Journal of the Neurological Sciences 325 (2013) 176–179

Contents lists available at SciVerse ScienceDirect

Journal of the Neurological Sciences

journal homepage: www.elsevier.com/locate/jns

Short communication

A case of exacerbated multiphasic disseminated encephalomyelitis after interferon beta treatment

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ARTICLE INFO

Article history:
Received 28 August 2012
Received in revised form 12 December 2012
Accepted 12 December 2012
Available online 9 January 2013

Keywords:
Acute disseminated encephalomyelitis
Multiphasic disseminated encephalomyelitis
Interferon beta
Multiple sclerosis
Neuromyelitis optica

ABSTRACT

Acute disseminated encephalomyelitis (ADEM) is an inflammatory demyelinating disorder of the central nervous system (CNS), which can be monophasic or with repeated episodes. Relapsing ADEM can be misdiagnosed as multiple sclerosis (MS). We describe here a 16-year-old female patient with multiphasic disseminated encephalomyelitis (MDEM), which was exacerbated after an interferon beta (INF-β) treatment. The patient presented with polysymptomatic and encephalopathic features at the first attack and was definitively diagnosed with ADEM. During the following 28 months, she had two relapses, with the lesions spatially disseminated in time and space, but without encephalopathy. She was diagnosed with MS and started on treatment with IFN-β injection. A severe relapse occurred 5 months after starting IFN-β treatment, with both the clinical and MRI characteristics worse than during the former 2 relapses, meeting the diagnostic criteria for MDEM. Treatment with IFN-β was halted, with no new relapses observed over the following 9 months. These findings suggest that treating MDEM patients with IFN-β may exacerbate the disease, similar to that observed during IFN-β treatment of patients with neuromyelitis optica. Caution should be exercised when treating these patients with IFN-β.

1. Introduction

Acute disseminated encephalomyelitis (ADEM) is an idiopathic immune-mediated demyelinating disease of the central nervous system (CNS), which usually starts with an abrupt onset of neurologic symptoms and signs within days to weeks after an infection or immunization. Although ADEM was long thought to be a monophasic disease, about 5% to 25% patients have been found to relapse [1–5]. According to the National Multiple Sclerosis Society (NMSS) consensus definitions for pediatric multiple sclerosis (MS) and related disorders, ADEM can be classified as monophasic, multiphasic or recurrent ADEM based on clinical features and lesion appearance on magnetic resonance imaging (MRI) [6]. Multiphasic ADEM (MDEM) was defined as ADEM followed by a new clinical event that also met the criteria for ADEM, but involving previously uninvolved anatomic areas of the CNS, as confirmed by patient history, neurologic examination, and neuroimaging. The occurrence of encephalopathy was considered necessary in diagnosing ADEM or relapsing ADEM.

To date, few double-blind, placebo-controlled studies have evaluated different treatment options for MDEM. Large doses of methylprednisolone have been reported effective. To our knowledge, there have been no reports describing interferon beta (IFN-β) treatment of patients with MDEM. We describe here a 16 years old female patient with MDEM with clinical characteristic and MR images difficult to distinguish from MS. This patient's condition was exacerbated after IFN-β treatment.

2. Case report

In March 2009, a 16-year-old girl gradually became agitated. Her symptoms progressed to stupor and aphasia within one month. Her past history and family history were normal. Paired serum and cerebrospinal fluid (CSF) samples were negative for antibodies to measles, rubella, varicella zoster and herpes simplex viruses. The white blood cell (WBC) count in her CSF was 22×10^6/L, with 90% being lymphocytes. The glucose concentration in her CSF was normal. Fluid-attenuated inversion recovery (FLAIR) T2-weighted imaging performed one month after disease onset showed large lesions with poorly defined margins located in her bilateral basal ganglia (Fig. 1A2 and A3), right hippocampus (Fig. 1A2) and cerebellum (Fig. 1A1 and A3), as well as an irregularly shaped small patch of gadolinium (Gd)-contrast enhancement (Fig. 1A4). Spinal MRI showed a T2 hyperintense lesion at the level of her fourth cervical vertebra (Fig. 1A5). Routine tests for autoimmune connective tissue diseases, including rheumatoid factor, antinuclear antibody, and antibodies to streptolysin-o and extractable nuclear antigens, were normal, as were tests for infectious diseases. She was diagnosed with ADEM and started on high dose methylprednisolone

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http://dx.doi.org/10.1016/j.jns.2012.12.019

