

SYNDROME OF INAPPROPRIATE ANTIDIURETIC HORMONE SECRETION IN POLYARTERITIS NODOSA

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ABSTRACT

Case Summary: A 55 year old female diabetic and hypertensive was admitted due to generalized body weakness. She was diagnosed to have polyarteritis nodosa (PAN) confirmed by muscle biopsy in 2002. She has been on Prednisone 5 mg per day since 7 years ago with poor compliance. On physical examination, she is generally weak with coarse crackles on the left lung base. Initial chest x-ray showed infiltrates on the left lung base, hence was initially treated as a case of community acquired pneumonia. During the course of admission, patient was persistently hyponatremic with worsening generalized body weakness. Thyroid function test of the patient showed normal results with increased cortisol levels. Further investigation revealed an elevated ESR and CRP levels. Though a rare complication of polyarteritis nodosa, syndrome of inappropriate antidiuretic hormone secretion (SIADH) was considered in the patient. She was started on Prednisone at 40 mg OD and was eventually discharged improved.

Conclusion: Polyarteritis nodosa can cause SIADH. Other possibilities should be first ruled out before considering such a rare scenario.

INTRODUCTION

The syndrome of inappropriate antidiuretic hormone secretion is a condition wherein there is an inappropriate secretion of the arginine vasopressin that causes the body to retain water, which leads to hyponatremia. There are numerous conditions that can cause this condition such as drugs, neoplasm, cerebrovascular disease, and infections. However, there are two published case reports that attribute SIADH to polyarteritis nodosa.^{1,2} It was postulated that the SIADH could be due to local vasculitis of the hypothalamic artery leading to decrease blood flow to the hypothalamus which is interpreted as a hypovolemic state or of the renal artery leading to renal ischemia that resulted to hyperangiotensinemia.

Case

A 55 year old female was admitted with a chief complaint of generalized body weakness. She is a known diabetic and hypertensive since 2002 maintained on Gliclazide and Imidapril. Last 2002, she also experienced the same symptom and was confined at a private hospital. Diagnostic work-up was done and she was confirmed to have polyarteritis nodosa by muscle biopsy. During this time blood chemistry was within normal levels including the sodium levels. She was maintained on Prednisone 5mg per day but due to financial constraints she would take it intermittently for symptomatic relief of the muscle pain. She was eventually lost to follow-up.

Thirteen days prior to admission at Ospital ng Makati, she was brought to the emergency room due to tingling sensation and pricking pain of the muscles of her lower extremities accompanied by generalized body weakness. Upon examination, she was generally weak and had a hard time raising her extremities. Diagnostics showed hyponatremia (131 mmol/L) and elevated random blood sugar (13 mmol/L) and CRP (93 mg/L). She was eventually sent home and prescribed with Prednisone, Tramadol, Imidapril, and Gliclazide.

Seven days after, she was admitted at a private

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hospital due to persistent muscle pain, generalized body weakness, undocumented fever and abdominal pain. Thyroid function tests showed increased FT₄ (28.29 ng/dL), and decreased TSH (0.86 uIU/mL). Urinalysis showed an increased in WBC count (40-50/hpf). The patient was admitted for 2 days and was eventually discharged with the following take home medications: Levofloxacin, Hyoscine-N-Butylbromide, Propylthiouracil, Simvastatin, Metformin, Gliclazide, Vitamin B complex, Domperidone, Bisacodyl and multivitamins. Prednisone and Imidapril were not prescribed.

After discharged, persistence of muscle pain, generalized body weakness, fever (38.1 °C), and abdominal pain accompanied by cough productive of yellowish sputum and loss of appetite prompted consult at our institution. On physical examination, there was a 4/5 muscle strength on all extremities. Coarse crackles were heard on the left lung base. The rest of the examination was normal. Laboratories showed leukocytosis (24.1 x 10⁹/L) with predominance of segmenters (80%), hyponatremia (127 mmol/L), glucosuria (+1), and pneumonia at left base on chest x-ray. Repeat thyroid function tests showed decreased levels of FT₃ (0.82 pg/mL) and FT₄ (0.82 ng/dL), and normal level of TSH (0.54 uIU/mL), which is compatible with the clinical condition of the patient. Creatinine was at 40 μmol/L and urine specific gravity was 1.025. AST and ALT are within normal range, and 12-lead ECG showed sinus rhythm. She was started on Ceftazidime and Amikacin.

In spite of continuous antibiotics, her weakness progressed to almost 0/5 on muscle strength test on the 5th hospital day with persistent fever. A cranial CT scan was done and this revealed normal findings. Because of persistent leukocytosis (17.1 x 10⁹/L), antibiotics were shifted to Piperacillin-Tazobactam.

Despite improvement of pneumonia with 8 days of IV antibiotics, patient remained weak. Repeat laboratory results showed increased serum cortisol levels (743.1 mmol/L) with persistent hyponatremia (125 mmol/L). A third thyroid function determination was done, which revealed decreased level of FT₃ (0 pg/mL) with normal FT₄ (1.29 ng/mL) and TSH (2.128 uIU/L) levels and was interpreted as Sick Euthyroid Syndrome. During this time, Syndrome of Inappropriate Anti-diuretic Hormone Secretion secondary to Polyarteritis Nodosa was considered. Hence, Prednisone 10mg OD was started. Fluid intake was then limited. Vasculitic activity was assessed showing elevated ESR (36 mm/hr) and elevated CRP (96 mg/L). Prednisone was then increased to

40 mg/day. She then gradually improved together with the sodium levels at 131 mmol/L with motor function of 4/5 on all extremities. She was discharged improved with home medications of Prednisone 40mg OD and was advised to follow-up every 2 weeks for dose adjustment depending upon the ESR and CRP levels.

