Creutzfeldt-Jakob Disease (CJD) is caused by misfolded prion protein (PrPsc), its typical clinical characteristic is progressive mental deterioration [1]. However, some cases can present atypically that lead to clinical misdiagnosis [2]. Some technical and laboratory examinations, such as EEG, MRI, laboratory tests (CSF 14-3-3 and RTQuIC), and prion protein gene (PRNP) sequencing, can help us make diagnosis more accurate [3]. Here, we report an atypical and sporadic CJD case and review some articles about CJD to help us better understand this rare disease.

Case Presentation

A sixty-three years old man who used to be a butcher presented to the emergency department with a two-month history of acute neurological disorders. At first, he was misdiagnosed as encephalitis or brucellosis during the first visit to the local hospital. After one month, the patient presented progressive walking unstable, myoclonus, gatism, anepia, eating disorder, and blindness had occurred in a short period. Then he was transferred to our department. When he arrived at our department, he was in akinetic mutism. Neurological examination revealed hypnody, anisocoria, paroxysmal tremor on double upper limbs, head and face, Babinski’s sign was positive on the right side. Magnetic Resonance Imaging (MRI) revealed hyperintensity of the cortex and the caudate heads on both sides on diffusion-weighted imaging (Figure 1). Electroencephalography revealed triphasic slow waves. The test of 14-3-3 proteins in cerebrospinal fluid, which are known markers of prion disease, was positive. The polymorphic codon 129 of the prion protein gene (PRNP) is homozygous for Methionine (M/M) genotype. Given the patient’s clinical characteristics and auxiliary examination results, he was diagnosed as sporadic CJD (sCJD). The patient died because of gastrointestinal tract hemorrhage nine weeks after the initial onset of symptoms.

Discussion

Prion disease is caused by the infectious proteins, misfolded forms of the prion protein (PrPsc). CJD is the most common human prion disease, it accounts for more than 90 percent of sporadic prion disease [1]. It exists in four forms: sporadic (sCJD), familial (fCJD), iatrogenic (iCJD) and variant CJD (vCJD) [2]. The typical clinical characteristics are progressive mental deterioration and myoclonus [3]. However, ten percent of cases may present atypically [4]. Some CJD patients may present with isolated neurological symptoms, or atypical neurological presentations, they can almost mimic all features of neurological disease, then leading to clinical misdiagnosis [5]. Here, we review some articles and conclude the mimicking diseases (Table 1). The PrPsc has transmissibility and can spread by cell-to-cell, tissue-to-tissue, host-to-host, and its main histology features are spongiform change, neuronal loss, and accumulation of the abnormal prion protein [6]. PrPsc can spread in several ways, such as the alimentary tract, the skin, and the nasal mucosa. Oral transmission and aerosol transmission have been reported [7,8]. The efficiency of intragastric infection is about 1/40,000 of
Table 1: Creutzfeldt-Jakob disease mimicking diseases.

