

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.



Nephron What do you have for us today, my dear apprentice?

Henle A 24-year-old woman with hematuria and acute rise in creatinine level.

Nephron I see that you have taken a break from the electrolyte disorders and moved to the world of glomerular disease again. This is why nephrology is so much fun. It has so much variety to offer to us diagnosticians.

Henle Hmm... getting back to the case, she was in her usual state of health until a few weeks ago, when she started noticing unexplained joint pains, weight loss, and a feeling of uneasiness. She also noticed subjective fevers.

Nephron What is her creatinine level now?

Henle It was 0.7 mg/dL four months ago and 1.2 mg/dL two months ago. Now it is 3.8 mg/dL.

Nephron OK; did you examine her urine?

Henle Yes, of course I did. There are a few red blood cells and many white blood cells. The red cells are dysmorphic, but no red cell casts that I could notice, and no signs of any granular casts.

Nephron Is there any proteinuria?

Henle Yes, 2 grams in a 24-hour urine collection.

Nephron I am sure they did serologies before they called you.

Henle Here are the results: antinuclear antibodies (ANA), anti-double-stranded DNA, myeloperoxidase (MPO), and proteinase 3 (PR3) all negative. Her HIV test result is positive. Hepatitis B and C results are negative.

Nephron Stop right there. So you are telling me you already have a diagnosis? Why are we presenting this case, then? Sounds like you have an HIV-related glomerular process.

Henle (*wondering to himself about quick decision by Nephron*): Hmm! I am not too sure whether this is a glomerular process.

Nephron Why is this not a rapidly progressive GN? That has five known presentations.

Henle But in this case, anti-neutrophil cytoplasmic antibodies (ANCA) is negative and HIV is positive.

Nephron My dear apprentice, you have a lot to learn still. First and foremost, can you give me this individual's medication list? Please go get that while I drink my coffee.

Henle leaves to get the information, and Nephron gets a cup of warm coffee. Henle returns after a few hours.

Nephron Please read all her medications to me.

Henle She is taking no medications.

Nephron (*shocked*): Interesting!

Henle Can we go back to the HIV test being positive? Did I mention that her CD4 is low and her HIV viral load is high! Is there a connection to the presentation?

Nephron Of course there is. HIV can present in the kidney in many ways. The most common is HIV-associated nephropathy, usually in black individuals, as collapsing focal segmental glomerular sclerosis. Given the degree of proteinuria in this case, I doubt this is HIV-associated nephropathy, but the acute renal injury favors that diagnosis. What is her race?

Henle White.

Nephron Hmm. If we still think this is a glomerular process, then HIV-associated immune complex disease is a possibility, given her race and the hematuria and dysmorphic red cells. On biopsy this can be IgA nephropathy, membranous GN, membranous proliferative GN, and any pathologic immune complex disease. What do you think, Henle?

Henle (*confused*): Hmm... so is that the connection? How about we start from a more basic approach? Why are we jumping into the glomerulus without a systematic approach?

Nephron I am assuming you want to go over a systematic approach to rule in and rule out other causes of acute kidney injury (AKI)?

Henle Yes... I don't think it is a prerenal condition, because her urine Na is high and FeNa is above 1 percent. I don't think it's a postrenal condition, because I personally inserted a Foley catheter, and a bladder sonogram shows no significant residual volume. She is not oliguric. That leaves us with intrarenal causes. A tubular cause is still possible, regardless of the hematuria and proteinuria. This could be garden-variety tubular necrosis, but I can't find any source of low blood pressure or any toxic medications. An interstitial cause still bothers me. She has a lot of white blood cells in her urine, and the result of her urine culture is negative, which suggests a sterile pyuria. She might have an acute interstitial nephritis, and the proteinuria could be of tubular origin. I don't think she has a vascular disease process, although her platelets are low and she has anemia. Perhaps we should check her lactate dehydrogenase and haptoglobin levels to make sure there is no thrombotic microangiopathy from HIV? You already discussed the glomerular causes. To help distinguish from HIV-associated nephropathy and HIV-associated immune complex disease, I might get complement levels as well.

