CREUTZFELDT-JAKOB DISEASE

including variant disease

(CJD, Jakob-Creutzfeldt syndrome, Subacute Spongiform Encephalopathy, vCJD)

REPORTING INFORMATION

- **Class B:** Report by the close of the next business day after the case or suspected case presents and/or a positive laboratory result to the local public health department where the patient resides. If patient residence is unknown, report to the local public health department in which the reporting health care provider or laboratory is located.
- Reporting Form(s) and/or Mechanism: The Ohio Disease Reporting System (ODRS) should be used to report lab findings to the Ohio Department of Health (ODH). For healthcare providers without access to ODRS, you may use the Ohio Confidential Reportable Disease form (HEA 3334).
- Key fields for ODRS reporting include: for patient demographics – deceased and death date (if deceased); for laboratory - specimen type, test name and organism; for clinical information - imported and country/state of exposure; travel history; and notes should indicate relevant clinical findings and EEG results and whether the case is considered sporadic, familial or variant.

AGENT

CJD is believed to be caused by a self-replicating host-encoded protein or prion protein. This is transmissible in the laboratory to many species, including wild and transgenic mice and non-human primates.

CASE DEFINITION

The Centers for Disease Control and Prevention (CDC) has not established a case definition for CJD. Reports should be based upon the clinical signs and symptoms and laboratory criteria described below. Diagnosis of sporadic CJD is based on clinical signs and a characteristic EEG. Variant CJD cases differ in that EEGs do not show the typical periodic complexes. Demonstration of an abnormal amyloid protein in biopsied brain tissue and a pair of abnormal proteins in the CSF can verify the diagnosis antemortem.

Case Classification

Suspect: A positive CSF test for 14-3-3 protein.

Probable:

- Positive CSF test for 14-3-3 protein *and*
- Positive T-tau protein test *and/or* Positive RT-QuIC test *and*
- Presentation of clinical signs and symptoms diagnosed by a physician with no history of other neurological disorders that might compromise test results.

Confirmed:

- Positive CSF test for 14-3-3 protein *and*
- Positive T-tau protein test and/or Positive RT-QuIC test *and*
- Presentation of clinical signs and symptoms *and*
- A physician's diagnosis of CJD through brain biopsy or conclusive postmortem autopsy.

Not a Case: This status will not generally be used when reporting a case, but may be used to reclassify a report if investigation revealed that it was not a case.

SIGNS AND SYMPTOMS

Sporadic CJD has an insidious onset with confusion, poor concentration, lethargy, progressive dementia, intermittent unsteadiness when standing or walking and variable ataxia. Approximately 80% of patients with sporadic CJD are between 50 and 70 years of age, although familial CJD cases usually have an onset around 40 years of age. Overall, more than 95% of cases are 35 years old or older. About one third of patients initially express vague feelings of fatigue, disordered sleep or decreased appetite. Another third initially have neurologic symptoms, such as memory loss, confusion or uncharacteristic behavior. The final third initially have focal signs, such as ataxia, aphasia, visual loss, hemiparesis or amyotrophy. Muscle jerks and other neurologic signs appear later. Routine laboratory analysis of CSF is usually normal and there is no fever. Electroencephalograms (EEG) typically show periodic high-voltage complexes and the CSF 14-3-3 protein is elevated in 90% of CJD cases. Sporadic CJD progresses rapidly and death usually occurs within 3-12 months (mean 7 months), while familial CJD cases may live for 5-11 years. Variant CJD is distinguished from other forms of CJD by younger onset; vCJD has a mean onset age of 28 years. Patients with variant CJD (vCJD) show early prominent psychiatric and behavioral manifestations, and other features, such as painful sensory symptoms, delayed onset of overt neurologic signs, absence of diagnostic EEG changes, and a more prolonged duration of illness. The EEG is non-specific and the CSF 14-3-3 is not elevated in vCJD. Variant CJD patients survive a mean of 14 months.

DIAGNOSIS

CJD must be differentiated from other forms of dementia (especially Alzheimer disease), other infections (including encephalitis), toxic and metabolic encephalopathies, and occasionally tumors. Diagnosis is based on clinical signs along with EEG, CSF 14-3-3 assay, and neuro-imaging. CJD patients have a characteristically periodic EEG; however, variant CJD (vCJD) does not show periodic complexes. A diagnosis of CJD is suggested by the typical inexorable progression of symptoms, with the dissolution of cognitive abilities from week to week or even day to day, and the development of myoclonic jerking, particularly startle myoclonus, in response to sound or touch. Pyramidal tract, cerebellar, extrapyramidal and lower motor neuron signs, cortical visual deficits, abnormal extraocular movements, vestibular dysfunction, seizures, sensory deficits and autonomic abnormalities are also seen. During the late stages of the disease, the patient becomes mute and akinetic, and even the myoclonic jerking subsides. In vCJD, psychiatric abnormalities, behavioral manifestations and sensory symptoms are common. Brain biopsy and, in vCJD, tonsil biopsy can provide antemortem diagnosis, but these are invasive procedures and a definitive diagnosis depends on postmortem examination of brain tissue.

EPIDEMIOLOGY

Source

There are four known variants: sporadic CJD (sCJD); genetic CJD (gCJD); iatrogenic CJD (iCJD); and variant CJD (vCJD). The agent for CJD is believed to be a self-replicating host-encoded protein called a prion. Human cases are the only known reservoir for sporadic and familial CJD. Cases of CJD have been linked to corneal transplants, contaminated neurosurgical instruments, neurosurgical placement and injection of human cadaveric dura mater and injection of hormones produced from cadaveric human pituitary glands. Approximately 10-15% of CJD cases have a family history consistent with an autosomal dominant inheritance of the disease. In most of these cases, there are coding changes in the gene for PrP. The causative agent for vCJD and bovine spongiform encephalopathy (BSE) may have a common origin. BSE infected cattle are believed to be the reservoir for vCJD. Variant CJD has been found primarily in the United Kingdom, following an outbreak of BSE in the 1980's.

