An Unusual Case of Neurosyphilis Manifesting as Syndrome of Inappropriate Antidiuretic Hormone Secretion (SIADH)

Hannah L. Seay
Loura Khallouf
Alyson Lieberman
Sandeep S. Jubbal

Patient: Male, 56-year-old
Final Diagnosis: Neurosyphilis
Symptoms: Abdominal pain • constipation • nausea
Medication: Penicillin
Clinical Procedure: Colonoscopy with colon biopsy • CT scan • lumbar puncture • MRI
Specialty: Infectious Diseases • Medicine, General and Internal

Objective: Unusual clinical course
Background: Syphilis has increased in prevalence in the United States by 72.7% from 2013 to 2017, with the highest rates recorded in men who have sex with men. There is an increased incidence of syphilis in patients with a concomitant HIV infection, estimated at a 77-fold increase.

Case Report: This report documents an unusual case of neurosyphilis manifesting as syndrome of inappropriate antidiuretic hormone secretion (SIADH) in a 56-year-old man with HIV/AIDS. A 56-year-old man who has sex with men with HIV/AIDS presented with a 4-day history of periumbilical abdominal pain, nausea, and constipation. A physical exam revealed slowing of baseline cognition, but was otherwise unremarkable. Urine and serum osmolality studies were consistent with SIADH as defined by the Bartter and Schwartz Criteria: serum osmolality <275 mOsm/kg, urine osmolality >100 mOsm/kg, urine sodium >20-40 mmol/L, euvoolemia, and no other cause for hyponatremia identified. He was fluid-restricted, with improvement in laboratory abnormalities, further supporting the diagnosis of SIADH. A diagnostic work-up included a CT abdomen/pelvis with perirenal lymphadenopathy, colonoscopy negative for malignancy, chest CT with lymphadenopathy, and a head MRI negative for intracranial processes. The patient was ultimately found to have positive results on rapid plasma reagin (RPR) and Venereal Disease Research Laboratory (VDRL) tests, and was diagnosed as having neurosyphilis. He underwent penicillin desensitization and received a 14-day course of penicillin G, with recovery of sodium to normal range on discharge.

Conclusions: Our case highlights SIADH as an initial presenting sign of neurosyphilis with HIV infection, which has only been documented in 2 prior case reports. Our case highlights the importance of recognizing atypical presentations of neurosyphilis in patients with HIV to prevent long-term complications.

Keywords: HIV Seropositivity • Inappropriate ADH Syndrome • Neurosyphilis • Syphilis

Full-text PDF: https://www.amjcaserep.com/abstract/index/idArt/929050
**Background**

Syphilis has increased in prevalence in the United States by 72.7% from 2013 to 2017, for a total of 30 644 cases in 2017, with the highest rates recorded in men who have sex with men [1]. There is an increased incidence of syphilis in patients with a concomitant HIV infection, estimated at a 77-fold increase [2]. Further, those with HIV are at a greater risk of developing neurosyphilis compared to non-HIV-infected patients, at 2.1% versus 0.6% [2].

Syphilis is caused by infection of the spirochete *Treponema pallidum* [3]. Syphilis is known as the mimicker of diseases due to the variety of its clinical presentations, potentially affecting every organ of the body. Neurosyphilis results from infections of the brain, meninges, or spinal cord by *Treponema pallidum* and can occur at any point after initial infection [3]. Neurosyphilis can take many forms, including asymptomatic, meningitic, meningovascular, parietic, or tabetic neurosyphilis [4]. The pathophysiology of SIADH in patients with neurosyphilis is not well understood [5]. It is hypothesized that infections of the central nervous system can mediate release of antidiuretic hormone from the pituitary gland [6].

This report documents an unusual case of neurosyphilis manifesting as syndrome of inappropriate antidiuretic hormone secretion (SIADH) in a 56-year-old man with HIV/AIDS.

**Case Report**

A 56-year-old man presented with a 4-day history of periumbilical abdominal pain, nausea, and constipation. The patient described the abdominal pain as a constant, colicky pain with episodes of abdominal “heaviness” after consumption of meals. The patient’s last bowel movement was on the day of admission, but was notable for minimal stool burden. He denied associated vomiting, abdominal distention, rectal pain, or bleeding/purulent discharge per rectum.

On admission, the patient was noted to be tachycardic to 103 bpm with a blood pressure of 102/69, respiratory rate of 18/minute, and a temperature of 36.9°C. On exam, the abdomen was soft, non-tender, and non-distended and had normoactive bowel sounds without muscular defense. Results of a physical exam were otherwise only remarkable for slowed cognition.

