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Case report

# Central pontine myelinolysis in Wilson's disease: MR spectroscopy findings

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**Abstract**

Although a pontine lesion on cranial MRI is frequently associated with an extrapontine lesion, few cases report solitary pontine involvement in Wilson disease, and it is usually recognized as central pontine lesions related to hepatic dysfunction. A patient with Wilson's disease having a solitary pontine lesion without basal ganglia involvement in cranial MRI with cerebellar symptoms is presented. Based on MR spectroscopy findings, this solitary pontine lesion could be regarded as central pontine myelinolysis rather than the neurologic involvement in Wilson's disease. © 2004 Elsevier Inc. All rights reserved.

*Keywords:* Central pontine myelinolysis; Wilson's disease; Magnetic resonance imaging; Magnetic resonance spectroscopy

## 1. Introduction

Wilson's disease (WD) is an autosomal recessive disorder of copper (Cu) metabolism affecting mainly the liver and brain. In the brain, WD may involve primarily the corpus striatum but also the talami, brainstem nuclei, cerebral cortex, cerebral and cerebellar white matter, and dentate nuclei [1]. Though the involvement of pons in WD is customary (85.7%), solitary pons lesion is rare. Those patients with this single involvement are thought to have central pontine myelinolysis (CPM) related to hepatic dysfunction rather than Cu accumulation in this spesific location [1].

This report presents a case with WD and hepatic dysfunction having a lesion in pons compatible with CPM in MRI concurrent with MR spectroscopy (MRS) findings revealing neuronal loss and gliosis.

## 2. Case report

A 35-year-old man was admitted to our hospital because of a short history of postural instability and recurrent falls. He had a history of bilateral hand tremor, head shaking, and difficulty in speech for the previous 2 years.

His family history included a deceased paternal uncle who had similar symptoms.

On neurologic examination, he was fully conscious, oriented, and responsive to commands. He had high amplitude, fast postural and intentional tremor in hands, severe dysarthria, and titubation. Deep tendon jerks were hyperactive, and Babinski sign was positive bilaterally. The patient was markedly ataxic while walking with a wide-based gait. An ophthalmologic examination confirmed the presence of Kayser-Fleischer rings.

Serum ceruloplasmin level was 8.8 mg/dl (normal, 20–55), serum copper level was 70 $\mu$g/dl (normal, 80–155), and urinary copper excretion was 202 $\mu$g/24 h (normal, 3–35). Ultrasonography of the abdomen showed a coarse, heterogeneous hyperechoic parenchymal texture of the liver.

The other laboratory data included serum electrolytes, liver alkaline phosphatase, gamma glutamyl transferase, creatin kinase, lactate dehydrogenase, prothrombin time, activated partial thromboplastin time, aspartate aminotransferase, total bilirubin, and serum albumin with in normal limits.

Cranial MRI showed an area of decreased signal in the dorsal and central portion of pons on $T_1$-weighted images and an increased signal intensity on $T_2$-weighted images

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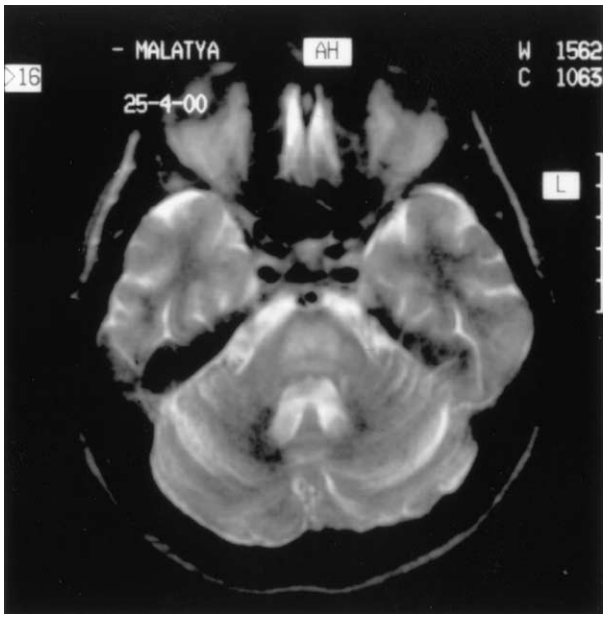


Fig. 1. Cranial MRI showed an area of increased signal intensity on T2-weighted images in brainstem.

(Figs. 1 and 2) with no additional findings suggesting neural pathology.