DISCUSSION

We have a 55 year old female, diagnosed with polyarteritis nodosa, who complained of acute onset of generalized body weakness, muscle pain, fever, and productive cough, who was persistently hyponatremic during the hospital stay.

There are many causes of hyponatremia. In a study conducted by Yawar *et al* in 220 patients with hyponatremia, the most common etiologies are: drugs (30%), gastrointestinal problems (25%), chest infection (11%), depletion hyponatremia (10%), syndrome of inappropriate antidiuretic hormone (6%), congestive heart failure (5%), malignancy (5%), and chronic liver disease (3.6%).³

Syndrome of inappropriate antidiuretic hormone secretion is a condition characterized as an excessive release of antidiuretic hormone from the pituitary gland that causes the body to conserve water, leading to hyponatremia. It is commonly seen in the clinical setting of malignancies, pulmonary disease, and CNS disorders.⁴ According to Decaux *et al*, the following criteria are needed to diagnose SIADH: serum hypoosmolality, inappropriately concentrated urine (>100 mOsm/kg H₂O), natriuresis >30 mEq/L, reversal of renal Na wasting and correction of hyponatremia after fluid restriction, and normal renal, adrenal, thyroid, cardiac, and liver function and with no signs of volume depletion.⁵ In relation to the patient, she was able to fulfil 3 out of these 5 criteria. Patient's serum osmolality was 269 mOsm/kg. Serum sodium improved from the lowest of 122 mmol/L to 131 mmol/L after sodium and water restriction. Patient has a normal renal, adrenal, thyroid, cardiac and liver function tests as shown by the laboratory results. She has no signs of volume depletion based on physical examination. Unfortunately at Ospital ng Makati, the urine osmolality and urine sodium are not available. In the algorithm presented by Singer *et al*, diagnosis of SIADH could be considered in a setting of serum hypoosmolality, urine specific gravity of >1.003, euvolesmia, and normal thyroid and adrenal function.⁶ With a serum osmolality of 269 mOsm/kg, urine specific gravity of 1.025, euvolesmia, and normal thyroid and adrenal function, syndrome of

inappropriate antidiuretic hormone secretion is most likely the cause of hyponatremia in this patient.

Based on her history and physical examination, the SIADH of the patient could also be caused by pneumonia. In pneumonia, there is a resetting to the vasopressin osmostat that causes the inappropriate antidiuretic hormone secretion.⁷ But due to the worsening of the general body weakness and persistent hyponatremia, despite adequate antibiotic treatment, other cause of SIADH had to be explored. Review of literature shows two case reports associating SIADH and PAN.

Polyarteritis nodosa is a necrotizing vasculitis that affects the small and medium arteries. In 1982, Fighali reported a case of a 40 year old male with fever, weight loss, abdominal and testicular pain, acroparesthesias and myalgias.¹ This patient was reported to have polyarteritis nodosa and SIADH, which was believed to be secondary to vascular irritation in the supra-optic and para-ventricular nuclei caused by polyarteritis nodosa that causes secretion of the antidiuretic hormone. Another reason provided was hyperangiotensinemia caused by renal ischemia caused by polyarteritis nodosa. In 1988, Gaston JS *et al* reported a case of a 64 year old male who presented with polyarteritis nodosa and hyponatremia.² He also gave two similar possible mechanisms: local cerebral vasculitis of the supraoptic or hypophyseal pathways or impairment of the kidneys to excrete water appropriately.

In the case of our patient, inappropriate antidiuretic hormone secretion could be attributed to the uncontrolled activity of polyarteritis nodosa involving the hypothalamic artery. Polyarteritis nodosa affects the small and medium sized arteries, and the hypothalamic artery. As inflammation in the lumen increases, blood flow to the hypothalamus also decreases. This would be interpreted by the hypothalamus as a decrease in blood volume. As a compensatory mechanism, the hypothalamus would increase production of antidiuretic hormone, increasing water reabsorption, and causing hyponatremia.

The other mechanism of hyperangiotensinemia as a cause of inappropriate antidiuretic hormone due to renal ischemia was less likely possible in the case of our patient. There was no evidence present in our patient that would suggest an ongoing renal ischemia such as elevation of creatinine levels and reduction in the glomerular filtration rate. Thus, vasculitis was more likely the pathogenesis behind the hyponatremia.

Also, it is important to correlate disease activity of PAN to the onset of SIADH. The elevated acute phase reactants seen in the patient is highly suggestive of disease activity of PAN which coincided with the occurrence of SIADH. With remission of PAN, we expect improvement of SIADH and her sodium levels.

In this case, we concluded that the hyponatremia is more likely due to PAN than to pneumonia. The persistence of hyponatremia despite the continuous administration of antibiotics proved that pulmonary disease was not the cause of SIADH. It was only after the starting the steroids did our patient showed signs of improvement and elevation of the sodium levels. Furthermore, the hyponatremia of our patient was already present even before the onset of her pneumonia.

CONCLUSION

In patients with polyarteritis nodosa, it is possible to have hyponatremia due to syndrome of inappropriate anti-diuretic hormone secretion. All other causes of hyponatremia should be first ruled out before entertaining this rare possible cause.

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