Unusual association of diseases/symptoms

An unusual cause for hyponatremia with seizures

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Summary

A 50-year-old Asian Indian female with known hypertension presented with persistent vomiting but no other symptoms of meningism. Clinical examination and basic laboratory parameters were entirely normal except for significant hyponatremia. Further investigation was suggestive of the syndrome of inappropriate antidiuretic hormone (SIADH) secretion. Subsequently, despite steady correction of hyponatremia, the patient developed generalised seizures. Cerebrospinal fluid (CSF) analysis performed was inconclusive. Screening for a chronic meningitis underlying SIADH, yielded positive blood and CSF titres for venereal disease research laboratory (VDRL), which were confirmed by *Treponema pallidum* haemagglutination (TPHA). The patient was treated for neurosyphilis and made a complete recovery. Hyponatremia resolved and she had no further episodes of seizures. She was tested for HIV infection which was negative. On follow-up, she remained TPHA positive but VDRL titres became negative.

BACKGROUND

This case illustrates the propensity of neurosyphilis for presenting with atypical features. This patient had no definite symptoms or signs of meningism, and the diagnosis of neurosyphilis could easily have been missed if not for the screening test. Furthermore, this case demonstrates that contrary to common perception, immunocompetence cannot rule out neurosyphilis, and a negative test for HIV should still lead clinicians to look for other sexually transmitted diseases with neurological manifestations such as syphilis, especially as it is easy and relatively inexpensive to screen for this disease. Finally, neurosyphilis presenting with isolated syndrome of inappropriate antidiuretic hormone secretion (SIADH) is unusual. We believe that this combination of features makes this report both interesting and a useful teaching case.

CASE PRESENTATION

A 50-year-old housewife, a known hypertensive since 12 years on therapy with atenolol, was admitted with complaints of vomiting since the past 10 days. She had never received thiazides as antihypertensives. Her husband had passed away 15 years ago from a febrile illness, the details of which were not available. She belonged to an educated middle-class urban family of moderate means.

At presentation, she was haemodynamically stable. She was conscious, alert and oriented. Neurologic examination showed preserved higher mental functions and no evidence of meningeal irritation or focal deficits. Specifically, there was no anisocoria, and no evidence of peripheral neuropathy in the form of sensory loss over her extremities, although her ankle jerks were only elicitable with reinforcement. Examination of other systems was also entirely normal.

After reviewing her preliminary biochemical parameters (see below), she was started on 1.6% hypertonic saline infusion with frequent monitoring of serum sodium.

Despite correction of her sodium to 123 meq/l by the fourth day of hospital stay, she subsequently suffered two episodes of generalised tonic-clonic seizures.

INVESTIGATIONS

Laboratory investigations at baseline revealed mildly elevated leucocyte counts ($11\,700/\text{mm}^3$) and marked hyponatremia (100 meq/l). Serum potassium was normal (3.5 meq/l). Further investigation of the hyponatremia was suggestive of the SIADH. Serum and urine osmolality were 214 mmol/l and 236 mmol/l respectively; urine sodium was 18 meq/l, serum thyroid stimulating hormone (TSH) was 0.6 mIU/ml, serum cortisol was 20.7 mcg/dl.

Cranial CT imaging was normal (figure 1). Electroencephalography showed bihemispherical generalised spike discharge with phase reversal (figure 2). Cerebrospinal fluid (CSF) analysis was inconclusive (CSF glucose 89 mg/dl, random blood glucose 100 mg/dl, serum protein 70 mg/dl, leucocytes $20/\text{mm}^3$, all lymphocytes, no erythrocytes). CSF was also negative for acid fast bacilli by fluorescein staining. Tuberculosis-PCR was negative and adenosine deaminase levels were low (2 U/l). The tap was non-bloody. HIV ELISA was negative. Thoracic radiogram was normal.

DIFFERENTIAL DIAGNOSIS

Preliminary differential diagnoses included various causes for SIADH include pulmonary and neurological disease. Consequent to the episodes of seizure despite partial correction of hyponatremia, a neurological condition was considered more likely. Cranial CT imaging ruled out stroke and neoplastic disease, making chronic meningitis a strong possibility. Screening for chronic meningitis in view of SIADH and inconclusive CSF analysis, revealed elevated venereal disease research laboratory (VDRL) titres in blood and CSF. Tests for tuberculous meningitis, the commonest cause of chronic meningitis

Figure 1 Cranial CT (plain and contrast) showing no evidence of meningeal enhancement, ischaemic areas or intracerebral gummata.