Single voxel $^{1}$H-MRS was performed by using the point-resolved spectroscopy sequence (PRESS) with TR 2000 ms, TE 30 ms, 256 averages, 13 × 13 × 13 mm voxel size. Volume of interest was positioned within pons. Spectrum was acquired after automatic gradient shimming with manual optimization and manual water suppression. Because the first MRS had a poor quality, MRS was repeated. The spectrum was referenced to creatine (Cr) peak (3 ppm). The signals from *N*-acetyl aspartate (NAA), Cr, and choline (Cho) were integrated (Figs. 3 and 4).

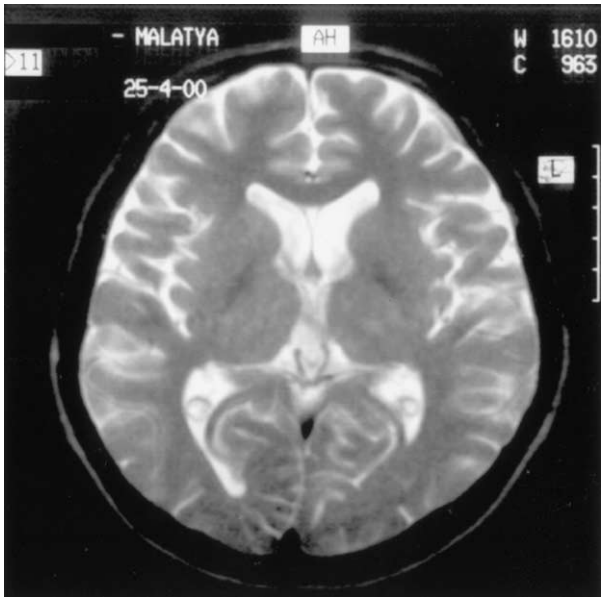


Fig. 2. MRI did not show any pathological finding at the level of basal ganglia.

MRS findings of the lesion showed a slight reduction of NAA and marked reduction of Cr and Cho (Table 1).

## 3. Discussion

WD is characterized by impairment in normal biliary excretion of copper, resulting in toxic accumulation of copper in potentially sensitive tissues of the body primarily liver and brain [2]. As a result of this accumulation, typical cranial MRI abnormalities of WD often mark as increased signal intensity and rarely as decreased signal intensity on $T_2$-weighted and decreased signal intensity on $T_1$-weighted scans [1]. In a large series, abnormal MR findings were putaminal (86%), pontine (82%), midbrain (77%), thalamic (54%), and in caudate nucleus (45%) [3]. Although, a pontine lesion on MRI is frequently associated with an extrapontine lesion, few cases report solitary pontine involvement [4,5]. These lesions are usually interpreted as CPM related to hepatic dysfunction due to copper accumulation [4,5]. In the large series presented by Saatci et al. [1], pontine involvement has been observed as two forms affecting the dorsal and central section of the pons. Central pontine lesions always appeared to be coexistent with the lesion of the pontine tegmentum and were diffuse or trapezoid, while anterior and lateral longitudinal fibers were preserved. However, they reported that their cases with central pontine lesions resembled CPM and were observed in all of the patients in neurologic form, i.e., central pontine lesions were not observed in any of the isolated hepatic forms. Therefore, Saatci et al. [1] considered that the cases of isolated hepatic form were directly associated with neurologic involvement of WD rather than the secondary central pontine myelinolysis due to the pontine lesions of the liver dysfunction [1]. But, Imia et al. reported CPM cases due to liver dysfunction in three patients with WD [4]. In addition, the clinicopathological study reported by Seitelberg et al. diagnosed CPM in seven WD patients [5].

Although CPM occurs frequently upon rapid improvement of hyponatremia or on the basis of alcoholism, electrolyte imbalance due to renal failure, hepatic dysfunction, diabetes mellitus, and WD have been reported as well [5–9].

The characteristic clinical manifestations of pontine myelinolysis are spastic tetraparesis and pseudobulbar paralysis due to destructive lesion in the corticospinal and corticobulbar tracts in the pons [8,10,11]. In fewer cases, lesions involving the pontocerebellar fibers can cause cerebellar signs such as ataxia, dysarthria, and intensional tremor [12]. Pirzada et al. suggested that the pontocerebellar fibers are more susceptible to the effects of myelinolysis but weakness due to involvement of the corticospinal tracts masks the cerebellar signs [8]. In our patient, cerebellar signs were prominent as ataxia, dysarthria, intentional tremor, and ti-

