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Creutzfeldt-Jakob Disease: An Outline

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ABSTRACT

A degenerative brain disorder that leads to dementia and death. Creutzfeldt-Jakob disease can develop suddenly, be passed down via the family, or be contracted through contact with tissue that is infected, such as after a transplant or by consuming contaminated meat. The most effective diagnostic tools is a magnetic resonance imaging (MRI) brain scan, which can reveal patterns of abnormal brain signals characteristic of CJD.Diagnosis of CJD is usually based on brain biopsy. Currently there is no cure for CJD, therefore treatment is based to relieve symptoms and to make the patient feel as comfortable as possible. Treatment includes antidepressants to help with anxiety and depression, painkillers used to relieve pain.

Keywords: *Prion,(MRI) brain scan, brain biopsy, Creutzfeldt-Jakob disease*

INTRODUCTION

A prion is a misfolded protein that can transmit its misfoldedness to normal variants of the same protein and trigger cellular death.Prion diseases can affect both humans and animals. The most common form of prion disease that affects humans is Creutzfeldt-Jakob disease (CJD) [1]. Prion disorders develop when the normal prion protein changes and damages the brain. This abnormal accumulation of protein in the brain can cause memory loss, personality changes, and difficulties with movement.

Subacute spongiform encephalopathy, often known as Creutzfeldt-Jakob disease (CJD), is a deadly degenerative brain condition.[2][3] Memory issues, behavioral modifications, and visual disturbances are early indicators.[3] Later indications include dementia, involuntary movements, loss of vision, weakness, and loss all physical and mental function.[3]Infectious prions are misfolded proteins that can cause normally folded proteins to also become misfolded.[3]

Around 85% CJD occur for unknown reasons, while 7.5% of cases are inheritedas genetic disorder.[3] Exposure to brain or spinal tissue from an infected person may also result in spread.[3] There is simply symptomatic treatment available for CJD; there is no particular treatment.[3] Opioids may be used to help with pain, while clonazepam or sodium valproate may help with involuntary movements.[3]The incidence of CJD cases worldwideis one person per million people, per year.[3]

However, researchers are hopeful that they will be able to identify the potential targets for disease modification. In this review, we will be discussing the epidemiology,

clinical features, pathophysiology, diagnosis and management (medical and surgical) of CJD.

EPIDEMIOLOGY

The majority cases of CJD (about 85%) are believed to occur sporadically, mainly by the rapid transformation of normal protein prions into abnormal prions.This sporadic disease occurs worldwide, at a rate of roughly 1 to 2 cases per 1 million populations per year.Ageing may trigger a rise in the incidence of CJD.

Death records are a good index of CJD because the disease is rapidly fatal, and the median duration of illness is between 4–5 months[4].However, the genetic pattern of CJD happens earlier, mostly between the ages of 30 and 50. Men and women were affected with equal frequency[5].

The initial symptoms of this diseaseare cognitive impairment, which can be seen in 35% of patients. Loss of intellect and memory, loss of balance and co-ordination, might probably be the first sign in about 17.5% of cases [6].Types of CJD includes: familial, iatrogenic, variant, and sporadic. The sporadic form of the disease is the most frequent and accounts for 85% of CJD cases [6,7].

The clinical diagnosis of CJD is different and includes prominent neurological and psychological symptoms. There is simply symptomatic treatment available for CJD; there is no particular treatment.

It presents differently depending on the patient, making a premortem diagnosis difficult. Clinical signs, tests, and image findings including magnetic resonance imaging (MRI), electroencephalograms (EEG), and cerebrospinal fluid (CSF) analysis are crucial investigation markers. The diagnosis of CJD is frequently suspect based on these factors. However, normal neuropathological procedures and immune cytochemical testing of brain tissue obtained either through a biopsy or an autopsy approach are necessary for the diagnosis of CJD [8].

PATHOPHYSIOLOGY

The pathophysiology of CJD is caused by misfolded proteins that steadily accumulate in the brain cells (neurons), causing damage and neuronal death. Prion proteins are produced in the brain when a normal protein folds improperly due to the nature of prions.

This occurs in a progressive rate, the CJD symptoms can vary from mild to severe in a short period of time. When CJD reaches its advanced stages, patients with all kinds of the disease will spend their whole lives in bed. They lose all awareness of their surroundings and require care around-the-clock [9].

The catalysis of the protein PrPC into the pathogenic prion protein (PrPSc) is a key component of the molecular pathogenesis of CJD. PrP is a normal cellular protein, functions in humans, is encoded by the PrP gene (PRNP), is located to chromosome 20. In prion disease, the post-translational modification of proteins, from the normal α-helical structure (PrPc) to a β-stranded form (PrPSc).The exact mechanism of this change is unclear, and this causes to vary with different prion diseases.

Once the process starts, PrPSc keeps converting PrPc by auto-catalytic changes. PrPSc and PrPc differ in their physio-chemical makeup. PrPSc tends to accumulate in tissues, is largely insoluble, and is resistant to protease destruction.

It also forms amyloid deposits. PrPSc is related to disease pathogenesis and infectivity, but the precise relationships are unclear [12,13].This post-translational

change in conformation leads to the generation of PrP^{Sc} and is involved in spongiform encephalopathy [10]. logical neuropath CJD characteristicsThe cortex, basal ganglia, thalamus, and white matter all exhibit severe cerebral atrophy. Bilateral lateral ventricular dilatation is noticeable, but the hippocampus is relatively preserved from atrophy[11].

