

Cerebral salt wasting syndrome in a renal transplanted child with tuberculosis meningitis

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ABSTRACT

Hyponatraemia is a common complication of intracranial diseases. We report the case of a 9 year-old boy, renal transplant recipient, with tuberculosis meningitis who developed hyponatraemia and excessive natriuresis as a result of hydrocephalus and cerebral salt wasting syndrome complicating the intracranial disease. A brief review of the syndrome is presented, emphasising the differential diagnosis with other forms of hyponatraemia of central origin.

Key-Words:

Cerebral salt wasting syndrome (CSWS); hydrocephalus; hyponatraemia; syndrome of inappropriate antidiuretic hormone secretion (SIADH).

INTRODUCTION

Hyponatraemia is a common complication of intracranial diseases such as infections, trauma, tumours and stroke¹⁻⁷. This electrolyte imbalance can increase the severity of neurological symptoms due to the risk of cerebral oedema and ischaemia¹⁻². Cerebral salt wasting syndrome (CSWS) and syndrome of inappropriate antidiuretic hormone secretion (SIADH) are two potential causes of hyponatraemia in patients with intracranial disorders¹⁻⁵. Their differentiation is essential as inad-

equately management can result in unnecessary hyponatraemia-related morbidity in unrecognised CSWS patients, as its treatment is markedly different to that of SIADH¹⁻⁴. Tuberculosis meningitis (TM) can be the most common infectious neurologic disease associated with CSWS in paediatric patients³.

CASE REPORT

A 9 year-old boy, submitted to a renal transplant at the age of 6, under triple immunosuppressive therapy (steroids, mycophenolate mofetil and tacrolimus), presented with a 3-day history of fever and vomiting. On examination he showed apparent weight loss and neck stiffness with positive signs of meningeal irritability. Initial laboratory tests showed white blood cell count of 16,200/mm³ with 58.8% neutrophils and 33% lymphocytes, C-reactive protein 9.6 mg/dL (normal <0.5 mg/dL) and erythrocyte sedimentation rate 62 mm/h (normal <10 mm/h). Lumbar puncture revealed a cerebrospinal fluid (CSF) white blood cell count of 250 cells/mm³ without predominance of any type; protein 122 mg/dL; glucose 11 mg/dL (serum glucose 90 mg/dL). A diagnosis of meningitis was made and treatment with ceftriaxone initiated. Two days later the patient complained of drowsiness and had a convergent squint. Brain computed tomography (CT) was normal. At this

time parents referred to contact with a neighbour with pulmonary tuberculosis. A diagnosis of TM was made based on the contact history, neurological focal signs and hypoglycorrachia and a 4 drug TM treatment was adopted with isoniazid, rifampin, pyrazinamide and streptomycin plus prednisolone (2 mg/kg/day). Three days later symptoms recurred, with severe headache, vomiting and impaired consciousness. This was associated with signs of dehydration and increased urine output (6 ml/kg/h). Laboratory tests showed: plasma urea 51 mg/dL, creatinine 0.6 mg/dL, sodium 127 mmol/L, osmolality 286 mOsmol/kg, uric acid 2.9 mg/dL, urinary sodium 90 mmol/L and fractional excretion of sodium of 2.3%. Brain CT revealed hydrocephalus. A diagnosis of CSWS was made. Volume replacement was given and, in addition, 3% saline to maintain positive sodium balance. An external ventricular drain was inserted, later replaced by a ventriculoperitoneal shunt. Symptoms started to regress a few days later and serum sodium normalised. Repeated chest X-rays were normal. The Mantoux skin test was negative. *Mycobacterium tuberculosis* was identified by polymerase chain reaction technique from CSF and gastric samples, and CSF cultures were also positive. The boy was discharged after 3 months. He is still under treatment and has homonymous left hemianopsia.

DISCUSSION

CSWS is characterised by hyponatraemia, excessive natriuresis and extracellular-fluid volume depletion, occurring in patients with intracranial pathologies, excluding the use of any therapies, namely diuretics^{1-4,7}. Information on its prevalence in childhood is scant, with few case reports described⁴⁻⁵. The aetiology and pathogenesis of CSWS are not clearly understood¹⁻⁴. Decreased sympathetic input to the kidneys and humoral mechanisms such as excessive release of natriuretic factors are possible explanations¹⁻⁵. The main differential diagnosis is SIADH¹⁻⁵. At present some authorities doubt that there is a difference between them, while many others feel that CSWS is a distinct entity^{6,7}. The major difference is that CSWS involves renal salt loss resulting in hyponatraemia and extracellular vol-

Table 1

Differential diagnosis between CSWS and SIADH^{1-4,6,7}

	CSWS	SIADH
Weight	↓	↑
Central venous pressure	↓	↑ or N
Clinical dehydration	Yes	No
Water balance	Negative	Variable
Blood urea-creatinine ratio	↑	N
Serum osmolality	↑ or N	↓
Serum uric acid	↓	↓
Urine sodium	↑↑	↑
Urine volume	↑↑	↓ or N
Response to saline infusion	Correct	Limited
N (normal)		
↑ (increased)		
↓ (decreased)		
CSWS (cerebral salt wasting syndrome)		
SIADH (syndrome of inappropriate antidiuretic hormone secretion)		

ume decrease while SIADH involves renal water retention with consequent euvolaemic or hypervolaemic hyponatraemia²⁻³. Differentiating CSWS from SIADH thus depends primarily on the presence of hypovolaemia, a negative salt balance and positive response to saline infusion in CSWS, but there are other factors that help to distinguish between them (Table 1)^{1-4,6,7}. Our patient had decreased volume plasma as demonstrated by dehydration and polyuria, as well as excessive natriuresis. In addition, he responded to salt and fluid replacement which favours CSWS. The mainstay treatment of CSWS consists of volume replacement and maintenance of a positive salt balance, generally using either isotonic or hypertonic saline⁵. Lowering intracranial pressure by a ventriculoperitoneal shunt or an external lumbar drain might be an additional effective treatment^{1,3}. Since natriuretic peptides can inhibit mineralocorticoid secretion in patients with CSWS, administration of an agent with mineralocorticoid activity, such as fludrocortisone, has also been shown to be effective in returning serum sodium levels to normal¹⁻⁵. Some authors suggest that it should be initiated after several days when the diagnosis is clear and management by replacement of salt and fluids is not effective⁵. In this case fludrocortisone was not used as the patient responded well to volume and salt replacement and to ventricular drainage.

Although rare, TM is a serious extrapulmonary complication of mycobacterial infections in immunocompromised patients, such as renal transplant recipients. Hydrocephalus and hyponatraemia are possible complications. The latter may be due to CSWS that needs to be differentiated from SIADH, as they have markedly different treatments. Determining the cause of hyponatraemia was essential in this case to institute the appropriate treatment. However, despite the prompt diagnosis and treatment, neurological sequelae of TM could not be avoided. Although TM is a growing threat in the transplant setting, early and aggressive diagnosis with meticulous monitoring of immunosuppression allows a successful outcome for both patient and graft. Optimal prophylaxis guidelines have yet to be completely defined.

Conflict of interest statement. None declared.

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