Sporadic onset Creutzfeldt-Jacob disease: Interesting MRI observations

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We describe a 60-year-old woman with “probable” sporadic Creutzfeldt-Jacob disease (CJD) who manifested with two months history of rapidly progressive dementia and abnormal behavior, speech and gait abnormality, excessive sleepiness and myoclonic jerks. Scalp EEG showed diffuse slowing of background activity to delta range and triphasic sharp wave complexes occurring periodically twice in one-second interval. Magnetic resonance Imaging (MRI) of brain revealed high signal intensity on T2 weighted image (T2WI) and fluid attenuated inversion recovery sequences in the caudate and putamen bilaterally. Diffusion weighted images showed bilateral symmetric hyperintense signals in the caudate and putamen. The role of MRI in the diagnosis of CJD is discussed.

Key words: Creutzfeldt-Jacob disease, creutzfeldt-jacob disease, magnetic resonance imaging, rapidly progressive dementia

Introduction

Creutzfeldt-Jacob disease (CJD) is a rare prion disease of the nervous system characterized by dementia, myoclonus, ataxia and other inconstant neurological signs. It can be sporadic as well as familial and is usually fatal within one year of onset of symptoms. Its diagnosis often rests on EEG. However, some recent studies have reported signal abnormalities in the deeper gray matter nuclei of the brain, which are characteristically observed in the disease.

We report the characteristic magnetic resonance imaging (MRI) observations of a patient with “probable” sporadic CJD and discuss their significance in the light of current knowledge.

Case Report

A 60-year-old lady manifested with two months history of rapidly progressive illness dominated by dementia in the form of abnormal behavior, irrelevant talk, unprovoked anger and inappropriate cry. During the next one month, she developed unsteady gait, slurring of speech and excessive sleepiness. Later she developed spontaneous jerky movements of legs and became bed-bound, incontinent and unresponsive. She did not have any systemic illness, neurosurgical intervention or hormonal treatment in the past. Her diet was adequate. At admission she had a blank stare with infrequent blinks and absence of vocalization and response to commands. She developed frequent brief-lasting myoclonic jerks involving the limbs, which increased with painful stimuli but not with sound. She developed rigidity of all limbs and stretch reflexes were brisk. Plantar response was flexor. She was subsequently lost to follow-up.

The following investigations were normal: hemogram, platelet count, peripheral blood smear, serum glucose, ammonia, electrolytes, renal, liver and thyroid function tests, X-ray of chest and CT brain (plain and contrast). Lithium was not detectable in the blood. Cerebrospinal fluid (CSF) analysis showed 9 lymphocytes/ cu. mm, protein of 49 mg/dl and glucose of 87 mg/dl. Cytospin analysis of CSF did not reveal any abnormality.

Discussion

There is no epidemiological data available from India, but the national CJD registry at NIMHANS, Bangalore, India have recorded 85 cases of CJD till September 2005. The diagnostic
Creutzfeldt-Jacob disease

Marked accumulation of protease resistant prion protein (PRP)

Dementia, Myoclonus, visual loss, Neuropathy, ataxia etc.

Periodic Triphasic waves (EEG)

CSF: 14-3-3 protein

Presence of florid plaques (like kuru)

Increased glycogen ratio on immunoblot of PRP

Genetics: PrP mutations

Table 1: Differences between the classical and variant Creutzfeldt-Jacob disease

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Classic CJD</th>
<th>Variant CJD</th>
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<tbody>
<tr>
<td>Median age</td>
<td>60 years</td>
<td>28 years</td>
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<tr>
<td>Median duration of illness</td>
<td>4 to 5 months</td>
<td>13 to 14 months</td>
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<tr>
<td>Symptoms</td>
<td>Dementia, Myoclonus, visual loss, ataxia etc.</td>
<td>Psychiatric symptoms, involuntary movements, ataxia, painful dysesthesia</td>
</tr>
<tr>
<td>Periodic Triphasic waves (EEG)</td>
<td>Present</td>
<td>Absent</td>
</tr>
<tr>
<td>Mode of Transmission</td>
<td>Sporadic, Familial, iatrogenic, dural graft, growth hormone etc.</td>
<td>From cattle with bovine spongiform encephalopathy</td>
</tr>
<tr>
<td>Pulsar sign (MRI)</td>
<td>Not reported</td>
<td>&gt;75% of cases</td>
</tr>
<tr>
<td>CSF 14-3-3</td>
<td>Detectable and useful</td>
<td>Not detectable</td>
</tr>
<tr>
<td>Presence of florid plaques</td>
<td>Sparse (10%)</td>
<td>Seen in large numbers</td>
</tr>
<tr>
<td>Presence of agent in lymphoid tissue</td>
<td>Not readily detected</td>
<td>Readily detected</td>
</tr>
<tr>
<td>Immunohistochemistry of brain tissue</td>
<td>Variable accumulation</td>
<td>Marked accumulation of protease resistant prion protein</td>
</tr>
<tr>
<td>Increased glycogen ratio on immunoblot of PRP</td>
<td>Not reported</td>
<td>Marked accumulation seen</td>
</tr>
<tr>
<td>Genetics: PrP mutations</td>
<td>Yes</td>
<td>No; homozygous for methionine at codon 129</td>
</tr>
</tbody>
</table>

CJD - Creutzfeldt-Jacob disease, PRP - Protease resistant prion protein, MRI - Magnetic resonance imaging

Figure 1: Scalp EEG (A) showing characteristic periodic triphasic waves occurring 2 per second with paucity of alpha waves in background activity. MRI brain (B, C, D) - Axial FLAIR image (B) and diffusion-weighted image (C) shows symmetrical hyperintensity (arrow-B, C) in bilateral putamen and caudate head and hypointensity (arrow -D) in same regions on ADC mappings (D) suggestive of restricted diffusion on diffusion weighted image

Additional involvement of the dorsomedial thalamic nucleus may look like “Hockey-stick” along with pulvinar changes. Bilateral pulvinar sign has a sensitivity of 78% and correlates with histological gliosis. The other notable MRI finding in variant CJD is periaqueductal grey high signal without any cerebral atrophy.
been noted that in sporadic CJD spongiosis is responsible for the signal changes, while gliosis in patients with variant CJD. The exact origin of the periodic triphasic complexes, a characteristic EEG abnormality in CJD, is not known but is hypothesized to originate or be modulated from deeper nuclei, especially thalami. These MRI observations and pathological changes noted earlier provide structural correlate for the electrophysiological changes.

This case highlights that MRI may be an additional tool in the diagnosis of CJD and might help in the better understanding of the pathophysiological process.

References

2. Languram MJ, Ayache N. Definition and evaluation of MRI based measures for the neuroradiological investigation of CJD. ECTRIM News No. 60; Jan 2005.

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