Immunoglobulin induced hyponatremia in Guillain-Barré syndrome: A rare occurrence

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ABSTRACT

Guillain-Barré syndrome (GBS) is an acquired, inflammatory peripheral neuropathy characterized by progressive ascending, symmetrical muscle weakness, and depressed or absent deep tendon reflexes. Here, we report the case of a 55-year-old male who presented to the emergency with a history of sudden onset weakness of bilateral lower and upper limbs, in ascending order for 3 days. He was diagnosed with GBS and appropriate treatment with intravenous immunoglobulin (IVIG) was started. The course of the treatment was assessed meticulously. Undesirable effects from IVIG are reported to occur in up to 5–15% of all IV infusions. Most of these are mild, reversible, and transient. Various studies have proven pseudohyponatremia to be a known complication of IVIG. In this case report, we demonstrate that IVIG administration can result in true hyponatremia and it can be deleterious if meticulous care and concern are not provided to the patient.

Key words: *Electrolytes, Guillain-Barre syndrome, Hyponatremia, Immunoglobulin, Power*

"Courage, Faith, Strength, Hope!" words of encouragement most commonly heard among Guillain-Barré syndrome (GBS) Survivors. GBS is an acquired, inflammatory peripheral neuropathy characterized by progressive ascending, symmetrical muscle weakness and depressed or absent deep tendon reflexes [1]. The diagnosis of GBS is based on the history, physical examination, and cerebrospinal fluid (CSF) evaluation [2]. The CSF characteristically contains a high protein concentration with a normal cell count, but these changes may take up to 2 weeks to develop.

The treatment with plasmapheresis and intravenous immunoglobulin (IVIG) is the ones with the most promising results [3]. However, undesirable effects from IVIG are reported to occur in up to 5–15% of all IV infusions [4]. Most of these are mild, reversible, and transient. Various studies have proven pseudohyponatremia to be a known complication of IVIG [5]. In this case report, we demonstrate that in a case of GBS, IVIG administration can result in true hyponatremia and it can be deleterious if meticulous care and concern are not provided to the patient.

CASE REPORT

A 55-year-old male patient visited the emergency department with a history of sudden weakness of the upper and lower limbs for 3 days. On being apparently alright 3 days earlier, he noticed that on waking up from sleep, he could not move his legs. The patient was taken to a local hospital nearby after which he was referred to Mahatma Gandhi Mission Hospital for further treatment. Gradually, he could not move his arms too.

On arrival at the hospital, the patient became very ill. On examination, the blood pressure was 150/90 mmHg and the pulse rate was 86 beats/min and regular. His oxygen saturation was 98% on room air and the temperature was normal. The clinical examination suggested weakness of 2/5 in the bilateral upper and lower limbs with absent reflexes and mute plantar reflex bilaterally. Sensations were intact on all four limbs suggesting no sensory involvement. The patient showed a Glasgow Coma Scale (GCS) of 15/15, absence of fever, well-oriented, a single breath count of 20 with no clinical evidence of dehydration.

Concerning his laboratory tests, complete blood count, urine routine, kidney function tests, and thyroid profile were within normal ranges. The laboratory results are shown in Table 1. His initial serum electrolytes were within normal range (Sodium = 136 mEq/L, and potassium = 4.5 mEq/L). Magnetic resonance imaging (MRI) brain (Plain) revealed no significant abnormality while MRI (whole spine screening) revealed disk desiccation and disk bulge at C5-C6, C6-C7, and C7-D1 and also at L4-L5, and L5-S1.The cardiac monitoring was normal throughout the hospital stay with no significant ST-T changes in the echocardiogram. His chest and abdominal X-ray had no obvious pathology.

Differential diagnoses such as diabetes mellitus and Vitamin B12 deficiency were ruled out on account of a lack of autonomic features. Small fiber neuropathies such as amyloidosis, heavy metal poisoning, and porphyria present with pain as their presenting complaint. Thus, with the demyelinating disorder at

the back of our minds, the most probable diagnosis suggested acute inflammatory demyelinating polyneuropathy – GBS. Lumbar puncture was performed the next day and yielded a clear and colorless CSF with 102 mg/dL of protein, 64 mg/dL of sugar. The CSF cell count was three with occasional lymphocytes.

After consultation with a neurologist, treatment with IVIG at 5 cc/hour was initiated through an intravenous infusion (test dose to watch for hypotension, anaphylaxis, and breathlessness). Later, the rate of IVIG infusion was increased to 21 cc/hour. Inj. Enoxaparin 0.4 cc subcutaneously was started as a measure for deep vein thrombosis prophylaxis. Neurophysiotherapy was initiated. On the 3rd day of IVIG administration, the patient complained of crampy pain in the left leg for which tab. Pregabalin 75 mg at bedtime (10PM) was started. With blood pressure being constantly elevated, tab. Propranolol 20 mg twice a day (9AM–9PM) was started. The rate of IVIG administration was gradually increased to 25 cc/hour–28 cc/hour and finally plateaued at 30 cc/hour.

