomography (PET) revealed hypo-metabolism in the left medial temporal region. An intracarotid amobarbital test revealed left hemisphere language dominance and equal memory scores bilaterally. The laser interstitial thermal therapy (LITT) was performed in August 2019 with left amygdalohippocampectomy. Her weight at the hospital admission was 110 lb, a 55-pound decrease over 15 months. The morning after LITT, while still inpatient, much to the surprise of the patient and family, she reported a complete resolution of nausea and began eating normally. MRI scan performed one month after LITT showed a bilobed lesion due to a previous ablation within the left medial temporal lobe that measured 4.7 cm anterior-posterior and 2.8 $\times$ 1.2 cm transverse, indicating no lesion outside the planned ablation. At her 17-month follow-up, she reported only a single seizure without alteration of awareness, had no nausea, regained her normal appetite, and had gained back 35 lb (BMI 24). At 36 month follow up she remained seizure free and had gained another 15 lbs. Her only post-surgical deficit was a slightly increased difficulty with verbal memory.

Discussion

To our knowledge, this is the first case report of a patient with dominant (left) temporal lobe epilepsy and associated anorexia that was temporally associated with escalating seizure frequency and stopped with the cessation of seizures. This temporality and association suggest a causal and pathogenic relationship. The patient had simultaneously increased symptoms of anorexia, nausea, lack of appetite, and a 55-pound weight loss along with an increase in seizure frequency over a two-year period. There was complete remission of symptoms in less than 24 h after laser ablation surgery of the left hippocampus and amygdala. The patient followed up at 37 months and described an absence of nausea, a 50-pound weight gain, and a single focal seizure without loss of awareness since ablation. No other cause for nausea and appetite loss was found despite extensive gastrointestinal workup.

Table 2
Timeline of antiseizure medication, seizures, and weight.

Date (office visit)	Antiseizure medications	Seizures	Weight (pounds)
November 2012	OXC, LEV	None × 4 years	149
March 2014	OXC, LEV	FA start November 2013	128
June 2014	OXC, LEV	FA multiple/mo	131
September 2014	OXC, LEV	FA multiple/week	130
October 2014	OXC, LEV, start TPM	FA ~ 1/mo	136
December 2014	TPM, LEV	FA rare	139
March 2015	TPM, LEV	No seizures	138
September 2015	TPM, LEV	No seizures	145
March 2016	TPM, LEV	No seizures	159
April 2017	TPM, LEV	FA mult/mo; FIA 1–2/mo	157
January 2018	TPM, LEV, add PER	FA mult/mo; FIA 1–2/mo	156
May 2018	TPM, LEV, stop PER	FA mult/mo; FIA 1–2/mo	165
September 2018	TPM, LEV	FA multiple/mo; almost constant nausea; FIA 1–2/mo	154
October 2018	TPM (start reduction), LEV, add OXC	FA daily; constant nausea; FIA 2–4/mo	143
January 2019	ESLI, LEV (TPM and OXC stopped)	FA daily; nausea; FIA 2–4/mo	135
February 2019	LCM, LEV	FA daily; nausea; FIA 2–4/mo	122
May 2019	LCM, LEV	FA daily; nausea; FIA 2–4/mo	117
August 2019	LITT performed		
January 2020	LCM, LEV	Seizure free	129
September 2021	LCM, LEV	Seizure free	158
September 2022	LCM, LEV	Seizure free	167

Table abbreviations: TPM = topiramate; LEV = levetiracetam; OXC = oxcarbazepine; ESL = eslicarbazepine; PER = perampanel. FA = focal aware; FIA = focal impaired awareness.

Some ASMs can be associated with weight loss including topiramate, which this patient received. However, topiramate initiation in this case reduced seizures and was associated with weight gain between March 2014 and October 2016 (Table 2). When seizures recurred, the weight loss started and persisted after topiramate was discontinued in January 2019. After the LITT, the ASM regimen remained unchanged other than reduction of lacosamide dose, and yet weight gain has persisted during the time of seizure freedom.

