Transient cerebral salt wasting following scrub typhus infection

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Abstract

Cerebral salt wasting (hyponatraemia associated with renal sodium loss and hypovolumia) has been reported secondary to intra-cerebral pathology and following certain infections. Cerebral salt wasting following typhus infection has been reported rarely. We report a case of transient cerebral salt wasting that occurred during the convalescent phase of scrub typhus infection resulting in severe symptomatic hyponatraemia.

Introduction

Scrub typhus is caused by *Orientia tsutsugamushi*; an obligate, intracellular, gram-negative bacterium. It is transmitted to humans accidentally by the bite of the larva of trombiculid mites. The infection causes a disseminated vascular and perivascular inflammation which results in significant vascular leakage and may progress to end organ damage.

It is one of the most important re-emerging Rickettsial infections in Sri Lanka, India as well as many other Southeast Asian countries and in the tsutsugamushi triangle.

Scrub typhus presents as an acute febrile illness after an incubation period of 6-21 days. An eschar, a dark scab-like lesion is characteristic at the chigger bite [1]. It is characterized by fever, headache, myalgia, cough, and gastrointestinal symptoms and may affect any organ system in the body resulting in sepsis with shock, ARDS, myocarditis, liver failure, renal failure, and encephalitis resulting in a mortality around 30% [2].

The recommended treatment is doxycycline, however, alternative regimens such as, chloramphenicol, azithromycin, rifampicin, and roxithromycin have been used successfully. Usually following treatment patients have a good recovery and rarely need reassessment.

However delay in the diagnosis and appropriate treatment may lead to complications such as bilateral hearing loss, tinnitus, and features of parkinsonism [3].

Cerebral salt wasting following scrub typhus infection has rarely been reported.

We present a middle aged male from Gampaha, who developed transient cerebral salt wasting during the convalescent phase following treatment for scrub typhus infection.

Case report

A 64 yr-old-male from the Gampaha district of Sri Lanka, presented with fever, chills and rigors for one week, having arthralgia and myalgia and loose stools, without respiratory, urinary or CNS symptoms. Apart for diabetes mellitus, he had no other medical illness.

He was found to have an eschar over his abdomen and a clinical diagnosis of scrub typhus was made.

He was started on oral doxycycline for which his fever settled rapidly and was discharged on a 7 day course of oral doxycycline.

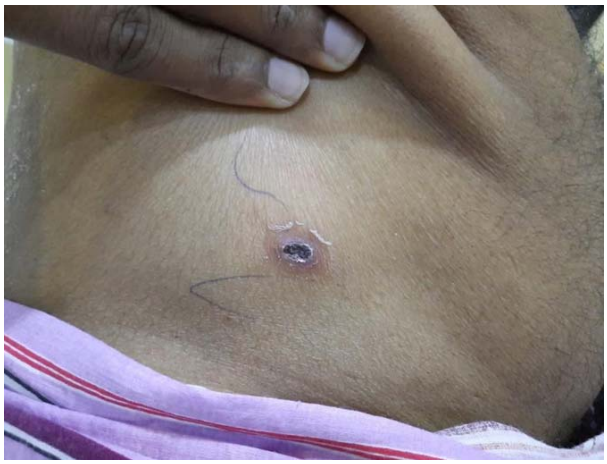

Figure. **Eschar on the abdomen in our patient, with permission.**

Ceylon Medical Journal 2022; **67:** 66-68

DOI: http://doi.org/10.4038/cmj.v67i2.9634

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One week later he was re-admitted to our ward, with progressive generalized weakness, difficulty in walking and severe lethargy with poor appetite, increased urinary frequency and urge incontinence. He had no dysuria, abdominal pain or new onset fever, vomiting or diarrhea, He denied photophobia or headache.

Although he consumed alcohol occasionally and smoked cigarettes infrequently he denied use during the post hospital stay. His diabetic control was satisfactory and he was not on any diuretics.

