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Magnetic resonance imaging of the brain in Wilson's disease

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Wilson's disease is an autosomal recessive disorder of copper metabolism with increased deposition of copper in the brain and liver. A case of Wilson's disease in a 22-year-old woman was examined by Computed Tomography (CT) and Magnetic Resonance Imaging (MRI) at 1.5 Tesla. MRI demonstrated lesions with hypointense signal on T1 weighted images and mixed hypointense and hyperintense signal on T2 weighted images in both lenticular nuclei. These abnormal signal intensity areas may be caused partly by gliosis, edema or cavitation as well as by copper and iron deposits.

Key words : *Wilson's disease - MRI.*

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โรคของวิลสัน (Wilson's disease) พบได้น้อย ถ่ายทอดได้ทางกรรมพันธุ์ ต้นเหตุอยู่ที่ความผิดปกติของเมตาโบลิสม์ของทองแดง (copper) ทำให้ทองแดงไปสะสมอยู่ในเซลล์ต่าง ๆ ของร่างกาย โดยเฉพาะสมองและตับ รายงานนี้ได้เสนอผู้ป่วยหญิงอายุ 22 ปี ซึ่งตรวจพบความผิดปกติของสมองโดยการตรวจด้วยเครื่องเอกซเรย์คอมพิวเตอร์ (Computed Tomography) และเครื่อง MRI (Magnetic Resonance Imaging) บริเวณเลนติคูลาร์นิวเคลียส (lenticular nucleus) ทั้งสองข้าง ภาพความผิดปกติที่ตรวจพบนี้เป็นผลมาจากไกลโอซีส (gliosis), การบวมเฉพาะที่ของสมอง (edema), ซีสต์ ร่วมกับการสะสมของทองแดง (copper) และเหล็ก (iron) มากกว่าปกติในบริเวณดังกล่าว

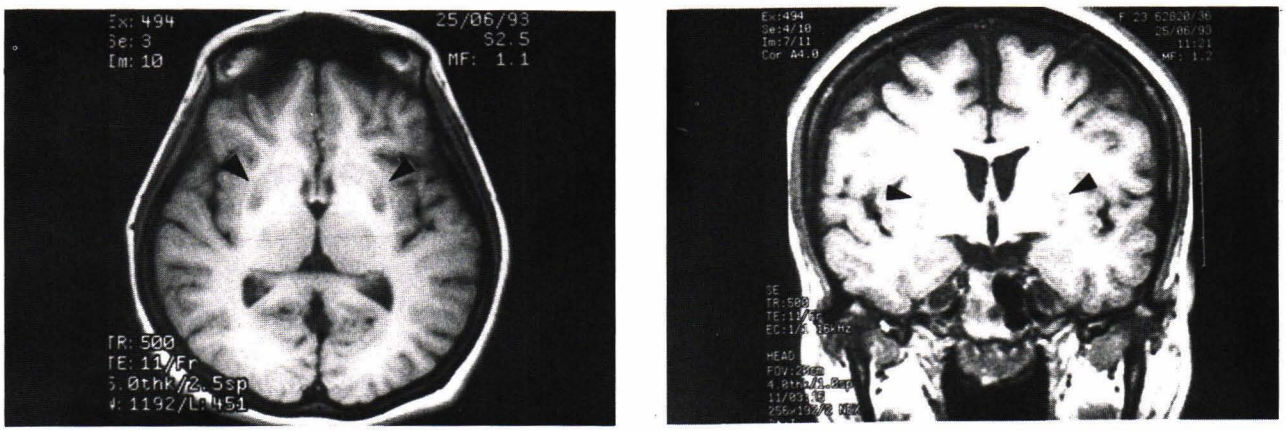
Wilson's disease (hepatolenticular degeneration) is an uncommon inherited autosomal recessive disorder of copper metabolism characterized by a deficiency of ceruloplasmin, the serum transport protein of copper. [1,2] As a result, copper is abnormally deposited in various tissues with resultant toxicity to them. [2] The most pronounced involvement is usually in the liver and brain. MRI (magnetic resonance imaging) provides more detailed anatomical information than CT (computed tomography) of the brain. It also provides biochemical information on the distribution of heavy metal in the brain substance. (3)

Case report

A 22-year-old woman presented with a two-year history of weakness and chronic liver disease. For a half-year period prior to admission, the patient developed emotional lability, deteriorating hand-writing due to rigidity, gait difficulty and dysarthria. Physical examination showed corneal Kayser- Fleischer ring and sunflower cataract of both eyes. Definite diagnosis of Wilson's disease was made biochemically by measuring a low level of serum ceruloplasmin (12 mg% [35 ± 6mg%]), and increased rate of urinary copper excretion to 123 μg/day (26-64 μg/day). A liver biopsy revealed cirrhosis.

