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MR of the Base of the Pons in Wilson Disease

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Summary: The authors describe unusual MR findings in three patients with Wilson disease, eg, white matter changes in the base of the pons, and speculate whether the changes are caused by Wilson disease or by concomitant disease, and whether the pontine lesions they observed are primary or related to lesions located more rostrally.

Index terms: Wilson disease; Pons, neoplasms; Degenerative brain disease

Wilson disease, or hepatolenticular degeneration, is an autosomal recessive disorder of copper metabolism characterized by the abnormal deposition of copper in various organs, particularly the liver and the brain.

Numerous articles have dealt with the magnetic resonance (MR) findings of the brain in Wilson disease (1–9), and the most common focal abnormalities have been found in the basal ganglia, especially in the lenticular nucleus. MR abnormalities in the pons have been occasionally reported (4–7, 9), and most of the authors have described the lesion in the pontine tegmentum (5, 6). This report describes three cases of Wilson disease with MR abnormalities evident in the base of the pons.

Case Reports

Three patients with Wilson disease were seen in our institution between 1988 and 1989. All had low serum ceruloplasmin (<2.0 mg/dL), low serum copper levels (<50 μg/dL), increased 24-hour urinary copper excretions (>70 μg/day), and the presence of Kayser-Fleischer rings. Medical histories and neurologic findings are summarized in Table 1.

Case 1

The patient was a 36-year-old woman experiencing gait disturbance, difficulty in writing, and mild dysarthria of 1-year duration. At age 31, she underwent splenectomy for splenomegaly and thrombocytopenia of unknown etiology.

On admission, she had moderate hepatomegaly. Neurologic examination revealed mild rigidity in all limbs, postural tremor in the hands, and mild truncal and limb ataxia. Muscle stretch reflexes were mildly hyperactive in all limbs. There was mild peripheral facial palsy and spasm on the right.

(CT) Computed tomography and MR examinations were performed prior to the implementation of penicillamine therapy. CT revealed mild cerebral cortical and brain stem atrophy with the lucency of the thalamus and basal ganglia, especially the putamen. MR, performed on a 1.5-T unit (Picker International, Cleveland, OH), was remarkable in low T1-weighted, IR 2500/30/600 (TR/TE/TI), and high T2-weighted, SE 2000/100/1 (TR/TE/excitations), signal intensity in the thalamus and the base of the pons (Fig. 1). In addition, there were abnormal signals in the putamen, internal capsules, and pulvinar (Table 2).

Case 2

The patient was a 22-year-old woman with 6-month history of intention tremor in the right arm, and a 4-year history of slow speech. Her neurologic examination at that time revealed mild dysarthria, intention tremor of the right arm, and mild truncal ataxia. She had a mild increase of muscle stretch reflexes of all limbs.

CT and MR examinations were performed. CT showed equivocal cerebral cortical atrophy. MR showed abnormal signals in the putamen, thalamus, internal capsule, external capsule, pulvinar, dentate nucleus, and base of the pons (Table 2). Thalamic and pontine signals were symmetrically

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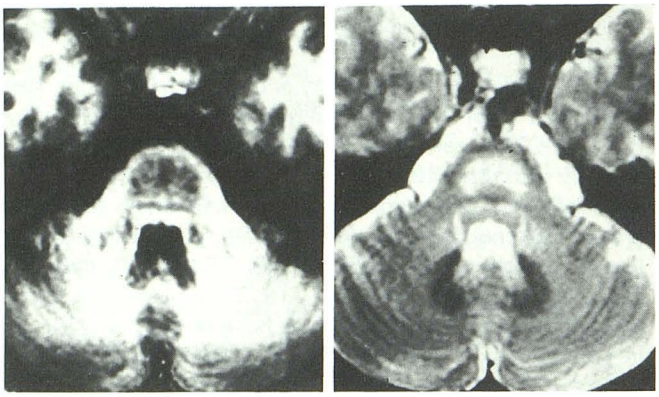
TABLE 1: Clinical findings

