

PRION INFECTIONS OF THE BRAIN

Prions (proteinaceous infectious particles) are infective agents comprised of protein, lacking nucleic acid. The actual protein, termed PrP^C is a normal cellular constituent. The infective particle is an isoform of PrP, resulting from partial refolding into a different configuration, which can then induce further conversion of the normal protein into the infective form. Clinically relevant infection occurs in the CNS in both animals and humans, resulting in varying degrees of spongiform neuronal degeneration, neuronal loss, and amyloid-like plaques predominantly affecting gray matter structures. Human forms of prion infection include sporadic, familial (inherited), and acquired. The sporadic forms are divided into sCJD and sporadic fatal insomnia (sFI), and sCJD is further divided into several subtypes, largely based on which amino acids in the prion gene. Sporadic CJD (sCJD) accounts for approximately 85% of human cases, with the remainder being predominantly hereditary, including familial CJD, GSS, and familial fatal insomnia. Iatrogenic causes include dura mater grafts, corneal implants and contaminated human growth hormone. New variant CJD (vCJD), which is thought to be transmitted via contaminated meat from cows infected with bovine spongiform encephalopathy (BSE), gained recognition from a public health perspective in the late 1990's. Overall, CJD is rare with an incidence of less than 1 per million. The sporadic form is more common amongst the elderly while the variant form is seen in younger patients. Sporadic CJD is characterized by a rapidly progressive dementia resulting in death over weeks to months.

MRI is the mainstay of imaging investigation. Typical findings of sCJD on conventional sequences include symmetric hyperintensity on FLAIR and DWI involving the basal ganglia, in particular, the corpus striatum, and/or cerebral cortex signal abnormality, either symmetric or asymmetric. DWI shows persistent restricted diffusion in the typical areas of involvement. The histopathology of CJD is characterized by neuronal loss and spongiform changes. DWI lesions co-localize strongly with the histopathologic lesions. MRI findings can precede the onset of characteristic clinical disease, particularly with the use of DWI. No mass effect or enhancement is seen and there is progression to atrophy in the terminal stages. MRS has shown decreased NAA, reflecting neuronal loss, but is nonspecific. The variant form of CJD (vCJD) shows distinctive imaging findings, in particular, symmetric high signal in the pulvinar compared to the signal in the remainder of the basal ganglia. This is termed the "pulvinar sign". There have been less than 300 cases of human iatrogenic prion disease worldwide. Most of these infections have been caused by the use and/or implantation of dura mater, corneal grafts and cadaveric human growth hormone. The most frequent MRI finding in these cases has been bilateral symmetrical hyperintensity of the caudate head and putamen, with the abnormalities appearing earlier on DWI than on T2WI. Inherited prion diseases comprise about 15% of human cases. There are very few published reports on imaging findings. Gerstmann-Straussler-Scheinker (GSS) disease is one of the inherited prion diseases. Clinically there is prominent cerebellar ataxia. Like sCJD, DWI demonstrates bilateral discontinuous ribbon-like hyperintensities throughout the cerebral cortex, and progressive cortical atrophy.

In summary, MRI plays an extremely important role in early diagnosis, especially with DWI and FLAIR images. The cortical and deep lesions may appear alone or together, and although usually bilateral and symmetric, they may be asymmetric or purely unilateral. When typical MRI findings are observed in an appropriate clinical context, the diagnosis of prion disease is very likely and brain biopsy can usually be avoided.