Detective Nephron

Detective Nephron, world-renowned for expert analytical skills, trains budding physician-detectives on the diagnosis and treatment of kidney diseases. L.O. Henle presents a new case to the master consultant.

Henle I have a case for us. Metabolic alkalosis.

Nephron Excellent.

Henle, prepared A 65-year-old male was just seen recently for fatigue and muscle weakness and found to have a serum bicarbonate level of 39 mEq.

Nephron, chuckling Give me a break, apprentice, this is a cake walk. Give some hydration and send him home.

Henle, with a curious look They tried that for three days. Perhaps you want to know that his pre- and posthydration urine chloride values are on or about 80 mEq/L

Nephron, confused Ahhah!, this is going to be fun!

Henle He has recently diagnosed prostate cancer, with metastatic disease to the liver and the bone. He was treated with leuprolide, and recently with cisplatin and etoposide.

The detective listens.

All of a sudden, a knock is heard, and a medical student in a nicely ironed short white coat enters the room.

She appears frightened.

Nephron Who are you and what do you want?

Henle, smirking She is a medical student who has been involved with this case. She wanted to join us today with our discussion. Her name is Ms. Curious Tubule.

Nephron Hello, Ms. Tubule, so here we have a case of metabolic alkalosis or alkalemia?

Tubule He did get an arterial blood gas that revealed a ph of 7.57 and $pC0_2$ of 41 mm Hg. The bicarbonate was 38. This suggests a case of mixed respiratory and metabolic alkalosis.

Nephron How so?

Henle His primary problem appears to be metabolic alkalosis, and to compensate, his $pC0_2$ should have been lower, at least 0.5 mm Hg for every rise of bicarbonate of 1 mEq/L. Hence, there is a respiratory alkalosis as well.

Nephron Great job, let's move on. Let's discuss the causes of this patient's metabolic alkalosis. Can either of you tell me why this patient's plasma bicarbonate level rose to 39?

Henle Two possibilities: either there was decreased effective extracellular volume or there was an exogenous or endogenous source of increased extracellular volume content.

Tubule That is so confusing. But wouldn't the urine chloride be helpful here? Since it's high, I don't think it's a low volume state.

Henle I am getting to that point. You can have a low volume state with diuretic use and have a high urine chloride. So don't assume that just because the urine chloride is high, it's not low effective volume yet.

Nephron You are both correct. Fascinating. So now what do we need to do? Find out if he is on a diuretic or taking any endogenous medications that might be increasing his HCO_3 load?

Tubule He refused to take any of the drugs you mention.

Nephron Are you sure? Go back and check again. It's very important to make sure.

Tubule and Henle exit and Detective Nephron resumes drinking his coffee.

Nephron (to himself) Henle and Tubule really were having a very powerful discussion. I love their passion for the subject.

Henle returns to the office.

Nephron You're back.

Henle, very excited No diuretics.

Nephron Good!

Henle But we noticed a few more things: worsening hypokalemia (2.9 mmol/L) and hypernatremia (147 mmol/L), and this has been getting worse for the past month.

Nephron Stop right there! So now you are telling me we have a case of a chloride-resistant hypokalemic metabolic alkalosis?

Henle Yes, you are correct.

Nephron, with confidence I assume normal renal function.

Henle Yes, as usual you are correct.

Nephron, looking around Where is your friend, Ms Tubule?

Henle She is gathering some more data for us. I asked her to get the blood pressure readings for the last few months.

They pause as Tubule enters.

Nephron Let me guess, recent onset of hypertension as well?

The detective pauses to see their response.

Tubule Yes, you are correct.

Nephron When the urine chloride is not zero, you asked if he was taking a diuretic; you said he wasn't. So now we are left with the question of whether he has hypertension or no hypertension. If he has no hypertension, you enter the world of "Bartter's and friends." You also confirmed normal renal function, another possibility if there was no hypertension.

Henle The presence of hypertension is important because it might be the only clue to a diagnosis of primary hyperaldosteronism, renal artery stenosis, or production of endogenous compounds in the body that can raise blood pressure and have profound metabolic derangements.

Tubule So you think he has a primary aldosteronism or something like that?

Nephron, pleased Excellent. By the way, does he have elevated blood sugars?

Henle As a matter of fact, he did mention that he was diagnosed recently by his oncologist with type II diabetes mellitus and he has been gaining weight. He had normal blood glucose levels as of last year and he sees a primary care physician regularly.

Tubule Is that a recent onset diabetes? That is strange?

