A Case of Creutzfeldt-Jakob Disease Showing Decreased Cerebral Blood Flow on Tc-99m ECD SPECT at an Early Stage

Pacient s Creutzfeldtovou-Jakobovou nemocí se sníženým prokrvením mozku na Tc-99 ECD SPECT v počátcích choroby

Abstract

This report presents the case of a Japanese man who presented with disturbed position sense in his left leg and later developed ataxia. Tc-99m ECD SPECT showed reduced perfusion in the parieto-temporal regions, especially in the left temporal area, although there were no abnormalities on the first MRI-diffusion-weighted images (DWI). After the first MRI, he developed a disturbance of short-term memory, disorientation, and myoclonus of the left upper extremity, and he could no longer utter words. One month after the first MRI, repeat MRI-DWI showed bilateral abnormalities in the cerebral cortex, putamen, and caudate head. A cerebrospinal fluid (CSF) test revealed that CSF 14-3-3 protein was positive, and the neuron-specific enolase (NSE) level was 300 pg/ml. The prion protein gene showed M/M polymorphism at codon 129. On the basis of his symptoms, clinical course, and laboratory findings, the patient was diagnosed as having probable Creutzfeldt-Jakob disease (CJD). These results suggest that SPECT may be more sensitive than MRI for detecting the abnormalities of sporadic CJD.

Souhrn

Prezentujeme kazuistiku pacienta japonského původu, u nějž došlo k poruše polohocitu na levé dolní končetině a později k rozvoji ataxie. Tc-99m ECD SPECT prokázal sníženou perfuzi v parieto-temporálních oblastech, obzvláště v levé temporální oblasti, přestože na prvních difuzně vážených MR sekvencích nebyly nalezeny žádné abnormity. Po prvním MR došlo u pacienta k rozvoji poruch krátkodobé paměti, dezorientaci a myoklonu levé horní končetiny, pacient nebyl schopen vyslovit jediné slovo. MR-DWI provedené měsíc po prvním MR prokázalo bilaterální abnormity v mozkové kůře, putamen a nucleus caudatus. Při vyšetření likvoru byl pozitivní nález proteinu CSF 14-3-3 a hladina neuron-specifické enolázy dosahovala 300 pg/ml. Pacient je nositelem M/M polymorfizmu na kodonu 129 genu pro prionový protein. Na základě těchto symptomů, klinického průběhu a laboratorních vyšetření byla u pacienta diagnostikována Creutzfeldtova-Jakobova nemoc (CJD). Tyto výsledky naznačují, že SPECT vyšetření by při zjišťování abnormit sporadické CJD mohlo být citlivější než MR.

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Accepted for review: 13. 4. 2010
Accepted for press: 18. 10. 2010

