

Case Summary

Case

- 21 yo F pt
 - Initial presentation to outside facility
 - Seizure
 - Delusional thinking, waxing and waning
 - Labs including CBC, CMP, TSH, inflammatory markers normal
 - MRI normal
 - EEG with mild nonspecific slowing Started on anti-seizure medication, Keppra, discharged for outpt follow-up

Case, cont.

- Presented back to care within days
 - Second seizure
 - Also with increased delusional thinking, psychosis
 - Content regarding demons, some religious content, paranoia
 - No other focal symptoms
 - Labs still normal
- No history of mental illness or medical illness
- Lives on farm, but no exposures
- Married, no children
- No substance use regularly, has used cannabis, but not regularly or recently
- No clear trauma history, brain injury history, previously healthy, no other medications

Case cont.

- Transferred to a psychiatric hospital after apparent stabilization of seizures, but with ongoing psychosis
 - Presumed psychotic disorder, new onset schizophrenia vs. schizoaffective, etc.
 - Seizures controlled on Keppra and Lamictal
 - 10 days of treatment without significant improvement on antipsychotics
 - Increasing confusion
 - Increasing delirium, waxing and waning
 - Agitation, anxiety
 - Increasing stupor
 - Increasing language dysfunction

Case, cont.

- Patient still without focal symptoms of infection, other illness
- No other ongoing seizure activity obviously noted
- Labs unrevealing without infection (HIV, syphilis, inflammatory markers, CBC)
- Meds altered without significant improvement
 - Confusion not improved with decreasing medications that may contribute
 - Antipsychotic increases not clearly improving symptoms
- Patient transferred to hospital for further work-up

Differential Diagnosis

Differential

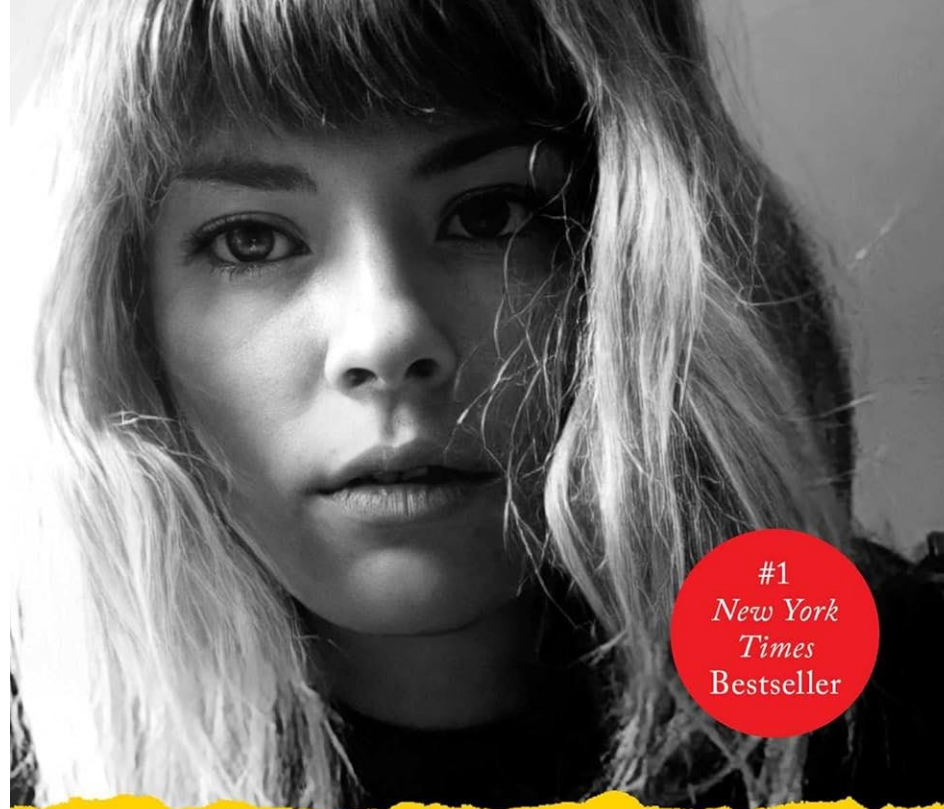
Substances and medications with capacity to induce psychosis

