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Case report

Hypersexuality in a patient with epilepsy during treatment of levetiracetam

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1. Introduction

Sexual dysfunction is commonly reported by patients with epilepsy, the prevalence is not clearly defined and is different by gender. Although older studies found higher frequencies, studies with structured interviews reported the prevalence to be 20% in male patients and 20–30% in female patients.[1,2] The most frequent epilepsy associated sexual dysfunctions are decreased libido and potency problems in men and hyposexuality and orgasmic dysfunction in women.[1,2]

Many hormones of the hypothalamic–pituitary axis related to sexual functions are affected in patients with epilepsy. Antiepileptic drugs such as carbamazepine and phenytoine are enzyme inducers which cause reduction in the levels of testosterone in men and estrogens in women and contribute to sexual dysfunction.[3] Lamotrigine and levetiracetam, which are neither enzyme inducers nor enzyme inhibitors, have been shown to improve sexual functioning in persons with epilepsy.[4] Specifically, female patients with epilepsy aged 18–45 treated with levetiracetam reported greater satisfaction with their sexual lives when compared to those who were treated with carbamazepine or even healthy controls.[4]

The focal epileptic discharges appear to play a role in sexual dysfunction.[1] Daniele et al. reported a reduction of sexual interest in patients with right-sided temporal lobe epilepsy (R-TLE) as compared with left-sided temporal epilepsy (L-TLE) and discussed that lateralized differences in the temporal lobe or hypothalamus may contribute to the different patterns of pituitary gonadotropin secretion.[5]

Hypersexuality is a relatively rare sexual dysfunction in epileptic patients. There are three reported cases of antiepileptic drug induced hypersexuality: one case of mania with hypersexuality induced by carbamazepine and two cases of hypersexuality without manic or hypomanic features induced by adjunctive lamotrigine to carbamazepine and oxcarbazepine.[6,7] We report a female patient who exhibited acute hypersexuality with the addition of levetiracetam while taking carbamazepine. To our knowledge this is the first reported case of hypersexuality triggered by levetiracetam.

2. Case

The patient was a 44 year-old woman with a history of mesial temporal lobe epilepsy since she was 15. Her lesion was surgically removed 13 years ago, pathology revealed a ganglioglioma. After being seizure free for 5 years, the patient had 1–2 seizures monthly while being treated with carbamazepine. Her last EEG in 2008 revealed left fronto-temporal epileptiform activity. Her MRI in 2009 noted left and temporo-occipital post-operative encephalomalacia. She had one depressive episode following her divorce 15 years ago, at which time she attempted to commit suicide with her anticonvulsant pills. She had partial response to pharmacotherapy. Her depressive features eventually resolved when she returned to work a few years ago. She had no sexual dysfunction her entire life and no sexual intercourse after her divorce. She masturbated 3–4 times a year for a few days when she was attracted by someone. After the patient developed osteoporosis, levetiracetam was initiated at 500 mg/day and titrated to 2000 mg/day while carbamazepine was decreased from 1000 to 800 mg/day. Three days after the initiation of 2000 mg/day, she experienced increased sexual drive without being stimulated visually or tactilely. She developed sexual daydreams and started to masturbate 8–9 times/day. She determined these experiences as unpleasant and disturbing. After reporting about her new sexual complaints to her long-standing epileptologist, levetiracetam was decreased and psychiatric consultation was requested. Whereas the psychiatric diagnostic interview suggested a prior major depressive episode or adjustment disorder with depressed mood at time of the prior

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suicide attempt, no current psychopathology was revealed with denial of all manic or hypomanic features including hypersexuality. Further, the patient had no prior or current medical history, including brain injuries, which could have predisposed her to hypersexuality excluding epilepsy and remote temporal lobectomy. Therefore levatirecetam was suspected as the causative factor. With gradual reduction of the levetiracetam dosage down to 1000 mg/day, her masturbation frequency decreased to 2–3 times a day and disappeared with discontinuation of the drug. The patient is now treated with carbamazepine 800 mg/day and has been seizure-free for 4 months and her sexual desire and activity returned to baseline.

3. Discussion

Hypersexuality is an excessive drive in frequency and intensity for an individual to engage in reccurent sexually arousing fantasies, sexual urges, or behaviors.[8] It is reported as a result of organic disorders such as dementia, stroke, brain injury, temporal lobe epilepsy, epilepsy surgery, treatment with stimulant drugs like methamphetamine and cocaine or dopaminergic treatment for Parkinson's Disease, moclobemide and bupropion.[9] It is a well known symptom of bipolar mania and antidepressant treatment may also induce manic switch in depressive patients, causing hypersexuality.[10]

Our patient did not meet any of the etiological causes cited above. Specifically, she was not having a hypomanic or manic episode, was not being treated with stimulants or antidepressant psychotropics and did not have history of neurologic disease associated with hypersexuality excluding epilepsy with her left-sided remote temporal lobectomy. As mentioned above, R-TLE is a greater risk factor for sexual dysfunction compared to L-TLE, and sexual dysfunction tends to resolve after surgical resection.[5,11] There are other case reports of hypersexuality after epilepsy surgery.[12] To our knowledge, there is no data suggesting a tendency for hypersexuality in patients with L-TLE and a review by Suffren et al. suggested that hypersexuality more often resulted from right hemisphere than left hemisphere lesions.[13] The onset of hypersexuality in our patient was temporarily related to the initiation of levetiracetam and resolved when it was discontinued. Therefore the authors concluded that hypersexuality was induced by levetiracetam.

