CLINICAL VIGNETTE

An Interesting Case of Hyperkalemia in a Patient with Normal Renal Function

Vito K. Rocco, MD and Susan C. Ahern, DO

A 70-year-old Caucasian male with a history of chronic hyperkalemia for about 8 years presented to Endocrinology for a second opinion about the etiology and appropriate treatment of his hyperkalemia. His past medical history was notable for GERD, Barrett's esophagus, PUD, celiac disease, hiatal hernia and gout. He was initially evaluated by an outside endocrinologist for a history of hyperkalemia up to 6.5 mg/dL. The details of the initial evaluation are not available but treatment with fludrocortisone 0.1 mg "a few times a week" and increased to 0.1 mg daily about 2 years ago. During this time, he experienced intermittent nausea, developed "gout" in toes, cold intolerance and a gradual weight loss of 10-16 lb. His serum potassium levels normalized.

He presented for a second opinion about his hyperkalemia. His BP was 106/61, pulse 58 regular, weight 139 lbs. He was taking fludrocortisone 0.1 mg three a day per week and indomethacin as needed for gout pain. His serum potassium was 5.2 mmol/L at that time. The patient inquired if chronic fludrocortisone was the best therapy for his condition. He was advised to continue potassium restricted diet and hold fludrocortisone and follow up labs were ordered.

One week later, the serum potassium was stable at 5.2 mmol/L, serum sodium 142 mmol/L, chloride 100 mmol/L, CO2 28 mmol/L, glucose 95 mg/dL, creatinine 0.95 mg/dL, and BUN 7 mg/dL. Random cortisol was 10 mcg/dL (4.0-31 ng/ml), serum aldosterone 4.7 ng/mL (4.0-31 ng/dl), plasma renin activity 0.2 ng/mL/hr (0.5 – 4.0 ng/mL/hr), and ACTH 31 pg/mL (NR 6 – 59). Cosyntropin stimulation study 3 weeks later revealed baseline cortisol 11 mcg/dL which increased to 27 mcg/dL, 1 hour after cosyntropin. His relatively low renin and aldosterone for his blood pressure was suggestive of hyporeninemic hypoaldosteronism. The normal cosyntropin stimulation test along with low renin ruled out primary adrenal insufficiency causing chronic hyperkalemia.

There was no clear endocrine explanation for his hyperkalemia. With normal potassium and absence of symptomatic hypotension, there was no clear role for chronic fludrocortisone. We advised periodic labs to ensure potassium remained normal off fludrocortisone. He was advised to avoid high potassium containing foods and avoid NSAIDS, angiotensin converting enzyme inhibitors and angiotensin receptors blockers.

At follow up, 2 months later, a basic metabolic panel showed normal serum potassium 4.6 mmol/L and metabolic acidosis with serum CO2 19 mmol/L. This raised concern about an underlying renal tubular acidosis as the cause of his hyperkalemia. At Nephrology consultation, he reported onset of diarrhea about two and a half weeks prior visiting Florida. The diarrhea had improved and nearly resolved. Repeat laboratory included serum sodium 136, potassium 4.7, chloride 94, total CO2 27, serum anion gap 15, glucose 89, serum creatinine 1.05, BUN 10 and serum osmolality 294 mOsm/Kg. Urine chemistries were also sent and returned showing sodium 26 mmol/L, potassium 17 mmol/L, chloride < 20 mmol/L, creatinine 43.9 mg/dL, osmolality 261 mOsm/Kg and urea nitrogen 433 mg/dL. The transtubular potassium gradient was 4.07, but this is difficult to interpret since serum potassium was well within normal limits at 4.7 at the time of the analysis. Fractional excretion of sodium was 0.46%, and fractional excretion of urea was 54.5% both of which suggest euvolemia. Urine anion gap was > 23 raising concern about renal tubular acidosis, rather than diarrhea-induced metabolic acidosis. In the absence of renal tubular acidosis, the renal response to diarrhea is to markedly increase urinary chloride which causes a negative urine anion gap. At this juncture, he is felt to have a mild distal renal tubular acidosis and will require close follow-up. Given the recent normal serum total CO2, he was advised to use sodium bicarbonate 650 mg 3 tablets once or twice a day if he has diarrhea and to notify our office if he starts sodium bicarbonate in order to arrange follow-up, including laboratory data.

Discussion

The differential of hyperkalemia in a patient with normal renal function includes increased potassium released from cells and reduced urinary potassium excretion.[1] Given the presence of relative hypotension, hyperkalemia, low serum aldosterone, low plasma renin activity and no evidence for adrenal insufficiency, this patient was felt to have isolated hyporeninemic hypoaldosteronism[2,3] or primary acquired hypoaldosteronism.[4] This form of hypoaldosteronism is distinct from other forms such as, pseudo-hypoaldosteronism type 1, which is resistant to mineralocorticoid therapy, and pseudohypoaldosteronism type 2 in which patients are typically hypertensive. NSAIDS, including indomethacin, are a known cause of reversible hyporeninemic hypoaldosteronism by inhibiting renin production and subsequent aldosterone release independent of a decrease in creatinine clearance.[5-7] Our patient had very sporadic indomethacin use and never had a concomitant decline in renal function. Other common causes of hyporeninemic hypoaldosteronism, which are not applicable to our patient, are diabetic nephropathy, AIDS, tubulointerstitial disease, and IGM monoclonal gamopathy.[8]

Aldosterone deficiency and the resulting hyperkalemia impaired renal ammoniagenesis, and can produce an acquired distal hyperkalemic renal tubular acidosis,[9,10] commonly referred to as RTA type 4. Hyperkalemic RTA occurs more frequently in adults than children and the degree of hyperkalemia is usually out of proportion to GFR.[8,11] Symptoms of postural hypotension and lethargy may be present (10). Fludrocortisone therapy stimulates sodium reabsorption and potassium excretion. Treatment with bicarbonate increases renal potassium excretion by increasing sodium delivery to the distal tubule and shifts potassium into cells with correction of acidosis.[1]

This case illustrates an unusual cause of chronic hyperkalemia. With collaboration of endocrinology and nephrology, we were able to determine the etiology as hyporeninemic hyperaldosteronism with resultant hyperkalemic RTA type 4. Fludrocortisone 0.2-1mg/day is most commonly recommended treatment for hyperkalemia in hyporeninemic hypoaldosteronism assuming there are no contraindications to fludrocortisone therapy.[2,7,8,10,12] For now, since the patient does not have hyperkalemia, we will address his acid base disturbance with bicarbonate therapy as needed. He does not have any contraindications to fludrocortisone such as edema, volume overload or hypertension; therefore, fludrocortisone is an option for him in the future if hyperkalemia returns.

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