CT AND MRI OF THE BRAIN IN WILSON DISEASE (WILSON'S DISEASE)

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ABSTRACT

Two cases of Wilson disease were presented. One case was 14 years old girl, had low density at pons, midbrain, thalamus, putamen and brain atrophy. New low density lesions and expanded areas of the previous low density areas were noted by CT scan after 4 months follow up. Another case of 31 years old male, his pons and thalamus contained bright signal on T2WI-MRI study. Brain atrophy, mild ventriculomegaly, were seen. Low signal at red nucleus, substantia nigra, globus pallidus and dentate nuclei was shown on T2WI-MRI study.

INTRODUCTION

Wilson disease (hepatolenticular degeneration) is a hereditary disorder characterized by the accumulation of copper in the body, especially in the liver, brain, kidneys and corneas. The excess copper leads to tissue injury and ultimately, if effective treatment is not instituted, to death (1).

The neurologic signs at onset may take a variety of forms. Patients may start with dystonic facies, dystonic postures. Tremor, loss of coordination of fine movements, dysarthria, rigidity, drooling and titubation could be seen. Seizures are infrequent and sensory abnormalities are absent.

Psychological symptoms of Wilson disease are prominent and consist of early development of intellectual deterioration, personality changes, and unstable behavior.

Pathologic changes primarily involve the basal ganglia with neuron loss, spongiform degeneration and demyelination in the putamina and the caudate nuclei. Later, similar changes are seen in the pallidum, dentate nuclei and substantia nigra. Thalamic and cerebellar involvement is less frequent. Scarring and cavitation of the globus pallidus represent late changes (2).

CASE REPORTS

Two patients presented with bradykinesia and dysarthria. One patient was 14 years old girl. Her first CT scan of the brain was on March 3, 1988. It showed multiple low density areas, involving pons, midbrain, both thalami, and putamen. Her second CT scan was on July 22, 1988. There were new low density lesions, at the left cerebellum, and the lesions at pons, thalamus and putamen have enlarged. There was no enhancement within the lesions. The ventricles were midly dilated without midline shift. The ventricles did not change in size after 4 months follow-up (Fig.1).

The second patient was male, age 31 years old. T1WI-axial view MRI scan showed mild brain atrophy with mild ventriculomegaly. T2WI-axial MRI scan showed bright signal, involving pons and both thalami (Fig.2). Dark signal was observed at red nucleus, substantia nigra, globus pallidus, and dentate nucleus (Fig.2)

