



Unusual cases of Creutzfeldt Jakob Disease (CJD)

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We report four cases of CJD in a county of 420,000 people, living within a few miles area within less than 2 years
The first two cases were hospitalized at the same institution around the same time and died within a few days of each other approximately three months after symptoms onset. There was no known relation between the two cases.

First case

First case is an 81-year-old man who presented at the office with confusion, memory loss and repetition for the past month associated with pressure in the frontal region. He was previously followed in our neurological practice and was in good health.

Has a history at young age, 30 to 40 years ago, going deer hunting and eating the meat with his family members. He continued to eat venison occasionally. They used to go hunting in New York State at younger age. No history of prior brain surgery, use of growth hormone, corneal transplant, blood transfusion. He enjoyed eating red meat regularly including oxtail and rarely rabbits.

During January of 2021 he developed severe bilateral COVID pneumonia that required prolonged hospitalization but recovered well. Neurological evaluation initially revealed poor recall. Initial MRI (Figure 1) revealed subtle increased signal on DWI on the left frontal region. ERP revealed attention impairment and slowing of processing speed. ERP revealed decreased P200 and P3b amplitude (Figure 2). P3b response tend to localize on the temporal cortex and may correlate with MRI.

EEG showing periodic discharges (Figure 3).

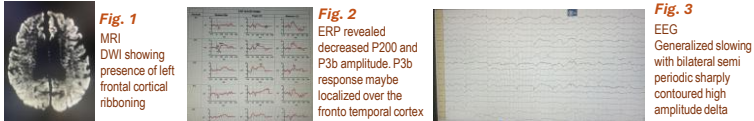
Progress was rapid, within a few weeks unable to recognize family members and had difficulties with comprehension and expression. Echolalia was pronounced. Subsequently developed asymmetrical postural myoclonus. Serial MRI showed left frontotemporal increased DWI signal.

MRI revealed presence of left frontotemporal increased DWI signal with cortical ribboning.

Serial EEG revealed generalized slowing and progressive asymmetrical and then more symmetrical bilateral sharp theta activity and triphasic waves. Lumbar puncture revealed TAU greater than 20,000 and positive RT Quick. Paraneoplastic antibodies, Lyme, West Nile, RPR were negative.

No family history of prion. Mother had dementia suggestive of Alzheimer's type. Was transferred to hospice care.

Unfortunately, autopsy was not obtained.



Second case

Patient was admitted to the hospital at the same time of the first case with progressive gait impairment and left arm clumsiness and tremors two months after having had COVID. Had still persistent cough. Initial neurological evaluation revealed left arm ataxia. Developed subsequently confusion, dysarthria, aphasia left-sided weakness with spasticity and myoclonus.

Symptoms progressed rapidly.

She previously had normal health, exercising regularly.

There was no history of previous corneal transplant, use of growth hormone, blood transfusion or prior brain surgery. No family history of prion.

Patient occasionally ate beef but no deer meat.

Lumbar puncture revealed TAU greater than 20,000, protein 14-3-3 was 90,875 and positive RT Quic. Paraneoplastic antibodies, Lyme, West Nile, RPR, viral PCR were negative.

MRI revealed abnormal DWI signal involving the putamen and head of caudate with cortical ribboning (Figure 4).

EEG revealed continued theta delta slowing and bilateral triphasic waves and sharp activity (Figure 5).

Developed aspiration pneumonia, was treated with IV antibiotics and steroids. Was intubated and eventually care was withdrawn.

No autopsy was performed.



Third case

Case was seen in the office with a 6 months cognitive decline. Maybe 3 months prior to that had some balance issues while traveling abroad. She presented with visual disturbances, short term memory loss, confusion, imbalance, later mild paranoia. Also noted mild tremors, involuntary movements of the left leg.

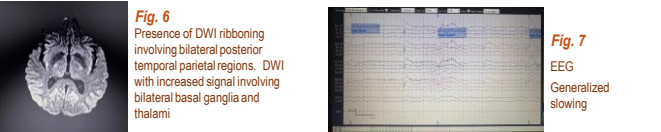
Brain MRI revealed cortical ribbon sign particularly involving parietal and posterior temporal areas (Figure 6). Optical Coherence Tomography (OCT) was normal. EEG revealed mild generalized slowing (Figure 7). Evoked Response showed signs of slowing of processing speed and attention impairment.

Normal CTA of head and neck.

Routine labs within the normal range. Para neoplastic panel negative. ANA, Lyme, HIV, negative.

No family history of neurological disorders. No history of corneal transplant, no prior blood transfusion, brain surgery or use of growth hormone. However, 20 years prior had a tooth implant using demineralized cortical allograft cadaveric bone.

Spinal fluid showed normal cell count, glucose and protein TAU, protein 14-3-3 were elevated. Positive RT Qulc.



Fourth case

Since abstract was submitted another case was diagnosed in the same area.

Presented with progressive imbalance and recurrent falls for approximately 6 months.

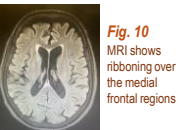
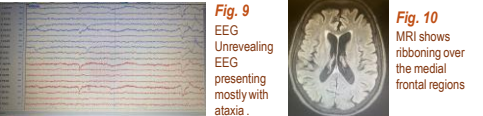
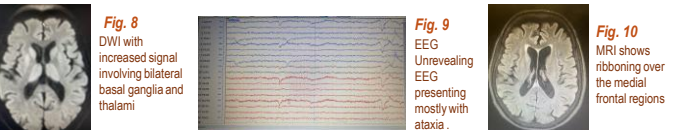
No significant past medical history. No previous corneal transplant, brain surgery, blood transfusion, travel abroad or family history of prion disorder. No recent infection such as COVID.

