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Case Report

Tubercular meningitis presenting as cerebral salt wasting syndrome in an adult: A case report

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ABSTRACT

Introduction: Cerebral salt wasting syndrome (CSWS) is a cause of hyponatremia in the setting of intracranial pathologies such as Central Nervous System (CNS) trauma, infections, and tumors. It is important to differentiate CSWS from the syndrome of inappropriate antidiuretic hormone secretion (SIADH) as their management differs. CSWS leads to hypovolemia as opposed to euvolemia or hypervolemia in SIADH. SIADH is managed with fluid restriction and this could worsen CSWS which is managed with adminstration of intravenous crystalloids to correct hyponatremia.

Case summary: A 42-year-old male was admitted after a week of low-grade fever with easy fatigability, hypersomnolence, and excessive thirst. He had polyuria which started 5 days before presentation, and unintentionally lost 3 kg of weight in the past month. He had orthostatic hypotension, and was dehydrated, but vital signs were normal with the exception of his temperature. Cerebrospinal fluid (CSF) analysis revealed a glucose of 42 mg/dl, protein 170 mg/dl, cell count 28/mm^3 with 65% lymphocytes which was consistant with tubercular meningitis. CSF AFB culture was positive in addition to a positive CSF PCR for *M. tuberculosis*.

Discussion: Presentation of CNS infection with tuberculosis may be non-specific and its insidious onset could lead to delayed or missed diagnosis; however persistent constitutional symptoms and signs with history of weight loss and a close contact with tuberculosis may raise the possibility of tuberculosis. Early diagnosis and treatment has an excellent prognosis, but any delay contributes to death and disability despite anti-tubercular drug therapy. CSWS should be managed with salt and volume replacement, but more importantly, the causative CNS insult should also be confirmed and addressed.

1. Introduction

Many intracranial pathologies can frequently give rise to hyponatremia – which could be due to cerebral salt wasting syndrome (CSWS) via a poorly understood mechanism [1]. However this is usually mistaken for the syndrome of inappropriate anti-diuretic hormone secretion (SIADH). CSWS causes natriuresis, hyponatremia, and volume contraction in the setting of CNS trauma, infections, and tumors [2]. CSWS is diagnosed when serum sodium is less than 135 mg/dl along with urine osmolality above 100 mOsm/kg and urine sodium more than 40 mEq/L in the setting of CNS pathology [3]. It is important to differentiate CSWS from SIADH as their management differ. CSWS leads to hypovolemia as opposed to euvolemia or hypervolemia in SIADH. SIADH is managed with fluid restriction and this could worsen CSWS which is managed with administration of intravenous (IV) crystalloids to correct hyponatremia. Here we present a case of CSWS in an adult caused by tubercular meningitis.

2. Case description

A 42 year old male presented to the emergency department with a chief complaint of mild fever (recorded up to 99.8 °F at home) for about a week with easy fatigability and excessive thirst. The patient further complained of polyuria without dysuria for five days prior to

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presentation. His only surgical history was an uncomplicated laparoscopic cholecystectomy a year ago and had no known past medical history. He also reported a 3 kg unintentional weight loss over last month. He was non-smoker and had no known contact with a history of tuberculosis. He was not taking any immunosuppressive agents or other medications. On presentation to emergency department, he was drowsy but arousable and was able to follow commands. His Glasgow Coma Scale (GCS) was 15/15. His initial blood pressure was 100/80 mm of Hg on sitting position and 85/60 mm of Hg on standing position, heart rate was 86/min, respiratory rate was 12/min and temperature was 100.6°F. His eyes and oral mucosa were dry and skin turgor was decreased. He was not noted to have icterus, pallor, lymphadenopathy or rash.

On neurological examination the Kernig's sign, Brudzinski's sign and neck rigidity were absent. The motor exam revealed normal muscle power on all limbs. Cranial nerves functions were assessed and revealed normal findings. All remainder of the physical exam were normal.

