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Conceptual Study on Creutzfeldt Jakob Disease

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A B S T R A C T
Creutzfeldt Jakob Disease belongs to the family of human prion diseases. It is a rapidly progressive rare transmissible universal fatal degenerative condition caused by prion proteins it occurs when the normal PrP proteins get converted into abnormal proteins (PrPsc). One person in one million populations is affected by the consumption of infectious cattle meat. There are three types of Creutzfeldt-Jakob disease. This disease mostly affects elderly patients aged between 50-70 years. The diagnosis criteria include Electroencephalogram (EEG), Magnetic Resonance Imaging (MRI), and Biomarkers in CSF but Creutzfeldt-Jakob disease is confirmed by Biopsy.

Keywords: Magnetic Resonance Imaging (MRI), Electroencephalogram (EEG), Creutzfeldt-Jakob disease

A R T I C L E I N F O

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1. Introduction

Creutzfeldt Jakob disease is a "KROTIS FELT- YAH-KOBE"[1] disease also known as a rare brain disorder that leads to dementia. This condition was first described in 1920 by Hans Creutzfeldt and later described in 1921 and 1923 by Alfons Jakob [3]. CJD belongs to the family of human prion disease, which is caused by misfolded, transmissible infection particles or prions [4]. The vCJD was first identified in March in the year 1996 in the UK [6]. CJD was found to have occurred in 179 cases worldwide [7].

2. Type of CJD

- Sporadic CJD
- Inherited /Familial CJD
- Acquired CJD

Sporadic CJD (SCJD) [3]: The sporadic CJD is a rare occurring disease. The exact cause for SCJD is not clear but results from the random structural changes in the normal Prp proteins leading to the formation of PrPSc or somatic mutations in their PRNP gene. SCJD is a very rapid disease and the mean time of survival of the patients is 6 months. SCJD has been detected in Europe, North America, Australia. The sporadic CJD is mainly seen in patients of age between 55-77 years old [3]. SCJD has been classified on account of its molecular and clinical characteristics [MM1, MM2, MV1, MV2, VV1, VV2] [12].

Inherited CJD/Familial CJD (FCJD):
The familial CJD is the CJD that passes from generation to generation and is mainly caused by genetic mutation [4]. The inherited forms of CJD are autosomal dominant with high penetrance. The most common type of familial CJD with the clinical phenotype of sporadic CJD is E200K-129M [13]. Fewer than 15% of people having CJD have a family history these people may test positive for the genetic changes associated with the disease [14]

Acquired CJD: The Iatrogenic CJD and Variant CJD fall under this category [3]

Iatrogenic CJD [15]:

Iatrogenic CJD occurs as a result of unintended exposure to prion during any medical or surgical procedures. The Iatrogenic CJD was first identified in the year 1974 in patients who had received transplants of corneal tissue from an infected cadaver. The two principle diagnosis for this is treatment with cadaveric pituitary-derived growth hormone(C-hGH) and Human dura meter.

Variant CJD (VCJD) [3]:

Variant CJD is the type of CJD that is caused when exposed to contaminated food products. It is also said that variant CJD is also transmitted by the transfusion of infectious blood. vCJD was observed in the year 1980 in the UK population which occurred after the ingestion of contaminated beef. This disease has a specific Neuropathology with florescence plaque in the brain, widespread deposition of abnormal PrP, and Thalamic gliosis in the brain.

Pathophysiology of CJD:

CJD is caused by prions/ transmissible infectious particle prions that can be found throughout the body in different concentrations but the concentration of CJD prions is mainly CJD high in the brain and posterior eye [retina optical nerve] the normal cellular prion proteins found on the cell membrane throughout the body is PRP When these normal prion proteins get infected [or]misfolded they form PRPCJD, PRPSC, PRPBSE Which are pathogenic. The prions that cause CJD exhibit at least low stable confirmations [3].

3. Diagnosis

The diagnostic criteria for Creutzfeldt-Jakob disease were published by WHO in the year 1998 which depends on clinical examinations such as EEG (electroencephalogram), MRI (magnetic resonance imaging), and CSF finding [17].

