Case Report: Autoimmune Encephalitis like presentation in a 38 year-old female with Bupropion Overdose

Anjali Chandra MD, Nathan Praschan MD, MPH

Department of Psychiatry, Brigham and Women's Hospital, Boston, MA

Introduction

SB is a right handed 38 y/o woman with a history of prior assault and ongoing IPV, migraines, likely ADHD, PMDD vs. MDD with PME and no prior IPLOCs who presented with tonic-clonic movements that progressed to status epilectus requiring admission to the neuro-ICU.

History
- Difficulties with inattention, procrastination and organization dating back to elementary school which persist
- History of cyclic mood symptoms starting in adolescence that include sadness, dysphoria, decreased motivation, irritability, anxiety, hopelessness and self-doubt
- No substance use

Med trials
- Citalopram 20mg (2020-2021), no benefit
- Buproprion XL 20mg (5/2023-9/2023), possible helpful
- Sertraline 25mg (10/2023-current), helpful
- Concerta 18mg (12/2023-current), helpful

Family Psychiatry History
- Brother with Schizophrenia

Medical History
- Hyperlipidemia and Anemia (baseline Hgb 8)

Key Symptoms
- *Preceding:* sleep wake disturbances
- *Acute:* tonic-clonic movements → status epilepticus
- *During hospitalization:* odd stereotypies of arms, oscillating periods of paranoia/agitation to stupor, initial autonomic instability (hypertensive/tachycardic)
- *Persistent:* psychomotor retardation, inattention (responded to medication)
- *Resolved:* Mood symptoms

May 2023	Referred by PCP for symptoms of depression and poor concentration Started on Bupropion
August 2023	Patient develops worsening headaches, sleep wake cycle disturbances
September 2023	Patient develops rhythmic jerking movements which progress into status epilepticus Admission to neuro-ICU Hospitalization complicated by QT prolongation, autonomic instability, periods of paranoia and stupor R IJ thrombus and R putamenal infarct
October 2023	Discharged and transitioned to partial-hospitalization program where she was treated for depression
November 2023	Persistent slowed cognition, concern for dissociative episodes in the context of IPV
Present	Inattention and slowed cognition somewhat improved on Concerta Continued remission of Depression on sertraline Ritalin too short acting for longer-days, in its absence, notes disorganization and lack of focus

Cultural Aspects

- **Patient has significant history of IPV**
  - Hx physical assault resulting in PTSD symptoms
  - Initial limited intramarital support
  - Active relationship discord
  - Physical and emotional abuse
  - Signs: too positive about relationship, discord observed by hospital staff during admission
- **IPV was main contributor to her overdose**
  - This became apparent over the course of hospitalization and subsequent follow up appointments
  - Persistent dissociative episodes in context of abuse (contributions to amnesia)

Differential Diagnosis

	Bupropion Overdose	Autoimmune Encephalitis	Epilepsy	HSV2
Timing	Same day as onset of symptoms	Weeks to Months	Presenting Event (although no prior history)	Days to Weeks
Mechanism	Leading hypothesis is due to increased sympathomimetic amines[6]	Autoantibodies triggering encephalitis; Inhibits NMDA receptors on GABAergic interneurons, leading to Glutamatergic excess	Genetics, environmental precipitants (EtoH)	CNS spread of HSV2, can cause epileptogenic foci, cortical irritation
Characteristics	Buproprion level >> Hydroxybupropion level consistent with acute overdose, Prolonged QTC	Predisposition Female > Male (4:1[7]. Viral + Seizures Malignant Catatonia like presentation, Patient did not have any of the following: Definite: CSF with IgG GluN1 antibodies, Probable: pleocytosis or oligoclonal bands, hyperintensity in medial temporal lobes, Abnormal EEG, may have prolonged executive dysfunction after neuro complications (dysautonomia/seizures resolve)	Administered intranasal versed, loaded with Keppra, and intubated with a Versed drip, with patient response	CSF weakly positive; Also tends to have enhancement in Mesial Temporal Lobes (which this patient does not have)
Likelihood	High, given ingestion and results of workup	Moderate, given high APE score and prolonged executive function deficits but less likely given no CSF, serum antibodies	Low given no EEG correlate, no prior seizure history and no subsequent episodes despite being off anti-epileptics	Low given no MRI/EEG correlate, the lack of progressive symptoms and no risk factors

Discussion

Rationale for not hospitalizing patient after overdose:
- Amnesia for the event
- Absence of mood symptoms
- Help-seeking and future oriented behavior
- Transition to partial-hospitalization program

