Creutzfeldt-Jakob Disease:
Case Reports Investigating Limitations in Rural Community Hospitals

Suhair Bhatti, DO, MPH, Arashpreet Gill, DO, William Duan, MD, Amy Sakazaki MSIV, Christine Skotzko, MD, FACLP

St. Joseph's Medical Center | Stockton, CA

Background

- **Creutzfeldt-Jakob Disease** (CJD) is a rare, rapidly progressive and assuredly fatal neurodegenerative human prion disease that is often difficult to diagnose premortem.
- Three subtypes:
  - **Sporadic** (85%) from protein misfolding w/o identifiable cause
    - 1-2/1 million in the U.S. Usually in >55 age group
  - **Familial/hereditary** (5-15%) due to mutation of prion protein gene
  - **Acquired** includes iatrogenic, and ingestion of beef infected with bovine spongiform encephalopathy ("Mad Cow")
- **Clinical symptoms** includes rapidly progressive dementia and a host of movement abnormalities as well as behavioral, personality changes, depression, anxiety, insomnia, hallucinations, and sensory disturbances
- Clinical diagnosis with CSF analysis, MRI, EEG
  - CSF studies can show increased Tau, 14-3-3, S100 proteins, etc.
  - Ultimately diagnosis with brain biopsy/autopsy

Discussion

- CJD initially difficult to suspect due to its varying presentation, numerous concurrent diagnosis, and wide differential
- **Case One:**
  - Reminder that an extensive and full history remains the foundation of medical practice
    - collateral about patient's long history of hunting, taxidermy, and eating wild game provided insight into possibly infectious etiology
  - Inability to complete LPs and EEGs, or obtain results for various investigations due to hospital resources led to delayed patient care, lengthened hospital stay incurring increased costs while also reducing patient's time at home before impending demise
- **Case Two:**
  - Continuous re-evaluation of a patient's condition against her presumed diagnosis
    - Remained in the hospital for three weeks with the presumptive diagnosis of acute encephalopathy likely secondary to infectious etiology
  - When faced with barriers to obtaining ideal neurological functional tests, it is important the health care team as a whole come together to try and find a solution to obtain needed evaluations

Conclusion

- CJD's rarity combined with the difficulty of recognizing its variable symptoms, can result in missed diagnoses before death especially in resource-challenged setting such as the community hospital.
- In both cases, extensive workup was pursued but diagnostics and lab work were delayed or did not result due to resource scarcity
  - not enough staff to do procedures, not enough resources to complete investigations/diagnostics
- Considerations for pursuing a prion disease workup in each case included sudden and progressive worsening of mental status, the lack of other infectious, vascular, or metabolic contributors.

Case One

History and Initial Investigation

- 70-year-old male with a past medical history of anxiety, atrial flutter, CAD, CHF, HTN, and HLD who presented to SJMC in Stockton, CA with sudden onset shortness of breath and confusion
- Two prior ED visits over last week, including day before for SOB and confusion. Both times he left AMA from ED
- ED's initial workup included CT Head, CTA Head, and MRI Brain - all negative for acute processes. Patient also fluid overloaded in setting of CHF.
- Neurology consulted, worked up: MOCA 13/30
  - Lumbar puncture, encephalitis testing, and EEG recommended
- CL consulted when patient became increasingly violent and combative, requiring sedation

Psychiatric Investigation and Course

- AOx1 (self), requiring redirection to not bite SpO2 monitor. Unable to meaningfully participate in interview
- Family noting no significant past psychiatric history except for heavy alcohol user and tobacco user in past. Social history notable for career as a plumber
- Collateral information: patient was at baseline until 3-4 weeks prior; suddenly having significant difficulties with basic tasks such as using TV remote, simple plumbing tasks (despite plumbing career), making strange remarks ("TV not working because of surges"), and behaving strangely (pulling all electric cords out of walls)
- Suspecting infectious encephalopathy of unknown etiology - metabolic, cerebrovascular, and oncological workups all negative
  - revisited imaging and lab work from prior
  - CT Head (Fig. 1) showing frontal and temporal atrophy, suggesting a possible frontotemporal dementia

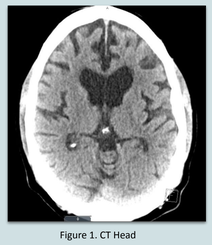

Figure 1. CT Head

- Findings discussed with family; investigative discussion revealing patient used to be an avid taxidermist and ate wild game frequently
- Prion disease now being considered, worked up

Challenges and Resolution

- CSF results negative for viral, bacterial, and fungal processes. Protein was significantly elevated, however, 14-3-3 and Tau markers not resulting as these labs had to be sent out to a third party lab
- In the interim, he remained violent, requiring continuous dexmedetomidine
  - Valproic acid, clonidine patch initiated to allow patient to transition down from ICU
  - Numerous days lapsed, patient condition only deteriorating while etiology remained unclear
  - Goals of care discussed and patient transitioned to home hospice, discharged, and sent home
    - Prion work up did not result by discharge

Case Two

Demographics and History

- 70-year-old female with a past medical history of a transient ischemic attack of unknown time, hyperlipidemia, chronic kidney disease stage III, hypertension, hyperparathyroidism, and chronic anemia with initial admission for acute encephalopathy secondary to a confirmed UTI
- Patient was treated for her initial UTI and her clinical picture improved, but her acute encephalopathy had not completely resolved
- Two weeks later, she returned with worsening encephalopathy and admittive with presumptive diagnosis of sepsis secondary to recurrent UTI
  - Despite recurrent treatment with broad spectrum antibiotics, there was only a worsening of her mentation
- Now refusing all food and IV intervention and requiring a Posey bed for severe agitation and violence against caregivers, even when taking vitals
- Patient's entire workup for toxic metabolic encephalopathy: CT Head, ammonia levels, urine toxicology screen were all negative

Investigation and Diagnostics

- Psychiatric History was taken from family members present- patient had no known personal or family history of psychiatric disorders, no history of substance use, and no environmental exposure to possibly known triggers
- At baseline, this patient was able drive, speak, and walk as well as perform most of her activities of daily living independently. This all changed the day before she was first diagnosed at the time of her initial UTI. She was unable to discuss her care or her situation, and did not recognize most of her family members.
- Further workup for a possible neurological cause was delayed by patient agitation and current state of presentation. As a result, MRI, EEG, and lumbar puncture were delayed by 2 additional weeks
- In this time, lorazepam, haloperidol, and olanzapine had been trialed with little to no change in her presentation
- Eventually, patient had to be placed on a continuous sedation with dexmedetomidine
- MRI showed a small focus of hyperintense signal in the frontal lobe,
  - the differential diagnoses provided by the radiologist:
    - early chronic microvascular ischemic disease, sequelae of migraines, demyelinating disease or remote infectious/inflammatory etiology
- EEG showed no epileptiform activity, diffuse cortical dysfunction of moderate degree (on sedation)
- Lumbar Puncture: elevated CSF protein, negative infectious encephalitis and meningitis, NMDA receptor antibody, CV2, SOX1 antibodies, LGI1 antibodies, and VDRL
  - CJD with the 14-3-3 Tau protein is still pending
- Remained on continuous sedation with a dexetemodine drip with goal of transitioning off, using valproic acid and clonidine

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