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LETTER TO THE EDITOR

Miller Fisher syndrome complicated by inappropriate secretion of antidiuretic hormone: a case report

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Introduction

Miller Fisher syndrome (MFS) is a variant of Guillain Barré syndrome (GBS) and is characterized by a triad presentation of ophthalmoplegia, areflexia and ataxia. Autonomic dysfunction is widely described in patients with GBS, occurring in up to two-thirds of patients [1]. Autonomic involvement is however less likely in patients with MFS. Herein, we describe a case of MFS associated with syndrome of inappropriate secretion of antidiuretic hormone (SIADH).

Case presentation

A 58-year-old male patient with no relevant medical history had a subacute onset of rapidly progressive dysesthesia in all four limbs in April 2020. He developed vertical binocular diplopia and inability to walk the next day, and was then admitted to the neurology department. He was afebrile and denied headaches. No preceding infection or vaccination was reported. A careful history ruled out long-term and/or chronic alcohol use. On admission, neurological examination revealed diffuse areflexia, lower limbs weakness (grade 3/5), severe extrinsic ophthalmoplegia and unsteady gait. He could not walk without assistance. There were no pyramidal signs and mental status was not altered. Routine blood tests showed decreased serum sodium concentration (123 mEq/L; N: 137–145). Serum osmolality and urine osmolality were 220 (N < 275) and 477 (N 400–800) mOsm/kg H_2O, respectively. Urine sodium was 20 mEq/L. Blood sugar level was normal (88 mg/dL), as well as thyroid function test. Serum creatinine was normal (0.68 mg/dl; N 0.66–1.25) and there was no adrenal insufficiency (morning serum cortisol 14.3 µg/dL; N 6.2–18). No vitamin/nutritional deficiencies were found. Infectious workup was unremarkable. Autoimmune serologies were negative, including GQ1b antibodies. Cerebrospinal fluid (CSF) analysis showed a cell count of 39 cells/µl (86% lymphocytes), elevated protein concentration (87 mg/dL; N < 45), and negative CSF-restricted IgG oligoclonal bands. No infectious agents were detected. Electroneuromyography (EMG) showed the absence of F-waves for the peroneal nerve. EMG was repeated 5 days later and showed the presence of an acute polyneuropathy with reduced amplitudes and slowed motor conduction velocities in the bilateral peroneal and tibial nerves. Brain and spinal cord magnetic resonance imaging was unremarkable, as well as whole body 18-fluorodeoxyglucose positron emission computed tomography. Computed tomography of the chest was normal. Based on the clinical picture, laboratory results and EMG findings, MFS associated with SIADH was diagnosed. The patient was thus treated with fluid restriction and intravenous hypertonic saline solution and was promptly started on IVIG at a dose of 2 g/kg over 5 consecutive days, resulting in progressive clinical improvement. Serum sodium levels normalized by day 7. The patient was then discharged to a rehabilitation center. A 3-month follow-up showed resolution of the ophthalmoplegia but persistent moderate ataxic gait, causing walking difficulties.

Discussion

Here, we describe a case of SIADH related to anti-GQ1b-negative MFS, an uncommon association. Although serum IgG anti-GQ1b antibody is the most specific biomarker for MFS, a negative result cannot exclude the diagnosis in

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our patient, given that 10–30% of patients with MFS are seronegative [2]. Occurrence of signs of polyneuropathy on the follow-up EMG supported the diagnosis of MFS. In the current case, other causes of SIADH were reasonably excluded as there were no demonstrable central nervous system lesions or pulmonary pathology, and since careful medication history ruled out drug-induced SIADH.

The involvement of the autonomic nervous system (such as blood pressure variability, cardiac arrhythmias, bladder and gastrointestinal dysfunction, or SIADH) is frequent in GBS [1]. A previous prospective study involving 50 patients with GBS showed that 48% developed SIADH during the course of their disease [3]. Although MFS is considered as a variant of GBS, its association with autonomic dysfunction, especially SIADH, is rather uncommon [4]. Only a few cases of MFS associated with SIADH have been reported [4, 5].

The exact underlying mechanisms of SIADH in patients with GBS/MFS remain yet unknown.

Several speculative mechanisms have been suggested, including (i) impairment of autonomic nervous function involving the peripheral afferent fibers arising from vascular stretch receptors, resulting in reduced vagal inhibitory action on the release of antidiuretic hormone from the neurohypophysis, (ii) increased renal tubular sensitivity to vasopressin, and (iii) a downward osmotic resetting and enhanced renal tubular sensitivity to antidiuretic hormone [3]. Some authors have also suggested that SIADH in anti-GQ1b-negative MFS may be an immune-mediated disorder involving hypothalamic nuclei, which abundantly express gangliosides GM1, GD1a, GD1b and GT1b, by other antiganglioside antibodies [6, 7].

In the study by Saifudheen and colleagues, SIADH was mostly asymptomatic in GBS patients, but was associated with a poorer prognosis and an increased mortality [3]. Although hyponatremia was also asymptomatic in our patient, this case is particularly relevant given that hyponatremia is a potentially life-threatening condition, as a result of cerebral edema and increased intracranial pressure [5]. In our case, serum sodium concentration rapidly normalized after fluid restriction and intravenous hypertonic saline solution, and neurological clinical outcome was gradually favorable after IVIG therapy and physiotherapy. Early recognition of this complication is essential to ensure appropriate and prompt management. Further work should determine whether SIADH contributes to worse functional outcomes and higher mortality in MFS, as already reported in GBS patients.

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Declarations

Conflict of interest The authors declare no conflict of interest regarding this case report.

Ethical approval All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

Informed consent For this type of study, formal consent is not required.

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