TYPES OF CJD
There are 4 main types of CJD.

Sporadic CJD
Sporadic CJD is the most common type.
The precise cause of sporadic CJD is caused by the spontaneous change of a normal brain protein into an abnormally ("misfolds") prion. Most cases of sporadic CJD occur in adult aged between 45 and 75. The Onset is commonly a rapid progressive dementia.

Variant CJD
Consuming meat from a cow that has the "mad cow" disease, or bovine spongiform encephalopathy, which is a prion sickness similar to CJD, is thought to be the cause of variant CJD (vCJD).It is currently unknown how long it typically takes for variant CJD symptoms to appear after the initial infection (the incubation period).

Familial or inherited CJD
Familial CJD is an extremely rare genetic disorder in which a person inherits the prion protein gene from one of their parents with a mutation that leads to prions forming in their brains during maturity and causing CJD symptoms. In most cases, sickness starts to manifest in one's 50s.

Iatrogenic CJD
Iatrogenic CJD refers to an infection that happened unintentionally as a result of medical treatment. If surgical equipment used for CJD-related brain surgery are not thoroughly cleaned between surgical procedures or are used on another patient, iatrogenic CJD may also result.

But increased awareness of these risks means iatrogenic CJD is now very rare in this prion disease.

CLINICAL SIGNS AND SYMPTOMS
The symptoms can vary depending on the type of Creutzfeldt-Jakob disease (CJD).

The neurological system is primarily affected by the symptoms of sporadic CJD, which progressively increase over the course of a few months.

In variant CJD, symptoms that affect a person's cognition and emotions.

After that, neurological problems appear, which subsequently worsen over the coming months.

The same pattern applies to familial CJD as it does to sporadic CJD, however the onset of symptoms is typically delayed by two years.

The pattern of iatrogenic CJD is unpredictable, most cases have resulted from hGH treatment or human dura mater grafts.

Early Neurological Symptoms
- Difficulty walking caused by problems with balance and co-ordination
- Slurred speech
- Numbness or pins and needles in different parts of the body
- Dizziness
- Vision problems, such as double vision
- Hallucinations (seeing or hearing things that aren't really there)

Early Psychological Symptoms
- Severe depression

- Withdrawal from family, friends and the world around you
- Anxiety
- Irritability
- Difficulty sleeping

Advanced Neurological Symptoms

- Weakness in physical co-ordination, , such as walking, speaking and balance (ataxia)
- Muscle twitches and spasms
- Urinary incontinence and bowel control
- Blurred vision
- Swallowing difficulties
- Loss of speech
- Coma

Later Psychological Symptoms

- Loss of memory, which is often severe
- Confusion
- Aggressive behavior
- Loss of appetite, which can lead to weight loss
- Irrational fear
- Unusual and inappropriate emotional responses

Final Stages

- People with various patterns of CJD are going to become bedridden as the illness closes.
- They become unaware of their surroundings.
- Loss the ability to speak.
- Following an infection, such as pneumonia, or respiratory failure where the person is unable to breathe, death will unavoidably occur [14].

CLINICAL DIAGNOSIS

Brain biopsy or an examination of brain tissue after death, known as an autopsy, are the only tests that can definitively determine whether Creutzfeldt-Jakob disease is present.

Before a patient passes away, doctors can accurately diagnose the situation. Your medical and personal history, a nervous examination, and certain diagnostic procedures are used to make the analysis.

A neurological exam may point to Creutzfeldt-Jakob disease (CJD) if you're experiencing:

- Muscle twitching and spasms
- Changes in reflexes
- Coordination problems
- Vision problems
- Blindness

In addition, health care providers commonly use these tests to help to detect CJD:

Electroencephalogram, also Known as an EEG

The electrical activity of the brain is captured by this test. It involves applying tiny metal discs to the scalp called electrodes, which can detect the peculiar patterns of variant CJDs.

Magnetic Resonance Imaging (MRI)

MRI is especially useful for brain disorders. MRI creates high-resolution images. The unique alterations that people with CJD experience can be seen on specific MRI scans and can reveal problems; MRI employs high magnetic fields to create a detailed image.

Spinal Fluid Tests

The brain and spinal cord are encased in and supported by spinal fluid. a method in which a needle is injected into the lower spine to extract a sample. This test can eliminate the possibility of other illnesses that manifest CJD-like symptoms.

Real-time quaking-induced conversion (RT-QuIC), a new technique to detect the presence of the prion proteins that causes

CJD. This test can diagnose CJD before death. [15]

Genetic Testing

Analyzing a sample of your blood or saliva can show if you have a genetic mutation that increases your chance of developing CJD.

Brain Biopsy

This test involves taking a sample of your brain tissue and analyzing it. A brain biopsy is the most definitive way to confirm CJD diagnosis. However, brain biopsies almost always happen after death, so they're only good for confirming or ruling out a CJD diagnosis.[16]

CONCLUSIONS

CJD is a rare disease with a poor diagnosis and rapid progression. CJD is a fatal neurodegenerative disorder, provides rapid loss of cognitive functioning and a wide range of neuropsychiatric disorders.

There is no effective treatment for CJD, which is uniformly fatal and hence supportive and symptomatic treatments are the keystones of therapy. Medication treatment is for symptomatic relief only, but none of them has so far clearly demonstrated a benefit. For this terminal illness to be treated, more future therapeutic intervention is needed.

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