3. Investigations

Routine laboratory tests revealed serum sodium of 128 mEq/L, potassium of 3.6 mEq/L and osmolality of 274 mOsm/kg. His ESR was elevated at 58 mm/h, and creatinine was 2.3 mg/dl. Urine specific gravity was 1.035, urine osmolality was 931.07 mOsm/kg, and urine sodium 57 mEq/L. He had 300–350 ml of fluid deficit on daily basis during his admission.

Tuberculin test and chest x-ray did not reveal any abnormalities. Sputum examination and sputum PCR (GeneXpert®) were both negative for *M. tuberculosis*. He was persistently somnolent and had an episode of generalized clonic tonic seizure for about 15–20 seconds on the second day of admission. A non-contrast MRI following the seizure episode did not reveal any structural abnormalities in brain (Figs. 1 and 2). Finally, CSF analysis revealed a glucose of 42 mg/dl, protein 170 mg/dl, cell count 28/mm^3 with 65% lymphocytes consistant with tubercular meningitis. CSF AFB culture was eventually positive along with CSF PCR for *Mycobactrium tuberculosis* (GeneXpert®). This confirmed the diagnosis of CSWS due to tubercular (TB) meningitis.

4. Treatment, outcome and follow up

The patient was treated with 3% hypertonic saline to correct hyponatremia, but failed to improve his hyponatremia or symptoms. He was started on anti-tubercular therapy (ATT) with isoniazid, rifampin, pyrazinamide and ethambutol followed by dexamethasone after confirmation of tubercular meningitis by PCR. We continued 3% hypertonic saline to replace sodium loss in the urine and added fludrocortisone.

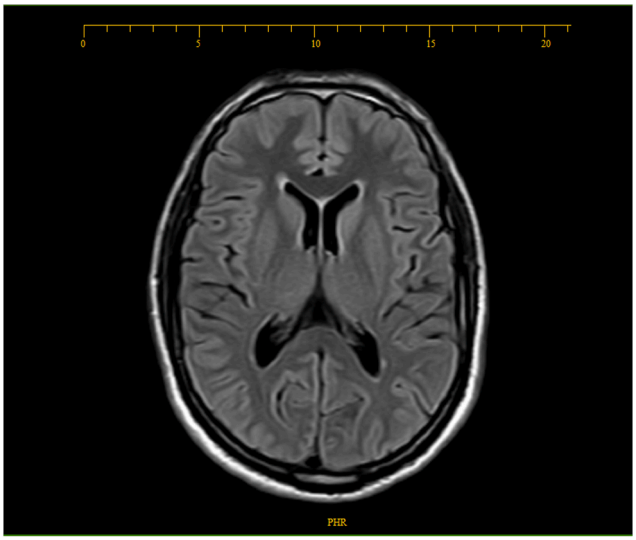

Fig. 1. MRI brain revealing normal findings.

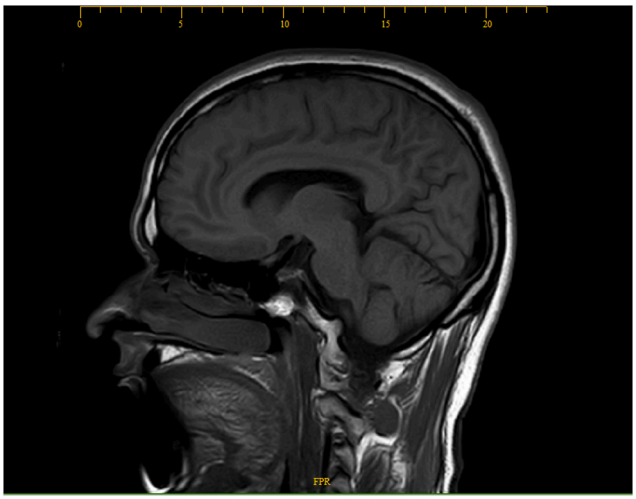

Fig. 2. MRI brain revealing normal findings.