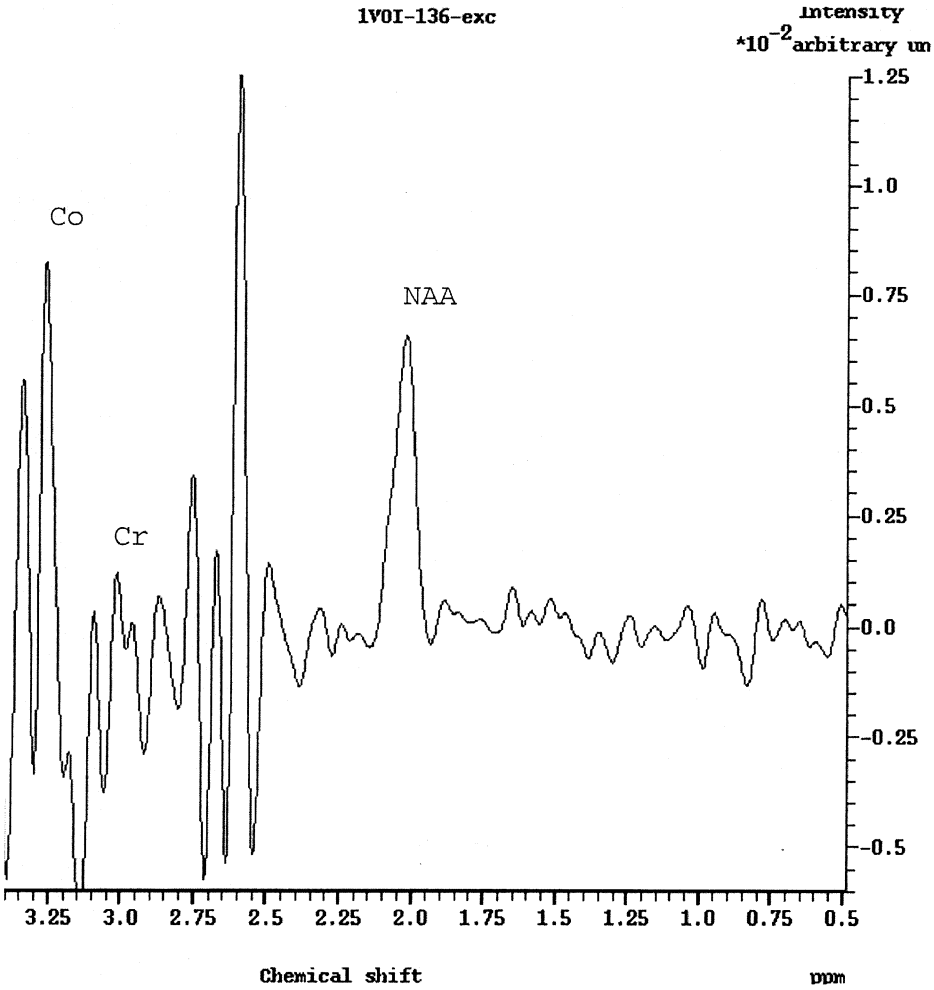


Fig. 3. Single-voxel H-MRS from pons showed a slight reduction of NAA and marked reduction of Cr and Cho.

tubation, which supported the involvement of pontocerebellar tracts.

Classic MRI findings in CPM show increased signal intensity of $T_2$-weighted scans and decreased signal intensity on $T_1$-weighted scans in the central pons [8,9,10]. The MRI findings in our patient were consistent with these findings.

Only limited spectroscopic data are as yet available in WD [2,13–15]. Van del Heuvel et al. had observed a reduction in the mI/Cr and Cho/Cr ratio compared to the controls [13]. The volume of interest included the right and left globi pallidus [13]. Kraft et al. reported a reduction in the mI/Cr and normal NAA/Cr and Cho/Cr ratios and found no difference in the absolute concentration of Cr between controls and treated WD patients. Volumes of interest were positioned within parietal white and gray matters and in nine patients also within the putamen [14]. Jayasundar et al. found a reduction in the NAA/Cr and Cho/Cr ratios in the basal ganglion [2]. It is seen that each of MRS studied have examined the patient at different stages of treatment using different voxel sizes in different locations. Although, it is difficult to compare these results, the most prominent finding is the decrease in myoinositol besides the decrease in NAA and Cho as reported in some of the recent literature [2,13].

A limited number of cases are reported focusing on the MRS findings of CPM. Smith et al. [16] demonstrated low Cho, low NAA, and lipidchatin in a patient with pontine osmotic myelinolysis due to electrolyte imbalance. MRS showed low Cho, low NAA, and lipid. MRS performed at the site of myelinolysis in another case disclosed a strong lipid triglycerid signals with no difference in Cr levels [16]. No MRS findings are reported previously on CPM with WD.

