Neuroimaging Highlight

Editors: Mark Hudon, Richard Farb

Sporadic Creutzfeldt-Jakob Disease with Worsening Depression and Cognition

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Can. J. Neurol. Sci. 2007; 34:464-466

A 58-year-old male presented with a one-year history of low mood, early morning awakening from sleep, apathy, difficulty with memory, concentration and organization. This had been associated with intrusive concerns of a recent social stressor. He was no longer able to work and was on medical disability. Except for a 20kg weight loss there were no other constitutional or neurological symptoms. He had hypertension and hypercholesterolemia and was on atorvastatin and aspirin. He scored 28/30 on mini-mental status examination (MMSE) with errors on object recall; however he could recall forgotten items after cueing. He had difficulty with concentration, was apathic and had a negative outlook to the future. His neurological examination and a detailed hematological work up including chemistry, cell counts, vitamin B12, folate, and renal, hepatic and thyroid function tests were normal. A brain magnetic resonance image (MRI) showed mild cerebral atrophy. Based on a formal neuropsychological assessment he was diagnosed with depression and started on Venlafaxine.

Three months later he noted gait imbalance, falls, and inability to drive due to worsening cognition and motor skills. His wife observed occasional jerking of the limbs during sleep. Examination showed that his score on repeat MMSE was 9/30, intention tremor of upper extremities, truncal ataxia with a wide based gait, and exaggerated reflexes with bilateral ankle clonus. Reflex tactile myoclonus was also observed. An EEG revealed right frontotemporal slowing. Two months later he was hospitalized after fracturing his ankle from a fall and was found to be severely demented with frequent and widespread myoclonus. A repeat brain MRI (Figure) showed abnormal signal in the basal ganglia and cingulate cortex bilaterally characteristic of Creutzfeldt Jacob disease (CJD). He died within two weeks of hospitalization and an autopsy showed spongiform changes in the brain confirming the antemortem diagnosis.

Creutzfeldt Jacob disease is a rare transmissible spongiform encephalopathy caused by abnormal conformational changes in prion proteins. Most cases are sporadic (sCJD) with an annual mortality rate in Canada of 1.03 per million.[1] Manifestations can range from rapidly progressing dementia, myoclonus, ataxia, visual disturbances, to psychiatric and extrapyramidal features.[2] Up to 92% of patients with CJD have at least one psychiatric manifestation, which is the presenting symptom in 26%.[3] Common psychiatric features include sleep disturbances, psychotic symptoms and depression.[3] In a correlative study, 80% of patients with CJD and hyperintense basal ganglia on MRI had dementia, 33% had depression and 14% had sensory symptoms,[2] our patient exhibited all three.

Brain MRI abnormalities on fluid attenuated inversion recovery (FLAIR) and diffusion weighted imaging (DWI) sequences have a >90% sensitivity and specificity for CJD.[4] Typical findings include simultaneous involvement of gray mater in the cortex and basal ganglia, as seen in our patient. The DWI signals may change with time but do not resolve completely, and corresponding hypointensities on apparent diffusion coefficient (ADC) sequences may last for up to two months.[5] Interestingly, abnormalities in the caudate are consistently associated with involvement of the putamen, while a reverse association is not uniform.[5] Thalamic abnormalities tend to occur late and are seen in 34% of patients with sCJD, in comparison the posterior thalami are involved commonly in new variant CJD and referred to as the "pulvinar sign" or as "hockey sticks" when there is additional mediodorsal involvement[5,6] (Figure-D). Magnetic resonance imaging (MRI) changes in familial CJD, which accounts for 5-10% of cases, are similar to sCJD.[6,7] The signal changes that involve grey matter structures correlate with the pathological changes of astrocytosis and vacuolation.[8] Vacuolation (spongiform changes) is considered to be a marker of degeneration rather than an etiology of the disease.[9] The differential for bilateral basal ganglia signals include carbon monoxide poisoning, hypoxic and/or ischemic injury, encephalitis, and Leigh's disease.[6] The clinical picture significantly limits the differential.