Substance or medication	Examples
Alcohol and sedatives/hypnotics	Alcohol (intoxication or withdrawal), barbiturates, and benzodiazepines (particularly withdrawal)
Anabolic steroids	Testosterone, methyltestosterone
Analgesics	Meperidine, pentazocine, indomethacin
Anticholinergics	Atropine, scopolamine
Antidepressants	Bupropion, others if triggering a manic switch
Antiseizure medications	Zonisamide, other antiseizure medications at high doses
Antimalarial	Mefloquine, chloroquine
Antiparkinsonian	Levodopa, selegiline, amantadine, pramipexole, bromocriptine
Antivirals	Abacavir, efavirenz, nevirapine, acyclovir
Cannabinoids	Marijuana, synthetic cannabinoids (ie, "spice"), dronabinol
Cardiovascular	Digoxin, disopyramide, propafenone, quinidine
Corticosteroids	Prednisone, dexamethasone, etc
Hallucinogens	LSD (lysergic acid diethylamide), PCP (phencyclidine), ketamine, psilocybin-containing mushrooms, mescaline, synthetic "designer drugs" (eg, 2-CB, "N-Bomb" [25I-NBOMe]), salvia divinorum
Inhalants	Toluene, butane, gasoline
Interferons	Interferon alfa-2a/2b
Over-the-counter	Dextromethorphan, diphenhydramine, some decongestants
Stimulants	Cocaine, amphetamine/methamphetamine, methylphenidate, certain diet pills, "bath salts" (MDPV [methylenedioxypropylvalerone], mephedrone), MDMA (3,4-methylenedioxymethamphetamine)/ecstasy
Toxins	Carbon monoxide, organophosphates, heavy metals (eg, arsenic, manganese, mercury, thallium)

Differential cont

- New onset psychosis DDx considered
 - Schizophrenia, psychotic disorder
 - Seizure—partial, ongoing
 - Med effect—(including antiseizure medications we were providing patient)
 - Infections—HIV, syphilis, encephalitis, systemic infection
 - Toxin/exposures
 - Substance use
 - **Autoimmune**

Anti-NMDA receptor encephalitis



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Anti-NMDA receptor encephalitis

- Initially described in 2007
- Young adults and children predominantly affected, infants can be affected
- Female predominance in young adults
- Symptoms
 - Initial headache, fever, viral illness
 - Prominent psychiatric symptoms: anxiety, agitation, bizarre behavior, hallucinations, delusions, disorganized thinking, psychosis. Rare cases of isolated psychosis
 - Sleep disorders
 - Memory deficits
 - Seizures
 - Decreased level of consciousness
 - Dyskinesias, abnormal movements
 - Autonomic instability
 - Language dysfunction

Diagnosis

- Must be made with spinal fluid analysis
 - MRI often normal
 - EEG with some abnormal activity, but does not correlate with abnormal body movements
 - CSF can have lymphocytic pleocytosis, oligoclonal bands, though parameters can be normal
 - Diagnosis is made by detection of IgG antibodies against the GluN1 (NR1) subunit of the NMDA receptor in the CSF. Serum can show false positives or negatives
 - Antibody testing often delayed due to specialized nature of testing (must be sent of academic facility)
- Associated with ovarian tumors
 - 45 percent of female patients found to have teratomas
- Associated with herpes simplex viral encephalitis

Treatment

- Immunomodulatory therapies
- Tumor resection
- Without treatment, there can be progressive neurologic deterioration and death
- Long term outcomes
 - Residual symptoms for more than one year, though improvement can be rapid
 - Cognition
 - Stable schizophrenia symptoms
 - At risk for relapse—if no trigger found or recurrent trigger (recurrent ovarian tumor, etc.)

Case, cont.

- Patient transferred to the ER with concern for anti-NMDA Receptor antibody syndrome
- Lumbar puncture completed and spinal fluid obtained
 - Specimen sent for evaluation
- CT scan of abdomen revealed ovarian teratoma, asymptomatic, small
- Patient given IVIG (antibody treatment) and IV methylprednisolone (steroid)
- Significant improvement in symptoms
- Scheduled for teratoma removal
- Diagnosis confirmed with result of antibody testing