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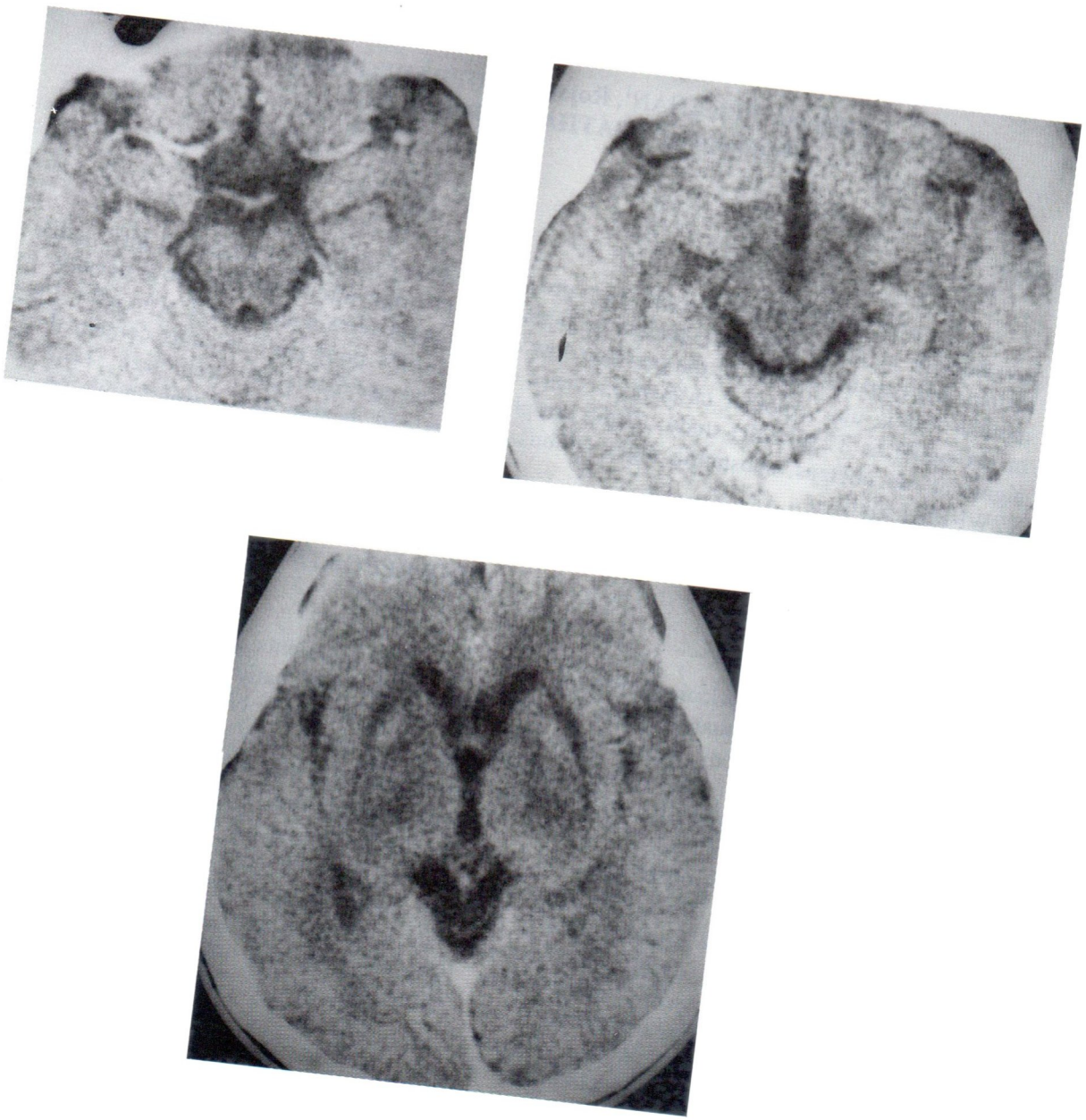

Fig.1A. Case 1. The 1st CT scan on March 3, 1988, showed low density areas at both sides of posterior aspect of pons, midbrain, both thalami and putamens, external capsules without significant contrast enhancement

