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Short communication

Transcranial magnetic stimulation in an adrenoleukodystrophy patient

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We experienced an 11-year-old boy diagnosed as having adrenoleukodystrophy (ALD), and studied his motor evoked potentials (MEPs) elicited by transcranial magnetic stimulation (TMS). He had intellectual and visual impairment, and MRI revealed high intensity of the parieto-occipital white matter. On evaluation of the long tracts, slight spasticity with equivocal Babinski signs was noted: however, the long tracts appeared intact on MRI, and short latency somatosensory evoked potentials (SSEPs) were completely normal. On TMS delivered through a circular coil, MEPs recorded from the relaxed first dorsal interosseous muscle showed that only the duration was significantly prolonged, which may be due to temporal dispersion of descending volleys in the pyramidal tracts, while the latency was not prolonged. TMS in ALD was considered sensitive and useful for detecting subtle involvement of the long tracts.

Keywords: Adrenoleukodystrophy; Transcranial magnetic stimulation

1. INTRODUCTION

The clinical phenotype of X-linked adrenoleukodystrophy (ALD) varies widely from no involvement of the central nervous system (CNS) to the childhood cerebral form manifested by the onset of symptoms generally between 4 and 10 years of age and rapid progression to a vegetative state within 2 years [1]. Therefore, monitoring of nerve conduction of the CNS is important to evaluate the progression of CNS involvement [2–5]. This paper reports that transcranial magnetic stimulation (TMS) of the motor cortex detected involvement of the long tracts prior to the development of abnormal MRI findings of the long tracts.

2. CASE REPORT

A 11-year-old boy had been treated for Addison disease since the age of 5 years. After an interval of 5 years, since the visual fields were narrowed, he was diagnosed as having ALD. Despite starting dietary therapy, visual and intellectual impairment was progressive over a year and he was referred to our hospital. Neurological examination revealed moderately impaired intelligence, normal optic fundi but reduced visual acuity (0.03) with narrowed visual fields, slight spasticity of the distal lower limbs, and equivocal Babinski signs. T2-weighted MRI images showed high intensity of the parieto-occipital white matter, but the pyramidal tracts were not involved (Fig. 1). Electrophysiological examination of the peripheral nerves yielded normal results. Brainstem auditory evoked potentials and both R1 and R2 of the blink reflex were well elicited with normal latencies. N11, P14, N17 and P20 of short latency somatosensory evoked potentials (SSEPs) were also obtained with a normal latency and interpeak amplitude of more than 2.0 μV. Pattern-reversal visual evoked potentials of N75 to N140 failed to be elicited.

3. MATERIALS AND METHODS

Motor-evoked potentials (MEPs) in the patient were compared with MEPs in six neurologically normal healthy control subjects with a mean age of 10.8 years (range, 9–12 years). The parents of all subjects gave verbal informed consent to the study. TMS was delivered by a Magstim Model 200 stimulator (Magstim) through a circular coil with a mean diameter of 90 mm (peak

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magnetic field strength, 2.0 tesla, here designated as 100% intensity). MEPs were recorded from surface electrodes placed over the first dorsal interosseous muscle (FDI) in the resting state. The coil was centered at the vertex or over the the fifth cervical spine (C5s). Threshold intensity for TMS, defined as the intensity needed to produce MEPs of more than 100 μV amplitude in at least three of six trials, was determined, and then MEPs were obtained by TMS at an intensity 10% above threshold. Magnetic stimulation of the spinal roots was performed using 35% intensity. Central motor conduction time (CMCT) was calculated by subtracting the latency of MEPs evoked by stimulation over C5s from that over the vertex. Statistical comparison was done using unpaired t-test with a $P \leq 0.02$ accepted as significant.

