

Case Report

Autonomic Dysfunction and SIADH as First Signs of Guillain-Barre Syndrome

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Abstract

A 68-year-old woman was admitted to our Internal Medicine Unit for severe hyponatremia and new onset resistant hypertension for two weeks. She also complained of nausea, weakness and paresthesia of the limbs in the previous 4 days. Several diagnostic tests were performed (blood, hormonal and urinary tests, echocardiography, ECG, renal arteries Doppler-US, total body CT scan), showing only severe hyponatremia, mild hypokalemia and mild hypochloremia. Hypertension was treated with isosorbide and doxazosin, whereas in the suspect of a Syndrome of Inappropriate Antidiuretic Hormone Secretion (SIADH), hyponatremia was treated with hypertonic saline solution with progressive normalization of serum sodium levels. Despite improvement in the presenting symptoms, after 10 days the neurological scenario worsened, with persistence of weakness and onset of areflexia of lower limbs, constipation and urinary retention. Therefore, the patient was evaluated by a neurologist who, hypothesizing a Guillain-Barre Syndrome (GBS), required an EMG, which confirmed this clinical suspect. Intravenous immunoglobulins were immediately started and administered for 5 days, with partial improvement of weakness and areflexia. The patient was then transferred to a rehabilitation institute for the recovery path.

We report a rare form of GBS where hypertension and SIADH, not frequent clinical features of this acute inflammatory polyneuropathy, preceded the neurological manifestation. In fact, the delay in the manifestation of the neurological pattern made harder and delayed the diagnosis. However, it is important to stress that a high clinical suspicious should rise in presence of multi-resistant hypertension with, even mild, neurological symptoms and electrolytes disturbances.

Keywords: demyelinating neuropathy; areflexia; paresthesia; hyponatremia; hypertension; urinary retention

Abbreviations

GBS: Guillain-Barre Syndrome; SIADH: Syndrome of Inappropriate Antidiuretic Hormone Secretion; EMG: Electromyography; US: Ultrasound; CT: Computed Tomography; ECG: Electrocardiography.

Case Presentation

A 68-year-old woman was admitted to our Internal Medicine Unit for severe hyponatremia and new onset resistant hypertension for two weeks. In the last two days she also complained of nausea, weakness and paresthesia of both upper and lower limbs. In her past medical history, she had dyslipidemia, bilateral moderate carotid stenosis treated with aspirin and Basedow disease diagnosed 10 years before.

Four days before our referral, she was admitted to the Emergency Department because of a hypertensive peak, but given the fairly normality of blood tests, 12-lead-ECG and echocardiography (which showed only an alteration in diastolic relaxation), she was discharged with indication to start an anti-hypertensive therapy. The general practitioner prescribed her ramipril/hydrochlorothiazide once daily, without any effect on blood pressure control, so that she returned to

the Emergency Room. Her physical examination and neurological evaluation were unremarkable except for high blood pressure (200/95 mmHg), which was resistant to several drugs. The 12-lead-ECG and echocardiography were unchanged, and the chest x-rays was normal. Blood tests showed only mild hypokalemia (3.2 mEq/L) and moderate hyponatremia (126 mEq/L). The latter was treated with physiological solution added with sodium chloride, however with worsening of Sodium (Na) serum levels (115 mEq/L). Once admitted to our ward ramipril/hydrochlorothiazide was stopped and continuous intravenous (IV) isosorbide and water restriction plus physiological solution added with sodium chloride were started, with a partial benefit on hypertension and mild improvement in hyponatremia (120 mEq/L). Blood tests were also repeated, showing normality of blood count, inflammatory markers and renal function but confirming electrolyte disturbances (Na 120 mEq/L, K 3.2 mEq/L, Ca 7.8 mEq/L, Cl 87 mEq/L, Mg 2.2 mEq/L). All hormonal tests (TSH reflex, adrenocorticotrophic hormone, urinary and plasmatic cortisol, urinary metanephrines) and urinary tests (chemical-physical urinary test and urinary second level sediment, urinary electrolyte dosing) were normal. The patient underwent also a renal arteries Doppler-ultrasound and a total body Computed Tomography (CT) scan, but both exams did not show any abnormal findings. Meanwhile, because

of a suboptimal control of hypertension with isosorbide, therapy was switched to doxazosin with normalization of blood pressure values. Given the persistence of hyponatremia (120 mEq/L), a SIADH consequent to prolonged effect of ramipril/HCT was suspected. The patient was then started with a treatment with hypertonic saline solution at 3%, with gradual improvement of sodium serum levels and normalization of other electrolyte disturbances. However, after 10 days of hospitalization the neurological scenario deteriorated: weakness and paresthesia of limbs worsened and complete areflexia of lower limbs, urinary retention and constipation suddenly developed. The patient was immediately evaluated by a neurologist, who in the suspect of Guillain-Barre syndrome, required Electromyography (EMG) which revealed marked suffering of demyelinating motor nerve fibers, thus confirming the diagnosis. Therapy with IV immunoglobulins was promptly started and continued for 5 days, with reappearance of lower limbs osteotendinous reflex and partial improvement of lower limbs motricity. After 19 days of hospitalization the patient was finally discharged and transferred to a rehabilitation structure to continue the recovery path.

