Variant CJD in the United States: An Analysis of 4 Cases

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Introduction

Variant Creutzfeldt-Jakob Disease (vCJD), has been linked to Bovine Spongiform Encephalopathy (BSE) - a prion disorder in cows. The emergence of vCJD has been linked to an earlier epidemic of BSE in the United Kingdom through the consumption of contaminated beef (1). Since the first report in 1996, a total of 229 vCJD cases have been recorded worldwide: 177 in the United Kingdom; 27 in France; and 25 cases distributed in 10 countries, including the United States (1).

Methods

Using publicly available data from the Centers for Disease Control and Prevention (CDC), the United States Department of Agriculture (USDA), and case reports including the newest confirmed diagnosed vCJD case (May 2014), we reviewed the cases of BSE and vCJD that have been found in the United States. For the vCJD patients, we compared age at symptom onset, symptom duration, clinical presentation, year of diagnosis and type of tissue confirmation for diagnosis.

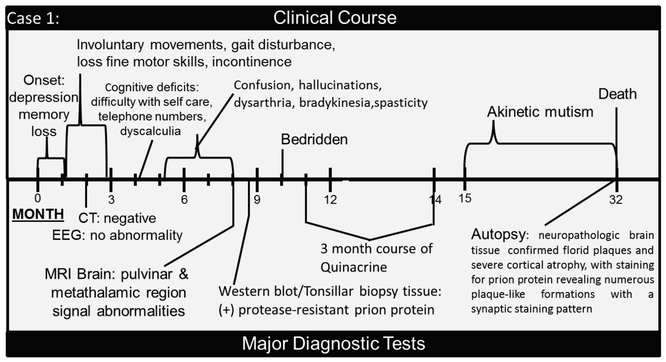
BSE Cases in the US

	Case 1: 2003	*Case 2: 2005*	*Case 3: 2006*	*Case 4: 2012*
History	**6.5 year old dairy cow, Washington State, Canadian import 2001**	**12 year old cow, Texas born, 1st endemic case**	**10 year old cow from Alabama, unknown origin**	**10.7 year old Californian dairy cow**
Strain	**unknown**	**Atypical**	**H-type**	**L-type**

Variant CJD Cases in the US

Case 1

Symptom onset occurred in November 2001 with depression and memory loss. She then moved back to the UK with her mother, where worsening ensued (3).



Case 2

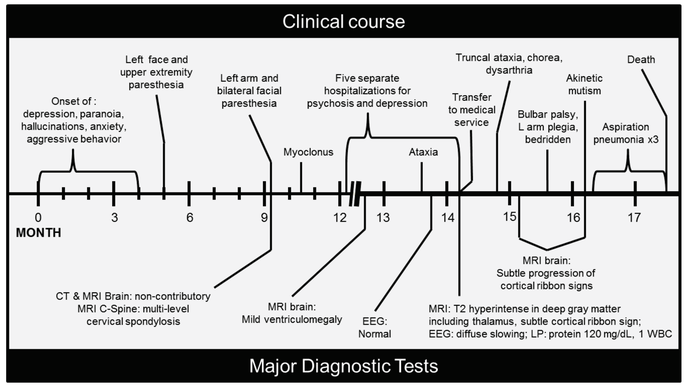
Onset of symptoms occurred in February 2005 with vertigo and ataxia. Subsequently developed depressive mood and “not feeling like himself”. MRI showed “pulvinar” sign. The patient passed away March 2006, 11 months after onset. Brain autopsy revealed florid plaques.

Case 3

Onset of symptoms occurred in Spring 2006. In late November 2006, the Clinical Prion Research Team at UCSF confirmed the vCJD clinical diagnosis by pathologic study of adenoid and brain biopsy tissues (1). Duration of symptoms was just over one year, with specific presentation and clinical symptoms and progression unknown. Per CDC reports, this case was attributed to consumption of BSE-contaminated cattle products in Saudi Arabia as a child (1).

Case 4

A male in his 40s, born and raised in the Middle East and moved to the United States in the late 1990’s. Between 1980-1996, he had lived in Kuwait, Russia and Lebanon. No evidence indicating stays in Great Britain, France, Ireland, or Saudi Arabia. Patient was high functioning with a professional degree attained in Russia. Onset of symptoms was in 2012 with anxiety and depression. The diagnosis of “probable vCJD” was given after imaging showed the “pulvinar sign” and his symptoms progressed despite treatment for other possible etiologies (2).