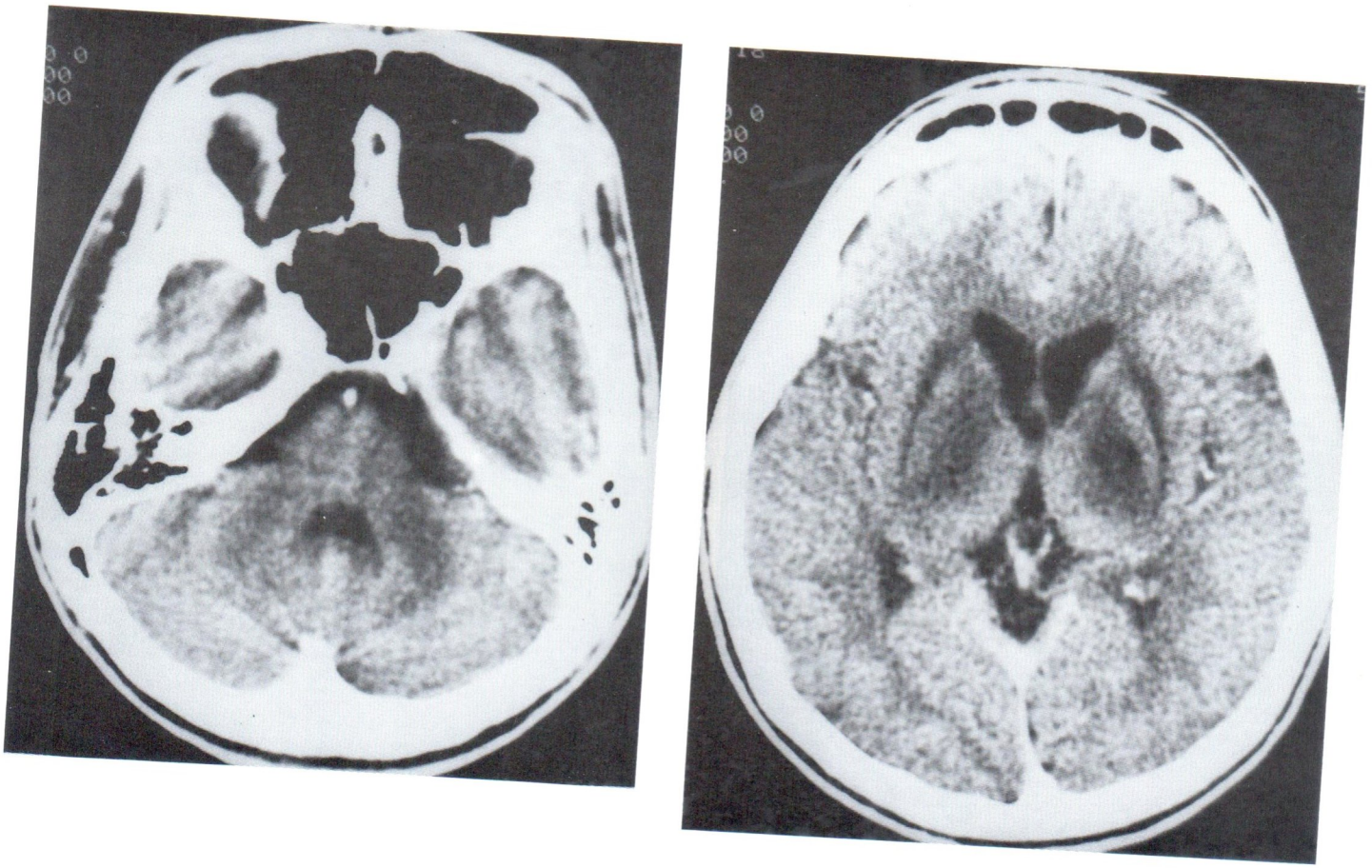

Fig.1B. Case 1. The 2nd CT scan on July 22, 1988 showed a new low density lesion in the left cerebellum. Larger lesions at pons, thalamus, putamen, internal capsules was noted without increasing size of the ventricles.