Figure 2 Electroencephalography showing bihemispherical generalised spike discharge with phase reversal in T3 (red arrowhead).

in India, were uniformly negative. Retrospectively, the initial CSF analysis was compatible with a diagnosis of neurosyphilis. Differential diagnoses included SIADH secondary to neurosyphilis, cerebral salt wasting syndrome and syphilitic nephritis. The latter diagnoses were ruled out by the absence of dehydration and the normal urinalysis respectively. Although urinary sodium was not very high, it was disproportionate to serum sodium. As the patient had given a history of recurrent vomiting, it is likely that in part, this reflects extra-renal sodium loss, with partial renal conservation of sodium. Nevertheless, the overall picture was clearly suggestive of an SIADH.

TREATMENT

The patient was immediately dilantinised in consultation with neurologists.

The patient was immediately initiated on a 2 week course of crystalline penicillin, followed by three doses of benzathine penicillin at weekly intervals.

OUTCOME AND FOLLOW-UP

She showed marked improvement with this therapy. There were no further episodes of seizures, and her sensorium returned to normal. Hyponatremia also resolved completely (serum sodium 137 meq/l).

On follow-up, serum and CSF tested weakly reactive for VDRL at 8 weeks and non-reactive at 16 weeks, although *Treponema pallidum* haemagglutination remained positive. She was kept on regular follow-up and remains asymptomatic.

DISCUSSION

Although once seen commonly, neurosyphilis has now become rare with the exception of immunocompromised individuals. It typically occurs in the late stage of infection with *T pallidum*. In the preantibiotic era, symptomatic neurosyphilis developed in about one-third of patients; parenchymal forms involving the brain and spinal cord that is, syphilitic encephalitis and tabes dorsalis were seen most often. With the advent of penicillin therapy, the typical

clinical presentation has shifted away from chronic forms of neurosyphilis, which involve central nervous system (CNS) parenchyma, to earlier forms that involve CNS meninges and blood vessels such as syphilitic meningitis and meningovascular syphilis with associated ischaemic stroke.¹ Meningovascular syphilis in particular, can be seen both in secondary syphilis as a part of systemic vasculitis, as well as in tertiary syphilis.² Our patient most likely suffered from tertiary syphilis; since systemic examination revealed no evidence of rash, lymphadenopathy or mucosal ulceration.

Unfortunately, in addition to being an uncommon disease, neurosyphilis can present in a multitude of forms, including stroke, myelopathy, seizures, delirium and dementia.³ This combination of rarity and protean manifestations can result in frequent misdiagnosis, especially in immunocompetent individuals with a low index of suspicion. Once suspected, however, it is relatively easy to confirm the diagnosis; VDRL reactivity in cerebrospinal fluid is considered relatively sensitive and specific for neurosyphilis.⁴

Although hyponatremia secondary to SIADH is a known complication of meningitis of any aetiology, it is rare for neurosyphilis per se to present with SIADH. Milger *et al*⁵ reported a retropositive patient presenting with hyponatremia secondary to SIADH. However, the case in question had central hypothyroidism, making the diagnosis of SIADH questionable. In our case although TSH was low normal, T3 and T4 were both normal ruling out hypothyroidism.

Other causes for hyponatremia in a patient with neurosyphilis, that need to be ruled out include cerebral salt wasting syndrome⁶ and syphilitic nephritis.⁷ The absence of signs of dehydration and the unremarkable urinalysis ruled out both these disorders respectively in our patient.

To conclude, our case is unique in several aspects; clinical presentation with isolated hyponatremia in the absence of signs of meningeal irritation, and the occurrence of meningovascular syphilis in an immunocompetent patient.

Learning points

- ▶ A high index of suspicion should be maintained for neurosyphilis in all cases with unexplained hyponatremia and SIADH.
- ▶ Neurosyphilis can occur in immunocompetent individuals.
- ▶ Neurosyphilis can be diagnosed easily by means of elevated VDRL titres in CSF.
- ▶ Neurosyphilis remains an easily treatable disease.

Competing interests None.

Patient consent Obtained.

REFERENCES

1. **Burke JM**, Schaberg DR. Neurosyphilis in the antibiotic era. *Neurology* 1985;**35**:1368–71.
2. **French P**. Syphilis. *BMJ* 2007;**334**:143–7.
3. **Timmermans M**, Carr J. Neurosyphilis in the modern era. *J Neurol Neurosurg Psychiatr* 2004;**75**:1727–30.
4. **Hart G**. Syphilis tests in diagnostic and therapeutic decision making. *Ann Intern Med* 1986;**104**:368–76.
5. **Milger K**, Fleig V, Kohlenberg A, *et al*. Neurosyphilis manifesting with unilateral visual loss and hyponatremia: a case report. *BMC Infect Dis* 2011;**11**:17.
6. **Momi J**, Tang CM, Abcar AC, *et al*. Hyponatremia-what is cerebral salt wasting? *Perm J* 2010;**14**:62–5.
7. **Hruby Z**, Kuźniar J, Rabczyński J, *et al*. The variety of clinical and histopathologic presentations of glomerulonephritis associated with latent syphilis. *Int Urol Nephrol* 1992;**24**:541–7.

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