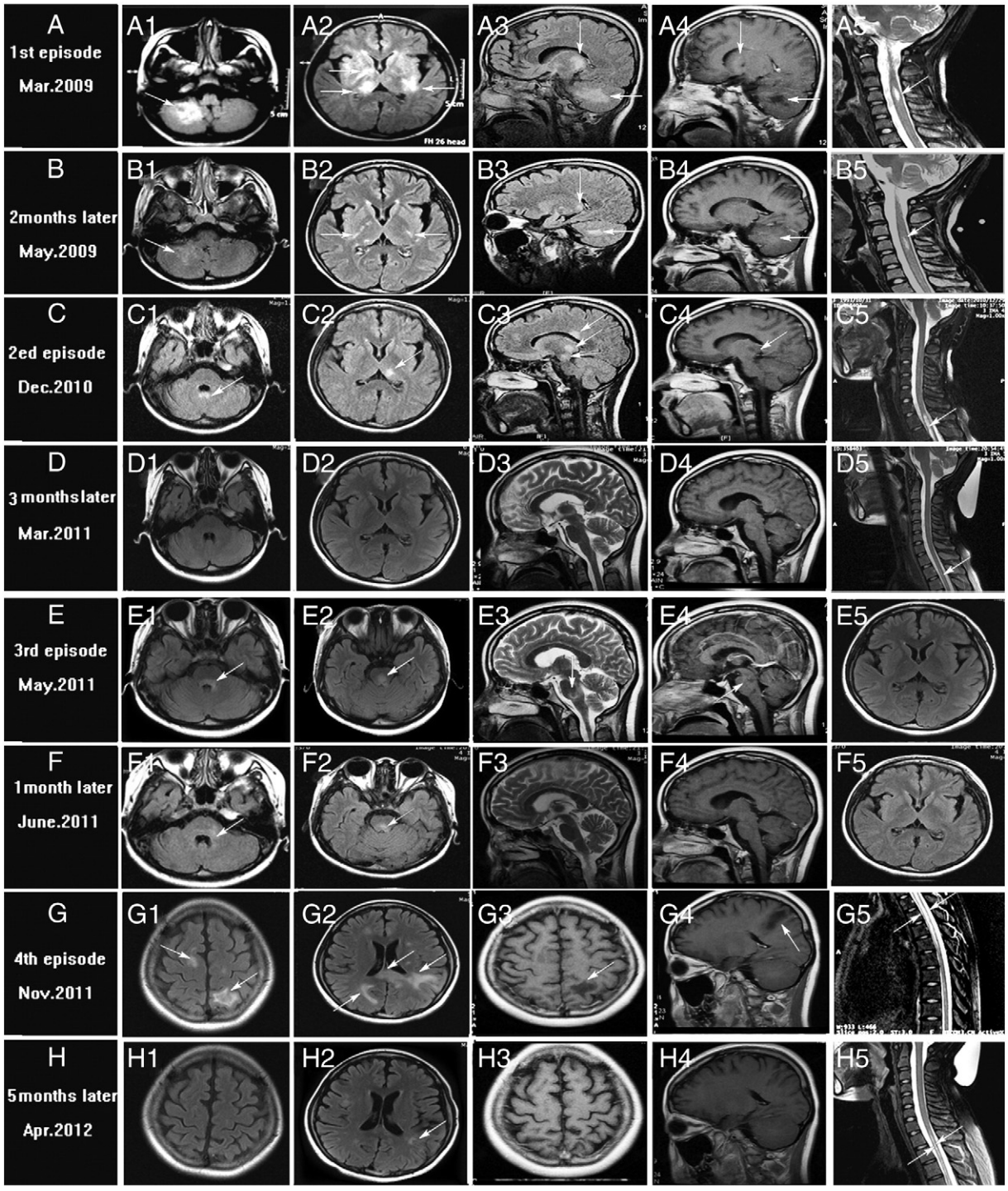

Fig. 1. Serial MRI findings in the brain and spinal cord. (A) Fluid-attenuated inversion recovery (FLAIR) T2 weighted image, showing large lesions with poorly defined margins in the right cerebellum (arrow, A1), the bilateral basal ganglia and thalamus (A2, A3) and cloud-like Gd enhancement on T1-weighted imaging (A4). Lesion in the spinal cord (A5). (C) T2-FLAIR showing new brain lesions in the midbrain (C1), thalamus, corpus callosum (C2,C3) without enhancement (C4)and a centrally located longitudinal spinal cord lesion from C7 to T12 (C5). (E) New lesion in the brain stem along the aqueduct with poorly defined margins on T2-FLAIR (E1, E2) and sagittal T2 MRI (E3), with no enhancement on Gd-T1 (E4). (G) T2-FLAIR showing large new lesions in the cortical (G1), corpus callosum and subcortical white matter (G2), without enhancement (G3, G4). Enlargement of the lesions in the spinal cord from C6 to T10 (G5). (H) MRI results 6 months after stopping INF-β therapy.

(1 g daily, for 5 days) immediately, tapering to tablets and stopped after 2 months. An MRI performed 2 months after therapy showed significant resolution of the lesions (Fig. 1B). Her condition gradually improved, resulting in a complete clinical recovery one year later without any residual deformity.

Twenty-one months later, she presented with diplopia, symmetrical weakness of the lower limbs and urinary retention. The results of fundoscopy and a visual field examination were normal, and electrophysiological tests were negative. The WBC count in her CSF was 320×10^6/L, with 95% lymphocytes. Oligoclonal band (OCB) analysis showed that the blood–brain barrier was damaged and that intrathecal synthesis of IgG had increased (Table 1), but she was negative for both OCB and neuromyelitis optica (NMO)-IgG. An MRI performed 2 weeks after disease onset showed new lesions in the thalamus