One in a Million: Diagnosis of Sporadic Creutzfeldt-Jakob Disease with Negative Imaging

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INTRODUCTION

Prion diseases are a diverse group of rare neurodegenerative conditions caused by abnormal prion proteins,.

In the US the incidence is about 1.2 per 1.000.000.

CDC diagnostic criteria for CJD include rapidly progressive dementia and additional characteristic findings on MRI, EEG and CSF.

We present a case of prion disease, most likely sCJD, diagnosed in the absence of typical MRI or EEG findings.

CASE DESCRIPTION

79-year-old Hispanic female independent at baseline presented with 3 weeks of disorientation, paranoia, hallucinations and generalized paralysis.. Physical exam on admission : AOx1, visual and tactile hallucinations, overall rigidity, muscle strength 4/5 throughout and a positive Babinski sign bilaterally, along with resting tremor, bradykinesia, slurred speech and echolalia. UA suggestive of UTI with positive nitrates and urine WBC 400. CT Head no acute findings. Admitted for treatment of delirium.

By day 5 of admission she became non-verbal, dysphagia, bladder and bowel incontinence, as well as decorticate posture. Vit D, Vit B12, CRP, ESR, RPR were all negative. MRI Brain with IV contrast with T1 and FLAIR images on day 5 showed chronic microvascular ischemic changes but no abnormal enhancement. EEGs diffuse severe slowing with triphasic appearance at 3-7 hertz. CSF showed >1,200 RBC raising concern for HSV encephalitis,. CSF sample was also sent for AFB +culture, HSV 1 and 2 PCR and antibodies, encephalitis panel, GAD antibodies, cryptococcal antigen all which were negative.

RT Quick, Tau protein and 14-3-3 protein were also sent to the National Prion Disease Pathology Surveillance Center (NPDPSC), and on hospital day 18 the results reported a positive RT Quick and elevated Tau protein>4000, reported as >98% likelihood of prion disease. The patient met criteria for Probable Prion Disease.

After having a conversation with the family explaining the poor prognosis, the consensus was to transfer the patient to inpatient hospice

	09/25	09/30
Clarity	Clear	Clear
Color	Colorless	Colorless
WBC	2	5
RBC	1280	140
Glucose	81	76
Protein	29	30

Table 1: CSF results with elevated RBCs but no other abnormalities.

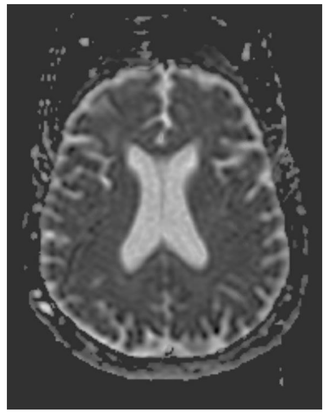

Figure 1: MRI on Day 5 showing chronic vascular ischemic changes but no other abnormalities.

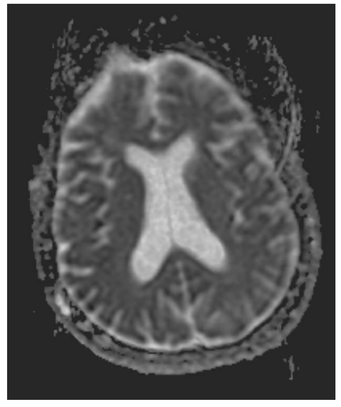

Figure 2: MRI on Day 10 showing same chronic vascular ischemic changes, no other abnormalities.

Table 2 (below): NPDPSC CSF report showing positive RT-QuIC result

Likelihood of prion disease: >98%

Test Name (specimen)	Result	Reference Range for Non-Prion Disease
RT-QuIC (CSF)*	Positive	negative

*RT-QuIC identifies the disease-causing agent

Test Name (specimen)	Result	Reference Range for Non-Prion Disease
T-tau protein (CSF) **	>4000 pg/ml	0 - 1149 pg/ml
14-3-3 protein (CSF) **	Inconclusive due to blood in the sample.	negative

** Indirect markers of neurodegenerative disease

DISCUSSION

Diagnosis of prion diseases is challenging. A high clinical suspicion must exist given the rarity of this cluster of diseases.

MRI with FLAIR and DWI/ADC has 91% sensitivity and 95% specificity .Typical patterns include cerebral involvement or “cortical ribboning” basal ganglia involvement and cerebellar atrophy,

EEG findings are typical periodic sharp wave complexes (PSWC) which are usually observed with or shortly after patients develop myoclonus and akinetic mutism.

RT-QuIC assay on CSF which has been shown to have 91% sensitivity and 98% specificity. Only done by NPDPSC. A positive diagnosis is equivalent to Probable Prion Disease.

Our patient had the typical clinical presentation, characterized by rapidly progressive dementia within 3 weeks of onset, associated with akinetic mutism and myoclonus, in addition to dysphagia. This warranted a high clinical suspicion. However multiple MRIs failed to show typical findings for prion disease, and two EEGs failed to show PSWC, reporting only severe diffuse slowing with triphasic morphology. Finally, a RT-QuIC assay from CSF sent thanks to having a high clinical suspicion came back positive, being consistent with the diagnosis.

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CONCLUSIONS

CJD is a rare but aggressive disease with fast progression and multiple comorbidities that are mostly due to deconditioning, with associated high mortality. In order to diagnose CJD and other prion diseases clinical suspicion must be high. Amongst our diagnostic tools we have MRI, EEG and CSF analysis. However, despite possible negative findings, it is important to use our clinical criteria and to proceed with CSF analysis with molecular studies (RT-QuIC) when we have a high suspicion, given they have better NPV and PPV. In our case, the patient was diagnosed thanks to multiple attempts to obtain LP despite patient having resting tremor which difficulted obtaining sample, and a high clinical suspicion of the disease.