

Introduction

Prion diseases are rare, fatal neurodegenerative diseases of animals and humans. Prion diseases are thought to occur when the prion protein, a normally occurring protein in mammalian cells, folds into an infectious and pathologic form. This abnormal folding results in a neurodegenerative process that is characterized pathologically by spongiform changes in the brain (“spongiform encephalopathy”). Creutzfeldt-Jakob disease (CJD) is the most common human prion disease and occurs at an incidence of one to two cases per one million population per year.

There are different types of CJD. Sporadic CJD (sCJD) occurs for unknown reasons and accounts for approximately 85–90% of cases. A smaller proportion of CJD cases (10–15%) result from an inherited mutation in the prion protein gene. Rare iatrogenic cases have been associated with human-derived pituitary hormone, dura mater grafts, corneal grafts and contaminated neurosurgical equipment. Variant CJD (vCJD) is associated with consumption of cattle products contaminated with the agent causing bovine spongiform encephalopathy (“mad cow disease”). There have been no reported cases of vCJD acquired in the United States.

In order to monitor the emergence of novel prion diseases and improve knowledge about prion diseases, all healthcare providers and facilities in Washington are required to report patients suspected to have human prion disease to the local health jurisdiction where the patient resides.

Clinical Features of Human Prion Disease

sCJD is most frequently characterized by a rapidly progressive dementia. Other observed manifestations can include myoclonus, visual deficits, cerebellar signs, pyramidal/extrapyramidal signs, psychiatric symptoms, and sleep disturbance. Given the wide variety of clinical manifestations, the most important characteristic is the rapid progression in the context of no other clear etiology.

Diagnostic Testing for Prion Diseases

Confirmatory testing for prion disease requires laboratory examination of brain tissue usually obtained at autopsy. Antemortem tests, such as CSF 14-3-3 and EEG are not confirmatory, but can improve diagnostic accuracy.

Postmortem Testing:

- **Brain Autopsy:** In suspected cases of prion disease, the Department of Health strongly recommends that physicians encourage an autopsy with the patient’s family to confirm prion disease and determine its type. Arrangements for autopsy and laboratory testing can be made through the National Prion Disease Pathology Surveillance Center (NPDPSC; see below) free of charge. This national reference center provides state-of-the-art prion disease diagnostics, including histopathology, immunohistochemistry, Western blot, and genetic analysis.

Antemortem Indicators:

- **Cerebral spinal fluid and protein markers:** Cerebral spinal fluid (CSF) findings in a patient with sCJD are generally unremarkable, although mild protein elevation is not uncommon. Testing CSF for the protein markers 14-3-3 and tau may be helpful in patients exhibiting rapidly progressive dementia, however these markers are not specific for sCJD and sensitivity decreases as the illness progresses. NPDPSC performs 14-3-3 and tau immunoassays.
- **Electroencephalogram (EEG):** Obtaining serial EEGs in suspected cases of sCJD can assist in the diagnosis. In early sCJD, the EEG may be normal or may show non-specific slowing. As disease progresses, patient with certain subtypes of sCJD develop biphasic or triphasic synchronous complexes on a slow background evolving into periodic sharp wave complexes occurring at about 1 per second. Importantly, this EEG pattern is transient in many patients, so its absence in a single test does not rule out CJD. However, when this pattern is observed, it does improve diagnostic certainty.

- **Magnetic Resonance Imaging (MRI):** Frequently, hyperintense signal in the basal ganglia, thalamus, and cortex, which is non-enhancing, may be seen on T2- and FLAIR-weighted sequences in cases of sCJD. Diffusion-weighted imaging (DWI) is particularly sensitive, and will often show signal abnormality at the cortical gray-white junction (“cortical ribboning”). While these findings are not specific for CJD, they are helpful in supporting the diagnosis of a clinically suspicious case. Suspicion of any form of CJD should be relayed to the interpreting radiologist.

Reporting a Suspect Case of Prion Disease to a Public Health Agency in Washington

Prion diseases in humans are notifiable per Washington Administrative Code 246-101. All suspected and confirmed cases should be reported to the local health jurisdiction where the patient resides. Contact information for local health jurisdictions is available at: <http://www.doh.wa.gov/LHJMap/LHJMap.htm>

Arranging Autopsy and Post Mortem Testing

Brain autopsy arrangements can be made through the NPDPS. Most autopsies in Washington are performed in Seattle. All expenses including transport of the body to and from the autopsy site, collection of brain tissue, and laboratory testing of brain tissue are covered by the NPDPS (see below). Patients or families interested in autopsy should complete the autopsy consent form available at: <http://www.cjdsurveillance.com/pdf/consent-autopsy.pdf>

Infection Control Considerations

- The abnormally folded prion proteins are resistant to many routine disinfectants and methods of sterilization used in medical facilities.
- **Invasive procedures:** If a patient with suspected or confirmed prion disease requires an invasive procedure, healthcare providers should contact the facility’s infection control division and implement appropriate infection control measures. Equipment that has been in contact with certain tissues (e.g., neurologic tissue) from these patients requires special decontamination measures.
- **Performing autopsy:** World Health Organization (WHO) Infection Control Guidelines for Transmissible Spongiform Encephalopathies should be followed during autopsy of a patient with suspected or confirmed human prion disease. These can be found at: <http://www.who.int/csr/resources/publications/bse/whocdscsraph2003.pdf>
- **Tissue/Organ donation:** Tissues and organs from patients confirmed, suspected, or at risk for prion disease should not be donated for transplantation or teaching purposes.

Additional information about infection control measures related to CJD is available from the Centers for Disease Control and Prevention (http://www.cdc.gov/ncidod/dvrd/cjd/infection_control_cjd.htm) and WHO (<http://www.who.int/csr/resources/publications/bse/whocdscsraph2003.pdf>).

Obtaining Clinical History to Determine Potential Risk Factors

Human prion disease has rarely been iatrogenically-acquired from human-derived pituitary hormones, dura mater grafts, corneal grafts, and contaminated neurosurgical equipment. It is important to obtain a history for these exposures on every patient with suspected prion disease. In addition, there have been rare cases of transfusion-associated vCJD transmission. Investigations of suspected vCJD cases should also include a history of transfusion products received and blood donations made by the patient.

Resource for Patients’ Families

The CJD Foundation operates a national toll-free line at (800) 659-1991 and a web site: <http://www.cjdfoundation.org/>

Contact Information

- Local health departments: <http://www.doh.wa.gov/LHJMap/LHJMap.htm>
- Washington State Department of Health, Office of Communicable Disease Epidemiology: (206) 418-5500 or (877) 539-4344 or <http://www.doh.wa.gov/EHSPHL/Epidemiology/CD/default.htm>
- National Prion Disease Pathology Surveillance Center (NPDPS), Division of Neuropathology, Case Western Reserve University: (216) 368-0587 or <http://www.cjdsurveillance.com>