

## MORNING REPORT

## AN INTERESTING CASE OF HYPOKALEMIA

Tariq N. Ali, MD, MBA (presenter) and Michele Fang, MD (discussant \*\*)

Dr. Ali (Tariq.Ali@uphs.upenn.edu) is a third-year internal medicine resident at the University of Pennsylvania Perelman School of Medicine. Dr. Fang (Michele.Fang@uphs.upenn.edu) is an associate professor at the University of Pennsylvania Perelman School of Medicine and associate editor of the SGIM Forum.

*\*\* The comments in italics are those of the discussant.*

A 19-year-old man with a family history of familial adenomatous polyposis (FAP) was admitted for evaluation and management of potassium 2.5 and hypertension from GI clinic. The patient was asymptomatic and was going in for routine follow up. He did not have any nausea, vomiting, palpitations, diarrhea, or lightheadedness. The patient denied headache, blurry vision, hematuria, chest pain, or shortness of breath. The patient stated he had “borderline hypertension” about a year ago, but no medications were prescribed.

*Hypokalemia is defined as a condition in which the serum potassium level is less than 3.5 mEq/L (3.5 mmol/L). Diuretics and gastrointestinal disorders are by far the most common causes of hypokalemia<sup>1</sup>. However, measurement of urine potassium establishes the pathophysiologic mechanism behind hypokalemia and, thus, aids in formulating the differential diagnosis. A serum magnesium assay is also important in the differential diagnosis, as well as in therapy, and is therefore performed as a first-line test as magnesium deficiency exacerbates potassium wasting by increasing distal potassium secretion<sup>2</sup>.*

The patient’s medical history is otherwise unremarkable. He has had multiple colonoscopies that did not show any polyps. His mother and maternal grandfather have familial adenomatous polyposis syndrome. He denies use of prescription drugs or illicit drugs and drinks on average less than a beer a week. He is an engineering student.

On physical exam, his vitals were BP 160/84, equal on both arms, pulse 57, Temp 36.8°C, R 15, Weight 67.1 kg, SpO<sub>2</sub> 100%, BMI 26.22. He was awake and alert in NAD. He had chronic benign cysts on scalp. His conjunctivae were clear and there was no papilledema. Lungs were clear. Heart was regular rate and rhythm, without S<sub>4</sub>. Abdomen was soft, nontender without masses or bruit. The patient had no peripheral edema, and he had no deficits neurologically or psychologically.

The patient’s potassium was repeated and found to be 2.4, magnesium 1.7. The patient also had U waves on EKG.

*In evaluating a young healthy individual with hypertension and hypokalemia with a normal diet on no medications, secondary causes of hypertension must be considered. The patient’s hypertension and hypokalemia were concerning for primary hyperaldosteronism. However, it is important to rule out other etiologies on the differential including pheochromocytoma, functional adenoma, and renal artery stenosis.*

Serum renin, aldosterone, plasma metanephrines, plasma normetanephrines, ACTH and cortisol levels were ordered. The patient’s potassium and magnesium were aggressively repleted. More than 300 meq of potassium were required to slowly bring the potassium level up to 3.6 by hospital day number two. The patient’s aldosterone was 72.9 ng/dL (upright 4.0-31.0 ng/dL, supine ≤16.0 ng/dL, unspecified ≤31.0 ng/dL). Direct renin 11.1 (2.5-45.7 pg/mL) making the aldosterone renin calculation 6.6. Plasma metanephrines and normetanephrines were normal. AM cortisol and ACTH were normal.

*Normal serum levels of aldosterone are dependent on the sodium intake and whether the patient is upright or supine. High sodium intake will tend to suppress serum aldosterone, whereas low sodium intake will elevate serum aldosterone. The reference intervals for serum aldosterone are based on normal sodium intake. An Aldosterone/Direct Renin Activity Ratio of greater than 3.7 is suggestive of hyperaldosteronism.*

*Given that cortisol levels were suppressible, pheochromocytoma and functional adenoma were much less likely.*

The patient’s urine potassium was 24.7 (indeterminant range).

