

Acute disseminated encephalomyelitis with tremor as the initial symptom

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Abstract

Multiple neurological deficits can occur in acute disseminated encephalomyelitis (ADEM) but rarely movement disorders. A 24-year-old female patient was admitted because of tremor in both upper limbs. After admission, her mental status progressively declined into coma. Brain magnetic resonance imaging and cerebrospinal fluid analysis were compatible with ADEM. Tests for central nervous system infection and autoimmune diseases were all negative. She was given steroid and IVIG, and the patient fully improved. We report here the first case of adult ADEM, who presented with tremor as the initial neurological manifestation.

INTRODUCTION

Acute disseminated encephalitis (ADEM) is a monophasic, multifocal central nervous system (CNS) disorder. Typically, ADEM occurs in children, and young adults are rarely affected. There is demyelination of the CNS, an autoimmune reaction and secondary inflammation after a predisposing infection or vaccination.¹ Various neurological manifestations can occur including changes in mental status, brain stem signs, weakness, and paresthesia. Abnormal movement disorders such as tremors, ataxia, and myoclonus are rarely described.² Here, we report a young woman who presented with tremor as her initial symptom of ADEM, who recovered after immune therapy with no residual tremor.

CASE REPORT

A 24-year-old female was admitted due to a fine tremor in both arms and hands for three days. She had a common cold two weeks prior to her visit. There was no recent history of vaccination or travel and no family history of seizures or movement disorders. She also had fever, nausea and headache; and the tremor became more severe as time progressed. On admission, she was alert, very cooperative, and had no abnormal neurological findings except tremor. The tremor was 6-7 Hz, symmetrical, occurred in both

action and at rest (Video 1). Her mental status progressively deteriorated to become stuporous. Brain magnetic resonance imaging (MRI) showed mild enhancing lesions in bilateral basal ganglia; and multifocal white matter change throughout the cervical spinal cord (Figure 1). The spinal tap opening pressure was 37 cm H₂O, and the protein level was 50 mg/dl. Analysis of the cerebrospinal fluid (CSF) showed the absence of the pleocytosis and oligoclonal bands. Tests for viruses, bacteria, fungi were all negative. Polymerase chain reactions (PCR) for Herpes simplex virus, Human immunodeficiency virus, Japanese encephalitis virus, tick-borne infection, and West Nile virus were also negative. Autoimmune tests such as rheumatoid factor, antinuclear antibody including antineutrophil cytoplasmic antibody (ANCA), fluorescent antinuclear antibody (FANA), anti-dsDNA antibody were negative. Anti N-methyl-D-aspartate (NMDA) receptor antibody was negative, and there was no abnormal mass on the abdominal CT. The test for the anti-aquaporin-4 (AQP4) antibody was negative in the CSF and serum by enzyme-linked immunosorbent assay (ELISA)³ and cell based assay (CBA).⁴

On third hospital day, her mental status deteriorated further, and she descended into a coma. She was transferred to the Intensive Care Unit. A newly appeared oromandibular tremor with quadriparesis, upper motor neuron sign was