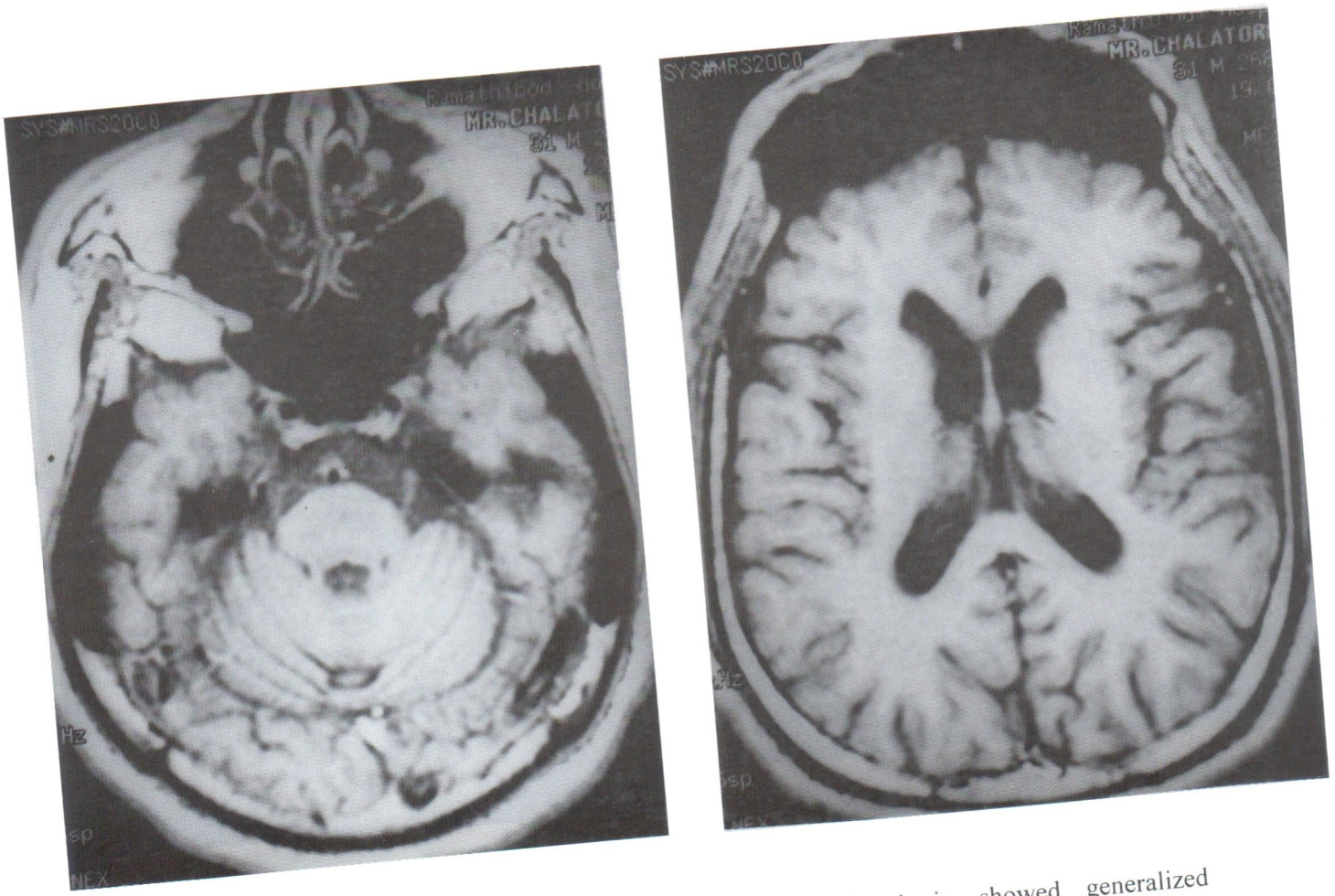

Fig.2A. Case 2. T1WI-Axial view MRI study of the brain showed generalized brain atrophy.

