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LETTER TO THE EDITOR

Rapid-eye-movement sleep behavior disorder secondary to acute aseptic limbic encephalitis

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Abstract Rapid-eye-movement (REM) sleep behavior disorder (RBD) is a parasomnia characterized by complex motor activity associated with dreaming during REM sleep. RBD may be idiopathic or associated with various neurological diseases involving the brainstem. The association of RBD and limbic system impairment was unclear. We report a 46-year-old man with acute aseptic limbic encephalitis in association with RBD. The patient presented with subacute onset of anterograde/retrograde amnesia and persistent fever. Abnormal nocturnal behavior during sleep consisted of waving hands to fight and kicking legs. Brain magnetic resonance imaging showed damage on the bilateral unci and medial temporal lobes. Cerebrospinal fluid analysis indicated aseptic encephalitis. A polysomnography revealed augmented phasic activity in the submental and bilateral tibialis anterior muscles during REM sleep. Our finding suggests that limbic system impairment may lead to the occurrence of RBD.

Keywords Aseptic encephalitis · Limbic system · REM sleep behavior disorder (RBD)

Sir,

Rapid-eye-movement (REM) sleep behavior disorder (RBD) is a parasomnia characterized by complex motor activity associated with dreaming during REM sleep [1, 2]. RBD may be idiopathic or associated with various neurological diseases involving the brainstem. Based on animal studies, lesions in the dorsolateral pons or in the medial medulla result in loss of muscle atonia in REM sleep [2]. RBD has been reported rarely with damage in the limbic system [3]. The association between RBD and acute aseptic limbic encephalitis has not been reported. We report a patient with acute aseptic limbic encephalitis who developed RBD coincidentally.

Case report

A 46-year-old man presented with acute onset of antegrade and retrograde memory impairment for 2 days. He had caught a common cold 2 weeks prior to admission. Past medical history was unremarkable. On admission, severe short-term memory impairment was noted. The mini-mental status examination (MMSE) score was 24, and the cognitive abilities screening instrument (CASI) score was 87. The laboratory investigation revealed mild leukocytosis (12,240/μl). However, persistent fever was found after admission, and the brain magnetic resonance image showed hyperintensity over the bilateral unci and medial temporal lobes on diffuse weighted image and FLAIR image (Fig. 1). Analysis of the cerebrospinal fluid showed normal pressure, increased cell count (19 monocytes and 1 polymorphonuclear cell/mm^3), increased protein concentration (77.1 mg/dl) and normal glucose concentration (72 mg/dl). Acyclovir therapy was given immediately, because we could not rule out herpes simplex encephalitis [4]. Antigens for cryptococcus and VDRL were negative. Antibodies to herpes simplex virus type 1, 2 (HSV-1, -2) and varicella-zoster virus were also negative. Although the definite pathogen was not identified, repeated analysis of the cerebrospinal fluid was normal. The repeated MMSE score was 29, and CASI score was 98.

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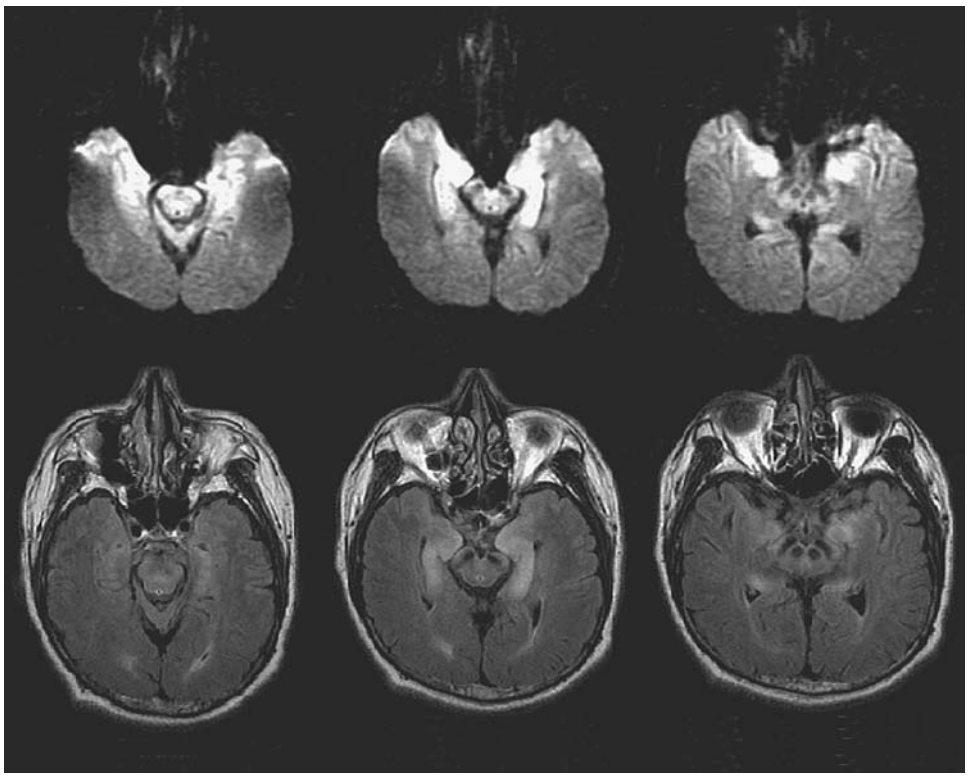