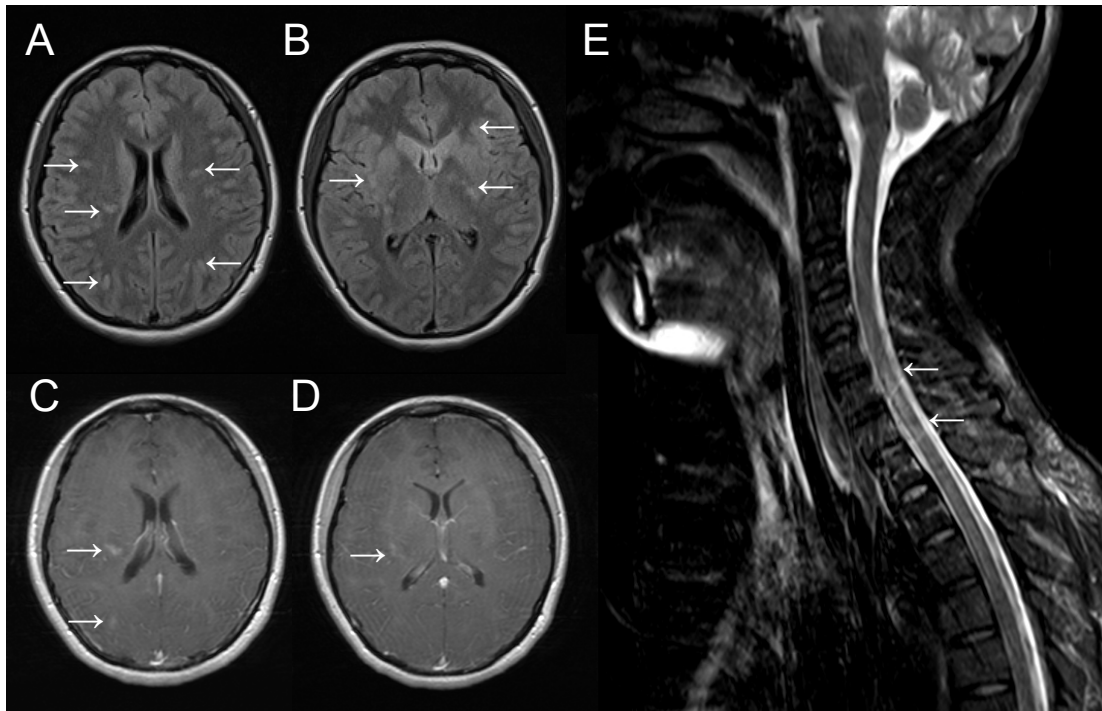


Figure 1. Brain magnetic resonance imaging (MRI) on third hospital day. T2-weighted fluid-attenuated inversion recovery (FLAIR) images (A, B) show small multifocal high signal intensities on bilateral white matter with subtle enhancement in the similar lesion (arrow) and leptomeninges on T1-weighted contrast images (C, D). Spinal MRI on sixth hospital day shows spinal cord lesions (arrow) in the C5, C6, C7 level on T2-weighted sagittal image (E).

observed. Because the electroencephalography (EEG) showed frequent electrographic seizures, antiepileptic drugs were also given. On her seventh day in the hospital, repeat CSF analysis showed a protein level of 90 mg/dl, and intracranial pressure was still elevated. Immunotherapies were given after ruling out CNS infection. Because there was no obvious clinical improvement with intravenous (IV) methylprednisolone 1000 mg for five days, IV immunoglobulin 400 mg/kg was administered for the next five days. The patient subsequently gradually improved with reduced tremor and became more alert. The EEG became normal, and the assisted ventilation was eventually removed. After two months, the patient did not show any neurological deficits except for partial weakness in her hands and feet with improved MRI findings. Visual evoked potentials (VEP), somatosensory evoked potentials (SEP), brainstem auditory evoked potentials (BAEP) and repeat test of AQP4 were all normal.

DISCUSSION

ADEM is a monophasic autoimmune neurological disorder with encephalopathy and brain

stem dysfunction associated with a preceding infection, or vaccination in about 50-75% of cases.¹ Neurological signs appear days to weeks after the predisposing event, with fever, headache, vomiting and nausea. In addition to ADEM lesions seen in MRI, various clinical neurological deficits can occur.⁵ While rare, movement disorders such as ataxia, myoclonus, dystonia and chorea have been reported.⁶⁻⁸ Unilateral thalamus or basal ganglia lesions with an enhanced and increased signal intensity on T2-weighted image have been shown to occur in 30% of ADEM patients with abnormal movement disorders.⁹ The prognosis of ADEM is generally good, often with a full recovery within several weeks or months after immune therapy. However, some patients have multiphasic disease or develop multiple sclerosis (MS).⁸ Pathophysiological mechanism of the disease is believed to be molecular mimicry, which is a structural homology between a pathogen and the myelin proteins, resulting in T-cell activation and a specific auto-immune response against the host CNS.

Because neither clinical presentation nor paraclinical tests can provide a specific diagnosis, the final diagnosis of ADEM has to be made by

exclusion. MS, Neuromyelitis optica (NMO), other demyelinating, autoimmune and infectious CNS diseases should be excluded. Various movement disorders such as ataxia, myoclonus, dystonia, chorea, parkinsonism and tremor have been described to occur in MS.⁸ In contrast, movement disorders are uncommonly reported in ADEM, and ataxia is said to account for 50% of pediatric ADEM cases with movement disorders.⁹

In our patient, the aggressive clinical progress of the patient and MRI findings do not support the diagnosis of MS. Although the patient had high signal intensity in three vertebral segments in the MRI, in view of the repeatedly negative AQP4 test, the patient was unlikely to have NMO. Furthermore, the patient did not have visual symptoms and the VEP was normal. Although the presentation was that of a young female with tremor in the lips and upper limbs associated with an altered mental status, the NMDA receptor antibody test was negative, and there was no evidence of associated tumor, thus anti-NMDA receptor encephalitis was unlikely. The laboratory results, family history and clinical course of the patient showed that other differential diagnoses such as Wilson's disease, Huntington's disease, adrenoleukodystrophy or early onset Parkinson's disease were also unlikely. However, genetic studies were not done.

In conclusion, this is the report of a young female adult with ADEM patient who presented with tremor. Tremor as presenting symptom of adult ADEM has not been previously described in literature.

DISCLOSURE

Financial disclosures of all authors for the past year: HJK has received honoraria for speaking or consulting from Bayer Schering Pharma, Biogen Idec, Genzyme, Merck Serono, Novartis, MedImmune, and Teva-Handok and has received research grants from Genzyme, Merck Serono, and Kael-GemVax. He serves on a steering committee for MedImmune and serves as an editorial board member of Multiple Sclerosis Journal - Experimental, Translational and Clinical. JYY has received funding for travel from Korea Research-Based Pharmaceutical Industry Association, Korean Pharmaceutical Manufacturers Association. Other authors have no financial disclosures.

Funding for study: None

Conflicts of interest: None

Video 1. [http://neurology-asia.org/content/21/1/neuroasia-2016-21\(1\)-89-v1.mp4](http://neurology-asia.org/content/21/1/neuroasia-2016-21(1)-89-v1.mp4)

Symmetric resting tremor on both hands and arms of 6-7 Hz is observed without any other neurological symptoms on admission. Finger-to-nose test shows action tremor on left hand.

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