Table 1 *Motor evoked potentials by magnetic stimulation*

	The patient	Control subjects ($n = 6$)
Age (years)	11	10.8 ± 1.2 (mean ± S.D.)
Centers of coil:		
Latency (ms):		
C5s	10.9	10.2 ± 0.9
Vertex	19.9	19.2 ± 2.1
Duration (ms):		
C5s	6.9	7.5 ± 2.0
Vertex	22.3 †	11.2 ± 3.1
CMCT (ms)	9.0	9.0 ± 1.6

† Significantly different from controls at $P < 0.01$ (unpaired t-test).
C5s, fifth cervical spine; CMCT, central motor conduction time.

4. RESULTS

The results are summarized in Table 1. Threshold intensity in control subjects varied between 50 and 80%, and that in the patient was 60%. Latency of MEPs and CMCT of the patient were normal. However, the duration of MEPs evoked by TMS was significantly prolonged compared with those in control subjects ($P < 0.01$), as shown in Fig. 2.

5. DISCUSSION

The present case manifested the characteristic course of the childhood cerebral form of ALD, and MRI revealed demyelination of the parieto-occipital white matter. On the other hand, long tract signs were slightly positive, and MRI showed intact pyramidal tracts. In the electrophysiological evaluation of the long tracts of the CNS, the only meaningful finding was that the duration of MEPs elicited by TMS was significantly prolonged, since variability of duration is less pronounced than amplitude variability, especially when recording from a relaxed muscle [6]. Prolonged duration may be caused by temporal dispersion of the descending volleys evoked by TMS, and suggests slight nerve conduction dysfunction in the pyramidal tracts in ALD, since conduction slowing in the peripheral nerves was excluded and hypoexcitability of the motor cortical neurons and the anterior horn cells was also excluded because of no increasing of threshold intensity. Masur et al. [7] and Kukowski [8] reported that CMCT is prolonged in patients with advanced adrenomyeloneuropathy (AMN) and ALD. Although CMCT in the present patient was not prolonged, an earlier change was detected in MEPs. TMS is thus

