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Learning from errors

Hyponatraemia masking the diagnosis of cryptococcal meningitis

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Summary

Patients with acute hyponatraemia present with neurologic symptoms resulting from cerebral oedema induced by water movement into the brain. The author reports a male patient who presented to our emergency department with headache for 3 days and confusion for a day. The reported patient was on two immunosuppressive drugs, namely prednisone and azathiorprine for his ulcerative colitis. Laboratory data were consistent with syndrome of inappropriate antidiuretic hormone secretion (SIADH) which was appropriately corrected; however his mental status deteriorated. The patient's initial presentation was considered to be secondary to hyponatraemia. There was lapse of 36 h where the hyponatraemia was corrected; however the cause of the SIADH was not investigated. On further investigation of the patient a diagnosis of cryptococcal meningitis was ascertained. This case highlights the importance of considering a central nervous system infection in an immunosuppressed patients presenting with hyponatraemia secondary to SIADH.

BACKGROUND

Hyponatraemia is commonly defined as a serum sodium concentration below 135 meq/l, but can vary in different clinical laboratories. Patients with acute hyponatraemia are more likely to develop neurologic symptoms resulting from cerebral oedema induced by water movement into the brain. The syndrome of inappropriate antidiuretic hormone secretion (SIADH) is a common cause of hyponatraemia and is associated with decreased serum osmolality, excessive urinary sodium excretion, and inappropriately elevated urine osmolality. Small cell lung cancer is the single most common cause of SIADH followed by central nervous system (CNS) lesions.[1 2] CNS infections including bacterial and tuberculous meningitis are among the common aetiologies while fungal infections are relatively rare causes of SIADH. The incidence of SIADH in patients with cryptococcal meningitis is estimated to be approximately 8%.[3]

CASE PRESENTATION

The author reports a 42-year-old male patient who presented to our emergency department with headache for 3 days and confusion for a day. He described his headache as generalised and without photophobia or any other visual abnormalities. He became increasingly confused in the past 24 h and hence was got to the emergency department. The patient had a history of ulcerative colitis, hypertension and diabetes mellitus. His home medications included prednisone (35 mg daily), azathioprine (150 mg daily), mesalamine, metoprolol and metformin. He denied nicotine or alcohol use and any risk factors for HIV infection.

On examination, he was disoriented in time and place. He was afebrile and hemodynamically stable. His physical examination including neurologic exam was unremarkable.

INVESTIGATIONS

Of note, his routine laboratory findings revealed a white bood cell (WBC) count of 16.2 k/mm^3 with an absolute neutrophil count of 15.2 k/mm^3. The patient had laboratory findings consistent with those of SIADH, which included serum sodium=115 mmol/l, serum osmolality=235 mOsm/kg, urine sodium=24mmol/l and urine osmolality=540 mosm/kg. His blood urea nitrogen was 4 mg/dl and creatinine was 0.4 mg/dl. His HIV test was negative.

TREATMENT

The patient was initially started on 3% hypertonic saline. This was switched to 0.9% normal saline after his sodium was adequately corrected. The patient's hyponatraemia was corrected from 115 mmol/l to 130 mmol/l in the first 36 h of admission. Although hyponatraemia was corrected, his mental status deteriorated. This was the time when more investigations were ordered to investigate for causes of SIADH as well as altered mental status. Initial CAT scan of the head and chest radiograph were within normal limits. A lumbar puncture was performed and the cerebrospinal fluid (CSF) had the following findings: elevated opening pressure (33 cm of water), WBC (34 cells/mm^3 with 62% neutrophils), elevated proteins (68 mg/dl), and normal glucose (53 mg/dl). The CSF fluid grew *Cryptococcus neoformans* and the cryptococcal antigen titres were greater than 1:512. HIV ELISA test for the patient was negative.

OUTCOME AND FOLLOW-UP

The patient was started on intravenous amphotericin B 0.7 mg/kg daily, but he was unable to tolerate it secondary to an anaphylactoid reaction. He was switched to intravenous flucanazole 800 mg/day. His mental status improved slowly over next week. The blood cultures turned negative for *C neoformans* 4 days after initiation of antifungal

medications. He was subsequently discharged home on oral fluconazole.

DISCUSSION

Cryptococcosis is an invasive fungal infection due to *C neoformans* or *C gattii* that has become increasingly prevalent in immunocompromised patients.[4] Cryptococcal meningo-encephalitis is a common encountered manifestation of cryptococcosis. Diagnosis of cryptococcal meningoencephalitis can be challenging because of the subacute onset of symptoms and non-specific presentation. Typically, headache, lethargy, personality changes and memory loss develop over 2 to 4 weeks.

Patients with cryptococcosis usually have a disease or a drug therapy known to cause immunosuppression. The most common forms of immunosuppression other than HIV include corticosteroid therapy; cytotoxic drug therapy; solid organ transplantation; cancer (particularly haematologic malignancy); and various conditions such as sarcoidosis, diabetes mellitus and hepatic failure.

The reported patient was on two immunosuppressive drugs, namely prednisone and azathiorprine for his ulcerative colitis. The patient's initial presentation was considered to be secondary to hyponatraemia. During the patient's admission there was lapse of 36 h where the hyponatraemia was corrected, however the cause of the SIADH was not investigated. On further investigation of the patient a diagnosis of cryptococcal meningitis was ascertained. This case highlights the importance of considering a CNS infection in an immuno-suppressed patients presenting with hyponatraemia secondary to SIADH.

Learning points

- The SIADH is a common cause of hyponatraemia and is associated with decreased serum osmolality, excessive urinary sodium excretion and inappropriately elevated urine osmolality.
- Small cell lung cancer is the single most common cause of SIADH followed by CNS infections.
- *C neoformans* or *C gattii* has become increasingly prevalent in immunocompromised patients.[4]
- Diagnosis of cryptococcal meningoencephalitis can be challenging because of the subacute onset of symptoms and non-specific presentation.
- CNS infection and SIADH are not mutually exclusive, and both should always be considered in immuno-suppressed patients presenting with acutely altered mental status.

Competing interests None.

Patient consent Obtained.

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