

Magnetic Resonance Imaging of Brain in Patient with Late-Onset Wilson's Disease: A Case Report and Review of Literature

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Abstract Wilson's disease is a worldwide inherent gene disorder leads to copper deposition in various tissues. Recently, wilson's disease is classified according to onset of symptoms into early-onset and late-onset wilson. Reported a 56-year-old male patient presenting with dysarthria and dyskinesia. Laboratory tests revealed elevated urinary copper without elevation of liver function tests. Magnetic resonance imaging of the brain was performed and revealed typical bilateral putamena and midbrain tegmental T2 hyperintensity "Face of giant Panda" sign which are reliable imaging features of wilson's disease and the case represents a late-onset type. Medical treatment was prescribed for the patient with regular follow up.

Keywords: copper, late-onset wilson, magnetic resonance imaging, brain, face of giant Panda

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1. Introduction

Wilson's disease (WD) or hepatolenticular degeneration is a worldwide autosomal recessive genetic disorder that occurs in 1 per 30,000 individuals with slight male preponderance [1,2,3,4].

The disease can present at any age, majority of cases present before age of forty. Few cases may present after the fourth decade [5]. In a recent study conducted by Ferenci, two different phenotypes of wilson's disease depending on the age of onset and symptoms were observed: either presenting in childhood and early years of life which usually presents with hepatic symptoms or a late-onset type that presents with neurological symptoms [6].

Diagnosis of Wilson's disease is established by detection of Kayser-Fleischer ring, reduced serum ceruloplasmin, elevated urine and hepatic copper level, hepatic and/or neurologic signs and histological liver changes on biopsy [7].

Magnetic resonance imaging (MRI) of the brain can depict brain changes in different metabolic and genetic disorders including wilson's disease [8]. This case report describes characteristic magnetic resonance imaging brain findings related to late-onset wilson's disease and presents a concise review on differential diagnosis of similar imaging conditions.

2. Case Report

A 56-year-old male patient was referred to the hospital presenting with unsteadiness of gait, abnormal posturing,

incoordination in speech and dizziness with gradual onset and progressive course of nine months duration. Neurological examination revealed dysarthria, ataxia and dyskinesia. No overt hepatic manifestations. Ophthalmic examination revealed Kayser-Fleischer ring. Laboratory tests included elevated 24-hour urinary copper excretion at level 250 mcg/day (Normal: 50-70 mcg/day) and no elevation in liver function tests.

Brain magnetic resonance imaging (MRI) was performed on a 1.5 Tesla (Achieva, Philips Medical System, Best, Netherlands) using head coil according to the following MR imaging protocol: T2 fast spin-echo (Time of repetition/Time of echo) (TR/TE 3732/100) in axial, coronal and sagittal planes, axial fluid attenuated inversion recovery (FLAIR) (TR/TE/TI 6000/120/2000), axial T1 spin echo (TR/TE 488/15) were applied. Field of view 24 cm, 256×256 matrix, 6 mm slices thickness, 1.5 mm slice gap.

MRI brain revealed bilateral symmetrical hyperintensities in T2 weighted images and in FLAIR involving both putamena mainly the peripheral rim (laminar pattern), both caudates (Figure 1, Figure 3), cerebellum, both thalami and both globi pallidi that appear with peripheral hyperintensity in T1 images (Figure 2). Typical hyperintense T2 signal was noted in the tegmentum of midbrain in axial section giving the characteristic "Face of giant panda" with preserved signal of the red nucleus (Figure 4), preserved hypointense signal of the lateral portion of pars reticulata of substantia nigra and hypointense superior colliculus.

The diagnosis of late-onset wilson's disease was concluded according to clinical, laboratory data and MRI brain. Copper chelator was prescribed and follow up was advised.

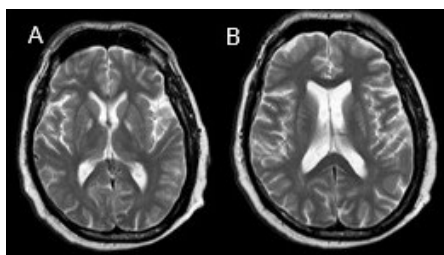


Figure 1. Axial T2 (A&B) MRI brain: Hyperintensities of both lentiform nuclei with laminar pattern