Patient had a habit for many years of eating deer meat, sometimes hunt by her husband. However, she didn't handle the carcass.

Patient used to cook with gas at home but there was no clear exposure.

Neuro exam was significant for ataxia. No myoclonus. MRI revealed bright DWI signal involving the bilateral basal ganglia and thalami (Figure 8). EEG was within the normal range (Figure 9). Routine CSF studies were normal. Prion studies were sent but not performed by the lab. Patient was transferred to another facility. She was treated as outpatient with few sessions of hyperbaric therapy due to presumed cooking gas exposure without improvement. Ataxia progressed with inability to walk, increasing confusion in addition to tremors. Lumbar puncture was repeated with positive RT Quic and elevated t-Tau/p-Tau ratio = 39 and normal p-Tau/ABeta 42 = 0,024.

Follow up MRI showed further cortical ribbon sign (Figure 10).



Discussion

Although no tissue obtained the likelihood of prion disease is greater than 99%. There has been recently described a noticeable increase in reported cases of prion disease worldwide. Unclear if due to better diagnosis or a real observation. These cases could possibly be another sporadic CJD however, since rarely prion cases have been reported with history of deer hunting and eating deer meat we believe is important to draw attention for this possibility. Public health study reported on a 6-year follow-up in a group of people that consumed contaminated deer meat. No case has been reported so far of prion disease, but incubation period could possibly amount to several decades. It's now known that Chronic Wasting Disease (CWD) has been found in both wild and farm-raised cervids from 31 North American states. Incubation period of CWD in naturally infected animals is unknown.

More recently a study using mice expressing human prion protein (PrP) inoculated with deer CWD isolates led to atypical symptoms with prion seeding in the brain and in the feces which could be a potential source of contamination. Infective cases of CJD related to dura graft and growth hormone may have a latency of symptoms of decades as well. And patients with codon 129 heterozygote might have longer incubation period.

Second case was noted to have symptoms onset after COVID infection.

Patient was in excellent health prior. COVID symptoms were upper respiratory related mostly. Soon after started with dizziness, left arm ataxia and imbalance.

A few cases of COVID followed by a diagnosis of CJD have been reported. Release of inflammatory drivers such as IL-1 and TNF during COVID infection may trigger glial activation and maybe inducing PrPSc production and virus spike protein may lead to tau deposition. In addition, COVID may affect the mitochondria which dysfunction may play a role in prion disease. Interestingly, MRI in COVID encephalitis may show ribboning pattern resembling CJD. Epidemiological studies might be able to show if the increase in reported CJD cases are secondary to COVID infections. If there is a cause relationship between them, we should expect a sharp increase in number of CJD cases in the future.

Our first patient had a severe case of COVID in January 2021 without neurological complaints at that time.

We just treated a patient who developed generalized subcortical myoclonus soon after COVID infection. CSF studies were negative for prion. Even more interesting, recently some patients who have received cadaveric growth hormone have been associated with amyloid angiopathy and Alzheimer's disease many decades later and not CJD. Current incidence of CJD is estimated at 1 to 2 cases per one million population per year. Their county has a population of 420,000 people therefore two simultaneous cases is quite unusual. Recently a report from west Michigan described 5 cases of CJD within a year in a 90-mile radius.

Interestingly, there was no relationship between both patients, although they resided within 8 miles from each other and shopped at the same grocery store. One patient was an avid meat eater including frequent eating oxtails. The second case ate meat occasionally although her husband ate it frequently. There were no other cases in their families.

A common cause for both cases could not be found. Pathological data could have shed some light if there were any similarities. The long incubation period that may span for several decades in some cases make it difficult to establish a causal relationship. The third case the only risk factor we possibly found was the bone tooth implant 20 years prior. We couldn't find any similar case. Her symptoms have been slowly progressive now with over a year, still functioning independently for daily living activities. Serial MRIs have been stable as well as EEGs. Serum p-TAU 217 was normal.

Infectivity has been already demonstrated in the plasma of patients with CJD, which maybe secondary to leak of the protein into the blood stream. In addition, high levels of infectivity in the bone marrow of sporadic cases of CJD has been published. Infectivity of the bone marrow has been demonstrated injecting bone marrow contains human prion into the brain of transgenic mice.

Lymphoid tissue has also found to harbinger prion.

Prion proteins have been found in bovine bone after inactivation procedures as well after deproteinization.

The local county health department did not report other cases in the area during last year. A total of four local cases were reported from 2015-2022. The author saw one of those in 2016 with no relation to the current cases. Tissue analysis then revealed presence PrPSc which pattern was not suggestive of variant CJD.

We will be monitoring for new cases in the area.

Conclusion

We hope to draw attention for four potential unusual cases of CJD. Two patient could potentially be secondary to consumption of deer meat which has so far been not described. However, if CWD can be transmitted to humans could potentially become much more common than Bovine Spongiform Encephalopathy (BSE) due to the easier dissemination.

The second case could have been triggered by COVID with so far only less than 10 cases reporting this association. If there is indeed a connection, we should expect to see an increase in CJD cases in the future, and this could possibly account for the increase in reported cases globally.

Sporadic CJD, of course, is a very plausible explanation. However, the increase in reported CJD may as well be more than just improvement in diagnosis and due to people living longer. Time invariably will provide the answer.

The third case raises suspicion for the risk bone materials utilization in dental and other surgical procedure in transmitting CJD and alert for awareness of new similar cases in the future.

At the time of this submission, case # 3 has been in hospice care, and case # 4 has passed.