Key words

Creutzfeldt-Jakob disease – early stage – MRI – SPECT – cerebral blood flow

Klíčová slova

Creutzfeldtova-Jakobova nemoc – počátek choroby – SPECT – prokrvení mozku

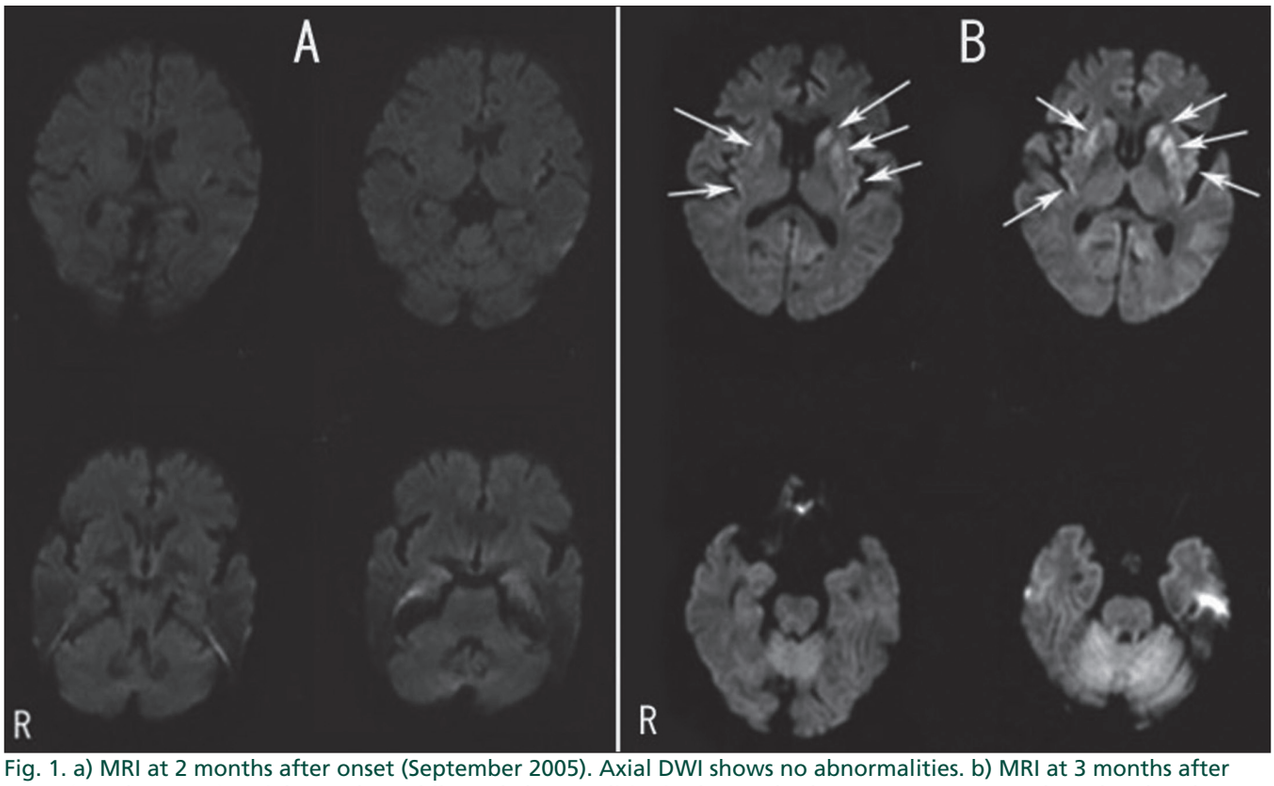

Fig. 1. a) MRI at 2 months after onset (September 2005). Axial DWI shows no abnormalities. b) MRI at 3 months after onset (October 2005). Axial DWI shows bilateral abnormalities in the cerebral cortex, putamen, and caudate head.

Introduction

Creutzfeldt-Jakob disease (CJD) is a neurodegenerative disorder caused by an abnormal prion that promotes refolding of native proteins, disrupts cell function, and causes cell death, because the number of misfolded protein molecules increases exponentially. Diagnosis is difficult unless the patient presents with typical symptoms, such as progressive dementia and myoclonus. MRI diffusion-weighted imaging (DWI) is useful for the accurate diagnosis of CJD at an early stage [1,2]. This report presents the case of a Japanese man who developed disturbed position sense in his left leg followed by ataxia. Single photon emission computed tomography using technetium-99m ethyl cysteinate dimer (Tc-99m ECD SPECT) showed reduced perfusion in the parieto-temporal regions, especially in the left