	Case 1	Case 2	Case 3
Sex	F	F	M
Age (yr)	36	22	32
Age at diagnosis (yr)	36	22	12
Tremor	1	1	2
Bradykinesia	0	0	2
Rigidity	1	0	1
Dysarthria	0	1	2
Spasticity	1	1	1
Ataxia	1	1	2
Abnormal gait	0	0	2
Hepatosplenomegaly	2	(1)[a]	1
Kayser-Fleischer ring	+	+	+
Serum ceruloplasmin (mg/dL)	1.5	1.8	1.0↓
Serum copper (μg/dL)	1.3	47	35
Urinary copper (μg/day)	160	79	464
Time of radiologic examination after therapy[b]	−1 mo	+4 yr	+2 mo

Note.—0 = absent, 1 = mild, 2 = severe.

[a] Parentheses indicate an equivocal finding.

[b] − = before treatment, + = after treatment.



A B

Fig. 1. Case 1: A 36-year-old woman (before treatment).

A, 1.5-T MR image (IR 2500/30/600) shows markedly a low signal in the pontine base.

B, 1.5-T MR image (SE 2000/100) shows a high signal in the base of the pons. These findings are the most marked of all of the three cases.

decreased on T1-weighted images and increased on T2-weighted images (Fig. 2).

Case 3

The patient was a 32-year-old man who was admitted because of deteriorating intention tremor of the both arms and gait disturbance after self-discontinuation of penicillamine. Wilson disease was diagnosed at age 12 when he experienced acute difficulty in walking. He was treated, and showed improvement; treatment was maintained on an irregular basis thereafter. He had a rigid mask-like face, and showed occasional drooling, and his speech was loud and he stuttered. He had brown skin and moderate hepatosplenomegaly. He had generalized cogwheel rigidity, and coarse resting tremor in the arms. There were truncal ataxia and intention tremors of all limbs. His posture was characteristically parkinsonian, and he walked with small and shuffling steps. Muscle stretch reflexes were increased in all limbs with extensor plantar responses. The palmomental reflexes were present bilaterally.

CT and MR were performed 2 months after the day of admission. CT revealed mild cerebral cortical and brain stem atrophy with equivocal basal ganglia lucency. MR revealed abnormal signals on the putamen, thalamus, internal capsule, external capsule, and pontine base (Table 2). The pontine signal aberrations were similar to those in cases 1 and 2 (Fig. 3).

Discussion

Several investigators have described the MR characteristics of Wilson disease. The lesions were visualized as the increased signal, and/or the decreased size of the affected structure involving putamen, caudate, subcortical white matter, thalamus, globus pallidus, midbrain, and cerebellum (1–9).

Previous reports (4–7, 9) described MR findings of the pons in which almost all the pontine lesions were found in the tegmentum (5, 6), whereas there have been no reported lesions in the base of the pons, such as those found in our cases.

An important question concerns the nature of the lesion in the base of the pons demonstrated in our patients. The MR findings within the pons base shown in our cases are characterized by an area of prolonged T1 and T2 relaxation, and the similar MR findings are well observed in infarct, metastasis, glioma, multiple sclerosis, encephalitis, and encephalopathy associated with radiation or chemotherapy (10); however, the histories and

TABLE 2: Findings in CT and MR imaging

	Case 1	Case 2	Case 3
CT			
Cortical atrophy	1	(1)	1
Brain stem atrophy	1	0	1
Ventricular dilatation	0	0	0
Basal ganglia lucency	1	0	(1)
Thalamic lucency	1	0	0
MR (T1W/T2W)			
Lenticular nucleus (putamen)	−1/−2	−1/−1	−1/−1
Caudate nucleus	0/0	0/0	0/0
Thalamus	−2/+2	−1/+1	−1/+1
Internal capsule	0/+1	0/+1	0/+1
External capsule	0/0	0/+1	0/+1
Pulvinar	−1/−1	−1/−1	0/0
Midbrain	0/0	0/0	0/0
Pons	−2/+2	−1/+1	−1/+1
Dentate nucleus	0/0	0/−1	0/(−1)

Note.—CT finding: 0 = absent, 1 = mild, 2 = severe; MR finding: −2 = markedly low intensity, −1 = mild low intensity, 0 = normal, +1 = mild high intensity, +2 = severe high intensity; Parentheses indicate an equivocal finding.

lack of mass effect in our cases lead us to exclude these possibilities.