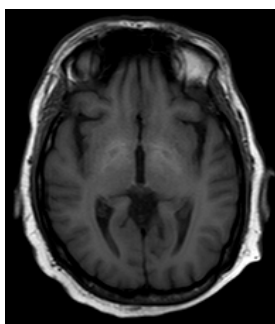


Figure 2. Axial T1WI MRI brain: Peripheral hyperintensity of both globi pallidi

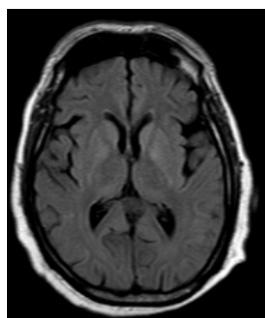


Figure 3. Axial FLAIR MRI brain: Hyperintensities in both basal ganglia and caudates

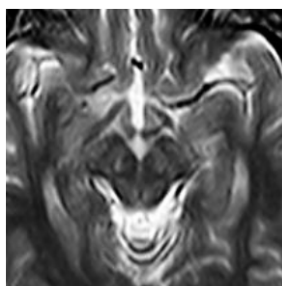


Figure 4. Axial T2WI MRI brain: Characteristic face of giant panda with hyperintense midbrain tegmentum

3. Discussion

Typical signal abnormalities in Wilson's disease could be depicted by MRI brain. The commonest MRI brain changes included symmetrical high T2 signal in both putamina with a concentric-laminar pattern [8,9]. Hyperintense T2 signal in globi pallidi, brainstem, both thalami, cerebellum were observed in many cases [10,11,12]. MRI may depict signal changes in early disease and can monitor cases during therapy [12,13]. The

high signal intensity on T2-weighted images of the basal ganglia may represent edema, gliosis, necrosis and cystic degeneration [12]. In a prospective study done by Sinha et al, a reported incidence of 12% was noted for "face of giant panda" sign in patients with Wilson's disease [14].

A characteristic MRI finding in Wilson's disease is "face of giant panda" sign with hyperintense tegmentum of midbrain in T2-weighted images with preserved signal of both red nuclei and both substantia nigra was reported in many studies [10,15,16].

The pathogenesis of Wilson's disease is based on dysfunction in copper metabolism due to encoded ATP7B gene mutation leading to dysfunction in hepatocytic copper transporter ATPase [7,17]. Disturbance in mechanisms regulating copper metabolism leads to deficiency in ceruloplasmin, a copper carrier in blood and consequently copper accumulation in various tissues including liver and brain [7,17,18,19].

The differential diagnosis of Wilson's disease include bilateral symmetrical basal ganglia hyperintensities that involve toxic, metabolic, degenerative and infectious brain diseases mainly: carbon monoxide poisoning, Wernicke encephalopathy (WE), Creutzfeldt-Jakob-Disease (CJD) and Japanese encephalitis [8].

MRI brain in carbon monoxide poisoning revealed bilateral symmetrical T2 and FLAIR hyperintensities in both globi pallidi, less commonly caudate nucleus, putamen, and thalamus could be affected [20,21]. MRI brain in Creutzfeldt-Jakob-disease detected bilateral symmetrical hyperintense T2 signal in the pulvinar nuclei of both thalami which is considered diagnostic of variant Creutzfeldt-Jakob-Disease (vCJD) [22]. While in Wernicke's encephalopathy, bilateral symmetrical T2 hyperintensities in medial thalami, mammillary bodies, tectal plate, periaqueductal area and periventricular regions of the third ventricle could be depicted in MRI brain [23]. Japanese encephalitis (JE) is caused by infection with the JE virus, which belongs to the mosquito-borne flavivirus group [24]. Definitive diagnosis is based on enzyme-linked immunosorbent assay test that allow detection of antibody in serum and cerebrospinal fluid of the patient [25]. In Japanese encephalitis, computed tomography of the brain can detect hemorrhagic lesions. Bilateral thalamic T2 hyperintensities are noted in MRI brain. Also involvement of basal ganglia, midbrain including substantia nigra and red nucleus, pons, hippocampus, cerebral cortex, cerebellum and subcortical white matter could be detected [24].

4. Conclusion

Brain imaging, particularly MRI brain can demonstrate changes related to metabolic dysfunction based on genetic etiology as in Wilson's disease. Characteristic MRI brain findings can reflect the pathophysiology of the disease and can be useful in monitoring patients during therapy.

5. Consent for Publication

A written informed consent was obtained from the patient participant in the case report.

Conflict of Interest

The author declares no conflicts of interest.

List of Abbreviations

Wilson's disease: (WD)
 Magnetic resonance imaging: (MRI)
 Time of repetition/Time of echo: (TR/TE)
 Fluid attenuated inversion recovery: (FLAIR)
 Wernicke encephalopathy: (WE)
 Creutzfeldt-Jakob-Disease: (CJD)
 Variant Creutzfeldt-Jakob-Disease: (vCJD)
 Japanese encephalitis: (JE)

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