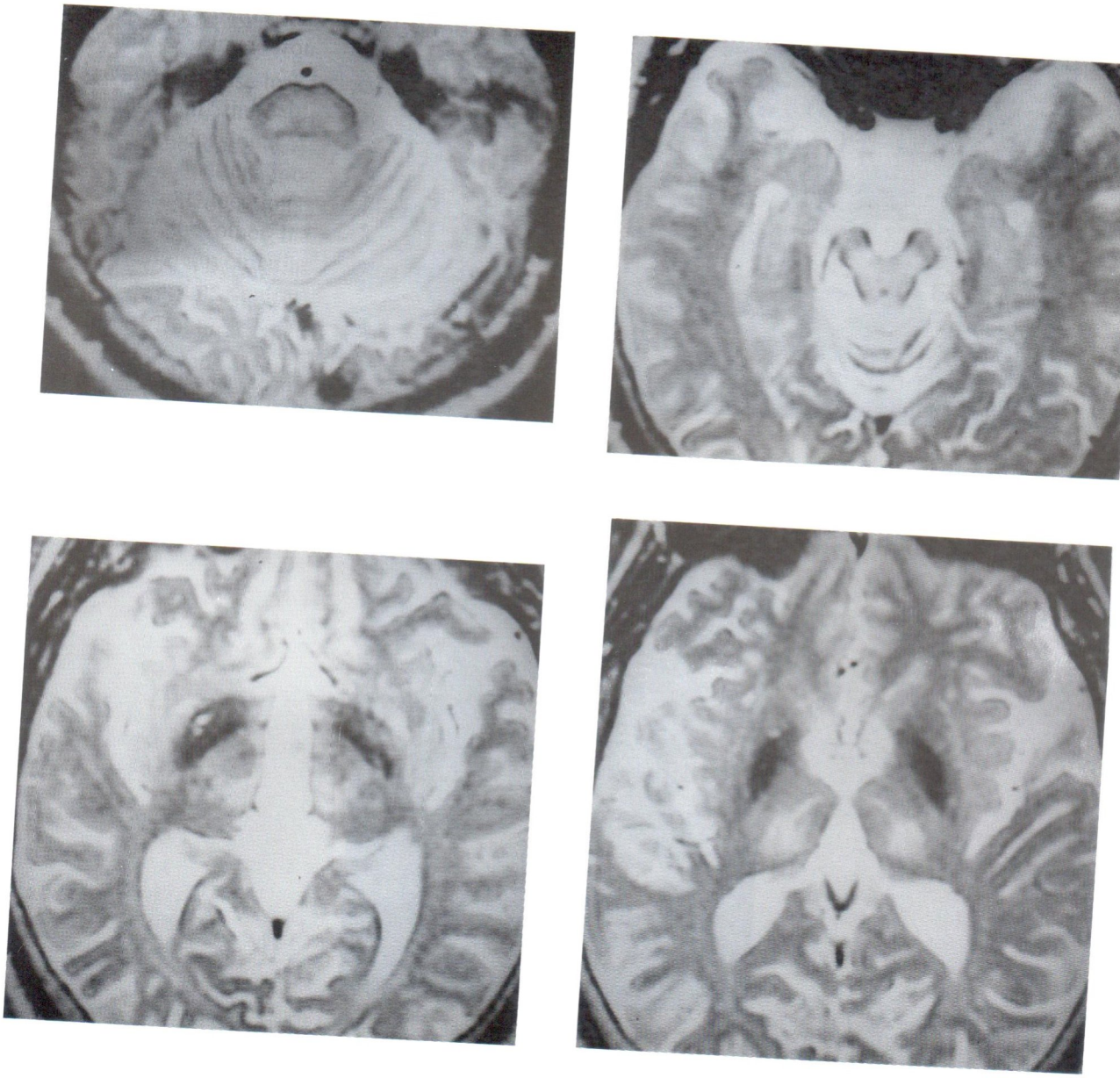

Fig.2B. Case 2. T2WI axial MRI of the brain showed bright signal at pons, thalami and midbrain.

