American Journal of Infection Control 42 (2014) 659-64

Contents lists available at ScienceDirect

American Journal of Infection Control

journal homepage: www.ajicjournal.org

Major article

Accuracy of administrative diagnostic data for pathologically confirmed cases of Creutzfeldt-Jakob disease in Massachusetts, 2000-2008

Jed A. Barash MD [a,b,*], James K. West PhD [c], Alfred DeMaria Jr. MD [d]

[a] Department of Medicine, Yale University School of Medicine, Robert Wood Johnson Foundation Clinical Scholars Program, New Haven, CT
[b] Department of Neurology, Veterans Affairs Medical Center, West Haven, CT
[c] Bureau of Infectious Diseases, Massachusetts Department of Public Health, Boston, MA
[d] Bureau of Health Statistics, Research, and Evaluation, Massachusetts Department of Public Health, Jamaica Plain, MA

Key Words:
Prion diseases
Surveillance
Death certificate

Background: Creutzfeldt-Jakob disease (CJD) is a transmissible disorder that is monitored by public health authorities at the state and national levels in the United States. Little is known about the current accuracy and concurrence of CJD diagnoses across national and state sources of surveillance data.
Methods: Using multiple sources, including the National Prion Disease Pathology Surveillance Center (NPDPSC) registry, we sought to identify all deceased Massachusetts patients with pathologically diagnosed CJD between 2000 and 2008. Pathologically verified CJD cases were then matched to their respective records in the Massachusetts hospital discharge and death certificate datasets. Using these data, we also aimed to estimate the sensitivity and specificity of death certificate diagnoses.
Results: Death certificate and hospital discharge dataset diagnoses of CJD combined accounted for 80% (35 of 44) of pathologically confirmed cases. The estimated sensitivity and specificity for death certificate diagnoses alone were 71% (27 of 38) and 75% (9 of 12), respectively.
Conclusions: Death certificate diagnoses were less sensitive for pathologically confirmed CJD than reported previously. Increasing reliance on autopsy over biopsy and an expanding spectrum of health care delivery may be responsible for this discrepancy. The findings reported here underscore the value of using multiple mechanisms in national CJD surveillance.

The human transmissible spongiform encephalopathies, or prion diseases, are rare and invariably fatal neurodegenerative disorders that include Creutzfeldt-Jakob disease (CJD). CJD is classified as sporadic, genetic, and acquired forms,[1] the latter of which represents a notable public health concern. Acquired cases of CJD have been associated with iatrogenic sources (iCJD; from procedures involving contaminated tissue, such as dura mater grafting, corneal transplantation, and human pituitary growth hormone administration)[2] and with exposure to beef and other products from cattle affected by bovine spongiform encephalopathy (BSE). With regard to iatrogenic sources, after a neurosurgical patient in New Hampshire was confirmed to have subsequently developed CJD in September 2013, there was concern that, along with other patients at the hospital where the surgery was performed, a small number of patients in other states (including 2 in Massachusetts) had been exposed to surgical equipment used in the earlier procedure. The unusual characteristics of the human prion disease associated with BSE, known as variant CJD (vCJD), include early age of onset and distinctive clinical and neuropathologic features. These attributes led to its identification in 1996 in the midst of the BSE epidemic in the United Kingdom.[3]

In the United States, surveillance for CJD is multitiered. At the national level, the Centers for Disease Control and Prevention (CDC) performs a periodic evaluation of mortality data for unusually young CJD patients and clusters, reviews spontaneous reports of individual cases from health care providers, examines outcomes from a long-term cohort study of growth hormone recipients for additional cases, and works with and financially supports the National Prion Disease Pathology Surveillance Center (NPDPSC), which it established in collaboration with the American Association of Neuropathologists shortly after the discovery of vCJD in the

* Address correspondence to Jed A. Barash, MD, Lahey Clinic, Department of Neurology, 41 Mall Rd, Burlington, MA 01805.
E-mail address: jed.a.barash@lahey.org (J.A. Barash).
J.A.B. was supported by a Robert Wood Johnson Clinical Scholars Fellowship through Yale University and the Department of Veterans Affairs.
Conflict of interest: None to report.

0196-6553/$36.00 - Copyright © 2014 by the Association for Professionals in Infection Control and Epidemiology, Inc. Published by Elsevier Inc. All rights reserved.
http://dx.doi.org/10.1016/j.ajic.2014.02.002

United Kingdom in 1996.[4,5] Although many reported cases of CJD might meet the criteria for a diagnosis of CJD based on clinical signs and test results (including magnetic resonance imaging [MRI], electroencephalography [EEG], and cerebrospinal fluid [CSF] analysis), definitive diagnosis requires pathological confirmation.[6]

The NPDPSC has been charged with the task of verifying diagnoses of transmissible spongiform encephalopathies in the United States through tissue analysis. Over time, the NPDPSC has become the primary mechanism for confirming prion disease in the United States and identified more than 250 CJD cases in 2011 alone.[7] Of note, 3 cases of vCJD and 6 cases of iCJD in US residents have been confirmed by the NPDPSC since 1996; the CDC-coordinated investigations of the vCJD cases indicated that all of the patients likely had acquired the disease abroad.[4,7]

