Hold the Benztropine: Prion Disease Masquerading as Medication-Induced Extrapyramidal Symptoms

Swetha Mummini, MD; Nisha S. Naik, MD; Samantha Latorre, MD

University of Maryland School of Medicine

Introduction

- Creutzfeldt-Jakob Disease (CJD) is a progressive neurodegenerative disease caused by misfolded prion proteins.
- Clinical manifestations of CJD include personality changes, anxiety, depression, visual hallucinations, sleep disturbances, aphasia, cerebellar symptoms, and extrapyramidal/pyramidal symptoms (1,5,6)
- We describe a rare case of a patient with a diagnosis of schizophrenia who was misdiagnosed with drug induced parkinsonism and later found to have probable Creutzfeldt-Jakob disease.

Case

67 y/o F with a history of schizophrenia and diagnosis of small cell lung cancer in June 2022 was brought to the emergency room after developing worsening tremors, confusion, and truncal ataxia over the course of 2 weeks.

Timeline Prior to Hospitalization

- **November 2022** - Seen at geriatric psychiatry clinic, MoCA 20/30; no abnormal movements but patient notes insomnia.
- **December 7th** - Family describes patient as increasingly combative and anxious. Risperidone increased from 2 mg BID to 3 mg BID.
- **December 14th** - Daughter calls concerned mother is more lethargic. Risperidone is decreased to 1 mg AM, 2 mg QHS
- **December 21st** - Patient seen in clinic. Has rigidity, cogwheeling, and with truncal ataxia. Risperidone further decreased to 1 mg BID and patient started on benztropine.
- **December 27th** - Daughter calls stating patient now cannot walk or feed herself. Psychiatrist urges patient to go to ED and patient admitted for hyponatremia (Na 122) and acute encephalopathy.

Hospitalization Course

- **Week 1** - Patient is delirious with minimal verbalization. Following 1-step commands, has myoclonus and pill rolling tremor. Neurology attributes motor symptoms to EPS-like reaction from risperidone Patient started on carbidopa/levodopa and diphenhydramine. MRI brain is read as unremarkable.
- **Week 2** - Hyponatremia improves. No longer following commands or verbalizing. Rigidity in upper extremities. No response to lorazepam challenge to rule-out catatonia. EEG shows lateralized periodic discharges, started on Depakene. Lumbar puncture obtained, pending multiple send-out results.
- **Week 4** - Akinetic, mute, minimal arousability. Repeat MRI results show restricted diffusion in head of caudate nuclei and anterior aspect of putamen, indicating probable CJD
- **Week 6** - Lumbar puncture results (elevated 14-3-3 gamma and T-tau) further support CJD diagnosis.

Diagnostics Obtained During Hospitalization

EEG Results

Week 2, 48-hour EEG – Shows lateralized periodic discharges in right hemisphere and right hemispheric slowing. Rare focal sharps seen in left temporal region.
Week 4, 72-hour EEG – Shows generalized sharp periodic discharges with sharp morphology. Focal right and left sharp waves in temporo-occipital region.

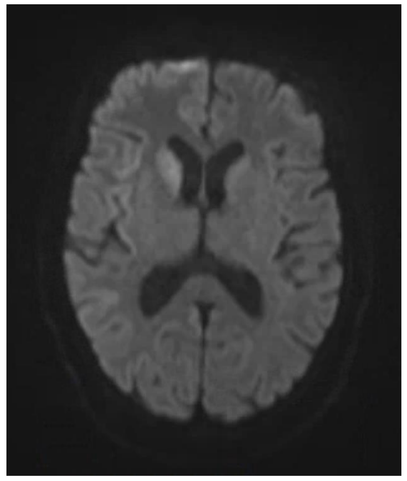
CSF results

T-tau protein, marker of neurodegeneration: >20,000 pg/mL (elevated)
14-3-3 gamma, marker of CJD: 105290 AU/mL (elevated)
RT-QuIC, prion detection assay: indeterminate

