healthy controls. Direct sequencing of the *PRNP* gene identified a heterozygous p.Asp179Asn mutation homozygous for methionine at codon 129 and for glutamate at codon 219. The results of the SPM analysis showed marked hypometabolism in the deep cerebral nuclei (including the bilateral thalami, caudate nuclei, and hypothalamus), association cortices (including the frontal, lateral temporal, inferior parietal lobule and posterior cingulate gyri), and midbrain. ***Conclusions:*** This is the first Korean report of FFI, in which the family showed male phenotypic predominance. The patient's SPM analysis demonstrated brain hypometabolism in the midbrain and the hypothalamus, as well as the thalami, caudate nuclei, and multiple cortical regions. These results contribute further to the overall understanding of the pathophysiology of FFI.

Introduction

Fatal familial insomnia (FFI) is a rare disease characterized by intractable insomnia, dysautonomia, and mental deterioration [1]. FFI is classified as a genetically transmitted human transmissible spongiform encephalopathy [1]. Point mutation at codon 178 of *PRNP* is the diagnostic genetic abnormality of FFI.

We herein report a patient with FFI, who, to our knowledge, is the first case in the Korean population. In addition to a detailed history and the results of comprehensive neuropsychological tests, we also present the patient's statistical parametric mapping (SPM) analysis of [^{18}F]-fluorodeoxyglucose positron emission tomography (FDG-PET) compared with 7 age-matched normal controls.

Case Report

Clinical Description

The patient was a 34-year-old Korean man who visited our emergency department complaining of intractable insomnia and progressive dementia. The patient suffered from intractable insomnia and irregular, coarse breathing during sleep, which began 9 months before admission. He consequently developed excessive sweating, bilateral action tremors, and restlessness. Memory disturbance and poor executive function were noticed 2 months before admission. Delusions of persecution and social withdrawal were also present. Three days before admission, the patient began to show gait disturbance with mild postural instability.

The patient had been in good health before disease onset. He had 16 years of education, majored in law, and worked as a civil servant at the district court until he lost his job due to memory disturbance.

His vital signs showed a marked fluctuation in blood pressure, tachycardia, and tachypnea. His initial body temperature was 38.0°C, which was stabilized after controlling his pneumonia.

Neurologic examination revealed disorientation and anomic aphasia with paraphasia. The Korean version of the Mini-Mental State Examination score was 17 out of 30. Hypophonia, dysarthria, both resting and action tremors, and akathisia were present. His gait was ataxic with a tendency of tilting backwards. Otherwise, cranial nerve functions, muscle volume, tone, and power as well as sensory functions were normal. Extrapyramidal signs such as rigidity or bradykinesia were absent. Deep tendon reflexes were normoactive without pathologic reflexes.

Routine blood labs showed no abnormalities. Both plasma and urine catecholamine levels were elevated. Cerebrospinal fluid analysis was unremarkable and the patient was negative for 14-3-3 protein.

Family History

The patient's four-generation pedigree is presented in fig. 1 . The patient's mother (III:7), who was a physically and mentally healthy 70-year-old woman, had the same mutation. An asymptomatic brother of the proband (IV:12) was negative for the *PRNP* gene mutation. The son of the patient's great-aunt (II:1) had gradually developed hypersomnia, gait disturbance, ataxia, and dysarthria. His cerebrospinal fluid study was positive for 14-3-3 protein. The genetic analysis of subject II:1 revealed a *PRNP* gene mutation at codon 178 (D178N) and homozygosity for methionine at codon 129. Total disease duration was 27 months.

Fig. 1

The pedigree of a Korean family with FFI. The diagonal bar indicates a deceased member. Arrow = The proband.