Creutzfeldt-Jakob Disease (CJD)

Creutzfeldt-Jakob disease (CJD) is the most common cause of spongiform encephalopathy. Spongiform encephalopathy consists of prion induced spongiform degeneration of the cerebral cortex and cerebellum. CJD is caused by the misfolded prion proteins which have a high affinity for brain tissue and induce further conformational changes of physiological prion proteins. These abnormally folded proteins accumulate and cause toxic plaque formation and neuronal death leading to spongiform encephalopathy. There are four subtypes: sporadic (sCJD), familial (fCJD), variant (vCJD) and iatrogenic (iCJD). The sporadic type is the most common. Once symptoms present, the progression is rapid and fatal. Symptoms include ataxia, cognitive impairment, behavioral changes myoclonus, and muscle weakness. There is no cure, and treatment is only supportive.

PLAY PICMONIC

Pathophysiology

Misfolded Prion Protein

Prawn folded protein

Normally, prion proteins are encoded by the $PRNP$ gene and exist in a mostly alpha-helix configuration. They are commonly found in the cell membrane of neurons. They play a function in the uptake of copper, have a protective function against free radicals, and are involved in normal synapse function. Prion disease is caused by a misfolded prion protein that has a predominantly beta-sheet structure. This misfolded protein is resistant to the actions of proteases and can induce conformational changes in normal cellular prion proteins.

Spongiform Encephalopathy

Sponge with Altered-brain

When physiological prion changes its composition from alpha helix to predominantly beta sheet, it induces similar changes in other prions. Misfolded prions are resistant to proteases, and their accumulation causes intracellular dysfunction as well as extracellular aggregation (plaques). The subsequent vacuolization without inflammation that occurs from neuronal cell death in the central nervous system gives the tissue a spongiform appearance on histology.

Subtypes

Sporadic Type

Sporadic-Spear

Sporadic type is the most common subtype (accounting for approximately 85%). In sporadic cases, there is no identifiable cause.

Familial Type

Familial-Family

The familial type accounts for approximately 10-15% of the cases and it is due to a mutation in the $PRNP$ gene that causes glutamic acid to be replaced by lysine leading to the formation of misfolded prions. In individuals with this type of CJD, there is a need for genetic counseling.

Variant Type

Varying-color

Acquired types account for less than 1% of cases and include variant and iatrogenic. Variant type (vCJD) is due to the consumption of meat from cows or sheep with prions in their muscle tissue. Prions in cows cause spongiform encephalopathy in cows, famously known as mad cow disease.

Iatrogenic Type

i-at-medic

Iatrogenic type is due to medical procedures with contaminated equipment. This has been reported in corneal transplants and neurosurgery.

Clinical Manifestations

Rapidly Progressive

Rapid-rabbit

CJD may not show up for decades but once symptoms emerge, it progresses rapidly leading to death. Rapidly progressive cognitive impairment leading to dementia and myoclonic jerks are the hallmarks of CJD.

Dementia

Demented-D-man

CJD presents with rapidly progressing dementia. It is characterized by memory impairments, deficits in speech, reasoning, and spatiotemporal awareness. After the onset of symptoms, patients with CJD also present with behavioral changes, depression, and other neuropsychiatric symptoms such as visual hallucinations.

Ataxia

A-taxi

Cerebellar compromise leads to ataxia and other extrapyramidal signs such as hypokinesia, bradykinesia, and dystonia. Other cerebellar manifestations include nystagmus.

Myoclonus

Mayo-clown

Myoclonus is brief, shock-like, involuntary muscle twitches. In CJD they are often triggered by a startling stimulus. Startles are reproducible exaggerated responses to trivial stimuli such as loud noises. Other muscular symptoms include muscle weakness. Patients may present with hyperreflexia, Babinski sign, and spasticity.

Diagnosis

Magnetic Resonance Imaging (MRI)

M-R-eyes Machine

Magnetic resonance imaging (MRI) findings include hyperintense signals involving the cerebral cortex, the head of the caudate, and the putamen on FLAIR, diffusion-weighted imaging (DWI), and T2-weighted images. Other areas involved include the superior frontal gyrus, superior parietal lobule, cingulate gyrus, and the insula.

Increased Levels of 14-3-3 Protein

(1) Wand (4) Fork and two (3) Trees

If CJD is suspected, a lumbar puncture is performed to evaluate if there are increased levels of 14-3-3 protein in the cerebrospinal fluid (CSF). Elevated 14-3-3 levels in the spinal fluid is a sign of neuronal destruction. The findings in the cerebrospinal fluid analysis include the presence of neuron-specific enolase, S100 protein, and tau protein.

Periodic Sharp Waves On EEG

Periodic Sharp Waves On EEG

Another finding in CJD is the presence of bi- or triphasic periodic sharp waves with a frequency of 1-2 Hz on electroencephalogram (EEG).

Management

Supportive Care

Supportive IV bags

There is no cure for CJD- death usually occurs within one year after the onset of symptoms. Current management is focused on supportive and symptomatic treatment.