- In a study of 1056 US-based, trans-identifying adults, perceived usefulness of hospitalization after suicidal ideation/attempts was low and patients reported their stay to be unhelpful. General trust and voluntary admission were positively related to perceived helpfulness[1]
- Literature looking at suicide risk amongst hospitalized versus discharged self-harm patients found that suicide risk was higher amongst hospitalized patients versus those who were discharged (males had 5.4 more suicides per 1000 patients (95% CI: 3.0,7.8), those aged 10-29 had 2.4 more suicides per 1000 (2.4 (95% CI 1.1-3.6), and those aged ≥50 had 5.8 (95% CI 0.5,11.2) more suicides compared to those discharged.
- Analyses controlling for confounding variables did not find clear evidence to support reduction in suicide risk or a significant difference in an estimated conditional average treatment effect of inpatient admission, in preventing suicide within this population[2]
- Interestingly, patients hospitalized for epilepsy are at a 3-fold increased risk for hospitalization due to suicide attempt[3]

Autoimmune encephalitis workup
- Our patient had APE2 score of 4 (elevated), with high suspicion for autoimmune encephalitis in the setting of negative CSF/serum studies
- In a study conducted on 1736 epilepsy cases, of which 387 cases met criteria for epilepsy, certain clinical features such as new-onset epilepsy, autonomic dysfunction, viral prodrome were significantly associated with positive antibody results.
- An APE score of ≥ 4 had a sensitivity of 97.7% and a specificity of 77.9% for the ability to predict the presence of an autoantibody.
- Amongst antibody studies, CSF studies are considered to be more sensitive than serum[4]. 85.6% of patients with anti-NMDA receptor encephalitis who had antibodies in CSF also had serum antibodies whereas, 100% of patients with serum antibodies had positive CSF antibodies[5].

Management
- Agitation managed with valproic acid, dexmedetomidine, and lorazepam
  - Transitioned to clonidine and quetiapine
- Empirically treated for Autoimmune Encephalitis with IVMP and IVIG
  - Data around empiric treatment
- Treated empirically for HSV2 infection (weakly positive CSF) with acyclovir
- Rationale
  - Used lorazepam due to initial concern for catatonia

References

1. Aboussouan A, Moscardini EH, Cerel J, Tucker RP. Experiences of hospitalization for suicide ideation and suicide attempt in gender diverse adults. Suicide Life Threat Behav. 2022 Jun;52(3):427-438. doi: 10.1111/sltb.12852. Epub 2022 Jan 27. PMID: 35083785.
2. Goldman-Mellor SJ, Bhat HS, Allen MH, Schoenbaum M. Suicide Risk Among Hospitalized Versus Discharged Deliberate Self-Harm Patients: Generalized Random Forest Analysis Using a Large Claims Data Set. Am J Prev Med. 2022 Apr;62(4):558-566. doi: 10.1016/j.amepre.2021.08.028. Epub 2021 Nov 19. PMID: 34810041; PMCID: PMC8945689.
3. Xu KY, Rossi KC, Kim AM, Jettté N, Yoo JY, Hung K, Dhamoon MS. Risk of readmission for suicide attempt after epilepsy hospitalization. Epilepsy Behav. 2018 Jun;83:124-130. doi: 10.1016/j.yebeh.2018.03.037. Epub 2018 Apr 25. PMID: 29702413.
4. Dubey D, Singh J, Britton JW, Pittock SJ, Flanagan EP, Lennon VA, Tillema JM, Wirrell E, Shin C, So E, Cascino GD, Wingerchuk DM, Hoerth MT, Shih JJ, Nickels KC, McKeon A. Predictive models in the diagnosis and treatment of autoimmune epilepsy. Epilepsia. 2017 Jul;58(7):1181-1189. doi: 10.1111/epi.13797. Epub 2017 May 26. PMID: 28558833.
5. Gresa-Arribas N, Titulaer MJ, Torrents A, et al. Antibody titers at diagnosis and during follow-up of anti-NMDA receptor encephalitis: a retrospective study. Lancet Neurol. 2014;13:167–7
6. Kara H, Ak A, Bayr A, Acar D, Istanbulluoğlu R, Değirmenci S. Seizures after overdoses of bupropion intake. Balkan Med J. 2013;30(2):248-249. doi:10.5152/balkanmedj.2012.094 [PubMed 25207109]
7. Dalmau J, Armangué T, Planagumà J, Radosevic M, Mannara F, Leypoldt F, Geis C, Lancaster E, Titulaer MJ, Rosenfeld MR, Graus F. An update on anti-NMDA receptor encephalitis for neurologists and psychiatrists: mechanisms and models. Lancet Neurol. 2019 Nov;18(11):1045-1057. doi: 10.1016/S1474-4422(19)30244-3. Epub 2019 Jul 17. PMID: 31326280.