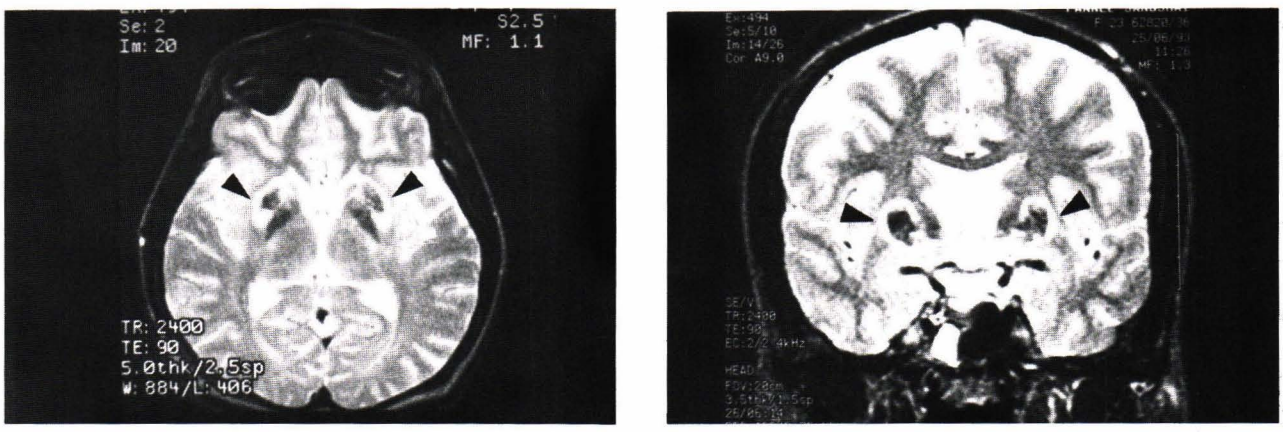
MRI of the brain was performed with a 1.5 Tesla (Signa, General Electric Medical System) using spin echo sequenecs, T_1 weighted images (TR 500 ms, TE 11 ms) and T_2 weighted images (TR 2,400 ms, TE 90 ms) in the axial and coronal planes. Additional noncontrast-enhanced CT of brain was performed with a Sytec 4000 (General Electric Medical System). The study revealed abnormal signal intensities in both basal ganglia, and hypointense signals on T_1 weighted images (Figure 1). These lesions were of mixed hypointense and hyperintense signals on T_2 weighted images (Figure 2). Noncontrast-enhanced CT revealed hypodense areas in both basal ganglia (Figure 3).

Small liver with multiple regenerated nodules, splenomegaly and ascites were demonstrated by CT and MRI (Figure 4).



A

Figure 1. A. Axial T1 weighted MRI (500/11) B. Coronal T1 weighted MRI (500/11). Hypointense signals are noted in both basal ganglia (arrowheads).



B

Figure 2. A. Axial T2 wighted MRI (2,400/90) B. Coronal T2 weighted MRI (2,400/90). Mixed hypointense and hyperintense signals are noted in both basal ganglia.

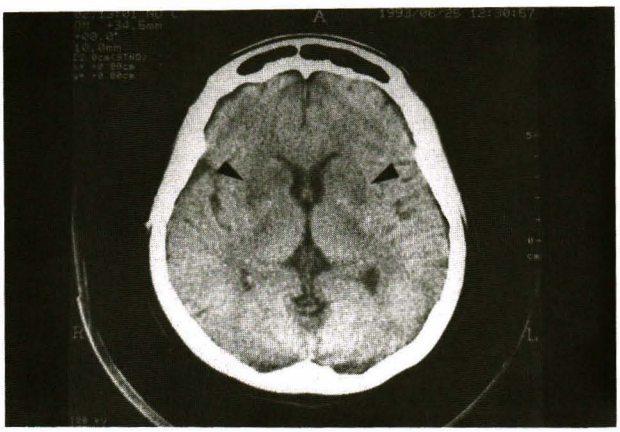


Figure 3. Noncontrast enhanced CT shows hypodense areas in both basal ganglia (arrowheads).