<table>
<thead>
<tr>
<th>Case</th>
<th>Sex</th>
<th>Age</th>
<th>Common early clinical symptoms</th>
<th>Mimicking disease</th>
<th>MRI</th>
<th>EEG</th>
<th>Histology/ Biochemistry</th>
<th>Duration</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heiso PS, et al. [16]</td>
<td>M</td>
<td>83</td>
<td>Mild headache, behavioral changes, cognitive impairment, and irritability</td>
<td>Focal epilepsy</td>
<td>Possible postictal changes</td>
<td>Seizure activity</td>
<td>CSF 14-3-3 protein (+)</td>
<td>3 m</td>
<td>sCJD</td>
</tr>
<tr>
<td>Miyake K, et al. [17]</td>
<td>F</td>
<td>82</td>
<td>Memory disturbance; unable to move her right hand well, right arm sometimes elevated involuntarily. Tonic convulsion</td>
<td>Status epilepticus</td>
<td>Ribbon-like high intensity</td>
<td>Showed spikes in the left parietal region, and slow wave bursts in the bilateral frontal areas</td>
<td>Diffuse cortical atrophy; typical spongiform changes; synaptic depositions of prion protein</td>
<td>3 y</td>
<td>sCJD</td>
</tr>
<tr>
<td>Ahn SW, et al. [18]</td>
<td>M</td>
<td>46</td>
<td>Lethargy, delusion of persecution, and auditory hallucinations depression and compulsive behavior</td>
<td>Schizophrenic</td>
<td>Cortical high signal intensities indicating a typical cortical &quot;ribbon&quot;</td>
<td>Periodic triphasic waveforms with background slowing</td>
<td>CSF 14-3-3 protein (+)</td>
<td>Sustained vegetative state; &gt;2 y</td>
<td>sCJD</td>
</tr>
<tr>
<td>Sharma DK, et al. [4]</td>
<td>F</td>
<td>68</td>
<td>Left frontal headache, word-finding difficulties, Dyslexia, apraxia, and some perseveration.</td>
<td>Stroke</td>
<td>Unremarkable and consistent with age.</td>
<td>Normal</td>
<td>CSF 14-3-3 protein (+)</td>
<td>3 m</td>
<td>sCJD</td>
</tr>
<tr>
<td>Goosse K [19]</td>
<td>F</td>
<td>65</td>
<td>Progressive cognitive impairment, drunken man’s gait and double vision.</td>
<td>Wernicke encephalopathy</td>
<td>Normal</td>
<td>Diffuse encephalopathic pattern with delta waves parietotemporally and sharp slow waves without triphasic complexes</td>
<td>Deposits of prion proteins CSF 14-3-3 protein (+)</td>
<td>2 m</td>
<td>sCJD</td>
</tr>
<tr>
<td>Dirzius E, et al. [20]</td>
<td>F</td>
<td>53</td>
<td>Blurred vision, dizziness, disturbed gait and coordination Impairment</td>
<td>Posterior reversible encephalopathy syndrome</td>
<td>Normal</td>
<td>Normal</td>
<td>Prion protein scrapie (PrPSc) (+)</td>
<td>13 m</td>
<td>sCJD</td>
</tr>
<tr>
<td>Winton-Brown T, et al. [21]</td>
<td>M</td>
<td>61</td>
<td>Confusion, word-finding difficulties, slurred speech, and right-hand clumsiness</td>
<td>Catatonia</td>
<td>Cortical and basal ganglia hyperintensity</td>
<td>None</td>
<td>CSF 14-3-3 protein (+) spongiform encephalopathy, neuronal loss, and gliosis</td>
<td>4 w</td>
<td>sCJD</td>
</tr>
<tr>
<td>Zuhorn F, et al. [22]</td>
<td>F</td>
<td>75</td>
<td>Rapid progressive cognitive impairment.</td>
<td>Autoimmune encephalitis with CASPR2 antibodies</td>
<td>Multiple microangiopathic lesions</td>
<td>Generalized periodic pattern with triphasic waves</td>
<td>CSF 14-3-3 proteins (+); spongiform encephalopathy</td>
<td>unknown</td>
<td>sCJD</td>
</tr>
<tr>
<td>Yang HY, et al. [23]</td>
<td>M</td>
<td>57</td>
<td>Depression, early morning awakening, anhedonia and chronic back pain</td>
<td>Psychiatric disorders</td>
<td>Hyperintensities in the cerebral cortex and bilateral basal ganglia</td>
<td>Normal</td>
<td>CSF 14-3-3 protein (+)</td>
<td>unknown</td>
<td>sCJD</td>
</tr>
</tbody>
</table>

Figure 1: Diffusion-weighted Imaging. Hyperintensity of the cortex and the caudate heads on both sides (Arrows).

Based on the data of China CJD surveillance network, this rare disease in China has been obviously underestimated [14]. Most Chinese sCJD patients often visit physician, psychiatrist or neurologist in local hospital at the early stage of disease, some atypical psychiatric and neurological symptoms and signs may be ignored in clinical diagnosis. Thus, differential diagnosis of sCJD remains challenging because of a huge overlap of clinical presentations [15]. Therefore, for possible CJD patients, CJD-associated technical/laboratory examinations, such as EEG, MRI, laboratory tests (CSF 14-3-3 and RT-QuIC), and PRNP sequencing, as much as possible are highly recommended in clinical diagnosis. In summary, in clinical work, it is very important that better recognition of sporadic CJD can help to increase diagnosis accuracy and decrease misdiagnosis of CJD.

Ethical Standards

The authors assert that all procedures contributing to this work comply with the ethical standards of the relevant National and Institutional Committees on Human Experimentation and with the Helsinki Declaration of 1975, as revised in 2008.

Acknowledgment

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References