Massachusetts monitors the occurrence of CJD. Surveillance for the disease has been ongoing since 1992.[8] In addition to reviewing death certificates (comprising the "death certificate" dataset) and investigating case reports, the Massachusetts Department of Public Health also has examined the Massachusetts Hospital Inpatient Discharge Database (hereinafter the "hospital discharge" dataset) for patients assigned a CJD diagnosis. Of note, a previous investigation in Massachusetts revealed 97 deaths attributed to CJD between 1991 and 2001, including 90 detected by the mortality data and 7 detected through supplemental sources.[8] However, much of that study period predated the significant developments occurring in the last half of the 1990s, including increased awareness of CJD after onset of the vCJD epidemic in Europe, establishment of the NPDPSC, and identification of CSF and MRI findings associated with CJD.[9-11]

Despite the presence of both national- and state-level surveillance in the United States, little is known about the accuracy and concurrence of CJD diagnoses across surveillance layers, particularly in the current clinical environment. In the present study, using cases sent for neuropathologic confirmation as the gold standard, we aimed to describe the accuracy and concurrence of associated hospital discharge and death certificate dataset diagnoses in Massachusetts between 2000 and 2008. Using these data, we also sought to estimate the sensitivity and specificity of Massachusetts death certificate diagnoses during this period.

METHODS

Our initial aim was to identify all Massachusetts patients with pathologically confirmed, definite CJD[12] through immunocytochemistry, Western blot analysis, or standard neuropathological techniques, including biopsy and autopsy) who died between January 1, 2000, and December 31, 2008, when the most recent hospital discharge dataset was available (Fig 1). All patients resided, died, or received their diagnostic evaluation in Massachusetts. From a public health perspective, we elected to focus solely on CJD, because it is the most common prion disease encountered and diagnosed by US clinicians. Thus, cases of other pathologically verified prion diseases not within the spectrum of CJD, including Gerstmann-Sträussler-Scheinker syndrome (GSS), variably protease-sensitive prionopathy (VPSPr), and prion disorders without sufficient pathological material for further classification, were excluded from our analysis.

We obtained a record of all Massachusetts CJD cases referred to the NPDPSC during the study period. For each patient, this register included basic demographic data, outcome of the pathological examination, and, in some cases, results of other diagnostic tests, such as CSF 14-3-3 protein.

We searched the Massachusetts hospital discharge and death certificate datasets for all patients whose records carried any diagnostic code for CJD (as a primary, secondary, underlying or contributing diagnosis) during the period of interest. We used both datasets because we anticipated a subgroup of CJD cases that were never evaluated, diagnosed, or treated in the hospital (and thus never discharged) and might have received strictly outpatient management; such patients might have been captured only in the death certificate dataset. Diagnostic codes were drawn from the *International Classification of Diseases*, *Ninth Revision* (ICD-9; code 046.1 for all hospital discharge dataset records) and *International Classification of Diseases*, *Tenth Revision* (ICD-10; code A81.0 for all death certificates).[13,14] Using dates of birth and death, as well as gender, patients with pathologically confirmed CJD were then matched to their respective CJD records in the hospital discharge and death certificate datasets, where available. For each case that lacked a CJD diagnosis on the death certificate, we manually searched the death certificate dataset for the listed diagnoses. We could not perform a similar search for cases lacking a CJD diagnosis in the hospital discharge dataset, given the limitations of hospital discharge data.

For all cases in the hospital discharge dataset (ie, cases in which the hospital associated with a CJD inpatient discharge could be identified), we obtained medical records to confirm clinical and diagnostic details, including sex, age at diagnosis, duration of illness, and results of MRI, EEG, and CSF analysis. In accordance with recent clinical criteria that incorporated MRI, EEG, and CSF findings,[6] 1 of the following documented test results was considered consistent with CJD: (1) MRI with high signal abnormalities in the caudate nucleus and putamen or at least 2 cortical regions on diffusion-weighted imaging (DWI) or fluid-attenuated inversion recovery (FLAIR) sequences considered consistent with CJD by the original radiologist and/or neurologist reviewing the scan; (2) EEG with periodic discharges considered consistent with CJD by the original neurologists evaluating the study; and (3) elevated levels of 14-3-3 protein in the CSF on the primary laboratory report or clinical note.

In an additional effort to ascertain pathologically confirmed cases from Massachusetts that were not referred to the NPDPSC, we also reviewed the Massachusetts death certificate dataset for cases coded for CJD associated with a variable indicating that they were sent to autopsy but were not included in the NPDPSC register for Massachusetts, as well as the Massachusetts Virtual Epidemiologic Network (MAVEN), a Web-based disease surveillance system that includes clinical, diagnostic, and administrative data for reportable diseases,[15] including CJD cases reported since 2002. For cases that could be matched to a CJD record in the hospital discharge dataset, we obtained and examined hospital records to confirm the pathological diagnosis and associated diagnostic details.

Finally, we reviewed the death certificates of Massachusetts cases that underwent pathological examination for suspected CJD during the period of interest but were histologically negative for prion disease. As described above, our search included cases referred to the NPDPSC as well as those not referred. Together with the data from the pathologically verified cases, we then determined the sensitivity and specificity of Massachusetts death certificates for pathologically confirmed CJD.

The project was approved by the Institutional Review Boards of the Massachusetts Department of Public Health and Yale University.

RESULTS

In the NPDPSC registry, we identified 48 Massachusetts patients with pathologically confirmed prion disease and a recorded date of death between January 1, 2000, and December 31, 2008. Seven of these 48 cases were excluded from our analysis, including 3 cases of VPSPr, 2 cases of GSS, and 2 cases of prion disease that could not be