Several reports link epilepsy with changes in appetitive behavior. Signer et al. described three cases of anorexia nervosa diagnosed by DSM III criteria in temporal lobe epilepsy patients [9]. In one case, a patient who suffered from depression and bulimic episodes since an early age received carbamazepine and lithium with subsequent improvement in her seizure disorder as well as a normalization of her affective state and eating disorder [9]. Ott et al. described a 33-year-old woman with bulimia nervosa diagnosed at the age of 28 with left temporal lobe epilepsy [10]. MRI brain showed a lesion over the medial tip of the lateral ventricle adjacent to the left hippocampus. She was treated with carbamazepine for 18 months with complete remission of the symptoms [10]. Although the above-mentioned studies demonstrate a resolution of eating disorders after medication use, the direct correlation of temporal lobe epilepsy resolution with medication use and resolution of the eating disorder is not clear as there could be a confounding variable that better explains these results.

There are previous cases of patients who underwent surgical treatment of temporal lobe epilepsy with a resolution of an eating disorder. Levine et al. described a case of bulimia in a 28-year-old woman with a history of drug resistant focal epilepsy manifest as complex partial seizures and secondarily generalized seizures since the age of 12 who underwent temporal lobectomy [1]. All binging/purging behavior and the compulsion to do so ceased after surgery [1]. Levine also reported a 36-year-old woman with a 6-year history of drug resistant focal epilepsy who became seizure-free after a left temporal lobectomy [1]. The patient had a head injury with a right-sided subdural hematoma and a two-month follow-up MRI brain showing right-sided inferior-frontal and temporal encephalomalacia. The patient reported symptoms of anorexia nervosa before the head injury that remitted following her lesion after the head injury [1]. Tachibana N et al. reported a 13-year-old girl with anorexia nervosa followed by generalized seizures and mood disorder that improved after a combination of valproate and clonazepam [11]. Uher et al. performed a literature review of cases that documented the relationship between brain lesions and eating disorders [2] and suggested that substantial evidence implicated frontotemporal circuits, not just the hypothalamus, in eating disorder pathophysiology. Kolstad et al. conducted a cross-sectional population-based study in patients between 13 and 19 years old with and without epilepsy [12]. The group with epilepsy was more likely to have an eating disorder or a poor-quality diet [12].

The hippocampus plays a prominent role in regulating food intake. Stevenson et al., in an extensive literature review, hypothesized that the hippocampus has an active role in food intake via a mechanism associated with memory and habit learning [13]. Impairment of the hippocampus may result in abnormal ingestion behavior. In animal studies, the hippocampus is vital for regulating higher-order aspects of feeding behavior [13]. Neurons in the hippocampus respond to a number of gastrointestinal signals for satiation and also utilize endocrine signals such as leptin, GLP-1, and Ghrelin to balance the use of energy and regulate food-motivated behaviors bi-directionally. The pancreas and hypothalamic cells secret the hormone amylin which has been thought to work synergistically with leptin to activate hippocampus neurons to regulate feeding behavior [14,15]. A subpopulation of neurons in mice expressing the dopamine receptor 2 within the hippocampus is also activated by food [16]. Azevedo et al. show that these neurons regulate food intake and the encoding of a food-place memory [16].

Despite being a single case, the dramatic change in appetite so closely tied to the hippocampal ablation and seizure cessation provides suggests that seizure activity emanating from the hippocampus may be a factor that alters eating behavior in a human. The influence of the hippocampus should be studied further in basic and clinical settings. When treating patients with eating disorders and seizures, clinicians should consider the contribution of the seizures to eating behaviors as well as the potential involvement of the hippocampus in seizure onset or spread.

Conclusion

This report demonstrates the resolution of anorexic behavior in a patient with dominant temporal lobe epilepsy after surgical ablation treatment. There are previous studies that suggest relationships between dysfunction of the hippocampus and eating disorders in the setting of epilepsy that is resolved with treatment. Further research is needed, however, to develop a robust causal relation. Thus, the onset of an eating disorder in a patient with

temporal lobe epilepsy should prompt consideration of an appropriate evaluation.

Ethical statement

Informed consent was obtained from the patient and family.

Funding

None is supported in this work.

Declaration of Competing Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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