His past medical history was significant for HIV and AIDS on antiretroviral therapy (CD4 count of 406 cells/mm² and undetectable viral RNA 3 months prior to admission), 3 prior small-bowel obstructions treated conservatively, an umbilical hernia status post surgical repair, anal dysplasia with HPV+ high-grade squamous intraepithelial lesion status post ablation, herpes simplex virus-2, and colonic polyps. His most recent reactive rapid plasma reagent (RPR) test result was negative 3 months prior to arrival.

On admission, the patient presented with an initial serum sodium of 124 mmol/L, osmolality of 264 mOsm/kg, creatinine of 0.81 mg/dL, and BUN of 10 mg/dL. Urine measurements revealed a sodium of 20 mmol/L, osmolality of 148 mOsm/kg, and specific gravity of >1.030. His CD4 count was 188 cells/µL with an RNA viral load of <20 copies/mL. All additional laboratory values are shown in Table 1. CT abdomen/pelvis, obtained due to his prior history of small-bowel obstructions, was significant for new-onset perirectal lymphadenopathy. The patient was given a 1.5-L IV bolus of normal saline with a repeat serum sodium of 125 mmol/L and was thus started on fluid restriction to 1500 mL/day. His sodium trended upwards to 130 mmol/L after initiating fluid restriction by day 2 of admission (Table 2).

On day 3 of admission, he underwent a colonoscopy due to concerns of malignancy. This revealed a large lipoma in the transverse colon, moderate inflammation in the descending/sigmoid colon suggestive of colitis, and evidence of chronic ischemic injury. Serum sodium/osmolality improved with fluid restriction, strongly suggesting SIADH as the etiology of hyponatremia (Table 2). A chest CT was obtained to evaluate causes of SIADH and revealed an enlarged right upper para-tracheal, mediastinal, and left supraclavicular lymph node.

On day 4 of admission, the patient was found to have a reactive rapid plasma reagin (RPR) with a 1: 256 titer and positive fluorescent treponemal antibodies, concerning for neurosyphilis. A head MRI was negative for acute abnormalities. Lumbar puncture was performed and the results were significant for a VDR titer of 1: 4, elevated protein of 107 mg/dL, and a leukocytosis of 33 cells/mm³. Additional lab values were negative, as noted in Table 1. The patient was diagnosed with neurosyphilis presenting as SIADH, and further work-up was halted at this time.

The patient was maintained on senna 17.2 mg, polyethylene glycol 17 g, docusate sodium 100 mg, and ondansetron 4 mg as needed throughout his hospital stay. He was maintained on a clear liquid diet with a 1500 mL/day fluid restriction, which was gradually progressed to a regular diet by day 5 of admission. He received IV ceftriaxone 2 g for 4 days prior to transferring to the intensive care unit for penicillin desensitization, given his history of penicillin allergy. A PICC line was placed and he received IV penicillin 4 000 000 units every 4 hours for a total of a 14-day course.

The patient’s constipation and nausea resolved following administration of treatment. His sodium normalized on a
| Laboratory values              | Day 1     | Reference range    |
|-------------------------------|-----------|-------------------|
| **Blood values**              |           |                   |
| Hemoglobin (g/dL)             | 13.1      | 13.2-17.1         |
| Hematocrit (%)                | 38.5      | 39-52             |
| White blood cell count (10^3/uL) | 8.4    | 4.3-10.8          |
| Sodium (mmol/L)               | 124       | 135-145           |
| Potassium (mmol/L)            | 4.4       | 3.5-5.3           |
| Creatinine (mg/dL)            | 0.81      | 0.60-1.30         |
| Blood urea nitrogen (mg/dL)   | 10        | 7-23              |
| Rapid plasma reagin           | Reactive  | Non-reactive      |
| Rapid plasma reagin titer     | 1: 256    |                   |
| Fluorescent treponemal antibody absorption | Reactive | Non-reactive |
| Chlamydia trachomatis, RNA    | Not detected | Not detected |
| Neisseria gonorrhoeae RNA     | Not detected | Not detected |
| Serum osmolality (mOsm/kg)    | 264       | 279-295           |
| HIV-1 RNA (copies/mL)         | <20 Detected | Not detected |
| HIV-1 RNA PCR (Log copies/mL)| <1.30 D.4  | Not detected |
| Absolute CD4 (cells/uL)       | 188       | 370-1540          |
| Cortisol AM (ug/dL)           | 12.9      | 6.7-22.6          |
| **Urine values**              |           |                   |
| Specific gravity              | 1.030     | 1.005-1.030       |
| Sodium (mmol/L)               | 20        |                   |
| Creatinine (mg/dL)            | 32        | 22-328            |
| Osmolality (mOsm/kg)          | 148       | 70-900            |
| **Cerebral spinal fluid (CSF) values** | | |
| Glucose (mg/dL)               | 68        | 50-80             |
| Protein (mg/dL)               | 107       | 15-45             |
| Cryptococcal antigen          | Not detected | Not detected |
| HSV 1 PCR                     | Not detected | Not detected |
| HSV 2 PCR                     | Not detected | Not detected |
| CSF culture                   | No growth  | No growth         |
| Venereal disease research laboratory test | Reactive 1: 4 | Non-reactive |
| CSF Gram stain                | No organism seen | |
| **Rectal PCR**                |           |                   |
| HSV 1 DNA                     | Not detected | Not detected |
| HSV 2 DNA                     | Detected  | Not detected      |

