Special report: Alzheimer’s disease vs. Creutzfeldt-Jakob disease

We’re living longer, but there is an ironic price to pay for our longevity — the incidence of certain age-related diseases is rising. As life expectancy increases, the incidence of neurodegenerative diseases such as Alzheimer’s disease (AD) also is growing.

Because there is such a high incidence of AD in the U.S., the question may be asked whether there are other neurodegenerative diseases with some symptoms similar to AD that might be misdiagnosed as Alzheimer’s. This paper will specifically examine the likelihood that sporadic Creutzfeldt-Jakob disease (CJD) may be misdiagnosed as Alzheimer’s.

Overview of neurodegenerative diseases
There are a number of neurodegenerative diseases, but, other than Alzheimer’s disease, which affects 15,000 people per million population, most are unfamiliar and rare. Creutzfeldt-Jakob Disease (CJD) is the rarest of all, affecting only one person per million population. Other neurodegenerative diseases include Parkinson’s disease (3,600 cases per million population); Frontotemporal dementia (140/million); Huntington’s disease (folk singer Woody Guthrie is the most famous victim of this disease which occurs at a rate of 110/million); Amyotrophic lateral sclerosis (also called Lou Gehrig’s disease, has an incidence of 70/million); Progressive supranuclear palsy (50/million); Spinocerebellar ataxias (40/million); and Pick’s disease (20/million).

According to Nobel Laureate Dr. Stanley Prusiner, the common characteristic of virtually all neurodegenerative diseases is abnormal processing of proteins in the brain. “Misprocessed proteins often accumulate because the cellular mechanisms for removing them are ineffective. The particular protein that is improperly processed determines the malfunction of distinct sets of neurons and thus the clinical manifestations of the disease.”

All of the neurodegenerative diseases, including CJD, occur sporadically or are genetically inherited. However, CJD differs from the other neurodegenerative diseases in one important respect: it also is transmissible.

Alzheimer’s disease background
Alzheimer’s disease is the most common neurodegenerative disorder in the U.S. According to the Alzheimer’s Association, an estimated 4.5 million Americans suffer from AD and, because increasing age is the greatest risk factor, the number of AD victims is expected to continue to increase as the population ages. AD affects one out of every 10 people over age 65, and the risk of AD doubles every five years after age 65. Nearly half of all 85-year-old individuals are affected. In addition, rare, inherited forms of AD can strike individuals who are in their 30s and 40s.

AD is the leading cause of dementia (conditions that gradually destroy brain cells) in the elderly, accounting for 50-75 percent of all cases of dementia. In addition, according to the National Center for Health Statistics, Alzheimer’s is the eighth leading cause of death in the United States. An individual with AD will live, on average, 7-10 years after the onset of clinical symptoms but may live as long as 20 years.

Creutzfeldt-Jakob disease background
Another neurodegenerative disease (but a very rare one) called Creutzfeldt-Jakob disease (CJD) has received, perhaps, more public attention in recent years than Alzheimer’s. CJD was first diagnosed in the 1920s, tends to occur sporadically (with no known cause), and affects approximately one in one million people annually throughout the world. Like AD, increasing age is a risk factor for CJD. The mean age at death in the U.S. for CJD is 68 years, and incidence among individuals aged 60 to 74 is about five cases per million population annually. Cases have been recorded in patients as young as 17 years and as old as 83 years. CJD is invariably fatal with mean illness duration of five months; death occurs within 12 months of illness in 80 percent of patients.

CJD has been thrust into public attention because of a similar sounding, but separate and distinct, disease called variant CJD (vCJD), first diagnosed in the United Kingdom (UK) in 1996. Variant CJD has been linked to consuming beef products contaminated with central nervous system tissue from cattle infected with Bovine Spongiform Encephalopathy (BSE, often called mad cow disease). Because of the similarity of names, there is substantial public confusion about CJD and vCJD in terms of incidence and causes. Worldwide, there have been (as of March 2005) a total of 166 cases of vCJD with 93 percent of those occurring in the UK. The United States has not had an indigenous case of variant CJD. The only diagnosed case of vCJD in the U.S. was a woman who had lived most of her life in the UK.

Disease mechanisms
Unfortunately, due to the difficulties in studying diseases associated with the brain, the disease processes for neurodegenerative diseases are not yet fully understood.
However, much is known about the pathological effects of these diseases on the brain.

Alzheimer’s destroys the nerve cells that process, store and retrieve information in the brain. This nerve cell destruction is thought to be the result of accumulation of amyloid plaques and neurofibrillary tangles. Amyloid is a general term for protein fragments that the body produces normally. In a healthy brain, these protein fragments would be broken down and eliminated. In AD patients, the fragments accumulate to form hard, insoluble plaques. Neurofibrillary tangles are insoluble twisted strands of a protein called tau that form inside brain cells. Scientists do not yet know whether the plaques or tangles cause AD or are a byproduct of some other process.

