Symptomatic Narcolepsy as a Presenting Feature of Neuromyelitis Optica

Pradeep Kallollimath, Amruth Gujjar[1], Megharanjini Patil[2]

Department of Neurology, Dharwad Institute of Mental Health and Neurosciences, Dharwad, Departments of [1]Neurology and [2]Radiology, Karnataka Institute of Medical Sciences, Hubballi, Karnataka, India

Abstract

Narcolepsy is a sleep disorder characterized by excessive daytime sleepiness. It can be either primary or symptomatic due to other neurologic disorders. Neuromyelitis optica (NMO) is an inflammatory demyelinating disorder in which symptomatic narcolepsy is being described as one of the core clinical features. Here, we report a patient with NMO who presented with narcolepsy. Signal changes on magnetic resonance imaging in hypothalamus and other periventricular regions of high aquaporin-4 expression should prompt considering NMO as diagnosis. Serum anti-aquaporin-4 IgG antibody testing should be done in such cases, and appropriate treatment should be initiated to prevent further neurological worsening and relapses.

Keywords: Aquaporin antibody, narcolepsy, neuromyelitis optica

Introduction

Neuromyelitis optica (NMO) is an inflammatory central nervous system disorder associated with antibodies to aquaporin-4. Wingerchuk's revised 2006 diagnostic criteria for diagnosis of NMO required optic neuritis, acute myelitis, and at least two of the following three supportive criteria: longitudinally extensive spinal cord lesions involving three or more contiguous vertebral segments, lack of brain lesions in the magnetic resonance imaging (MRI) fulfilling multiple sclerosis (MS) criteria at the disease onset, and serum positivity for aquaporin-4 antibody.[1] However, clinical spectrum of NMO is rapidly expanding, and many atypical presentations such as intractable hiccups and vomiting and hypersomnolence are being recognized as core clinical features.[2,3] This has led to the revised international consensus diagnostic criteria by the International Panel for NMO Diagnosis in 2015.[4] Here, we report a patient of NMO who presented with narcolepsy.

Case Report

A 20-year-old female presented with complaints of excessive sleep for 10 days. Her sleep duration gradually increased to 16–17 h/day and later to 20–22 h/day, getting up only for her daily needs. Three days after the onset of hypersomnolence, she developed swaying while walking which gradually progressed to require support while walking. Five days after the initial symptom, the patient developed double vision, which was binocular and more for distant objects.

On examination, the patient was conscious, responding to verbal commands, and lapsing into sleep in-between. Fundus examination was normal. She had binocular diplopia for distant objects but no obvious gaze palsy. Power was normal in all limbs. There was finger-nose and heel-knee incoordination bilaterally. She had wide-based gait and used to require one person support while walking.

Two years ago, the patient had fever for 20 days following which she developed right hemiparesis, aphasia, and seizures. Differential diagnosis of acute disseminated encephalomyelitis (ADEM), meningoencephalitis, and vasculitis were considered at that time. MRI brain had shown fluid-attenuated inversion recovery (FLAIR) hyperintensities in the left half of pons,

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Address for correspondence: Dr. Pradeep Kallollimath, H.No. 121; "Prapoorna", Renuka Nagar, Gokul Road, Hubballi - 580 030, Karnataka, India.
E-mail: pradeepkallollimath@gmail.com

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midbrain, left frontal lobe, insular cortex, and medial temporal lobe. Cerebrospinal fluid (CSF) study was within normal limits (protein of 23 mg/dL; cell count of 4 lymphocytes/dL; sugar of 69 mg/dL; ADA: 14 U/L; India ink negative; Gram stain negative). HIV and HbSAg tests were negative. ANA screening was negative. The patient was treated with oral prednisolone, levetiracetam, and supportive measures and improved.

The patient was readmitted after 2 months with dysphagia and nasal regurgitation after she had discontinued oral steroids. Repeat MRI showed persistent signal changes in the left side of midbrain and pons, newly appeared subtle signal changes in medulla around the central canal, gliotic changes in the left frontal lobe, insular cortex and medial temporal lobe, and no focal-enhancing lesions. Her symptoms improved after restarting steroids. She was taking oral prednisolone 10 mg/day which she had again discontinued 3 months before the present admission.

Based on the history and examination findings, differential diagnosis of relapsing-remitting demyelinating illness, recurrent ADEM, and vasculitis were considered.

Routine hematological and biochemical investigations were within normal limits. MRI of the brain and whole spine was done. There were hyperintense signal changes on T2 and FLAIR sequences in hypothalamus, periaqueductal gray, and pontine tegmentum [Figure 1a-c]. There was hypointensity on T1 imaging in the left cerebral peduncle suggestive of previous insult. Whole spine MRI showed T2 hyperintense lesion at D10 vertebral level [Figure 1d].

Serum NMO antibody test (by immunofluorescence method) was done, and the result was positive.