In Wilson disease, the most dramatic finding in the brain is cavitation in the lenticular nucleus and the tip of the frontal lobe (11), but pathologic changes are widespread throughout the brain (including the brain stem) and gray matter is predominantly involved. These changes range from focal degeneration to cavitation and a diffuse loss of myelinated fibers (12, 13). 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 (14). On the other hand, several pertinent articles have described focal demyelinating lesions of the pons base in Wilson disease as central pontine myelinolysis (CnPoMy) (15–18); Goebel and Herman Ben-Zur postulate that Wilson disease accounted for 14% of associated disorders in 112 cases of CnPoMy (15).

It has been suggested that the etiology of CnPoMy may include alcoholism, malnutrition, or liver disease, and that the disease is not solely caused by the iatrogenic correction of hyponatremia (15). Our patients were not alcoholics and had not undergone iatrogenic correction of hyponatremia, but they did have liver disease. Although the severity of the liver disease is difficult to judge clinically, case 1 underwent splenectomy

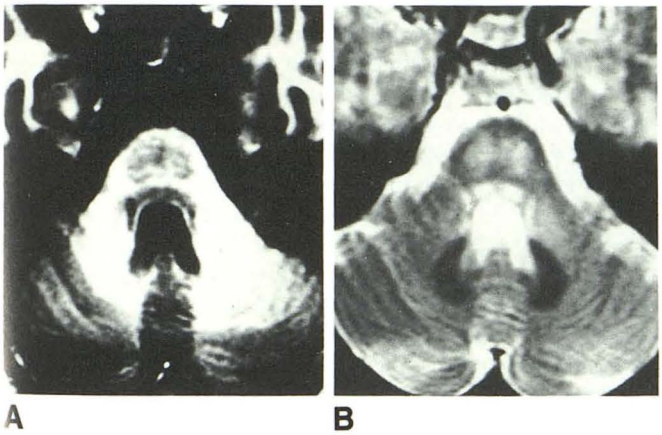


Fig. 2. Case 2: A 22-year-old woman (4 yr after treatment).
A, 1.5-T MR image (IR 2500/30/600) reveals a similar but less marked finding than that in case 1.
B, 1.5-T MR image (SE 2000/100) reveals a high signal in the base of the pons and a low signal in the dentate nucleus. These findings are the least marked of all of the three cases.

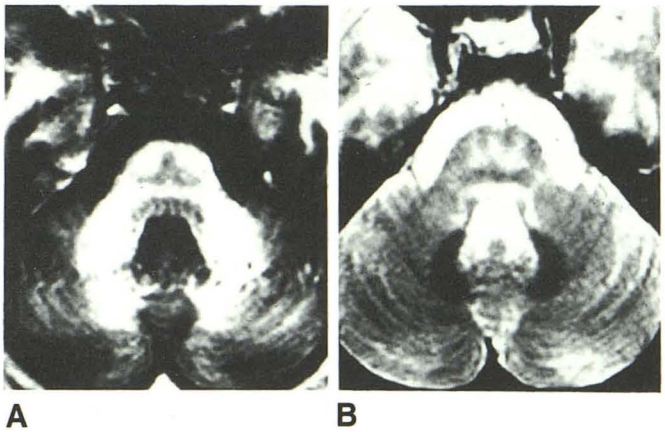


Fig. 3. Case 3: A 32-year-old man (2 months after treatment).
A, 1.5-T MR image (IR 2500/30/600) demonstrates a low signal in the base of the pons.
B, 1.5-T MR image (SE 2000/100) demonstrates high signal in the base of the pons and an equivocally low signal in the dentate nucleus.

and might have the most severe liver disease. MR abnormalities in the pontine base of case 1 were most prominent, indicating that the liver disease might be related to the pontine abnormalities. Therefore, the MR abnormalities of the pons might be those of CnPoMy, and the MR findings were quite similar to those previously reported as CnPoMy using MR (10).

To conclude, these MR abnormalities cannot be considered specific for more accurate diagnosis, and must be followed to determine whether or not they change with treatment. Further studies using high-field MR in combination with postmortem verification are required.

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