

Unusual Complication of Varicella Zoster (Vzv) Infection in a Bone Marrow Transplant Recipient

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ABSTRACT

Disseminated zoster in immune-compromised patients has been reported to have high mortality and can have atypical complications. Here we report a patient post-allogeneic bone marrow transplant (BMT) who presented with profound and prolonged hyponatremia secondary to SIADH complicating disseminated VZV infection. We also briefly review the literature related to this possibly under-appreciated complication.

Keywords

Hyponatremia, SIADH, Varicella zoster.

Introduction

Syndrome of inappropriate ADH secretion (SIADH) has been reported in association with viral infections like EBV, CMV and less commonly VZV [1-3]. Disseminated zoster in immune-compromised patients has been reported to have high mortality and can have atypical complications. Some authors have even suggested that the immunological breakdown associated with VZV may predispose to leukemic relapse [4]. Here we report a patient post-allogeneic BMT who presented with profound hyponatremia secondary to SIADH complicating disseminated VZV infection.

Case report

Our patient was a 36-year-old gentleman, 7-months post matched unrelated donor stem cell transplant for AML with a history of GVHD of the skin, gut, and liver for which he was on immune-suppression with Cyclosporine. He presented with a 3-day history of nausea, vomiting, hiccups, and abdominal discomfort, which was preceded by a vesicular multi-dermatomal skin rash affecting chest, back, and upper arms.

He was clinically euvolemic, there were no neurological deficits and cardiac function was normal. Blood work revealed normal renal function, mildly deranged transaminases and sodium of 100.

Blood urea was high normal, and endocrine work up including TSH and ACTH were normal. Swab from the rash was positive for VZV, and he was started on iv Acyclovir 10 mg/kg every 8 hours, which he received for 14 days. CT chest showed bilateral lung infiltrates, BAL fluid was positive for Varicella zoster virus and CT abdomen showed liver and spleen nodularity presumed related to the viral infection.

Urine osmolality was elevated at 518 mmol/kg, serum osmolality was reduced at 229 mmol/kg, and urine spot sodium was increased at 52 mmol/l confirming the diagnosis of SIADH. He also had mild hypokalemia. As he was quite symptomatic with nausea and vomiting, he received hypertonic saline infusions initially followed by normal saline infusions and oral sodium chloride along with oral fluid restriction. Plasma sodium recovered to normal after 15 days and he had resolution of the rash with iv Acyclovir therapy.

Discussion

The clinical and laboratory profile in our patient was consistent with SIADH and its resolution with treatment of varicella infection points to this as the likely etiology. Our patient also had mild hypokalemia which could be secondary to aldosterone release triggered by lowered serum osmolality [5].

Both pneumonia and encephalitis occurring as complication of varicella infection is well-documented to cause SIADH

[6,7] through the resetting of central osmostats. Our patient had radiological evidence of pneumonia and VZV was isolated from BAL fluid. However even in the absence of pneumonia or encephalitis, both localized and disseminated varicella zoster has been associated with SIADH [8]. In localized zoster infection one possible mechanism suggested is that the signals from peripheral osmo-receptors reach the dorsal root ganglion (DRG) of the spinal cord where the VZV resides, and this leads to dysregulation in mechanisms of ADH regulation [9,10]. Interestingly many SIADH cases in localized zoster infections have been in association with herpes zoster ophthalmicus [11]. One mechanism hypothesized is that the nucleus tractus solitarius in the brain stem is the key centre for processing signals from peripheral osmo receptors and baro receptors and is also the first central relay for sensory axons from V1 leading to potential for cross talk between trigeminal inputs and osmolar regulation [12].

The hyponatremia observed in our patient was severe with serum sodium hovering around 100-110 mmol/l for several days despite treatment. The amount of free water intake, genetic pre-disposition, severity of infection and concurrent drugs and co-morbidities influence likelihood and severity of hyponatremia in such patients. The combination of water restriction and high sodium and protein diet is effective in treating most patients with SIADH, the latter by inducing osmotic diuresis by increase in plasma urea. Loop diuretics may also be used either alone, or in combination with other drugs like demeclocycline which block ADH action or ADH receptor antagonists like tolvaptan [13].

Complete recovery of serum sodium levels in our patient took 14 days. The duration of hyponatremia reported in patients with zoster reactivation and SIADH has been variable (2 weeks to 4 months) and can be longer in patients who develop post herpetic neuralgia (PHN). This may be a reflection of the greater viral load and more extensive neural damage in PHN [14,15]. Severe pain as is common in PHN can also act as a non-osmotic trigger for ADH secretion [16].

Conclusion

This case highlights the rare, potentially severe and possibly under-appreciated association between SIADH and varicella zoster. Awareness of this association may lead to early diagnosis and treatment of hyponatremia associated with varicella infection.

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