PALLIATIVE CARE CASE OF THE MONTH

"Movement Disorder in Human Prion Disease"

by
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Case: Ms. V is a 59 year-old woman with history EtOH use disorder complicated by withdrawal seizures, opioid use disorder on Suboxone, hypertension, hypothyroidism, depression, and anxiety presenting with rapid progression of encephalopathy, delusions, intermittent mutism, myoclonic jerks, and hyperreflexia. Over the two weeks prior to admission, she had lost the ability to walk. MRI brain without contrast was notable for diffusion restriction involving right parietal, occipital, and frontal lobes, and "cortical ribboning" with caudate involvement. EEG showed frequent right occipital sharps with concern for focal seizure. Suspected diagnosis of Creutzfeldt-Jakob Disease (CJD) was given. Diagnosis was confirmed by cerebrospinal fluid testing sent to the National Prion Disease Pathology Surveillance Center which resulted positive on quaking-induced conversion (RT-QuIC) assay. Palliative care service was consulted for goals of care and symptom management. Given Ms. V's rapid neurologic decline, neurology delivered a prognosis of likely weeks. Family elected no further escalation of care, with transition of focus to comfort. She had discomfort and agitation related to increasing myoclonic jerks and other involuntary movements.

Background: CJD is a human prion disease that results in rapid neurodegeneration and death. In this disease, abnormal cellular prion protein (PrPC) misfolds and forms self-propagating multimeric assemblies known as prions. It is a rare disease, with about 500 new cases per year in the United States. The majority of cases are sporadic (~85%), some are genetic (10-15%), and very few (<1%) are acquired via contaminated neurosurgical instruments, dura mater transplants, corneal transplant or human growth hormone obtained from cadavers. Clinical criteria for diagnosis include rapidly progressive dementia; and at least two out of the following four clinical features: myoclonus, visual or cerebellar signs, pyramidal/extrapyramidal signs, and akinetic mutism. EEG classically shows periodic sharp wave complexes. Brain MRI often shows increased signal in caudate/putamen or at least two cortical regions. The National Prion Disease Pathology Surveillance Center evaluates CSF for RT-QUIC, 14-3-3, and for Tau proteins.

Discussion: What is the treatment approach for myoclonus and movement disorder in prion disease?

Movement disorders and dystonia are diagnostic criteria for CJD which lead to significant distress and morbidity. A recently published study from the National Prion Monitoring Cohort in the United Kingdom described the movement disorder characteristics in a prospective, longitudinal cohort of 700 patients with prion disease4. This study reported a wide spectrum of hyperkinetic to akinetic movement disturbances, including ataxia, myoclonus, dystonia, tremor, choreoathetosis, hemiballismus, and atypical parkinsonian movements.157 patients were prescribed medications for myoclonus. Antiepileptics and benzodiazepines were the 2 most common medication classes. Levetiracetam and sodium Valproate were both reported to have observed clinical benefit in 86% of patients treated with either. Patients treated with either clonazepam or midazolam had observed clinical benefit in 95% and 94% respectively. Baclofen was prescribed to 10 patients for increased tone; only 22% showed benefit. Previous studies have trialed prednisolone, high-dose levodopa and haloperidol without effect3, 5-6.

Case Conclusion:

Ms. V's condition rapidly declined and she became unable to swallow or tolerate oral medication. Per neurology recommendation, she was transitioned to IV epileptics – levetiracetam and lacosamide. A clonidine 0.1mg patch was also applied but did not significantly improve her agitation. Suboxone was discontinued due to patient distress with attempts to administer, and she was transitioned to IV hydromorphone scheduled to prevent opioid withdrawal with additional doses available as needed for pain. IV Ativan 0.5mg q6hr was initiated for abnormal movements and agitation. These symptoms improved with benzodiazepine treatment. She was transferred to an inpatient hospice unit where benzodiazepine dose and frequency was titrated up. She died peacefully several days after transfer with her family at bedside.

Case Reserve University offers an autopsy coordination program for patients with suspected prion disease to contribute tissue to research. Participation in post-mortem research, including brain and tissue donation, was offered to the family7. Family elected not to pursue autopsy. No special interment or cremation requirements are needed for patients with CJD. Although prion disease is potentially transmissible post-mortem, standard universal precautions are adequate for embalming. The funeral home was notified prion disease, however there was no anticipated handling of brain of lymphatic tissue.

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