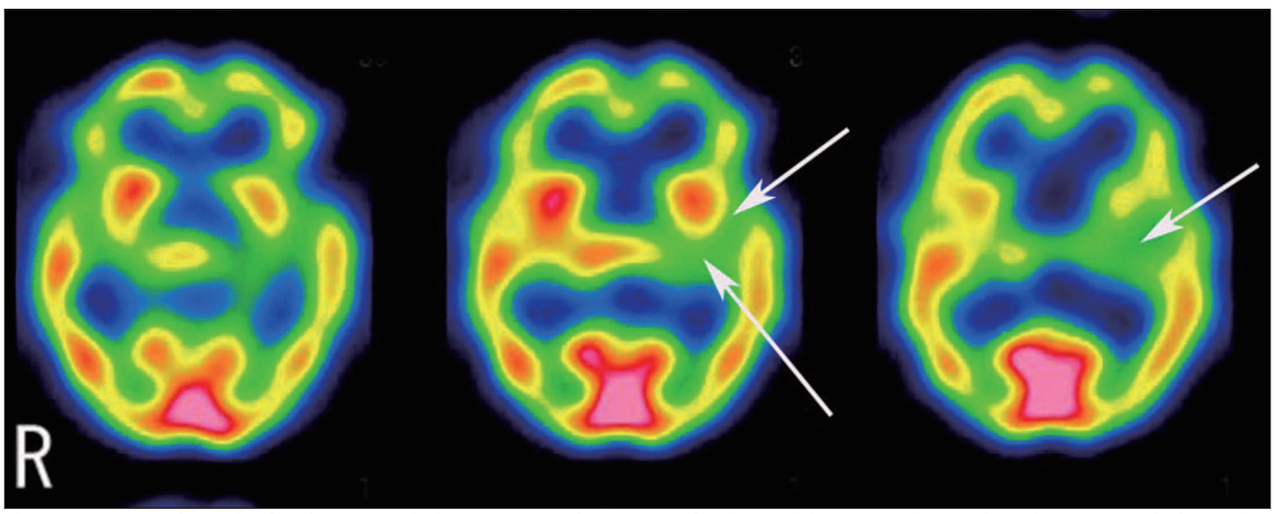

Fig. 2. In September, single photon emission computed tomography (SPECT) images using technetium-99m ethyl cysteinate dimer (ECD) show reduced perfusion in the parieto-temporal regions, especially the left temporal area.

temporal area, although there were no abnormalities on MRI-DWI and there was no periodic synchronous discharge (PSD) on electroencephalography (EEG) in the early stage.

Case report

The patient was a 73-year-old farmer. He had previously undergone thoracoplasty because of pulmonary tuberculosis at the age of 23 years and an appendectomy at the age of 40 years. He noticed stiffening of both ankles in August, 2005. His ability to walk became unstable later that month. He was admitted to our hospital in early September 2005. A neurological examination at the time of admission revealed mild ataxia of both feet, a slightly disturbed position sense in the left foot, and a wide-based gait. Mini-mental state examination (MMSE) score was 28 (normal, >24). No hand or foot myoclonus was observed. No abnormalities other than mild age-related atrophy were observed on CT and MRI, including DWI (Fig. 1a). Tc-99m ECD SPECT was performed and showed reduced perfusion in the parieto-temporal regions, especially the left temporal area (Fig. 2). The patient showed no signs of cognitive deterioration at the time of the SPECT examination. A thorough examination showed no malignancies, thus ruling out paraneoplastic cerebellar syndrome. In addition, anti-neuronal antibodies such as anti-Hu and anti-Yo were negative. Electroencephalography (EEG) showed a small number of slow waves (6–7 Hz) among the normal waves (Fig. 3a). In gradual fashion, his speech became explosive. Disturbance of short-term memory and disorientation developed in late September. He then lost the ability to form words, and myoclonus in the left upper extremity developed in early October, followed by an involvement of the right upper extremity later that month. CJD was therefore suspected, and MRI was repeated. MRI-DWI showed bilateral abnormalities in the cerebral cortex, putamen, and caudate head (Fig. 1b). Cerebrospinal fluid (CSF) examination revealed that 14-3-3 protein was positive, and the neuron-specific enolase (NSE) level was 300 pg/ml. The prion protein gene showed M/M polymorphism at codon 129. On the basis of his symptoms, clinical course, and laboratory findings, the patient was diagnosed as having probable CJD. In November, EEG showed increased theta and delta waves, and continuous, periodic, synchronous discharges (PSD) at 1 Hz (Fig. 3b). The patient then developed akinetic mutism and died eight months after the onset of symptoms. An autopsy was not performed.

Discussion

MRI, especially MRI-DWI, is useful for the diagnosis of CJD even at an early stage. Abnormalities on MRI-DWI can be detected in patients with prion disease prior to development of brain atrophy or typical symptoms such as progressive dementia and myoclonus [1,2]. Decreased regional cerebral blood flow (CBF) can be seen on SPECT before brain atrophy appears on CT [3]. However, few studies have addressed the sensitivity of MRI or SPECT for detecting CJD abnormalities. Generally, some inherited prion diseases (Gerstmann-Sträussler-Scheinker syndrome, familial CJD, and fatal familial insomnia) demonstrate cerebellar symptoms, normal cerebellar MRI, and decreased CBF on SPECT [4,5].

