

# 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, a budding nephrologist, presents a new case to the master consultant.**

*Ms. Curious Tubule enters the room along with L.O. Henle to present a case.*

**Nephron** My apprentice, what do you have for me? And I see we have our medical student back... good!

**Henle** I have a calcium level of 16 mg/dL in a 40-year-old male.

**Nephron** Well, then, let's begin... it's always fun to discuss hypercalcemia. Symptomatic or not?

**Tubule** Symptomatic, but aggressive treatment with hydration has been started. The cause is uncertain.

**Nephron** That's always the problem. Figuring out the cause is important, but for now you have to just put out the fire.

**Henle** Broadly speaking, I usually categorize hypercalcemia into hormonal causes: malignancy, medications, infections, or other rare causes.

**Nephron** That's a good place to start. But what do I also want to hear about when I hear calcium levels?

**Tubule** Phosphorus levels?

**Nephron** Good! And...?

**Tubule** I thought you could do this with just one value. Why do you need the phosphate level?

**Nephron** It may give me an idea about what the patient might have ingested. Let's take this case from an "inpatient admissions" standpoint. The most common cause of hypercalcemia in the inpatient setting is primary hyperparathyroidism, followed by hypercalcemia of malignancy and then calcium or milk alkali syndrome. What is the phosphorus level?

**Tubule** It was 3.0 mg/dL, which is normal.

**Henle** Primary hyperparathyroidism might cause a low normal phosphorus level, but ingestion of calcium tablets that could be binders, such as Tums, or calcium alkali syndrome could also result in low levels of phosphorus. However, we can't rule out primary hyperparathyroidism or malignancy yet.

**Nephron** Good thinking. Since you've started, let's complete the hormones. What other hormones can result in elevated calcium?

**Tubule** Elevated vitamin D in some cases of lymphoma, thyrotoxicosis, and adrenal insufficiency are a few that come to mind.

**Nephron** Good. In cases of lymphoma, there is an increased

amount of the enzyme that converts 25-OH vitamin D to 1,25-OH vitamin D, resulting in hypercalcemia. In thyrotoxicosis, bone resorption causes hypercalcemia. The reasons are a little more complex for adrenal insufficiency—it could be increased calcium resorption by the kidneys due to hypovolemia or increased release of calcium from the bone. I don't think this patient has that.

**Tubule** His vitals were normal except for a fever of 101°F. He had no clinical signs of adrenal insufficiency. His parathyroid hormone level, cortisol level, both 25-OH and 1,25-OH vitamin D levels, and thyroid-stimulating hormone level were all normal.

**Henle** I would consider medications a potential culprit. The patient is relatively young and may have ingested Tums.

**Tubule** Dr. Henle, we went over this already. His phosphorus level is normal, so it's unlikely he ingested any Tums tablets. Besides, I took a complete history, and he denies ingestion of Tums, lithium, or any thiazide diuretics. No theophylline, either.

**Nephron (smiling)** Nice work, Tubule. That's a good working list.

**Tubule** Also, a thiazide screen was negative.

**Nephron** You really didn't need that. What are the other electrolytes showing?

**Tubule** Normal potassium, normal sodium, and a slight increase in serum creatinine to 1.5 mg/dL.

**Henle (smiling)** No other signs of thiazide toxicity. No hypotension, either.

**Nephron** Tubule, I'm curious... what did you do next?

**Henle (jumping in)** She ordered an angiotensin-converting enzyme test, and it was normal.

**Nephron (confused)** What is his race?

**Tubule** He's black, but I don't know where he's from originally.

**Henle** He's from the West Indies.

**Nephron** I see...

**Tubule** A normal angiotensin-converting enzyme level and a normal chest x-ray put a disease like sarcoidosis lower down on my list of causes in his case...

**Henle (interrupting)** ...a tuberculin (ppd) test was also normal.

**Nephron** I already had a diagnosis when you told me his country of origin. Take 15 minutes and see what else you can come up with.

**Henle and Tubule leave the room.**

**Henle (to himself)** Tubule isn't even a full MD yet, but she's trying to jump in with impressive answers. Why is she being so competitive?

**Tubule (to herself)** I think I can come up with this diagnosis faster than Henle can.

**Henle and Tubule pace back and forth, reading books and checking Google, and go back in after 15 minutes.**

**Henle (jumping right in)** I think we should go step-by-step in the next category: malignancy.

**Tubule** Yes, malignancy can cause hypercalcemia via several mechanisms, including increased parathyroid hormonal production, production of parathyroid hormone like peptide, bone resorption, and interleukin-6 production.

**Nephron (smiling)** Good start!

**Nephron (to himself)** I'm enjoying this passionate discussion between my two apprentices. It makes them think and learn!

**Henle** Could he have a malignancy? He did have an enlarged parotid gland.

**Tubule** Serum-free light chains and serum immunofixation were normal, ruling out myeloma. Lactate dehydrogenase is elevated, but I don't know what to make of that.

**Nephron (interrupting)** Has his hypercalcemia corrected?

**Henle** It corrects down to 10–12 mg/dL after hydration and furosemide but returns quickly back to 15–16 mg/dL. In desperation, steroids and bisphosphonates were begun.

**Tubule** Infectious work-up revealed a negative HIV test and a negative bronchoscopy to rule out granulomatous infection, although his ppd was negative. His parathyroid hormone-like peptide was mildly elevated. Might he have cancer? A full body scan didn't reveal anything.

**Nephron (stopping both of them)** Where is he from again?

**Henle** The West Indies.

**Nephron** Go ask him for a thorough history of his recent travels, sexual activity, and transfusions. I need a good history and physical exam!

**Henle and Tubule return in a few hours.**

**Tubule** He was in the West Indies last year for four to five months for work-related purposes. While there, he had a blood transfusion during an urgent orthopedic procedure after a fall.

**Henle** Might he have a human T lymphotropic virus type 1 (HTLV-1) infection?

**Nephron** Bingo!

**Henle** ...and perhaps even an acute T cell leukemia/lymphoma?

**Nephron** Yes and yes! My advice is to get him tested quickly and conduct a bone marrow biopsy.

**Three days later...**

**Nephron (curious)** So, what was it?

**Henle** His HTLV-1 polymerase chain reaction test was positive, and a bone marrow test confirmed smoldering T cell leukemia. He was started on zidovudine and interferon and is planning to undergo high-dose chemotherapy as well.

**Nephron** So... as the "kidney police," what would you have to monitor in this individual in terms of renal disease?

**Tubule** Both interferon and HTLV-1 have been associated with collapsing focal segmental glomerulosclerosis, so it might not be a bad idea to check his urine protein to creatinine ratio once every few weeks to monitor for development of this entity.

**Nephron** Acute T cell leukemia/lymphoma can be smoldering, acute, or chronic and can occur in this age group. One of the causes is HTLV-1. Smoldering T cell leukemia rarely causes hypercalcemia, though it can happen sometimes. High calcium and lactate dehydrogenase are poor prognostic factors. HTLV-1 has a high prevalence in Jamaican patients—mostly women, but men have it, too. It's transmitted in the same manner as HIV, and can be spread via blood donation. Hypercalcemia occurs in 50 percent of patients with HTLV-1-induced adult T cell leukemia. The mechanism is not clear, but it is likely mediated by parathyroid hormone-like peptide and possibly interleukin-6. No one knows!

Once again, from a single entity of hypercalcemia, you diagnosed a life-threatening cancer from a strange virus. Remember, in addition to laboratory data and clinical acumen, you need a good history and physical exam—neither of these tools can ever be replaced. No online tool or laboratory test will ever give you as much information as the patient can. ●

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