CJD also destroys nerve cells in the brain. However, while extensive amyloid plaque accumulation is the prominent feature of Alzheimer’s, only about 10 percent of CJD cases exhibit amyloid plaque. CJD is characterized as a prion disease because it is caused by an infectious protein particle known as a prion. Prions are the only known pathogens that are devoid of nucleic acid (prions contain no DNA or RNA). Unlike Alzheimer’s disease, which is not transmissible, CJD can be transmitted through exposure to the pathogenic form of the prion protein molecule that causes it.

CJD causes cell death through accumulation of an abnormal form of cellular prion protein. All mammals produce normal cellular prion protein (PrP) in cells of the central nervous system and other tissues. This normal protein can change its shape into an abnormal, misfolded form called a prion, which is pathogenic and can destroy nerve cells. Scientists believe that when abnormal prion protein comes in contact with normal prion protein, the normal protein alters its structure to become like the abnormal protein. The accumulation of abnormal PrP in brain cells results in altered function and eventual cell death or loss of cell function. Scientists do not know what factors trigger this conversion. Some believe the abnormal PrP itself causes the conversion, while others believe a virus-like entity may be involved.

Symptoms

While there are some similarities in the symptoms of AD and CJD, an experienced clinician usually can distinguish between the diseases. Once AD begins, it progresses relatively slowly. The first symptom may be mild forgetfulness, which may include difficulty remembering recent events, activities, the names of familiar people or things and inability to solve simple math problems. As the disease progresses, more serious symptoms emerge such as difficulty in speaking, understanding, reading, or writing. Later, people with AD may become anxious or aggressive, or wander away from home. Late in the disease, motor and sensory abnormalities and gait disturbances may occur.

CJD symptoms typically consist of a rapidly progressive dementia, visual abnormalities, or cerebellar dysfunction including muscle incoordination and gait and speech abnormalities. During the course of the disease, most patients develop motor dysfunction with abnormal reflexes, spasticity, tremors and rigidity; some patients may also show behavioral changes with agitation, depression or confusion. These symptoms often progress very rapidly, and patients develop a state of akinetic mutism (inability to talk or carry out purposeful behavior even though the eyes are open) during the terminal stages of the illness. Myoclonus (muscle contractions in the form of “jerks” or twitches) is the most constant physical sign and is present in more than 80 percent of CJD patients.

Diagnosis

A definitive diagnosis of both AD and CJD requires an autopsy and examination of brain tissue. However, a trained clinician can diagnose either disease with a high degree of accuracy. The Alzheimer’s Association notes that diagnostic tools and criteria make it possible for physicians to diagnose AD with an accuracy of 90 percent. Diagnostic tools used by physicians include tests of memory, problem solving, attention, counting, and language; medical tests such as tests of blood and urine; and brain scans.

In the case of CJD, certain diagnostic tests are indicative of the disease. Specifically, periodic short wave complexes on an EEG, certain signals on an MRI and the presence of a protein called 14-3-3 in cerebrospinal fluid are, in conjunction with the clinical picture, considered to be diagnostic of CJD.

Dr. Richard Johnson, Eisenhower Professor of Neurology and Neuroscience at Johns Hopkins University School of Medicine, feels it is unlikely that CJD would be misdiagnosed as Alzheimer’s disease. Dr. Johnson has said that Johns Hopkins had reviewed all its case files on Alzheimer’s and CJD and found no misdiagnoses. Dr. Johnson said, “There has, in the entire program here, never been a case of Creutzfeldt-Jakob disease misdiagnosed. And I don’t think it would be in most institutions, certainly at the present day, where when a patient has that rapid a course, has other movement disorders that are routinely seen in Creutzfeldt-Jakob disease, you’re not going to call that Alzheimer’s disease. It’s not going to be missed.”
Conclusion

In nearly all cases, the differences between the clinical presentations of Alzheimer’s disease and CJD will be sufficient to clearly distinguish these two neurodegenerative diseases. Nevertheless, because some early CJD symptoms may be similar to those of AD, it is possible for some misdiagnoses to occur early in the course of the disease. However, the incidence of such misdiagnoses is likely to be very small and, given the slow progression of AD versus the rapid progression of CJD, most of those early misdiagnoses likely would be quickly corrected.

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References and further reading

- Alzheimer’s Association. www.alz.org
- Creutzfeldt-Jacob Disease Foundation, Inc. www.cjdfoundation.org