Sporadic CJD is classified into six types, MM1, MV1, VV1, MM2, MV2, and VV2, in combination with a band pattern (type 1 and type 2) of prion protein on Western blots and M or V of codon 129 polymorphism (M/M, M/V, V/V) [6]. MM2 type is further classified into cortical and thalamic forms. However, the thalamic form does not show PSD, and no abnormalities are observed on MRI [7,8]. Hamaguchi et al [9] reported a case of MM2 thalamic form with decreased blood flow in the bilateral thalamus from the early stage. On the basis of his symptoms, clinical course, and laboratory findings, the patient was diagnosed as having probable CJD. MM1 was suspected in the present case because myoclonus and PSD on EEG were seen during the disease course, although an autopsy and Western blotting were not performed. Thus, decreased CBF on SPECT might also be observed earlier than abnormalities on MRI even in sporadic CJD,

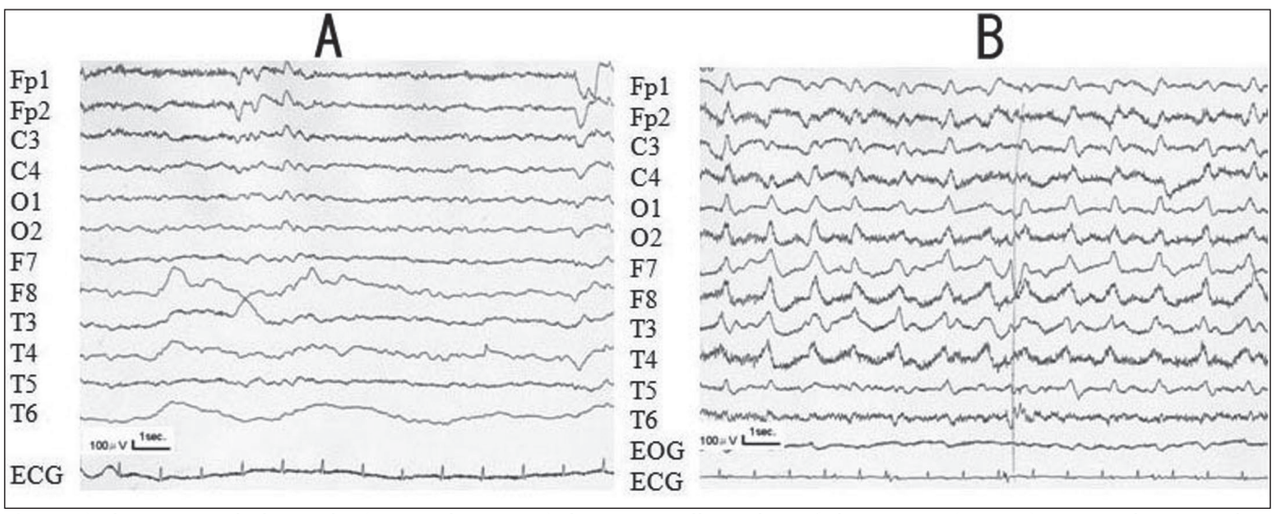

Fig. 3. a) Electroencephalography (September, 2005) shows a small number of slow waves (6–7 Hz) among the normal waves. b) Electroencephalography (November, 2005) shows continuous periodic synchronous discharges (PSD) at 1 Hz.

including MM1. SPECT may be more useful for visualizing the affected area at an early stage. Although the detailed mechanism is unclear, the deposition of prion-impaired neurons and glial cells may decrease CBF.

MRI is usually performed earlier than SPECT in patients who develop ataxia of unknown origin. However, CJD should be suspected if reduced CBF is observed in patients without any abnormal findings on MRI, and MRI should then be repeated, while other examinations, such as CSF NSE and 14-3-3 protein levels, should also be performed.

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