Familial Creutzfeldt-Jakob Disease with a Codon 200 Mutation Presenting as Thalamic Syndrome: Diagnosis by Single Photon Emission Computed Tomography using $^{99m}$Tc-ethyl Cysteinate Dimer

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Abstract

The clinical features of familial Creutzfeldt-Jakob disease with a codon 200 point mutation [fCJD (E200 K)] are similar to those of sporadic CJD (sCJD). MRI diffusion-weighted imaging (MRI-DWI) has been reported to be useful for the early diagnosis of CJD. We describe a Japanese fCJD (E200K) case in which thalamic symptoms were the initial manifestations. On admission, electroencephalography (EEG) showed no periodic synchronous discharge (PSD), and MRI showed no abnormalities. However, single photon emission computed tomography (SPECT) using $^{99m}$Tc-ethyl cysteinate dimer ($^{99m}$Tc-ECD) revealed hypoperfusion in the right thalamus. We conclude that the thalamic form of CJD tends to show no high-intensity area (HIA) by MRI-DWI, and that SPECT may be more useful for visualizing the affected area responsible for the thalamic symptoms at an early stage.

Key words: familial Creutzfeldt-Jakob disease, E200K, diffusion-weighted MRI, SPECT, thalamic syndrome

(DOI: 10.2169/internalmedicine.47.0307)

Introduction

The neurodegenerative disorders fCJD, Gerstmann-Straussler-Scheinker syndrome and fatal familial insomnia (FFI) have been recognized as the three major forms of inherited prion disease, based on their distinct disease phenotype and association with various mutations of the prion protein (PrP) gene. More than 20 mutations of the PrP gene have been described. The E200K mutation is the most frequent cause of fCJD, seen in more than 70% of families with CJD worldwide. Regarding the degree of clinical heterogeneity associated with this mutation, some authors have reported similarity to that observed in sCJD (1), and others have indicated that it is present in some cases of the thalamic form of CJD (2, 3).

Here, we present the first reported Japanese case of fCJD (E200K) manifested initially as thalamic symptoms in which no HIA was evident by MRI-DWI, but focal hypoperfusion was identified in the thalamus by SPECT.

Case Report

The patient was a 62-year-old Japanese woman. Her nephew had died of CJD at the age of 45 years. PrP gene analysis showed E200K, with methionine/methionine polymorphism at codon 129 and glutamine/glutamine polymorphism at codon 219. The presenting clinical symptoms in the nephew were insomnia, appetite loss and dementia. Involuntary movements such as tremor and myoclonus developed rapidly. EEG showed PSD and MRI-DWI showed high-intensity areas (HIA) in the basal ganglia two months after onset. Akinetic mutism then developed. The duration of illness was 7 months.

In July 2004, the patient developed insomnia, and also dysesthesia on the left side of the face, which spread pro-
The present patient had ataxia, hemichorea, disturbance of both superficial and deep sensation, and spontaneous pain on the left side. These symptoms closely resemble the features of thalamic syndrome reported by Dejerine and Roussy (5). She also suffered from insomnia. A case of fCJD (E200K) characterized clinically by insomnia and autonomic disturbance and neuropathologically by severe thalamic involvement has been reported by Chapman et al (2), and Taratuto et al (3) concluded that insomnia may be a prominent early symptom in cases of CJD linked to the E200K-129M haplotype in which the thalamus is severely affected. These findings suggested that the present patient had the thalamic form of fCJD (E200K).

The thalamic form of CJD, characterized by severe degeneration of the thalamus and inferior olivary nuclei, has been reported in some prion diseases including FFI (6), the MM2-thalamic form of sCJD (2), and fCJD (E200K) (3). Sporadic CJD has been classified on the basis of the genotype at polymorphic codon 129 of the PrP and the physicochemical properties of the pathologic PrP; various classification systems have been proposed (7-11). A simple classification for sCJD has been widely accepted, and now at least six phenotypes are recognized: MM1, MV1, VV1, MM2, MV2, and VV2 (9). In the MM2 thalamic phenotype, the clinical features are insomnia and psychomotor hyperactivity in addition to ataxia and cognitive impairment (9). This phenotype may be called sporadic fatal insomnia (SFI) because the clinical and pathologic features resemble those of FFI (12, 13). In the MM2 thalamic form or SFI, lack of PSD on EEG, positivity or negativity for 14-3-3 protein in CSF, and normal findings of brain MRI have been reported (12, 13).

The clinical features of fCJD (E200K) are reportedly similar to those of the classical form of CJD, usually presenting as rapidly progressive dementia associated with myoclonus, cerebellar, pyramidal and extrapyramidal signs, akinetic mutism, and PSD on EEG (1). However, in the present patient, PSD did not appear until 14 months after onset.
This feature resembles those of previously reported patients with MM2 thalamic sCJD (9) or SFI (12, 13).

In the present patient MRI-DWI revealed a HIA in the right caudate nucleus 8 months after onset. Our patient had no HIA in the thalamus, and SPECT demonstrated thalamic hypoperfusion, findings that are compatible with the thalamic form of CJD, as described below. It is likely that, in the thalamic form of fCJD (E200K), thalamic degeneration never appears as an abnormal signal on MRI-DWI during the disease course, although the appearance of spongiform degeneration in other areas would be revealed as hyperintensity. In our patient, hypoperfusion in the right thalamus revealed by SPECT corresponded to the patient’s neurological symptoms. When these symptoms spread to the bilateral extremities, the area of hypoperfusion extended to the bilateral thalamus (Fig. 1b). Mastrianni et al reported thalamic hypometabolism in SFI (13). Thalamic hypoperfusion or hypometabolism revealed by CBF-SPECT or [18F]2-fluoro-2-deoxy-D-glucose ([18F] FDG) and positron emission tomography (PET), which have been reported in FFI (14) and the MM2-thalamic form of sCJD (15), is useful for the diagnosis of this form of CJD.

In summary, the thalamic form of fCJD (E200K) at the early stage does not show any HIA by MRI-DWI, but SPECT demonstrates focal hypoperfusion in the affected area of the thalamus, which is helpful for diagnosis of the thalamic form of CJD.

Acknowledgement
The authors would like express their gratitude to Drs. T. Kitamoto and K. Doh-ura from the Department of Prion Research, Tohoku University Graduate School of Medicine, for searching the PrP gene and measuring 14-3-3 protein.

References

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