Summary of Cases	Case 1	Case 2	Case 3	Case 4
Birth Country	UK	UK	Saudi Arabia	Middle East
Age at Onset	22 yo female	30 yo male	Unknown age male	Male in his 40s
US Stay	Florida 1992-2004	Texas 2001-2005	Various US visits with residence in 2005	Texas 2000-2014
Onset/Death	2001/2004	2005/2006	2006/2006	2012/2014
Symptom Duration	36 months	11 months	Approx >1 year	18 months
MRI Imaging	Pulvinar sign	Pulvinar sign	Unknown	Cortical ribbon & pulvinar sign
Neuropath	Tonsillar & brain biopsy	Brain biopsy	Adenoid & brain biopsy	Brain biopsy

Conclusions

- The 4 US cases of vCJD exhibited a similar presentation to vCJD cases worldwide. One notable finding in the most recent case is the presence of the cortical ribbon sign on MRI brain.
- There are 4 neuropathologically confirmed vCJD cases in the US, most recently in May 2014, and 4 confirmed BSE cases (1,2,3,5).
- There is no evidence for indigenous transmission of vCJD in the United States and all 4 affected individuals have evidence supporting contraction of the disease outside of the United States (1,2).
- The most recent confirmed case underlies the need for continued surveillance and the continued need for physicians to identify possible cases of vCJD.
- Increasing evidence points to different strains of BSE: the typical BSE strain responsible for the outbreak in the United Kingdom and two atypical strains (H and L strains) for 3 of the US BSE cases (5).
- There is still a vital role of worldwide surveillance of vCJD since the incubation period of vCJD can last for decades and the presentation at onset can be non-specific.

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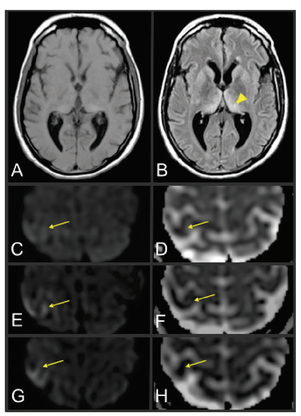
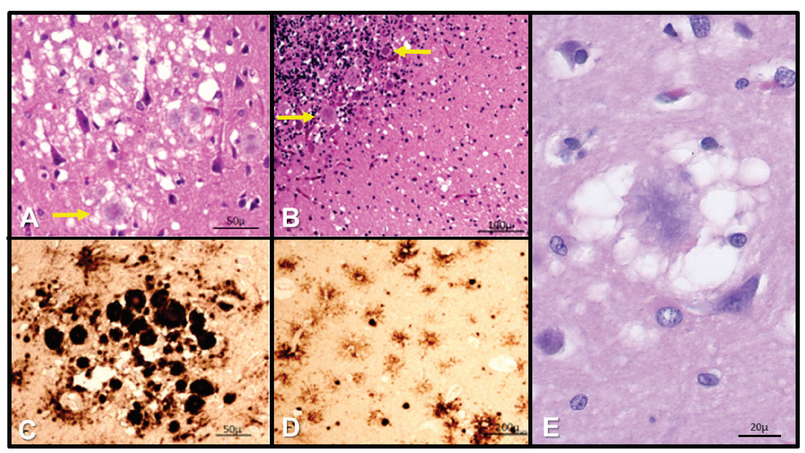
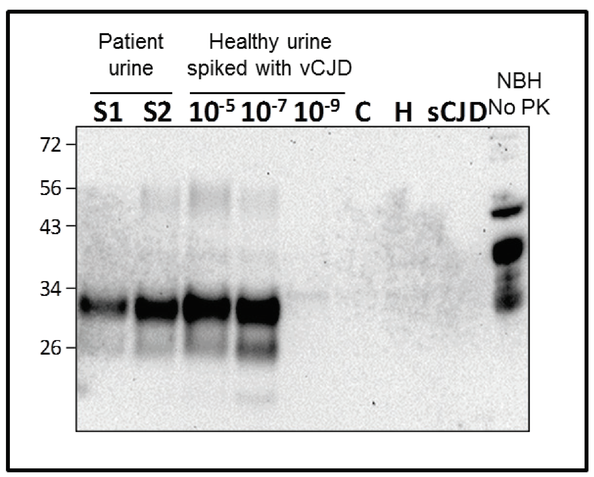


MRI brain with T2 hyperintensity and subtle restricted diffusion in pulvinar nuclei of bilateral thalami (pulvinar sign, arrowhead, panel B) & subtle restricted diffusion of right frontal cortex (cortical ribbon sign, panels C-H) (2).



Numerous typical florid plaques (panel A, arrow). Prion plaques in the granule cell layer of the cerebellum (panel B, arrows). Prion protein immunostaining showed intense immunoreaction of the core of the florid plaques and patchy and granular deposits that were arranged in rounded clusters (panel C). Immunostaining of cells in a spoke wheel–like fashion (panel D). High magnification of kuru plaques in the cerebellum (2).



PrP^{Sc} detection in urine by protein misfolding cyclic amplification (PMCA) (4). Western blot with patient’s sample (S1, S2), positive control, and negative control (no sample); lane H, urine from a healthy person; sCJD, urine from an sCJD patient (2).

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