Discussion

In our case we report a very rare manifestation of Guillain-Barre Syndrome (GBS), characterized by SIADH and autonomic dysfunction. GBS is the most frequent acute inflammatory polyneuropathy, which classic form is characterized by progressive ascending weakness and areflexia (or hyporeflexia) of limbs, sensory symptoms and neuropathic pain. However, a significant part of patients affected by GBS can manifest autonomic dysfunctions during the natural history of the illness [1-3]. Indeed, a recent American study found that 38% of patients with GBS admitted to Intensive Care Unit had at least one dysautonomic manifestation, namely hypertension/hypotension, ileus, tachycardia/bradycardia and urinary retention. Finally, the presence of dysautonomia was associated with a higher probability of mechanical ventilation and mortality [4]. SIADH is also a common finding in GBS patients. An Indian prospective study showed that among a population of 50 patients affected by GBS, the 48% of them developed SIADH during the illness course. Furthermore, patients with SIADH had longer mean duration of hospitalization, higher risk of ventilation support and poorer prognosis compared to GBS patients without it [5]. Conversely to our patient, either SIADH or dysautonomic manifestations often rise after neurological symptoms and perhaps this odd temporal clinical sequence may explain the delay in our diagnosis [1,3]. In the case we describe, at admission the patient had a completely normal neurological examination, developing weakness of upper and lower limbs, weakness of face muscles and areflexia after 10 days of hospitalization and even more from dysautonomic and electrolytes disturbances. In literature only few case reports describe a scenario like that of our patient. Hoffmann et al. reported the case of a 38-year-old woman who was admitted to Internal Medicine Unit for severe hyponatremia secondary to SIADH and who was diagnosed with GBS with limbs paresis and areflexia at least three days later. However, conversely to our patient, dysautonomic symptoms were absent [6]. On the other hand, Ramanathan et al. reported the case of an 82-year-old woman with paresthesia, back pain, blood pressure instability, constipation, urinary retention and hyponatremia secondary to SIADH that after 10 days of hospitalization developed

neurological symptoms (weakness of upper and lower limbs, weakness of face muscles and areflexia), suggesting the diagnosis of GBS (that was then confirmed). The scenario reported by Ramanathan was similar to ours, with both the presence of SIADH and dysautonomic symptoms preceding neurological manifestations. But, in his patient the neurological involvement was more important so that she needed a short period of stay in Intensive Care Unit and the recovery of motricity was only partial [3].

The pathogenesis of GBS, as well as that of autonomic dysfunctions associated with the inflammatory polyneuropathy is not yet fully understood. For sure, an aberrant autoimmune response against peripheral nerves caused by trigger factors, mainly respiratory and gastrointestinal infections, has been proven for GBS. Probably the inflammatory process that involves the peripheral nervous system can also affect sympathetic and parasympathetic nerves, causing alterations or failure of these systems [1,3]. Likewise, the pathogenesis of SIADH is unclear. Some hypotheses encompass an increased renal tubular sensitivity to anti-diuretic hormone and alterations of osmoreceptor's response [5].

The clinical presentation drives the diagnosis of GBS; nevertheless, it can be supported also by Cerebrospinal Fluid (CSF) examination showing albumin-cytological dissociation, and Electromyography (EMG), defining three different electrophysiological subtypes: Acute Motor Axonal Neuropathy (AMAN), Acute Motor and Sensory Axonal Neuropathy (AMSAN) and Acute Demyelinating Polyneuropathy (AIDP). In our case report, the clinical suspect was confirmed by the EMG showing the third subtype.

The treatment of GBS is based on the administration of intravenous immunoglobulins (IVIg), as we have done with our patient, or plasma exchange. Both these two treatments should be started as soon as possible to prevent an irreversible nerve damage. It is also necessary to monitor the vital parameters, especially the respiratory function and the hemodynamic, and if necessary, to transfer the patient to Intensive Care Unit to treat complications of GBS such as acute respiratory failure or pressure instability. Finally, physiotherapy and rehabilitation are important for a partial or complete recovery of motricity [1,2].

Conclusions

Our case of atypical GBS where SIADH and dysautonomic dysfunction preceded neurological manifestations, stresses on the difficulty that clinicians could face when diagnosing a disease with unusual clinical presentation. In fact, the delay in the manifestation of the neurological pattern made harder the diagnostic algorithm, despite a high clinical suspicion should have raised in presence of multi-resistant hypertension, electrolytes disturbances and even mild neurological symptoms which were present at the very beginning. In fact, limbs paraesthesias were present at the first stage of the illness, suggesting a possible neurological involvement, but they were misleadingly classified as secondarily to hypertension and severe hyponatremia. This could have been possibly caused because clinicians focused only on each symptom rather than on the whole scenario. The multidisciplinary approach finally solved the dilemma and drove the diagnosis and the optimal therapy, suggesting the need of collaboration between specialists when facing a complex clinical pattern.

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