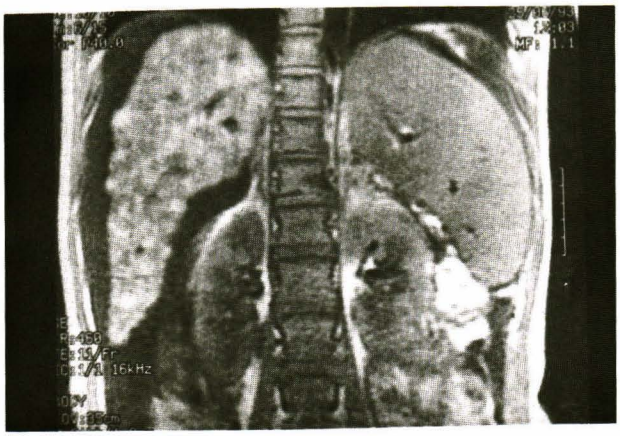


Figure 4. Coronal T1 weighted MRI show small liver with multiple regenerated nodules, splenomegaly and ascites.

Discussion

Several descriptions have been given for the abnormalities found in Wilson's disease, as shown by CT [4-7] and MRI. [2,7-13] The diagnosis of Wilson's disease was based on neurological or hepatic symptoms, the presence of a Kayser-Fleischer corneal ring (a granular deposit of copper in Descemet's membrane), decreased serum levels of ceruloplasmin, elevated urinary copper excretion and increased liver copper content. [7]

Typical sites of cerebral involvement are the deep gray matter and white matter. Involvement of gray matter nuclei is more common and usually bilateral symmetrically with variable involvement of the putamen, caudate nucleus, thalamus, globus pallidus, dentate nucleus, pons and mesencephalon (substantia nigra, periaqueductal gray matter, tectum, and red nucleus). White matter lesions usually are asymmetric, located in the subcortical region or centrum semiovale, and are often in the frontal lobe. Atrophy of the cortex of the cerebral and cerebellar hemispheres and the brain stem has also been described.

Pathologically, gliosis, edema and variable necrosis with cavitation occur [2,6] due to the toxicity of copper and/or secondary changes to ischemia. [8] These changes likely account for the hypointense signal on T_1 weighted images, hyperintense signal on T_2 weighted images and hypodensity on CT. Hypointensity on T_2 weighted images is due either to the paramagnetic effects of copper deposition itself, or some other paramagnetic agent such as iron, causing shortening of T_2-relaxation time. [7] Shortening of T_1-relaxation due to paramagnetic influence of copper was not seen; a possible explanation could be intracellular deposition. [10]

Cerebral MRI findings are correlated well with neurological deficits. Most patients without neurological symptoms have normal MR images, while most patients with neurological symptoms have abnormal studies. [2,8]

Quantitative analysis of the iron and copper content of the brains of patients with Wilson's disease has shown increased amounts of copper in the caudate nucleus, lenticular nuclei and the thalamus. [14] Iron is assumed to play a more important role than copper in reducing the signal intensity in the T_2 weighted images, because the content of iron is much greater in cases of Wilson's disease than copper. [12]

In our patient, we found abnormal signal intensity in the bilateral basal ganglia. Lesions with prolonged T_1 and T_2 relaxation time may reflect gliosis, edema or small cavitary lesions. On the other hand, areas with shortened T_2 relaxation time may be caused by copper and iron deposits. [2,7-13] No abnormality was seen in white matter.

In summary, Wilson's disease is established biochemically. Pathologically, gliosis, edema and variable necrosis with cavitation occur in deep gray matter and white matter of the brain due to the toxicity of copper. We have shown the abnormal density and abnormal signal intensity of the brain demonstrated by CT scan and MRI, respectively. MRI shows not only abnormal signal intensity caused by edema and brain death but also the probable existence of copper and iron deposits. The therapeutic efficacy of chelating agents can be monitored by this imaging.

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