Hypovolemic hyponatremia after trimethoprim use

Sir,

A 49-year-old deceased donor renal allograft recipient presented a year after transplantation with complaints of fatigue, nausea, and vomiting of 2 days duration. A week prior to presentation, he was diagnosed to have urinary tract infection with *Escherichia coli* and was prescribed tablet trimethoprim (20 mg/kg/day) -sulfamethoxazole (100 mg/kg/day) in two divided doses. At presentation, patient had sunken eyes, dry mouth, decreased skin turgor, tachycardia and postural hypotension. He was afebrile, normal respiratory and cardiovascular examination. Central nervous system examination showed no focal neurological deficit. Investigations showed serum creatinine 1.0 mg/dl, blood urea 64 mg/dl, serum sodium 115 mEq/L, potassium 5.6 mEq/L, uric acid 7.8 mg/dl, chloride 90 mEq/L, bicarbonate 17.3 mmol/L, and pH 7.36. The urinary sodium and potassium were 142 and 41 mEq/L respectively. The serum and urine osmolality 248 and 161 mOsm/kg respectively. The fractional excretion of sodium was <1%, uric acid: 6.19%, transtubular potassium gradient 3.01, serum thyroid stimulating hormone 0.5 μIU/L (0.17–4.05 μIU/mL) and serum cortisol 5.5 μg/dl (6.7–22.60 μg/dl). Ultrasound showed normal renal allograft and collapsed inferior vena cava. Trimethoprim-sulfamethoxazole combination was stopped. He was encouraged to consume high salt diet. With this, serum sodium increased to 127 mEq/L after 48 h and 135 mEq/L after 96 h.

Hypotonic hyponatremia can be divided according to volume status as hypovolemic, euvolemic, and hypervolemic. High urinary sodium excretion in patients of hypovolemia is inappropriate. It is possible in adrenal insufficiency, hypothyroidism, metabolic alkalosis, diuretic use, cerebral salt wasting, and salt wasting nephropathy.[1] Our patient had no feature suggestive of these etiologies. Trimethoprim-sulfamethoxazole can cause hyperkalemia, hyponatremia, and metabolic acidosis. Hyperkalemia is common than the others.[2]

Trimethoprim at high doses acts as reversible direct sodium channel inhibitor at the level of the eNaC in the distal tubule. It acts as a potassium sparing diuretic.[3] It also causes a distal acidification defect, with hyperkalemia contributing to reduced net acid excretion by inhibition of ammoniagenesis. However, there are reports of hyponatremia with the standard doses of trimethoprim.[4]

The diagnosis of trimethoprim induced hyponatremia depends on recognition of hypovolemia and elevated urinary sodium concentration. It has to be distinguished from syndrome of inappropriate anti diuretic hormone secretion (SIADH), the leading cause of hyponatremia in hospitalized patients[5] in whom fluid restriction is desired, while in trimethoprim induced hyponatremia liberal salt intake is the remedy.[6] Urine sodium excretion is elevated in both the conditions. SIADH is euvolemic condition while trimethoprim induced hyponatremia is hypovolemic condition. The latter, therefore, is associated with tachycardia, orthostatic hypotension, increased blood urea, increased rennin, aldosterone, and antidiuretic hormone.[1] The high antidiuretic hormone is also a feature of SIADH. However, SIADH is characterized by hypouricemia due to volume expansion resultant decrease in proximal tubular reabsorption of uric acid and hence elevated fractional excretion of uric acid (<10% suggestive of prerenal causes, >10% suggestive of SIADH or renal causes). For the same reason, SIADH patients also have high fractional excretion of sodium.[7]

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Conflicts of interest

There are no conflicts of interest.

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