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Sir,

a 56-year-old woman presented with moderate epigastric pain, nausea, vomiting, hiccups and mild orthostatic intolerance. Gastroenterological assessment, including esophagogastroduodenoscopy and abdominal ultrasound were normal. One month later she developed mild memory impairment together with depressive demeanor and excessive daytime sleepiness when she was referred to our Center. On admission, neurological and physical examination, except mild cognitive impairment (MMSE 25/30) was unremarkable. Brain MRI showed hyperintensive lesions in the brainstem, hypothalamus and periventricular white matter surrounding third ventricle (Figure 1 c and d). Cervical and thoracic MRI showed extensive hyperintense lesion extending from C3 to Th3 level (Figure 1 e and f). Predominantly lymphocytic pleocytosis together with oligoclonal bands were found in the CSF. NMO-IgG antibodies were positive (101.5 units/ml; normal values <5 (EIASON® Aquaporin-4 Ab, ELISA)) and she was diagnosed with NMO spectrum disorder.
Visual evoked potentials were normal. Overnight polysomnography showed sleep fragmentation; low sleep efficiency and diminished percentage of N3 and REM sleep stage (Figure 1 a). Mean Sleep Latency in Multiple Sleep Latency Test was 3 minutes, which indicates excessive daytime sleepiness. However no sleep onset REM period was observed which excluded secondary narcolepsy. Neuropsychological testing showed mild cognitive impairment primarily in domains of attention, verbal memory and executive functions. Head-up tilt table test together with serum dopamine, epinephrine and norepinephrine analysis revealed postural orthostatic tachycardia syndrome (POTS) (Figure 1 b) associated with significantly elevated norepinephrine levels in both, standing and supine position (norepinephrine – supine 4.84 nmol/L, norepinephrine – standing 13.95 nmol/L; normal values < 2.49 nmol/l). Urine metanephrine and normetanephrine levels and serum cortisol, prolactin, LH and FSH levels were within normal reference range.

Patient was treated with intravenous corticosteroids for five consecutive days with subjective improvement of daytime sleepiness and orthostatic intolerance and she was discharged with recommendation to take azathioprine and oral corticosteroids.

Follow-up MRI three and six months later showed no signs of new lesion and as of November 2013 she is without any new symptoms.

NMO is an idiopathic demyelinating disorder of the central nervous system affecting primarily optic nerves and spinal cord. However, discovery of disease specific serum NMO-IgG antibodies, enabled to consider additional clinical features as a part of NMO spectrum disorders (1). Brain MRI lesions parallel location of high AQP4 concentration like hypothalamus, area postrema and periaqueductal brainstem with consecutive clinical manifestation (2). Hypothermia, hypothermia, hypotension, hypersomnia and obesity were previously described as a consequence of the hypothalamic lesions (3) together with the vomiting and hiccups as the most frequent clinical manifestation of the periaqueductal brainstem lesions (4).

POTS is an autonomic disorder characterized by heart rate (HR) increment >30 bpm in standing without orthostatic hypotension. Two major types of POTS are recognized on the basis of standing plasma norepinephrine levels (5). Hyperadrenergic POTS is characterized by an excessive increase of plasma norepinephrine with an increase in blood pressure (BP) on standing. Most cases of POTS are idiopathic, and secondary form of POTS occurs in association with a variety of other medical illnesses among which is multiple sclerosis (6).

Here we present a case of hyperadrenergic POTS in the patient with NMO spectrum disorder and periaqueductal brainstem lesion. Considering analogy with multiple sclerosis in which autonomic dysfunction is explained by lesions in regions responsible for autonomic regulation, such as nuclei in the periventricular region of fourth ventricle in the brainstem (7), causative relationship between brainstem lesions in NMO and POTS seems plausible.

Comprehensive assessment of autonomic function in NMO patients and further research in this field should additionally elucidate this concept.

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Figures

Figure 1. a and b) Brain MRI, FLAIR sequences showing hyperintensive lesions in the brainstem and periventricular white matter surrounding third ventricle; c and d) spinal cord MRI, T2 sequences showing extensive hyperintense lesion extending from C3 to Th3 level.