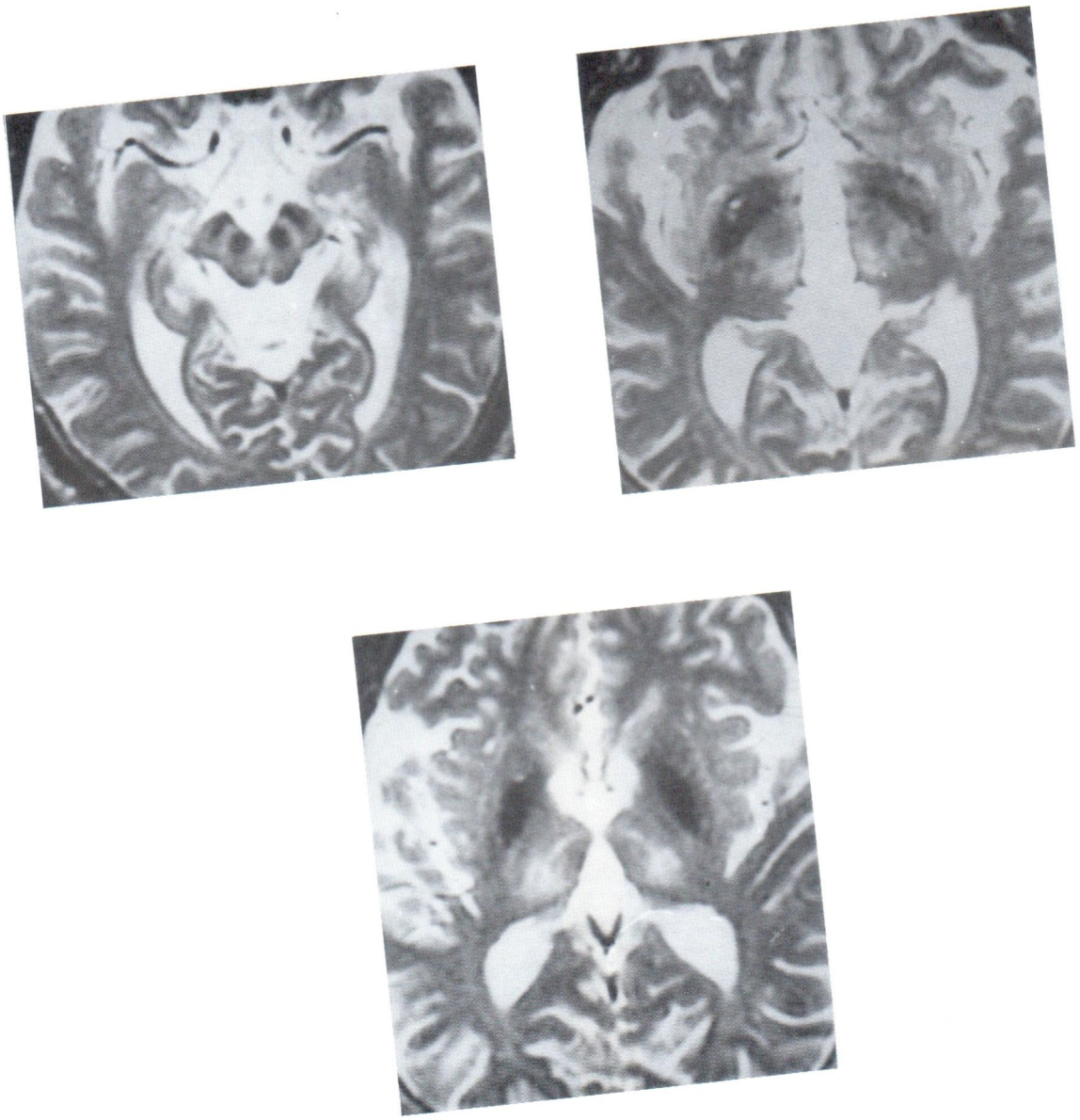

Fig.2C. Case 2. T2WI-axial MRI of the brain showed dark signal at red nucleus, substantia nigra, globus pallidus and dentate nucleus.

DISCUSSION

In Wilson disease, the most dramatic finding in the brain is cavitation in the lenticular nucleus and the tip of the frontal lobe (3), but pathologic changes are widespread throughout the brain (including brain stem) and gray matter is predominantly involved. These changes range from focal degeneration to cavitation and a diffuse loss of myelinated fibers (4-6). In the brain stem, there is an increased number of astrocytes and occasional Alzheimer glia in both the gray and white matter; focal degeneration has been reported in various locations, including the base of the pons (7). On the other hand, several articles have described focal demyelinating lesions of the pons base in Wilson disease as central pontine myelinolysis (8-11).

Wilson disease in an inborn error of copper metabolism. The precise biochemical defect is unknown, but likely involves inadequate synthesis of ceruloplasmin, a serum alpha-2-globulin for copper transport (12,13). Defective copper transportation and utilization results in abnormal deposition of the metal in the liver, brain and other organs. Here the copper is sequestered into lysosomes where it may disrupt membrane lipids and cause cellular degeneration (14).

In the brain, copper deposition takes place mainly in the basal ganglia, which appear brick-red at autopsy. The putamen, globus pallidus, and caudate are most involved, in that order. Neuronal loss occurs, but the pathologic picture is dominated by a marked gliosis, mainly composed of astrocytes (14,15). It is this gliosis rather than paramagnetic effects of copper that account for the imaging changes noted on MRI.

Copper deposition and lesser degenerative changes also occur in the brain stem, cerebellum, substantia nigra, and convolutional white matter.

Wilson disease is slightly more common in males than females. The age of onset is usually 10 to 40 years old. Computed tomography abnormalities are seen in about two-thirds of patients with Wilson disease (16-18). These include atrophy (focal or diffuse) and areas of hypodensity in the basal ganglia, brain stem, and white matter. CT has not proven particularly useful in correlating clinical symptoms, in assessing prognosis, or evaluating response to therapy (16-19).

About 80 percent of patients will have abnormal MRI scans, making MR more sensitive than CT (20,21). Symmetric areas of increased signal on T2WI were seen in the lenticular, thalamic, caudate, and dentate nuclei. A smaller number of patients showed brain stem and asymmetric white matter lesions. Clinical correlation was generally good. Dystonia correlated with putamen, caudate, and nigra lesions; bradykinesia with putamen lesions (21). The lesions detected as bright signal on T2WI on MR likely represent gliosis and edema rather than paramagnetic effects of copper, which would serve to decrease signal intensity.

Sener (22) reported bright claustrum on T2WI-MRI in his four cases of symptomatic Wilson disease.

The hyposignal seen on T2WI at red nucleus, substantia nigra, globus pallidus and dentate nuclei in our patient could reflect copper deposition in the basal ganglia, since copper is paramagnetic (23). The hypointensity of these mentioned structures are also found in normal aging (24). A possible explanation of such a signal is represented an iron deposition which accumulates commonly in areas which already have excessive copper accumulation. Phagocytes containing iron pigment are commonly observed in Wilson disease, in the pallidum and the substantia nigra (25). Furthermore siderophages are seen in relation to the cavitation observed in the putamen in late stages of Wilson disease or in relation to recent hemorrhages (25).

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