Occurrence

The disease occurs worldwide with an incidence 1 to 2 cases per million population per year. The highest age-specific average mortality rate (>5 cases per million) occurs in the 65 to 79-year-old age group. There is no seasonal distribution, no evidence of changing incidence over the years and no convincing geographic clustering, except for areas with large numbers of familial cases and variant CJD cases.

Mode of Transmission

The mode of transmission of most cases is unknown, but consistent experimental transmission of infectivity has been possible with homogenates of brain, spinal cord and eye tissue. Transmission occurred in less than half of the attempts with preparations of lung, liver, kidney, spleen, lymph node and cerebrospinal fluid. Iatrogenic cases have been linked to human pituitary hormone therapy, human dura mater grafts, corneal grafts, and neurosurgical instruments. Variant CJD cases appear to have a relationship to consumption of cattle brain or spinal cord in sausage, hamburger and other processed meat from BSE infected cattle starting in the 1980's and now thought to have ended because of changes in animal feeding and slaughtering practices.

Period of Communicability

CNS tissues are highly infectious late in the incubation period and throughout symptomatic illness. Infection present in lymphoid tissues from early in the incubation period, other tissues and CSF are sometimes infectious. In vCJD higher levels of infectivity are present in lymphoid tissues during clinical illness and incubation than in sporadic CJD. Blood may be infective in some forms of prion disease.

Incubation Period

The incubation period appears to range from 15 months to >30 years.

PUBLIC HEALTH MANAGEMENT

Case

Investigation

A complete medical history should be obtained. This should include previous surgical or dental procedures and possible exposure to human hormones or transplanted tissue, as well as a family history of dementia.

Treatment

No effective treatment is available. The disease appears to be uniformly fatal.

Isolation

There is no isolation for CJD. Standard precautions should be applied when caring for patients with CJD. Since evidence for communicability or increased risk for caregivers is lacking, additional isolation precautions, such as gowns or masks, are unnecessary.

Follow-up Specimens

There is no requirement for follow-up specimens.

Special Information

Avoid using tissues from infected patients in transplants. EEG electrodes or any surgical instruments used on any patient must be sterilized before further use.

Contacts

Since the mode of transmission is not established, there is no requirement to report contacts. Genetic differences in susceptibility resembling those of autosomal dominant

traits have been shown to explain patterns of occurrence of disease in families. CJD is dominantly inherited, so sequence analysis of the gene for protease-resistant protein (PrP) is not indicated unless there is a history of dementia in a first-degree relative.

Prevention and Control

Vaccination

There is no immunization available for CJD.

What is Creutzfeldt-Jakob Disease?

Creutzfeldt-Jakob Disease (CJD) is a rare neurological disease that usually afflicts people over 35 years of age. One type of CJD, variant CJD (vCJD) (found primarily in the United Kingdom), is seen in younger people. CJD is one of a group of diseases known as Transmissible Spongiform Encephalopathies (TSE). As a group, TSE affects humans and animals, but the agents affecting animals are not known to affect humans. However, there is increasing evidence that vCJD and bovine spongiform encephalopathy (BSE) are causally related. CJD was first identified in the 1920s.

Who gets CJD?

CJD has been diagnosed in humans aged 16 to 80 years, but almost all cases are people over 35 years of age (average age is 68 years). Variant CJD, found primarily in the United Kingdom, affects younger people (average age is 28 years).

How common is CJD?

There are about 1 to 2 cases of CJD per million population per year.

How is CJD spread?

The mode of transmission is not known, but experimental transmission has been possible with homogenates of brain, spinal cord, and eye tissue. A prion or prion protein (protease-resistant protein) is suspected of causing the disease. There does not appear to be person-to-person transmission.

What are the signs of CJD?

Early symptoms of CJD include poor concentration, a lethargic nature, and intermittent unsteadiness when standing or walking. As the disease progresses, there may be agitation, dementia, and chronic muscle spasms or twitching. The disease progresses rapidly with vision impairment and worsening of the dementia with death following shortly thereafter.

What is BSE?

BSE (bovine spongiform encephalopathy) or mad cow disease is a degenerative disease affecting the central nervous system of cattle. BSE is found primarily in the United Kingdom and a few other European countries. It is one of a group of diseases known as Transmissible Spongiform Encephalopathies (TSE). Other diseases in this group are scrapie in sheep and goats, chronic wasting disease in deer and elk, and transmissible mink encephalopathy in mink. All are rare neurologic diseases. In ruminants, the disease appears to spread by ingestion of BSE-contaminated meat or bone meal protein supplements derived from ruminants. The United Kingdom and U.S. have banned feeding ruminant-derived protein supplements to cattle and other ruminants. In 2008, the Food and Drug Administration (FDA) prohibited the use of the highest risk cattle tissues in ALL animal feed. These high risk cattle materials are the brains and spinal cords from cattle 30 months of age and older, and the entire carcass of cattle not inspected and passed for human consumption, unless the carcasses are shown to be from cattle less than 30 months of age, or the brains and spinal cords have been removed.

Is CJD related to BSE?

CJD cases in the U.S. have no apparent relationship to BSE. Recent research with variant CJD, found primarily in the United Kingdom, supports an association between variant CJD and BSE. In the past, the United Kingdom permitted brain and spinal cord to be mixed in sausage, hamburger or other meat products. This is speculated to be a link between

variant CJD and BSE. In 1989, the United Kingdom banned the use of brain and spinal cord in human foods.