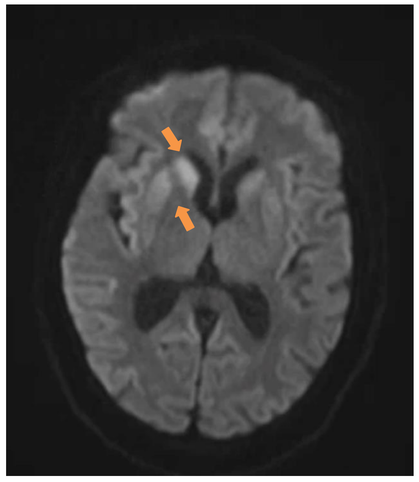
Additional CSF studies ordered

- CSF cytology negative
- CMV, VZV, VDRL negative
- Paraneoplastic markers ENC2 and ENS2 negative

Imaging During Hospitalization



Week 1: MRI brain, DWI image. Shows various areas of hyperintensity in subcortical white matter of frontal lobes, likely compatible with chronic small vessel disease



Week 4: Repeat MRI brain, DWI image. Shows restricted diffusion at head of caudate and anterior aspect of putamen.

Diagnostic Criteria

Probable diagnosis of CJD can be made based on clinical presentation and lab studies (2,3,4,6):

- Neuropsychiatric disorder with positive RT-QuIC result

OR

- Progressive dementia WITH
  - at least 2 of these: myoclonus, visual or cerebellar disturbance, pyramidal/ extrapyramidal dysfunction, akinetic mutism
    AND
  - Supportive diagnostic testing (EEG with sharp wave complexes, positive 14-3-3 assay with clinical duration to death <2y, MRI showing characteristic hyperintensity in caudate nucleus/putamen, or at least 2 cortical regions on DWI or FLAIR)
    AND
  - No alternative more suitable diagnosis to explain findings

Conclusions

- In patients with an underlying psychiatric disorder on neuroleptic medication, workup of the development of new neuropsychiatric symptoms should include consideration of autoimmune disease/other neurodegenerative diseases such as CJD.
  - Specifically for this patient, examination of the development of patient's neuropsychiatric decline week-to-week during inpatient hospitalization led to further exploration of neurologic etiologies and thus uncovered findings consistent with probable CJD.

References

1. Krasnianski A, Bohling GT, Harden M, Zerr I. Psychiatric symptoms in patients with sporadic Creutzfeldt-Jakob disease in Germany. J Clin Psychiatry. 2015 Sep;76(9):1209-15. doi: 10.4088/JCP.13m08915. PMID: 25938948.
2. Global surveillance, diagnosis, and therapy of human transmissible spongiform encephalopathies: Report of a WHO consultation, February 9-11, 1998, Geneva, Switzerland;
3. Manix, M., Kalakoti, P., Henry, M., Thakur, J., Menger, R., Guthikonda, B., & Nanda, A. (2015). Creutzfeldt-Jakob disease: updated diagnostic criteria, treatment algorithm, and the utility of brain biopsy. Neurosurgical focus, 39(5), E2. https://doi.org/10.3171/2015.8.FOCUS15328
4. Meissner B, Körtner K, Bartl M, Jastrow U, Mollenhauer B, Schröter A, Finkenstaedt M, Windl O, Poser S, Kretzschmar HA, Zerr I. Sporadic Creutzfeldt-Jakob disease: magnetic resonance imaging and clinical findings. Neurology. 2004 Aug 10;63(3):450-6. doi: 10.1212/01.wnl.0000136225.80445.c9. PMID: 15314808.
5. Wall, C. A., Rummans, T. A., Aksamit, A. J., Krahn, L. E., & Pankratz, V. S. (2005). Psychiatric manifestations of Creutzfeldt-Jakob disease: a 25-year analysis. The Journal of neuropsychiatry and clinical neurosciences, 17(4), 489–495. https://doi.org/10.1176/jnp.17.4.489
6. Zerr I, Kallenberg K, Summers DM, et al. Updated clinical diagnostic criteria for sporadic Creutzfeldt-Jakob disease. Brain 2009, 132; 2659-2668; and c) National CJD Research & Surveillance Unit.

Acknowledgements/Disclosures

Thank you to Dr. Latorre and the rest of the UMMC C/L Psychiatry Department for their guidance and mentorship!
The authors of this poster are physicians employed by the University of Maryland Medical Center. Fees related to attendance/presentation were in part financially compensated for by the University of Maryland Medical Center.