CREUTZFELDT-JAKOB DISEASE - TWO CASE REPORTS

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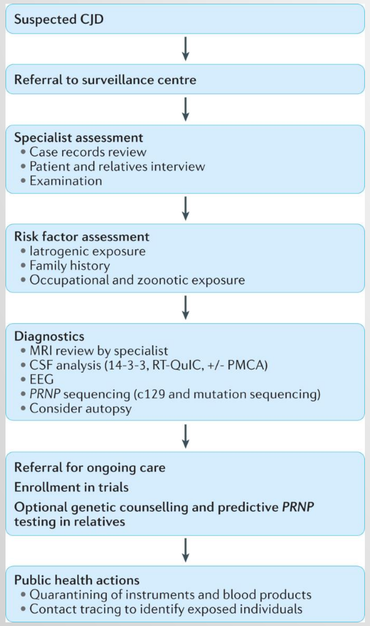
INTRODUCTION

- Creutzfeldt-Jakob Disease (CJD) is a rare, transmissible neurodegenerative disorder that is rapidly progressive and often fatal within 12 months. CJD manifests with dementia, vision impairments, poor coordination, behavioral changes, and eventually death. The early, non-specific clinical symptoms are often difficult to diagnose, and typically lead to an incorrect or late diagnosis. Given the non-specific presentation of CJD and its rate of progression, it is important to keep rapidly progressive dementias in a differential for neurocognitive changes.

- When evaluating patients for a rapidly progressive dementia, a host of laboratory studies are recommended including CBC, CMP, magnesium, RPR, ESR, ANA, CRP, thyroid function tests, B12 level, HIV screen, Lyme titer, autoantibodies, UA, CSF studies: glucose, oligoclonal bands, and cell count with differential, CSF 14-3-3 protein (specific for prion disease), VDRL test. Initial imaging would likely include CT Head and MRI w/wo Contrast + fluid-attenuated inversion recovery (FLAIR) and diffusion-weighted imaging (DWI).

- We report the cases of two individuals who presented to the same community hospital, approximately one month apart with neurological symptoms and unremarkable initial imaging. Both patients were ultimately diagnosed with CJD.

WORKUP



CASE DESCRIPTION

- **Patient 1**: A 73-year-old female with past medical history of hypertension, PE/DVT, HLD, and monoclonal gammopathy of undetermined significance.

- Initial symptoms: Altered cognition and vision (a right upper quadrant visual field defect). Ophthalmologic evaluation revealed L eye cataracts with a negative outpatient MRI. At her two-week follow-up, she developed worsening symptoms. Extensive workup for causes of AMS were negative, including CVA, autoimmune, paraneoplastic, and infectious etiologies. The patient received high-dose steroids x 3 days, and her mental status continued to deteriorate rapidly. The patient was transferred to a tertiary care facility where repeat MRI, EEG, and LP with CSF analysis later confirmed the diagnosis of CJD, and the patient was placed on comfort care.

- **Patient 2**: A 71-year-old female with past medical history of hypertension, hyperlipidemia, GERD, and chronic right shoulder arthritis status-post total shoulder replacement in 2019.

- Initial symptoms: presented with progressively worsening RUE/ RLE “tremor” and poor coordination for six weeks. Outpatient MRI and EMG were unremarkable, and her symptoms progressed with the addition of LUE/LLE, speech disturbances, stimulus-induced myoclonus, and increased startle reflex. Repeat MRI on admission W/O contrast revealed chronic white matter changes and cortical loss. AMS lab workup and LP were unremarkable. EEG with features consistent with CJS when correlated with clinical decline. Pt was placed on hospice and died three months after initial presentation. RT-QuIC, a highly accurate assay for detecting misfolded proteins in prion disease, was found to be positive post-mortem to suggest a diagnosis of CJD.

DISCUSSION

- Both cases presented with nonspecific symptoms encompassing a variety of neurological disorders with late recognition via cerebrospinal fluid detection of the proteins specific for prion disease. The diagnostic gold standard remains an autopsy with brain tissue biopsy. Though CJD is uncommon, and these clinical findings are nonspecific, it is important to always thoroughly measure the progression of dementia through time, as to not miss a CJD diagnosis, or other rapidly progressive dementias.

- It is uncertain whether these were sporadic genetic cases of CJD or whether they indicate an epidemiological public health crisis. Since 2020 cases of CJD have been on the rise. This has been thought due to the COVID-19 pandemic and whether the virus may a role. Another possibility includes “mad cow disease.” Since 2020 the ban on imported meat from the United Kingdom was lifted. Other potential forms of prion transmission include from surgical instruments infected with the prions, blood from blood transfusions, and any other iatrogenic cause where human protein can be transmitted such as cadaveric pituitary growth hormone.

CONCLUSION

- While there is no definitive treatment for CJD, a first-in-human protocol using Prion protein monoclonal antibody (PRN100) was run in 2018 demonstrating sustained CSF concentrations in a therapeutic range without toxicity. These findings are encouraging, and given the rapidly progressive nature of CJD, early detection and intervention will be crucial in this patient population.

- It is important to not dismiss altered mental status or nonspecific neurological and clinical findings as simply an advanced form of Alzheimer’s dementia especially when the patients are rapidly declining during their hospitalization. Identification of biomarkers suggestive of CJD in the CSF are indicative of prognosis. Using a classification system such as the European CJD Surveillance Network diagnostic criteria for sCJD (sporadic) can help to identify patients earlier in their clinical course and assess for family members at risk.

- More research is needed on reasons why cases of CJD are on the rise and the potential etiologies and transmission.

REFERENCES

- Dong TT, Satoh K. The Latest Research on RT-QuIC Assays-A Literature Review. Pathogens. 2021 Mar 5;10(3):305. doi: 10.3390/pathogens10030305. PMID: 33807776; PMCID: PMC8000803.

- Shir D, Lazar EB, Graff-Radford J, et al. Analysis of Clinical Features, Diagnostic Tests, and Biomarkers in Patients With Suspected Creutzfeldt-Jakob Disease, 2014-2021. JAMA Netw Open. 2022;5(8):e2225098. doi:10.1001/jamanetworkopen.2022.25098

- Watson, N., Brandel, JP., Green, A. et al. The importance of ongoing international surveillance for Creutzfeldt–Jakob disease. Nat Rev Neurol 17, 362–379 (2021). https://doi.org/10.1038/s41582-021-00488-7.

- Wilson P. Why are Prion Diseases on the Rise? Neurology Reviews. MDEdge Neurology Commentary. 2023 Dec 12.