Nephron Amazing thought process, Henle. I am proud of you! Regardless, go ahead, and let's get some answers with the tests you ordered. Also, do you think a renal sonogram might help?

Henle I suppose. Why not? The size of the kidney might give us a clue regarding a differential diagnosis.

Henle exits.

Nephron *(to himself)*: Fine work by Henle.

A day later:

Henle She is not doing well. Her renal function, anemia, and thrombocytopenia are worsening. Her complements are normal. Her renal sonogram shows massively enlarged hyperechoic kidneys: 23.5 cm bilaterally in the longitudinal axis. To me, the large size suggests HIV-associated nephropathy, amyloidosis, obstruction, or some combination—but she does not have an obstruction. Another possibility is diabetic disease, but she doesn't have long-standing diabetes. But a size over 20 cm sounds rather large to me.

Nephron Let me complete your differential. Her lactate dehydrogenase level is likely above 1000 U/L, and one more process can create this enormous kidney size. Please examine her for lymphadenopathy.

Henle, puzzled, leaves the room but returns quickly.

Nephron And?

Henle No lymph nodes anywhere, neither on examination nor on imaging. I scheduled her for a kidney biopsy.

Nephron Henle, your initial hunch was correct. You were thinking of causes of sterile pyuria and came up with interstitial nephritis? What else can cause leaking of white blood cells into the urine and interstitial nephritis and large kidneys?

Henle Infiltrative disease?

Nephron Yes, please get a kidney biopsy as soon as possible. I suspect a hematologic neoplasm.

Henle leaves the room in a rush and returns a day later.

Nephron And?

Henle Large B cell lymphoma infiltrating the kidney is the final diagnosis.

Nephron *(with confidence)*: Infiltrating lymphoma in the kidney can lead to large kidneys, sterile pyuria, and AKI, as in this case. In addition, the proteinuria might have been tubular in origin, given that the glomeruli appear normal.

Henle is stunned.

Nephron My dear apprentice, the kidney is the most common extranodal site for lymphoma infiltration. Usually it is bilateral, and symmetric large kidneys can be seen.

Henle *(puzzled)*: But presenting only in the kidneys and in no other place? Is that possible?

Nephron Yes, that has been reported as well: primary renal lymphoma. In addition, in autopsy studies of patients with lymphoma, renal involvement ranged from 6 percent to 60 percent of the cases. Hence, it might be clinically silent and perhaps more common than we think. Painless hematuria, nonnephrotic proteinuria, and large kidneys in a patient with lymphoma should prompt one to think about lymphoma infiltrating the kidney (LIK). Non-Hodgkin's lymphoma is the most common primary malignancy.

Henle Is AKI that common with LIK?

Nephron AKI occurs in only around 0.5 percent of all cases of LIK; hence it is not that common. And what happens? The mechanism by which lymphomatous infiltration causes renal failure is not known. It has been postulated that dense tumor infiltration of the kidney parenchyma may cause compression of the tubular lumen, producing intrarenal obstruction. In our case, it led to interstitial nephritis, but tubular necrosis can also be seen.

Henle I assume treatment with chemotherapy will reverse this quickly?

Nephron What are you waiting for?

Henle leaves to discuss the case with his hematology colleagues. A few weeks later:

Henle What a dramatic response. After chemotherapy was initiated, the patient's renal function improved, and her proteinuria and hematuria resolved. In addition, I repeated a sonogram, and the kidneys are now 16 cm bilaterally. This is amazing!

Nephron Well done, apprentice. Keep an open mind. Again, with a renal disorder you diagnosed a systemic disease that saved this patient's life. Onconephrology is an important part of nephrology that deals with cancer, chemotherapy, and the kidney. Most nephrologists should be familiar with the effects of cancer on the kidney. Cancer rates are rising, and newer chemotherapeutic agents are being used, and with this we are likely to see more renal injuries. Henle, let's get a cup of my favorite coffee. ●

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