On the 5th day of IVIG administration, the patient became intermittently disoriented and drowsy. He complained of crampy pain in both legs. Serum electrolytes revealed severe hyponatremia (sodium = 117 mEq/L, and potassium = 4.9 mEq/L). The single breath count narrowed to 18. Symptomatic treatment with Inj. 3% normal saline at 10 cc/hour was initiated. Serum osmolality = 265.05 mOsm/kg, urine osmolality = 399.75 mOsm/kg, and urinary sodium = 40 mmol/L; thus, suggesting of hyponatremia. On the next day, serum electrolytes were again reviewed (sodium = 119 mEq/L, and potassium = 4.8 mEq/L) and single breath count further dropped to 16. Tab. fludrocortisone 50 mcg BD (9AM–9PM) was started and a repeat chest X-ray was done as chest auscultation revealed bilateral basal crepitations. The chest X-ray was suggestive of the bilateral lower lobe pneumonitis for which the patient was started on antibiotics.

IVIG was administered for duration of 5 days and significant hyponatremia lasted for a period of 8 days post-IVIG treatment.

Table 1: Laboratory tests of the patient

Laboratory parameter	Normal range	Observed value (Day 1)
Hemoglobin	12–16.2 g/dL	13.5
Total Leukocyte Count	3540–9060/mm^3	7620
Platelet count	165,000–415,000/mm^3	265,000
Hematocrit	35.4–46.4	38.9
Mean corpuscular volume	80–96 fl	85.3
Urea	7–20 mg/dL	26
Creatinine	0.5–1.2 m/dL	0.8
Serum sodium	136–146 mEq/L	136
Serum potassium	3.5–5.5 mEq/L	4.5
CSF analysis	CSF sugar	64
	CSF protein	102
	CSF adenosine deaminase (ADA)	<1.0
	Cell count	03 (Occasional lymphocytes)

CSF: Cerebrospinal fluid

However, on completion of IVIG therapy supplemented with Tab. fludrocortisone, the patient improved with a GCS back to 15/15. Muscle strength on all four limbs did not show a drastic improvement as even literature suggests that most recovery near baseline occurs over a period of 1 year. The patient was discharged on the 18th day with muscle strength of 2/5 in the bilateral upper and lower limbs, normal sensations, no pain and most importantly, with a wonderful smile. Since then, the patient is on regular follow-up every 2 weeks.

DISCUSSION

Immunoglobulins produced from human plasma were first used in 1952 to treat primary immune deficiency [3]. IVIG is a proven effective treatment for GBS (Class 1 Evidence) [1]. However, it has been reported to result in post-infusional hyperproteinemia and would, therefore, be expected to cause pseudohyponatremia [4].

In a prospective study of 50 patients diagnosed with GBS, hyponatremia was noted in 48% cases and motor dysfunction. The underlying etiology of this phenomenon is presumably related to syndrome of inappropriate antidiuretic hormone (SIADH) [6]. A study examined the effect of IVIG infusion on serum sodium level measured by direct ion-selective electrodes and found that hyponatremia was also present in addition to pseudohyponatremia [7]. This "True Hyponatremia" is related to the osmotic translocation of water from intracellular to extracellular space mediated by an increase in the intravascular osmolality secondary to sucrose-based IVIG infusion [8].

In our patient, the normal serum sodium level at the time of presentation undoubtedly suggests that "True Hyponatremia" resulted due to sucrose-based IVIG Infusion. Another key point to be noted is that the patient did not improve symptomatically to hypertonic saline infusion or continuous administration of salt capsule. It was only when fludrocortisone was used, that the patient started showing signs of improvement.

Various studies demonstrate the use of dludrocortisone in subarachnoid hemorrhage, SIADH and cerebral salt wasting syndrome to prevent natriuresis and further hyponatremia [9]. Our patient case is unique in two aspects: (a) It confirms the theory that true hyponatremia occurs due to IVIG Infusion and not due to GBS, itself; and (b) administration of Tab. fludrocortisone proves beneficial to the patient, symptomatically, and results in a better prognosis.

CONCLUSION

Although pseudohyponatremia is a known complication of IVIG, in this case report, we demonstrated that IVIG administration can result in true hyponatremia and it can be deleterious if meticulous care and concern are not provided to the patient.

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