10 - 4. Creutzfeldt Jakob Disease (CJD)

4. Creutzfeldt-Jakob Disease (CJD)

 Three forms exist: sporadic (most common), familial and variant CJD (vCJD - related to bovine spongiform encephalopathy). There are no characteristic gross pathologic features of CJD because of the typical short course of the disease. Persons living beyond 6 months to a year may have some degree of generalized cerebral atrophy. Microscopically CJD shows a spongiform encephalopathy secondary to neuropil vacuolisation. Many round to oval vacuoles are seen in the neuropil of cortical gray matter - vacuoles may be single or multiloculated. The vacuoles may coalesce to microcysts. Most cases of CJD also demonstrate neuronal loss and gliosis. Prion protein (PrPc) is a normal neuronal cell surface protein encoded by a gene on chromosome 20. In CJD, this is converted via a conformational change to an abnormal form designated as PrPSc. This abnormal form is protease-resistant and can accumulate in the central nervous system of affected persons. This accumulation triggers further conversion of normal PrPc to PrPSc and accounts for the degenerative changes in the cerebral cortex. The PrP can be identified in tissues with immunoperoxidase staining. These abnormal PrPSc can be transmitted from one person with spongiform encephalopathy to another person via pituitary extracts, corneal transplants, dural grafts, and contaminated electrodes from neurosurgical procedures. In variant CJD, there is a marked accumulation of the prion protein, and the plaques are florid. An abnormal protein called 14-3-3 can be found in the CSF by immunoassay, but this protein is nonspecific and may be found in association with viral encephalitis and stroke. It is less frequent in variant CJD. In familial cases of CJD, the typical EEG changes are often lacking, and the 14-3-3 proteins are absent in CSF in more than 50% of cases. The presence of particular polymorphisms at codon 129 of PrP may have an influence on susceptibility to disease. The amino acids methionine (M) or valine (V) may be present at this locus. In 37% of healthy persons, both inherited PrP genes code for methionine (M/M), and 50% have M/V. In contrast, 73% of persons with sporadic CJD have the M/M phenotype, and 100% of persons with variant CJD have this phenotype. MRI is the most useful supportive diagnostic test in variant CJD. A characteristic abnormality seen in the posterior thalamic region (pulvinar sign) is highly sensitive and specific for variant CJD. The pulvinar sign has been found in

more than 90% of pathologically proven vCJD cases. FLAIR sequences of MRI are most likely to show the abnormality.

© SPMM Course Feature Classic CJD Variant CJD Age Elderly 7th or 8th decade of life Adults in 3rd/4th decade of life Course Shorter course (5 months) More prolonged (1 year) Symptoms Early neurological signs and dementia Early psychiatric/behavioural signs with delayed neurological features EEG Triphasic sharp waves often seen Triphasic waves are rare, and changes are often nonspecific MRI Pulvinar sign is not seen Pulvinar sign is present Biopsy Only a few plaques noted Large number of plaques Tonsils Prion protein cannot be isolated from lymphoid tissue Tonsillar tissue carries prion agent

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