Levetiracetam is an anticonvulsant with unique neuromodulary and neuroinhibitory properties. It binds to synaptic vesicle protein 2A, opposes the activity of negative modulators of GABA and inhibits N-type calcium channels.[14] Levetiracetam treatment has not been reported to cause any drug-specific sexual or endocrine side effects in men or women. It has also been reported to improve sexual function in women.[4]

A recent original research suggested that genetic variation of dopaminergic activity in patients might predispose to psychiatric complications under treatment with levetiracetam.[15] Dopamine is a neurotransmitter that has been implicated in human and animal sexual behavior and is believed to be the core of the excitatory neurotransmitter of sexual desire.[16] In our patient, hypersexuality might be triggered via dopamine pathways as in the cases of irritability and aggression. Since levetiracetam is believed to enhance the activity of GABA and GABAergic pathways are known to be a part of inhibitory system for sexual behavior,[16] this neurotransmitter is less likely to be involved in hypersexuality in this patient.

This is a record of a single case, more elaborative clinical studies are needed to assess the actual prevalence of this phenomenon among patients treated with levetiracetam. Clinicians should consider this adverse effect and the patient's sexual state when choosing levetiracetam in the treatment of epilepsy or in the off-label treatment of multiple psychiatric disorders.

References

1. Herzog AG. Disorders of reproduction in patients with epilepsy: primary neurological mechanisms. *Seizure* 2008;**17**(March (2)):101–10.
2. Harden CL. Sexual dysfunction in women with epilepsy. *Seizure* 2008;**17**(2):131–5.
3. Isojärvi JI, Taubøll E, Herzog AG. Effect of antiepileptic drugs on reproductive endocrine function in individuals with epilepsy. *CNS Drugs* 2005;**19**(3):207–23.
4. Svalheim S, Taubøll E, Luef G, Lossius A, Rauchenzauner M, Sandvand F, Bertelsen M, Mørkrid L, Gjerstad L. Differential effects of levetiracetam, carbamazepine, and lamotrigine on reproductive endocrine function in adults. *Epilepsy & Behavior* 2009;**16**(2):281–7.
5. Daniele A, Azzoni A, Bizzi A, Rossi A, Gainotti G, Mazza S. Sexual behavior and hemispheric laterality of the focus in the patients with temporal lobe epilepsy. *Biological Psychiatry* 1997;**42**:617–24.
6. Myers WC, Carrera 3rd F. Carbamazepine-induced mania with hypersexuality in a 9-year-old boy. *American Journal of Psychiatry* 1989;**146**(March (3)):400.
7. Grabowska-Grzyb A, Nagańska E, Wolańczyk T. Hypersexuality in two patients with epilepsy treated with lamotrigine. *Epilepsy & Behavior* 2006;**8**(3):663–5.
8. Diagnostic Statistical Manuel of Psychiatry. American Psychiatry Association. http://www.dsm5.org/proposedrevisions/pages/proposedrevision.aspx?rid=415.
9. Krueger RB, Kaplan MS. Disorders of sexual impulse control in neuropsychiatric conditions. *Seminars in Clinical Neuropsychiatry* 2000;**5**(4):266–74.
10. Dumlu K, Orhon Z, Özerdem A, Tural U, Ulaş H, Tunca Z. Treatment-induced manic switch in the course of unipolar depression can predict bipolarity: cluster analysis based evidence. *Journal of Affective Disorders* 2011;**134**(1–3):91–101.
11. Baird AD, Wilson SJ, Bladin PF, Saling MM, Reutens DC. Sexual outcome after epilepsy surgery. *Epilepsy & Behavior* 2003;**4**:268–78.
12. Baird AD, Wilson SJ, Bladin PF, Saling MM, Reutens DC. Hypersexuality after temporal lobe resection. *Epilepsy & Behavior* 2002;**3**:173–81.
13. Suffren S, Braun CM, Guimond A, Devinsky O. Opposed hemispheric specializations for human hypersexuality and orgasm? *Epilepsy & Behavior* 2011;**21**(May (1)):12–9.
14. Carreno M. Levetiracetam. *Drugs of Today (Barcelona Spain 1998)* 2007;**43**(November (11)):769–94.
15. Helmstaedter C, Mihov Y, Toliat MR, Thiele H, Nuernberg P, Schoch S, Surges R, Elger CE, Kunz WS, Hurlemann R. Genetic variation in dopaminergic activity is associated with the risk for psychiatric side effects of levetiracetam. *Epilepsia* 2012 [Aug 6, Epub ahead of print].
16. Pfaus JG. Pathways of sexual desire. *Journal of Sexual Medicine* 2009;**6**(June (6)):1506–33.