Brain MRI, Tc-99m HMPAO SPECT and F-18 FP-CIT PET/CT Findings in a Patient with Wilson Disease: A Case Report

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Abstract A 34-year-old female had experienced head and hand tremors with a dystonic component for 8 months. Brain MRI showed T2 high signal intensity in the periaqueductal region, dorsal midbrain and dorsal upper pons. No abnormal uptake was noted on Tc-99m HMPAO SPECT or F-18 FP-CIT PET/CT. Wilson disease was diagnosed according to the 2008 consensus guideline from the American Association for the Study of Liver Disease and 2012 guideline from the European Association for the Study of the Liver. This case demonstrates T2 signal change in the basal ganglia, excluding the putamen, in a Wilson disease patient with relatively severe clinical findings, but normal Tc-99m HMPAO SPECT and F-18 FP-CIT PET/CT.

Keywords Wilson disease · MRI · Tc-99m HMPAO SPECT · F-18 FP-CIT PET/CT

Introduction

Wilson disease is an uncommon, autosomal recessive, inborn defect in copper metabolism characterized by abnormal accumulation of copper in various tissues, particularly the liver and brain.

Magnetic resonance imaging (MRI) is helpful in the clinical diagnosis of neurodegenerative disorders, because MRI

enables visualization of the degenerative process showing either atrophy or abnormal signal intensity in affected areas.

Tc-99m HMPAO (hexamethylpropyleneamine oxime) SPECT (single photon emission computed tomography) provides information on the regional perfusion status of the brain.

Fluorinated N-3-fluoropropyl-2 β -carbomethoxy-3 β -(4-iodophenyl) nortropane (F-18 FP-CIT), a cocaine analog, binds to the dopamine transporter of presynaptic nerve endings of nigrostriatal neurons in the striatum and is used to evaluate degeneration of presynaptic dopaminergic neurons.

These imaging studies demonstrate morphological and functional changes in patients with Wilson disease. We here describe the brain MRI, Tc-99m HMPAO SPECT and F-18 FP-CIT PET/CT findings of a patient with Wilson disease.

Case Report

A 34-year-old female experienced head and hand tremors with a dystonic component for 8 months. She had been on panic disorder medication for 5 years and was a social drinker. No history of substance abuse and no risk of extrapyramidal side effects were reported. On neurological examination, she showed a head tremor (yes-yes type), which was relieved by a sensory trick, and wing-beating tremor. Her serum ceruloplasmin level was 1.96 mg/dl (normal range: 17.6–53.3 mg/dl) and copper level was 20 μ g/dl (normal range: 70–130 μ g/dl). The 24-h urinary copper excretion was 62 μ g/day. Ultrasonogram revealed mild splenomegaly and coarse hepatic echogenicity with suspicious surface nodularity, suggesting chronic hepatitis or early liver cirrhosis. Slit-lamp examination revealed a Kayser-Fleischer ring in both eyes, a pathognomonic sign. The patient was diagnosed with Wilson disease according to the 2008 consensus guideline from the American Association for the Study of Liver Disease [1] and

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2012 guideline from the European Association for the Study of the Liver [2].

Structural and functional brain imaging was performed, and brain MRI showed T2 high signal intensity in the superior cerebral peduncle, dorsal midbrain and dorsal upper pons (Fig. 1).

There was no perceptible abnormality on Tc-99m HMPAO SPECT (Fig. 2). F-18 FP-CIT PET/CT showed normal findings (Fig. 3).

Discussion

In Wilson disease, a genetically caused copper storage disease, hepatolenticular degeneration manifests as hepatic cirrhosis and basal ganglia damage. Damage to the nervous system is thus caused both directly by copper toxicity and indirectly by hepatic encephalopathy [3].

T2 high signal intensity in the putamen is the most common MRI finding [4]. This is because the copper concentration is the highest and astrocytic reaction is prominent in the putamen in Wilson disease, while under physiological conditions, concentrations of copper can be found in the locus. However, high signal intensity was not observed in the putamen in our patient, and T2 signal change was instead noted in the superior cerebral peduncle, dorsal midbrain and dorsal upper pons. With the exclusion of the putamen, the basal ganglia is affected relatively infrequently [5].

Fig. 1 Brain MRI shows T2 hyperintensity (arrows) on the dorsal midbrain (a), superior cerebral penduncle (b) and dorsal upper pons (c). No abnormal findings were observed in the putamen (d)

Fig. 2 Tc-99m HMPAO SPECT shows no abnormal perfusion

Slight signal abnormalities on T2 images are also often seen in the striatum, thalamus, midbrain and white matter in nonneurological patients [5]. The degree of signal change on MRI increases with disease severity [6], and signal abnormality regresses following decoppering drug therapy [7].

In this case, no abnormal perfusion was noted on SPECT. It is possible that neuronal degeneration was not coupled with perfusion abnormality. Also, because spatial resolution of brain MR surpasses Tc-99m HMPAO SPECT, minimally diminished perfusion could not be excluded.

However, Piga et al. [8] described diffuse or focal hypoperfusion of the superior frontal, prefrontal, parietal, occipital and temporal cortices, caudate and putamen on SPECT.

FP-CIT findings for our patient were normal. As yet, not much has been reported on FP-CIT in Wilson disease. [^{123}I] β -CIT (2 β -carbomethoxy-3-(4-iodophenyl)tropane) SPECT is known to show symmetrically reduced striatum activity in neurological patients compared to healthy controls or nonneurological patients [7, 9]. Severity of neurological symptoms was significantly correlated with [^{123}I] β -CIT binding ratios [10]. Both presynaptic and postsynaptic

Fig. 3 F-18 FP-CIT PET shows no reduced striatal activity

compartments are affected in neurological Wilson disease [9, 10]. This symptomatic patient may have shown negative findings on FP-CIT because the postsynaptic dopaminergic degeneration was more dominant.

We herein report findings of a Wilson disease patient displaying neurological symptoms, whose brain MRI findings involved infrequent sites, without any abnormalities on functional imaging.

Ethics Statement This study was approved by the ethics committee in our hospital and was performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki and its later amendments.

Conflict of Interest Seungyoo Kim, In Uk Song, Yong An Chung, Eun Kyung Choi and Jin Kyoung Oh declare that they have no conflict of interest.

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