EEG (Electroencephalogram):

EEG records the brain's electrical pattern and finds a specific type of abnormalities in major types of CJD. Periodic sharp wave complexes (PSWCS) are found in EEG recordings of nearly one-third of patients with sCJD and therefore it has been included in the diagnosis criteria of sCJD by WHO [17]. In sCJD the EEG set out characteristic changes depending on the stages of the disease. Such as diffuse slowing and frontal intermitted rhythmic delta activity (FIRDA) in the initial stages of the disease, typical periodic sharp wave complexes (PSWC) in the middle and last stage to reactive coma traces or even alpha coma in preterminal EEG recordings [18]. The time duration between the onset of the disease and the indication of PSWC findings on EEG is 3.7 months [17]. Not all patients with CJD develop PSWC there are only seen in patients who have MV1 and MM1 genotypes [17]. The EEG pattern associated with CJD is sensitive to benzodiazepines and external stimuli. The benzodiazepines mask the PSWC findings on EEG for patients with sCJD [17].

MRI (Magnetic resonance imaging):

Mostly the patients who are suspected of having CJD are studied with MRI throughout the disease to support the diagnosis of CJD [19]. MRI has been recorded as important for the diagnosis of sCJD. High signals in the head of the caudate nucleus and the putamen as compared with the thalamus and the cerebral cortex are seen in the MRI of sCJD patients [19]. The advanced technologies in MRI allowed the physicians to use FLAIR (Fluid attenuated inversion recovery), DWI (Diffusion-weighted imaging) and ADC apparent diffusion coefficient improving both the negative and positive predictive value [19]. Patients with new variant CJD show bilaterally increased signals on MRI in the pluvial thalami with a reported 78%sensitivity and specificity of 100% [19].

Biomarkers in CSF: [17]

The most commonly studied CSF biomarkers for CJD are 14-3.3 proteins which are replacement markers for CJD and appear after neuronal destruction. Several studies conclude that the sensitivity of positive 14-3.3 proteins CSF for classic sCJD is 92%-96%. Biomarkers like Tau proteins are released when the damage occurs to neurons and in classic sCJD have a sensitivity of 81% when these biomarkers are tested in combination the positive predictive value is 91% and this has a lower sensitivity of 53% in vCJD. Real-time quacking included conversation (RT-QUIC) is a recently described laboratory technique that provides a definitive diagnosis of CJD from CSF samples by detecting PrPSc. This test has a sensitivity of 80%-90% and is considered a better test than 14-3.3 proteins as it is 100% specific. Recent studies have shown that the RT-QUIC technique is the most sensitive and specific diagnostic test that can replace brain biopsy for accurate CJD diagnosis.

Brain Biopsy [14]:

Brain biopsy is done by removing a tissue sample from the frontal lobe by performing neurosurgical procedures. Biopsy gives the pathological confirmation of disease and is said as the golden standard for CJD.

Causes [4]: CJD is a prion disease caused by the abnormal transmissible proteins known as prions. when the healthy prion proteins change in their shape this leads to damage to the tissues present in the brain and shows the symptoms of CJD.

Symptoms: [16,14]

- Lack of coordination.
- Problems with walking and balance.
- Personality change.
- Impaired thinking.

Treatment:

There is no effective treatment for it and no medications are effective to stop the progression but the previous studies showed that doxycycline is effective in in-vitro and in-vivo models of disease, and patients with CJD who received compliant treatment with doxycycline showed increased survival time compared with other historical series. [20]

Preventions:

- Cover cuts and abrasions with waterproof dressing.
- Wear surgical gloves when handling the patient's tissues and fluids or dressing the patient's wounds
- Avoid cutting or sticking themselves with instruments contaminated by the patient’s blood or other tissues[14]

4. Conclusion

Creutzfeldt-Jakob Disease is a rapidly progressive rare, transmissible, universally fatal degenerative condition

caused by prions. CJD is also called a 'great mimicker'. Sporadic CJD is the most common form of CJD which affects 1-2 persons per million each year. This CJD affects elderly people. Real-time quacking included conversation [RT-QUIC] is a recently described laboratory technique that provides a definitive diagnosis of CJD. EEG is the main diagnosis used to detect SCJD. EEG patterns associated with SCJD are sensitive to sedatives and hypnotics (Benzodiazepines). The majority of symptoms caused by CJD are covered. Sodium Valproate which is commonly used for epilepsy and seizures is used for treating symptoms like myoclonus.

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