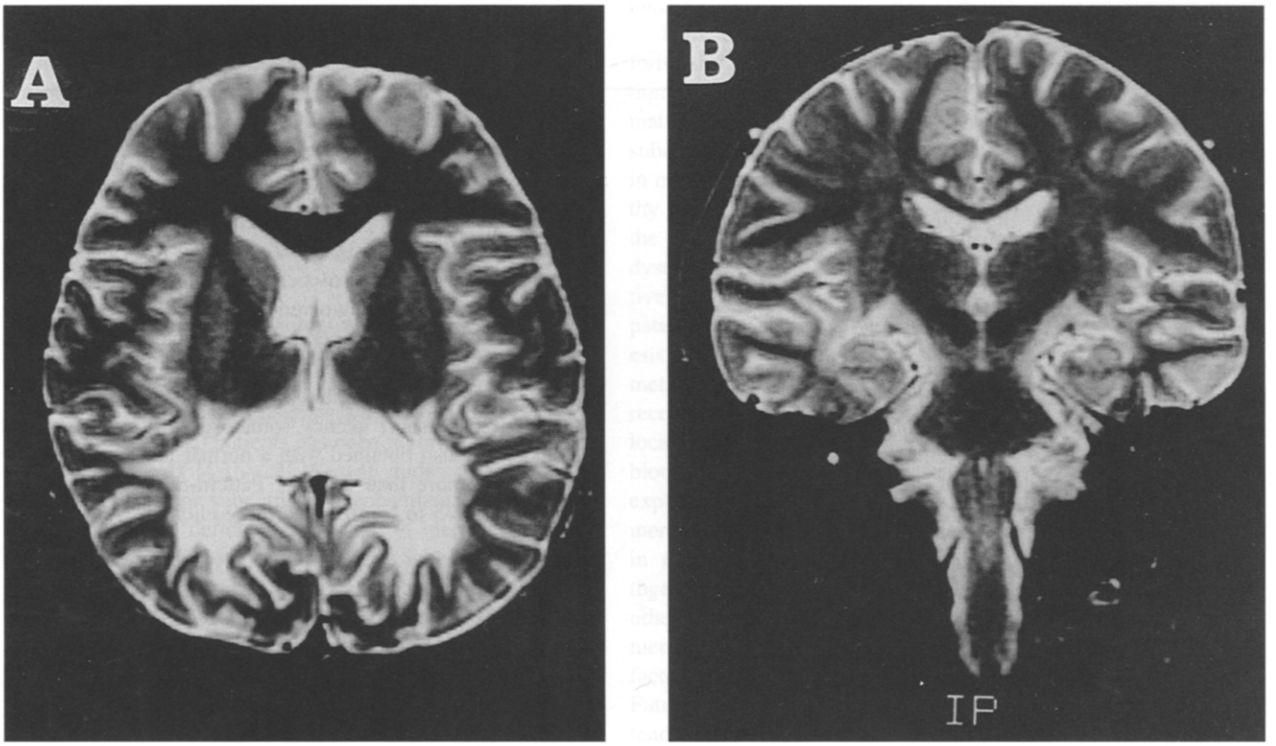

Fig. 1. MR images of the present case. A: the parieto-occipital white matter in the T2-weighted, 2500/100, axial image shows markedly high intensity. B: the pyramidal tracts, including the cerebral peduncles and the corticospinal tracts in the pons, in the T2-weighted, 2500/100, coronal image are not involved.

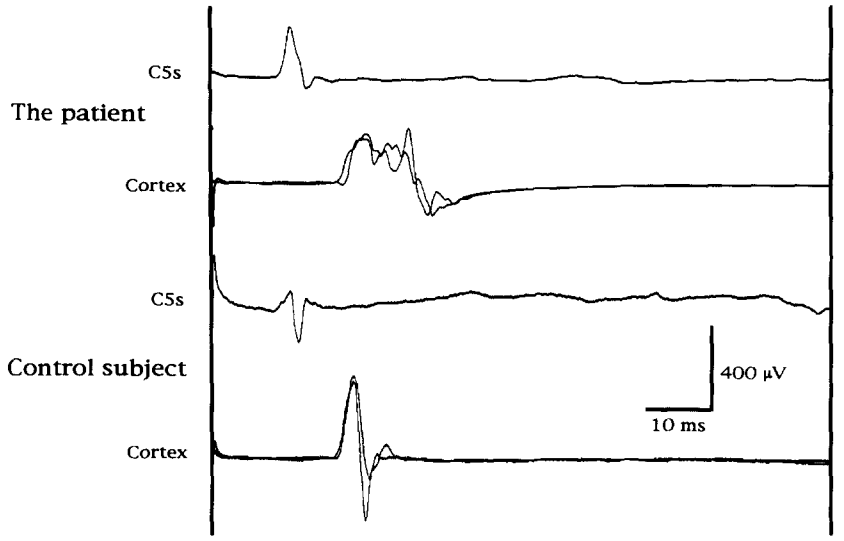

Fig. 2. Motor-evoked potentials recorded from the first dorsal interosseous muscle elicited by magnetic stimulation of the motor cortex (cortex) and of the anterior roots of the cervical spinal cord (C5s). On transcranial magnetic stimulation, the trace of the patient reveals significantly prolonged duration, compared with the trace of a control subject.

suggested to be a more sensitive examination to detect involvement of the long tracts than MRI.

Bone marrow transplantation (BMT) is recommended only in selected cases of early cerebral involvement, since it does not improve neuronal impairment resulting from demyelination [9]. Therefore, it is important to differentiate, as accurately as possible, patients with the initial findings of nerve conduction dysfunction prior to development of MRI findings caused by demyelination from those who are free of CNS involvement. Because the present case had gross involvement of the parieto-occipital white matter and the TMS findings were obtained not at the initial stage of CNS involvement, but at the advanced stage, further detailed study is required to determine whether the same MEP change is found in neurologically asymptomatic patients with ALD or AMN just prior to the onset of symptoms or changes on MRI, and whether findings of TMS examination would influence the decision to proceed with BMT.

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