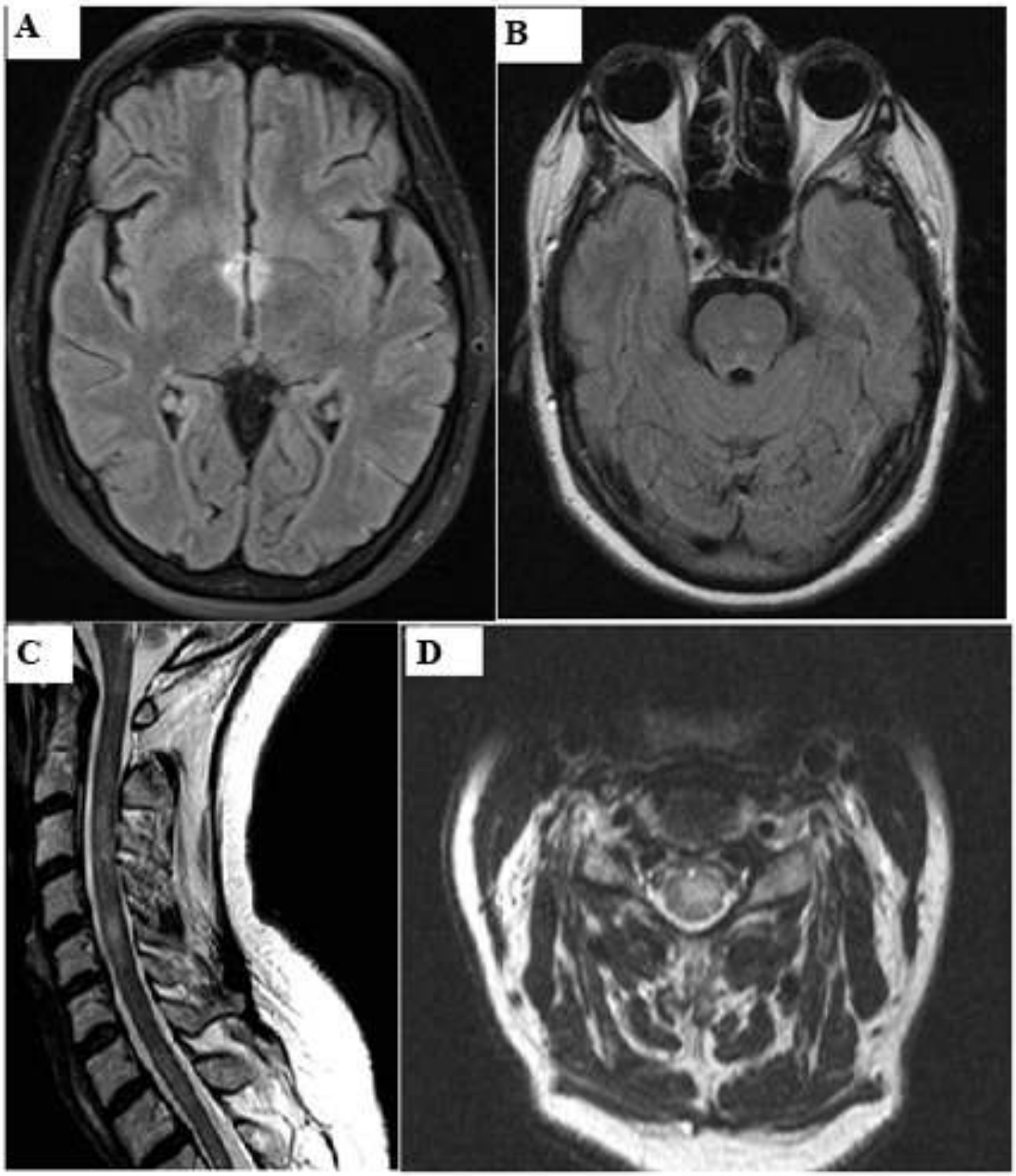

Figure 2. a) Hypnogram showing short sleep latency, excessive sleep fragmentation; low sleep efficiency and diminished percentage of N3 and REM sleep stage. b) Results of the head-up tilt table test. The upper line represents the heart rate and lower line represents blood pressure; second, 3rd and 4th vertical lines present Valsalva maneuver which was normal, 5th vertical line presents heart rate response to deep breathing which was normal; note the increase in hart rate after tilt (6th vertical line) without significant drop in blood pressure.