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Received April 23, 2007. Accepted in final form July 23, 2007.
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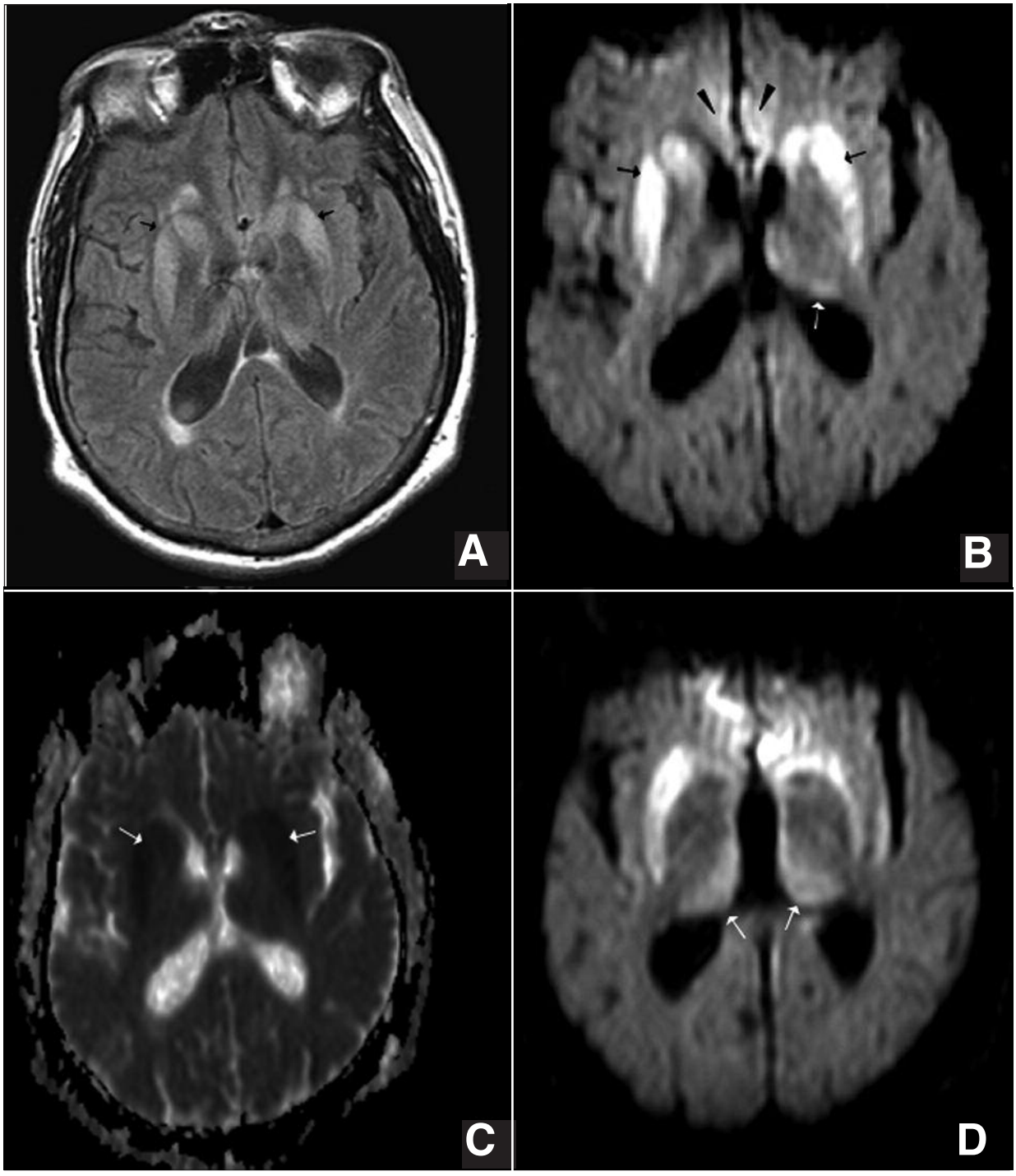

Figure : *Image A: Bilateral hyperintensities involving the putamen and caudate symmetrically on FLAIR sequence (arrows). Image B: DWI reveals pronounced hyperintensities in the striatum (black arrows) and cingulum bilaterally (arrow heads), and left thalamus (white arrow). Image C: ADC showing reduced signal in the striatum bilaterally corresponding to the DWI signals (white arrows). Image D: DWI showing bilateral "hockey-stick" involvement of the mediodorsal thalami.*

https://doi.org/10.1017/S031716710000737X Published online by Cambridge University Press

The typical periodic sharp wave discharges seen on EEG in CJD, have a sensitivity of 58% - 66%[10,11] with a 74% specificity.[11] The discharges tend to correlate with the presence of myoclonic jerks,[12] are more common in patients >50 years of age, and are seen in approximately 50% of cases after six months from disease onset and less often as time goes on.[10]

In addition to the utility of MRI with DWI in the antemortem diagnosis of CJD, this case re-iterates that psychiatric manifestations may mask cognitive changes. Thus, depression or behavioral abnormalities in the setting of rapidly progressive cognitive decline should alert the clinician to the diagnosis.

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