On examination he was drowsy, looking quite ill. He was clinically dehydrated as he had decreased skin turgor with dry mucous membranes and marked wrinkling in both legs with dry flaky skin. His blood pressure was 130/80 mmHg having a postural drop of more than 20mmHg systolic, on standing. With a prolonged capillary refilling time and pulse rate 88 beats per minute having postural tachycardia.

His lungs were clear. There was no neck stiffness, and his orientation and cortical functions were normal.

He had generalized reduction of muscle tone and grade 3-4/5 weakness in all muscle groups of the lower and upper limbs. The knee and ankle reflexes were diminished and plantar reflex were down-going. There was no demonstrable sensory deficit or cerebellar signs.

Investigations revealed severe hyponatraemia (106mmol/L) with normal potassium levels. Capillary sugar was 168mg/dL, his renal functions and liver profiles were normal while his inflammatory markers were within normal limits. His serum osmolality was 270mOsm/kg, urine osmolality was 404mOsm/kg and urinary sodium was 116mmol/L. Ultrasound abdomen showed normal kidney sizes without hepatosplenomegaly, however collapsibility of the IVC was noted.

On the first day of admission he was found to have a urine output of 5500ml for an intake of 2300ml. BUN creatinine ratio was 23.7 (upper limit - 20). His hematocrit was not elevated as he had a mild anaemia with a hemoglobin level of 10.3mg/dl.

Together with hyponatraemia, reduced serum osmolality and normal urine osmolality with increased urinary sodium loss (>20mmol/L), while being clinically hypovolemic and dehydrated a diagnosis of cerebral salt wasting was made. He was hydrated with normal saline and as he was symptomatic he was given 3% hypertonic saline, which gradually raised his serum sodium levels, resulting in improvement of his symptoms.

Non contrast CT brain was performed which didn't reveal any gross abnormality.

Nerve conduction study excluded Gullian barré syndrome and ruled out acute or chronic demyelinating polyradiculopathy.

Serum TSH and 9am cortisol measurements were normal. He was discharged with oral salt and followed up serum electrolyte measurements.

Serological analysis for Rickettsial infection was positive for *Orientia tsutsugamushi* (scrub typhus), IFA IgG titre>1:128 (3+) with a rising titre.

At three months, he was completely asymptomatic and his serum electrolytes were normal, therefore transient cerebral salt wasting induced by scrub typhus infection was considered.

Discussion

Cerebral salt wasting (CSW). Even though the entity of CSW is still in debate, to our best knowledge according to current literature it describes salt and water depletion from the kidneys causing hypovolemic hypernatremia. Urinary and serum osmolality as well as urinary sodium is similar to that of SIADH, however it can be differentiated from SIADH as these patients will be dehydrated and those with hyponatraemia resulting from SIADH will be euvolumic [4].

The pathophysiology of cerebral salt wasting is not fully understood but may involve natriuretic factors and direct neural influence on renal function [5]. The main etiology is following CNS disease such as intra-cerebral hemorrhage, infection or tumors, although it can occur in the absence of cerebral disease.

Differentiating between the two is important as the treatment is almost opposite in each. In SIADH the mainstay of treatment is fluid restriction and salt replacement, whereas in cerebral salt wasting it is volume repletion and salt replacement.

In order to confirm the diagnosis we performed osmolality studies of serum and urine samples and assessed urinary sodium levels. We performed a non-contrast CT brain which excluded any gross CNS pathology. TSH and cortisol levels were within normal limits.

Although cerebral salt wasting following scrub typhus has been rarely reported, we believe the actual burden may be a lot more, as scrub typhus is seen in many resource poor countries where investigations to confirm the diagnosis and exclude other causes of hyponatraemiais limited.

Furthermore mild hyponatraemia may be missed as most patients are not actively screened during the recovery period and after discharge from hospital.

Therefore cerebral salt wasting should be considered in patients who develop hyponatraemia following treatment of scrub typhus.

Author contributions

Kingsley Rajivasan Francis was involved in gathering patient details, investigations, literature search, corresponding, and drafting of this article.

Ranjan Premaratna was involved in literature search, formatting and drafting of this article.

Competing interests

The authors declare there are no conflicts of interests.

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