The decrease in NAA levels in the present case is compatible with the results of Smith et al. found in CPM cases and may be related with neuronal loss. The minimal increase in Cho levels may support the gliosis in this region and contradicts with the MRS findings in WD. The decrease in Cr neither reported in WD nor CPM. The decrease in Cr in the present case may be due to the mitochondrial dysfunction with an anticipated elevation of cerebral lactate levels. Low Cr peak and no lactate peak might be related to the possible paramagnetic effect of Cu and Fe being the

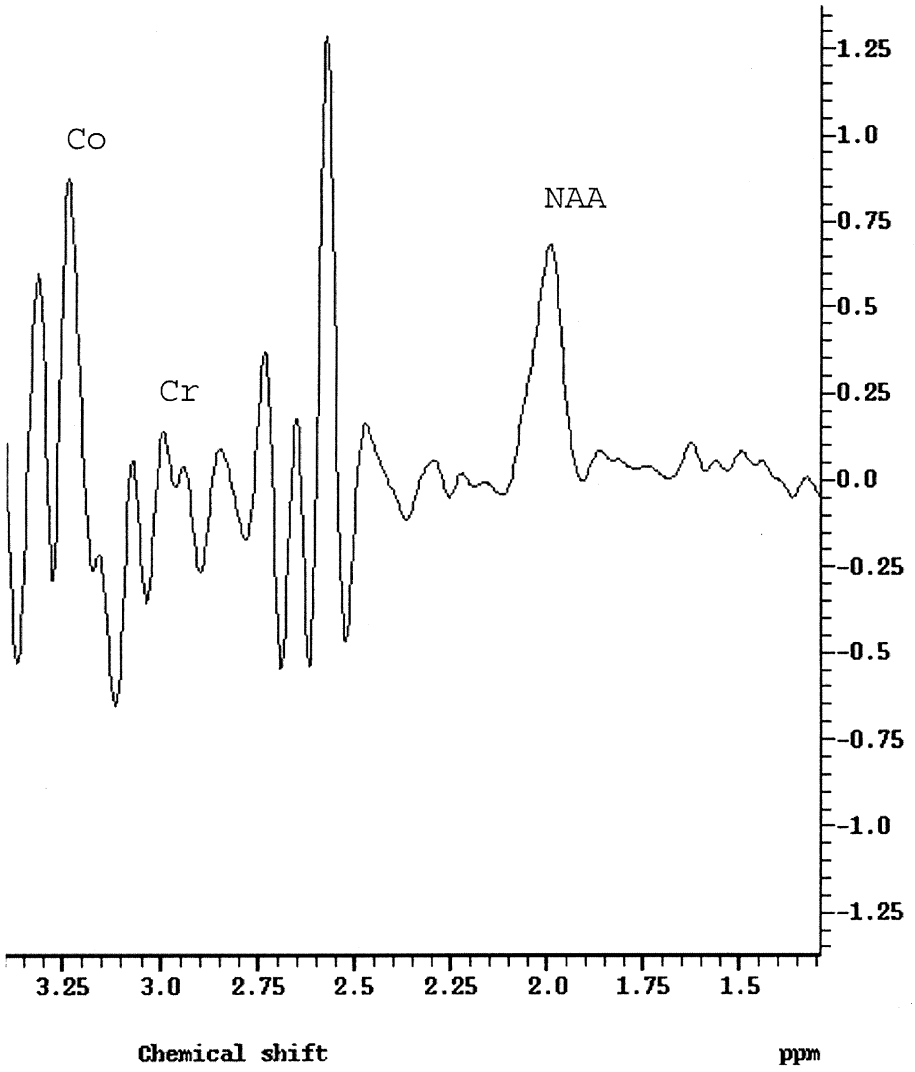


Fig. 4. Because the first MRS had poor quality, MRS was repeated.

cause of reduction in signals. Two consecutive MRS studies with unsatisfactory quality can be a natural cause of this paramagnetic effect [2,14].

Having only cerebellar manifestations with no other cerebral and cerebellar lesions, apart from pons in cranial MRI and decrease in NAA and Cho levels in MRS, which is attributable to WD, and decrease in Cr, which may be due to hepatic dysfunction besides Cu accumulation in the disease, the case is evaluated as a patient with CPM. MRS may be useful for the etiologic investigation of the pontine lesions in WD.

Table 1
Comparison of metabolite ratios from MRS (TE: 136 ms) revealing findings of pontine lesion in the present case with normal values of radiodiagnostic department

| Metabolite Ratios | Present Case | Control Value |
|---|---|---|
| Choline | 0.075 | 0.131 ± 0.086 |
| Creatine | 0.024 | 0.079 ± 0.048 |
| *N*-acetyl aspartate | 0.144 | 0.167 ± 0.118 |

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