The patient improved symptomatically after starting steroids. Her sleep duration reduced from 22 h to 16 h during hospital stay, and diplopia and ataxia were improved. She was started on azathioprine along with oral steroids and was discharged.

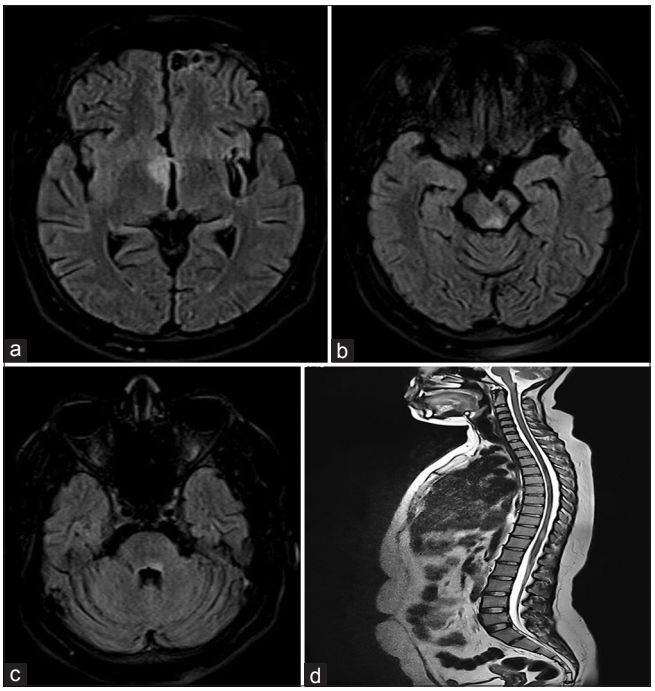

Figure 1: (a) Fluid-attenuated inversion recovery magnetic resonance imaging showing hyperintense signal changes in hypothalamus. (b) Fluid-attenuated inversion recovery magnetic resonance imaging showing hyperintense signal changes in periaqueductal gray. (c) Fluid-attenuated inversion recovery magnetic resonance imaging showing hyperintense signal changes in pontine tegmentum. (d) T2 sagittal magnetic resonance imaging of spine showing hyperintense lesion at D10 vertebra

Discussion

Narcolepsy is a sleep disorder characterized by excessive daytime sleepiness. Primary narcolepsy is caused by selective loss of hypocretin-1-producing neurons. An autoimmune process is thought to be the likely cause as certain human leukocyte antigens (HLAs) that increase the risk of autoimmune disorders are strongly associated with primary narcolepsy. HLA DQB1*0602 is found in more than 85% of people with primary narcolepsy.[5] Symptomatic narcolepsy occurs rarely with neurologic disorders such as tumor, stroke, or demyelinating disorders that directly damage hypocretin-1-producing neurons in the hypothalamus.[6] Narcolepsy has been reported in autoimmune demyelinating disorders, MS and NMO.

Our patient had narcolepsy as the presenting symptom with signal changes in hypothalamus on MRI. Her previous symptoms of hemiparesis and dysphagia could be part of symptomatic cerebral syndrome and acute brainstem syndrome of NMO. However, anti-aquaporin-4 antibody test was not done at that time as diagnosis of NMO was not considered at that stage.

Kanbayashi *et al*. reported 7 cases of excessive daytime sleepiness with symmetrical inflammatory hypothalamic lesions, of which 3 patients were anti-aquaporin-4 antibody positive. CSF hypocretin-1 levels in all the patients were significantly reduced. Aquaporin 4 is expressed in astrocytes, predominantly in periaqueductal and periventricular regions. An immune attack on aquaporin 4 in periventricular regions in the hypothalamus may secondarily affect the hypocretin neurons.[7]

Carlander *et al*. reported a case of NMO who was anti-aquaporin-4 antibody positive and had associated excessive daytime sleepiness and hypocretin deficiency.[8]

Poppe *et al*. reported two additional NMO cases presenting with excessive daytime sleepiness with symmetrical hypothalamic lesions although anti-aquaporin-4 antibody titer was not measured in these cases.[9]

Traditionally, NMO was considered as a disease of spinal cord and optic nerves. The discovery of aquaporin-4 IgG antibodies specific for NMO has broadened the clinical and neuroimaging spectrum of NMO with increasing recognition of nonopticospinal forms. This lead to introduction of the term NMO spectrum disorders in 2007.[10] Further advances have rendered the 2006 criteria inadequate leading to the revised international consensus diagnostic criteria in 2015.[4] Symptomatic narcolepsy is one of the core clinical characteristics in the revised diagnostic criteria.

Conclusion

This case demonstrates the importance of nonopticospinal features in the diagnosis of NMO. Our patient did not have classical optic neuritis or longitudinally extensive transverse myelitis but presented with diencephalic syndrome. Serum aquaporin-4 IgG antibody test should be done in patients presenting with nonopticospinal features such as narcolepsy, intractable hiccups, and vomiting. This will help in confirming the diagnosis of NMO and initiating proper treatment to prevent subsequent relapses.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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