

Familial Creutzfeldt–Jakob Disease with M232R Mutation Progressed Slowly like Alzheimer’s Disease

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Abstract:

Creutzfeldt–Jakob disease (CJD) is a rare, rapidly progressive, and typically fatal neurodegenerative disorder. Approximately 10–15% of all CJD cases are familial and result from autosomal dominant mutations in the prion protein gene (PRNP) located on chromosome 20. Among these, the Met232Arg (M232R) mutation has traditionally been associated with clinical features resembling sporadic CJD. However, recent case reports have described M232R-associated CJD (CJD232) patients presenting with atypical, slower clinical progression.

We report a case of a 62-year-old male patient with the M232R PRNP mutation who initially presented with gait disturbance and memory impairment over a two-year period. Although initial clinical findings, including Mini-Mental State Examination (MMSE) and electroencephalography (EEG), did not support a diagnosis of CJD, diffusion-weighted MRI (DWI) incidentally revealed high-signal intensity lesions in the cortex, prompting further investigation. Cerebrospinal fluid (CSF) analysis showed weak positivity for 14–3–3 protein, and genetic testing confirmed the M232R mutation in both the patient and his children. Despite this, the patient exhibited an unusually slow disease course, with preserved cognitive function and minimal neurologic deterioration for over 26 months. Follow-up MRI and FDG-PET scans showed no significant progression, and myoclonus appeared only after two years.

Compared to previous literature, which classifies CJD232 into rapid and slow progression subtypes, this patient’s clinical course was even slower than the previously reported slow-type cases, whose average time to akinetic mutism was approximately 20.6 months. This case highlights the phenotypic variability of the M232R mutation, which can closely mimic Alzheimer’s disease and suggests a possible overlap or interaction between prion disease and other neurodegenerative mechanisms. Further studies are needed to elucidate the pathogenic role of the M232R mutation and its contribution to disease heterogeneity in familial CJD.

Keywords:

Creutzfeldt–Jakob disease, PRNP gene, M232R mutation, familial CJD, slow progression, Alzheimer’s disease mimicry, diffusion-weighted MRI, neurodegeneration.