His fever subsided, orthostatic hypotension improved, and his sodium level gradually normalized by day nine of hospital admission. No further seizures occured. We discharged him after two weeks of hospital admission on ATT as per WHO category I [4]. Steroids were tapered over a month. Patient was asymptomatic on 10th day follow-up and compliant with ATT.

5. Discussion

TB meningitis is common in resource-limited countries such as Nepal. It is classified into three stages based on neurological signs and level of consciousness [Table 1]. Clinical presentation may be non-specific and its insidious onset could lead to delayed or missed diagnosis; however persistent constitutional symptoms and signs with history of weight loss, and a contact with TB may raise the possibility of tuberculosis [5]. The most common complications of TB meningitis are hyponatraemia, hydrocephalus, stroke, cranial nerve palsies, epileptic seizures, diabetes insipidus, tuberculoma, myeloradiculopathy and hypothalamic syndrome [6].

Partial and secondary generalized seizures are the most common seizure types in patients with TB meningitis [6]. The seizure in this case was most likely due to hyponatremia and was successfully treated with the correction of his sodium level. Early diagnosis and treatment of tubercular meningitis has an excellent prognosis, but any delay contributes to death and disability despite of ATT.

WHO category I ATT consisting of isoniazid, rifampin, pyrazinamide and ethambutol with the addition of a parenteral corticosteroid to prevent sequelae is used to treat TB meningitis in resource-poor settings [4].

Exact mechanism being still unclear, hyponatraemia occurs in up to 49% of patients with TB meningitis [6]. Although the link between hyponatremia due to CSWS and tubercular meningitis has been described by many case reports, this is still a rare association [7].

CSWS is characterized by hyponatremia along with increased urinary sodium excretion and extracellular volume contraction, as was the case in our patient [3]. Excessive secretion of atrial natriuretic peptide (ANP)

Table 1
Clinical classification of TB meningitis based on level of consciousness and neurological signs [10]. GCS = Glasgow Coma Scale.

Stage 1	GCS of 15 with no focal neurological signs.
Stage 2	Either GCS of 11–14 or GCS of 15 with focal neurological signs.
Stage 3	GCS<10 with or without focal neurological signs.

and brain natriuretic peptide (BNP), along with a direct neural influence on renal function could be possible pathogenetic mechanisms [8]. CSWS should be managed with salt and volume replacement, but more importantly, the underlying causative CNS insult should also be addressed – as we did with ATT in this case.

This patient's presentation was unusual in several ways. CSWS is mostly a late complication of TB meningitis, often seen in critically ill patients. Patients are usually admitted due to symptoms of TB meningitis, but this patient presented first with CSWS symptoms before TB meningitis was diagnosed. Meningeal signs were absent, and imaging studies were unrevealing, as normally one expects to find cerebral edema or hydrocephalus on MRI [9]. He did not improve after just sodium and volume replacement, so we added fludrocortisone. Fludrocortisone is a potent mineralocorticoid which increases renal collecting tubule sodium and water reabsorption and helps correct hyponatremia in CSWS, as in our case [8]. It is likely that his rapid recovery and avoidance of major complications in our patient was the result of timely diagnosis and prompt intervention.

Provenance and peer review

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Ethical approval

This case report was conducted in compliance with ethical standards. Informed written consent has been obtained and all identifying information is omitted.

Consent

Written informed consent was obtained from the patient for publication of this case report and accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal on request.

Author contribution

1.Kamal Pandit took relevant history, clinical examination, collected relevant investigations and follow up assessment of the patient. He wrote and edited the report.

2. Shashwat Pokharel, Sarita Kathayat, Sushil Khanal, Prabhat Adhikari, Andrew B.Trotter also wrote the report and revised it with relevant references.

Registration of research studies

1 Name of the registry:

2 Unique Identifying number or registration ID: Not applicable.

3 Hyperlink to your specific registration (must be publicly accessible and will be checked).

Guarantor

Kamal Pandit.He is the first author and corresponding author for this case report.

Declaration of competing interest

There is no any conflicts of interest.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.amsu.2020.11.008.

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