*Low urine potassium (<20 mEq/L) suggests gastrointestinal loss (eg diarrhea or laxative use), poor intake, TPN contents, or a shift of extracellular potassium into*

*continued on page 2*



## MORNING REPORT (continued from page 1)

intracellular space (with insulin and/or excessive bicarbonate supplements). High urine potassium (<40 mEq/L) suggests renal loss such as from diuretics. Our patient's urine potassium was in the indeterminate range. In these cases, calculation of the transtubular potassium gradient (TTKG) can be useful. The use of the transtubular potassium gradient (TTKG) was developed to account for the potentially confounding effect of urine concentration on the interpretation of the urine potassium concentration. The TTKG is equal to (urine potassium x serum osmolality)/(Serum potassium x urine osmolality).

Our patient's TTKG = 8.

A TTKG of 8 is suggestive of the kidney wasting excessive potassium, and is consistent with primary hyperaldosteronism.

The patient was diagnosed with hyperaldosteronism. The term primary hyperaldosteronism (or primary aldosteronism [PA]) refers to a renin-independent increase in the secretion of aldosterone. This condition is principally a disease of adulthood, with its peak incidence in the fourth to sixth decades of life. More than 90% of cases of PA are due either to an aldosterone-producing adenoma, which accounts for around 35% of cases (30-40%), or to idiopathic hyperaldosteronism, which accounts for around 60% of cases (almost all of which are bilateral). About 1% of patients present with adrenocortical carcinomas that are purely aldosterone-secreting and are usually large at the time of diagnosis; 1% present with familial hyperaldosteronism, and 1% present with an ectopic aldosterone-producing adenoma or carcinoma<sup>3</sup>.

The patient underwent abdomen and pelvis CT followed by

MRI which showed a 4.9 cm right retroperitoneal mass superior to the right kidney that was anatomically inseparable from the right adrenal gland. The patient was evaluated by endocrinology who felt that that radiographic differential diagnosis for the adrenal mass included functional adenoma, non-functional adenoma, myelolipoma or "collision tumor" which is a combination of a lipoma and adenoma.

Patients with familial adenomatous polyposis are considered to be at risk for extra-intestinal tissue growth including the development of thyroid and pancreatic cancer, CNS tumors and various benign growths including adrenal adenomas<sup>4</sup>. In one prospective study, patients with FAP were revealed to have a 4 times greater incidence (13%) of adrenal adenomas than expected in the general population (3%)<sup>5</sup>. It is notable though that most are considered to be clinically insignificant with most not overproducing hormones.

Endocrinology felt that because the patient was young (<45 years old) and had elevated aldosterone and elevated aldosterone>renin ratio, primary hyperaldosteronism was confirmed and he did not require adrenal vein sampling (as imaging alone will lead to 30% incorrect diagnosis which is more common in with older age—e.g., bilateral hyperplasia and nonfunctional incidentoma). The patient was started on amiloride 5 mg po daily to help with hypokalemia.

Most antihypertensive meds do affect plasma renin and aldosteronism; however, hydralazine, alpha blockers (prazosin, doxazosin, terazosin), and verapamil do not.

The patient was discharged on amiloride and potassium chloride

supplementation. He underwent laparoscopic right adrenalectomy five months later with resolution of hypertension and hypokalemia.

Take home points:

1. In patients with unexplained hypokalemia especially with hypertension, primary aldosteronism should be considered.
2. Workup for primary aldosteronism includes plasma renin and aldosterone and abdominal imaging. While workup in place, use of hydralazine, alpha blockers (prazosin, doxazosin, terazosin), and verapamil can be used for blood pressure control. Potassium sparing diuretics such as triamterine and amiloride can be used.

### References

1. Zacchia M, Abategiovanni ML, Stratigis S, et al. Potassium: From physiology to clinical implications. *Kidney Dis (Basel)*. 2016 Jun;2(2):72-9.
2. Huang C, Kuo E. Mechanism of hypokalemia in magnesium deficiency. *JASN*. October 2007;18(10):2649-2652.
3. Aronova A, Fahey TJ, Zarnegar R. Management of hypertension in primary aldosteronism. *World J Cardiol*. 2014 May 26;6(5):227-233.
4. Groen EJ, Roos A, Muntinghe FL, et al. Extra-Intestinal manifestations of familial adenomatous polyposis. *Ann Surg Oncol*. 2008 Sep;15(9):2439-2450.
5. Smith TG, Clark SK, Katz DE, et al. Adrenal masses are associated with familial adenomatous polyposis. *Dis colon rectum*. 2000 Dec;43(12):1739-1742.