**Table 1.** Laboratory values on admission.
fluid-restricted diet and remained within normal limits after discharge. One week after discharge, his sodium remained within normal limits at 136 mmol/L. He tolerated penicillin sensitization and successfully completed a 14-day course of IV penicillin. His RPR titer decreased to 1:8 by 3 months, 1:4 by 5 months, and 1:2 by 6 months. The patient is being followed by the infectious disease service and continues to do well. He is scheduled for a follow-up CT chest and CT pelvis with contrast at 6 months after admission to ensure resolution of lymphadenopathy. He did not undergo a repeat lumbar puncture.

**Discussion**

The ability to recognize the diverse presentation of neurosyphilis becomes increasingly important as the rates of syphilis continue to rise in the United States [1]. This poses a great challenge in patients with HIV co-infection due to the high variability in disease progression and presentation [5]. We present an unusual case of neurosyphilis manifesting as SIADH in a patient with known co-infection with HIV.

In our patient, other causes of SIADH and hyponatremia were excluded, including cerebral salt wasting syndrome, syphilitic nephritis, and adrenal insufficiency. Cerebral salt wasting syndrome was excluded given the lack of evidence of volume depletion. The patient presented in a euvoletic state with his baseline blood pressure, no clinical signs of dehydration, and a normal BUN/creatinine ratio. Syphilitic nephritis was ruled out by urinalysis without evidence of proteinuria. Adrenal insufficiency was unlikely given an AM cortisol of 12.9 mcg/dL. The most likely mechanism of hyponatremia in this patient was SIADH secondary to neurosyphilis given the inappropriate elevation of urine sodium and osmolality. The diagnosis of SIADH was made based on the Bartter and Schwartz Criteria, including a decreased plasma osmolality of <275 mOsm/kg, increased urine sodium ranging from >20 to 40 mOsm/kg, increased urine osmolality of >100 mOsm/kg, euvolemia, and no other identified cause [7,8]. SIADH was further supported by worsening of hyponatremia with 0.9% saline infusion and improvement after sodium restriction [8,9].

To the best of our knowledge, neurosyphilis presenting as SIADH has only been documented in 2 prior case reports. The first was a patient with known HIV infection who presented with hyponatremia, hypothyroidism, unilateral vision loss, generalized lymphadenopathy, and painless genital/oral ulcers diagnosed with neurosyphilis [5]. The patient’s hyponatremia was attributed to SIADH, although it may have been confounded by the diagnosis of hypothyroidism. The second case was a patient who presented with a 10-day course of vomiting, seizures, and hyponatremia, ultimately found to have neurosyphilis [10]. The hyponatremia in this patient was suggestive of SIADH, but hypovolemic hyponatremia secondary to profound vomiting may have contributed.

**Conclusions**

Our case documents SIADH as the exclusive presenting sign of neurosyphilis in an HIV-infected patient, which has only been documented in 2 prior case reports. This highlights the importance of recognizing atypical presentations of neurosyphilis, including SIADH, in patients with HIV to prevent long-term progression of the disease. Further, our patient developed neurosyphilis over a 3-month time course, highlighting the possibility of rapid progression of this disease in HIV-infected individuals. We propose that in HIV-infected patients presenting with SIADH, neurosyphilis should be considered in the differential diagnosis.

Table 2. Trends in critical lab values throughout admission.

| Laboratory values | Day 1 | Day 2 | Day 3 | Day 4 | Day 5 | Day 6 | Day 7 | Reference range |
|-------------------|-------|-------|-------|-------|-------|-------|-------|-----------------|
| Serum values      |       |       |       |       |       |       |       |                 |
| Serum sodium (mmol/L) | 124   | 130   | 133   | 133   | 131   | 133   | 131   | 135-145         |
| Serum osmolality  | 264   |       |       |       |       |       |       | 279-295         |
| Urine values      |       |       |       |       |       |       |       |                 |
| Urine sodium (mmol/L) | 20    | 31    |       |       |       |       |       |                 |
| Urine osmolality  | 148   | 274   |       |       |       |       |       | 70-900          |

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