Henle So we have a chloride-resistant, hypertensive metabolic alkalosis with hyperglycemia and hypokalemia. Could he have Cushing's syndrome or disease?

Nephron, with a smirk Again, my dear apprentices, I have a diagnosis for you! Perhaps you are correct.

Henle His plasma renin and serum aldosterone levels were low. His urinalysis revealed >1000 glucose, and urine potassium was 45 mmol/L for a serum potassium of 2.9 mmol/L. He is having renal losses of potassium.

Tubule Perhaps he is producing too much ACTH? Or too much cortisol?

Nephron What are you waiting for, you want to check the levels? I shall see you in a few days.

Tubule and Henle exit and Detective Nephron starts reading* ASN Kidney News*. A few days later…

Nephron My coffee is good, less sweet than usual.

Tubule Sweet is the key word. ACTH level was significantly elevated with a 24-hour urinary cortisol level in the astronomical range.

Henle So this patient is producing ACTH? Where?

Nephron Did you see his prostate biopsy? He probably has neuroendocrine features and is producing ACTH. I would start ketoconazole soon. Perhaps his ACTH production could be a marker of his cancer.

Tubule Fascinating!

A few weeks later…

Henle Dr. Nephron, his prostate cancer is producing ACTH. The octeotride scan and immunohistochemistry staining for ACTH on the prostate biopsy confirmed it. He is responding very well to the therapy. His hypertension, diabetes, alkalosis, and hypokalemia all resolved with the treatment.

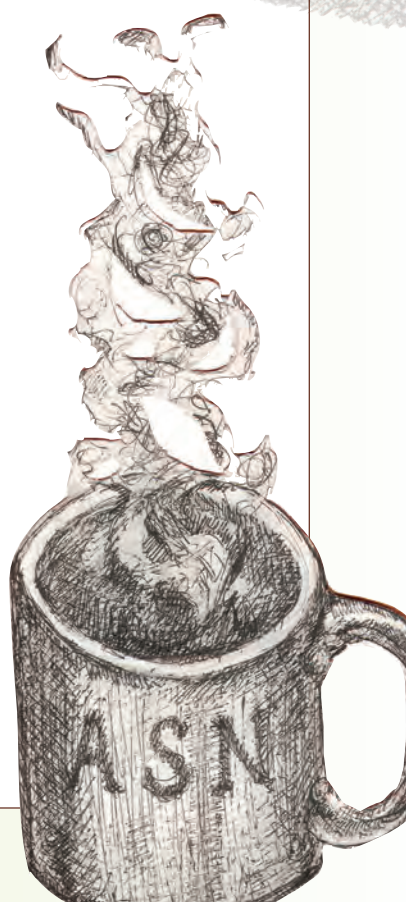
Nephron Remember, this patient presented with Cushing's like syndrome. In patients with the classic form of ectopic ATCH syndrome, the degree of ACTH and urinary cortisol and hypokalemia is much greater than classic Cushing's disease (pituitary cause). Usually ACTH ectopic production is classically seen in small cell and non-small cell lung cancer, but there are cases of thyroid cancer, prostate cancer, and ovarian carcinoid that have been reported with ectopic ACTH production.

Tubule In ectopic ACTH production, is the hypertension more profound?

Nephron, smiling Good question. Cushing's syndrome is the cause of hypertension in approximately one in 400 hypertensives. Among patients with Cushing's syndrome, hypertension is very common, affecting some 80 percent of patients. The number of patients with ectopic ACTH production who are hypertensive is usually lower than in other forms of Cushing's syndrome. This is likely due to the shorter duration of the disease or the underlying cancer. No one knows really. As you saw, this patient had hypernatremia, hypokalemia, and initial sodium retention. You see this when there is excess glucocorticoid effect. There is increased urinary retention leading to increased extracellular volume, and there is volume-mediated hypertension. The plasma renin activity will be low. Cortisol, a classic glucocorticoid hormone, might have some mineralocorticoid activity and hence raise blood pressure through its hypertensinogenic activity. These are the two mechanisms usually that can lead to hypertension in ACTH elevations—but again, usually lower chances in ectopic ACTH than in primary Cushing's disease.

Henle He is doing very well. His cancer is stable with no further progression.

Nephron Again, my dear apprentices, from a diagnosis of metabolic alkalosis, you made a diagnosis of a life-threatening systemic disorder. Always be a good detective. Observe, think, read, and apply. If it doesn't cross your mind, you will never diagnosis it. Great case, Henle.



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