Fig. 1 Axial FLAIR brain magnetic resonance image (MRI) and diffuse weighted imaging (DWI) showed hyperintensity over the bilateral unci and medial temporal lobes

Abnormal behavior during sleep began 3–4 days after admission. The patient waved his hands and kicked his legs, as if he wanted to reach something or to fight with someone during sleep. His recent memory was so impaired that he could not recall any dream upon awakening. The polysomnography recording revealed augmented phasic activity in the submental and bilateral tibialis anterior muscles during REM sleep (Fig. 2). An electroencephalogram showed no epileptiform discharge. A diagnosis of symptomatic RBD was made on the basis of his clinical presentation and polysomnography recording. RBD improved with clonazepam, and repeated PSG also showed no abnormal EMG activity during REM sleep.

Discussion

RBD frequently occurs in the setting of neurodegenerative disease involving the brainstem, and the relationship between RBD and synucleinopathies has been established [5, 6]. RBD also occurs in some neurological conditions involving the brainstem, including ischemic lesion, neoplasm and demyelinating lesion [7]. The mechanisms and anatomic factors of RBD are not completely clear. An anatomic framework and schema have been proposed in which the structure in humans is analogous to the subcoeruleus region in cats and is crucial to RBD pathogenesis [8]. Neuroimaging data from the literature on human RBD also reveal that lesions in the brainstem may induce RBD, such as brainstem astrocytoma and multiple infarcts, in which the dorsal midbrain and pontine tegmentum were speculated [1].

RBD can be associated with autoimmune disorders involving the limbic system. Iranzo et al. [3] reported six patients with nonparaneoplastic limbic encephalitis associated with antibodies to voltage-gated potassium channels (VGKC). Another case report demonstrated that limbic disorder with anti-Ma2-associated encephalitis might cause RBD and narcoleptic features [9]. Previous imaging studies have shown that during REM sleep, regional cerebral blood flow significantly increased in the pontine tegmentum, thalamic nuclei and limbic areas [10, 11]. The interaction within the limbic system activates during REM sleep, suggesting that the limbic system may play a role in REM sleep.

The etiologies of limbic encephalitis include viral infection, autoimmune disorders and paraneoplastic disease [12, 13]. Patients with paraneoplastic limbic encephalitis partially respond to antineoplastic therapy and usually have a poor prognosis. Limbic encephalitis related to VGKC antibody should be treated with immunotherapy, and this is different from our case [14]. Due to the benign course in our case, the diagnosis of aseptic encephalitis was more likely. In our case, the occurrence of RBD was due to direct damage of acute limbic encephalitis without primary brainstem impairment. Our report is important to support

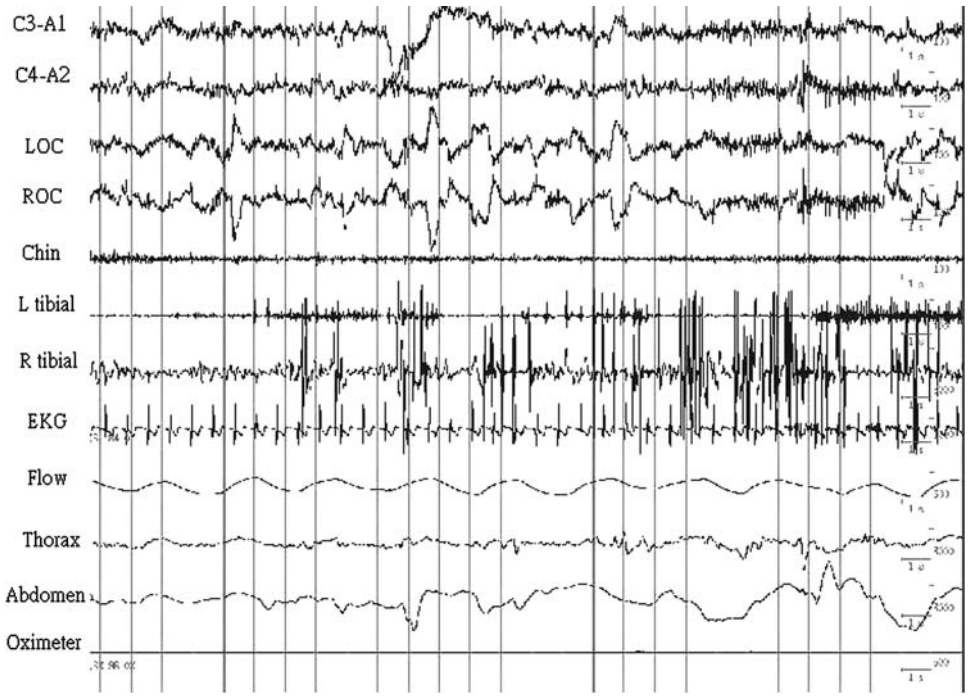

Fig. 2 A polysomnography revealed augmented phasic electromyogram activity over the submentalis and bilateral anterior tibialis channels during REM sleep

previous findings that limbic system impairment could be implicated in the pathogenesis of RBD.

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