Case Study #2: Post-Infectious Glomerulonephritis

Capt Jonathan Beatty, CPT Jennifer Corey, MAJ Imshin Kim,

CPT Jeffry Negard, & MAJ Audry Torres

Uniformed Services University of the Health Sciences

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Kurt LaBell is a 24-year-old male who presents to the clinic with a 4-day c/o blood in his urine and swelling in his hands and feet. During his evaluation he notes that he was on antibiotics a couple weeks ago for what he describes as an "Upper Respiratory Infection." You note that his blood pressure is 162/92.

1. **What Other Historical Information Would Be Most Helpful in Developing A Differential Diagnosis?**

I would ask the patient:

- Are you in pain (OLDCARTS)? Colicky flank pain would be a significant feature in the diagnosis of renal stones. Pain when urinating would be a significant finding in a UTI and severe flank pain would be significant for pyelonephritis. Painless hematuria could indicate a malignancy or glomerulonephritis. Chest pain could indicate endocarditis, which would also be a concern with our patient's history.
- What are your urinary patterns, urine color, timing of hematuria, clots? The color of urine would help to differentiate the diagnosis. Patients with glomerulonephritis typically have "tea" colored urine that is consistent throughout the urine stream (Welch, 2012). A prostatic or urethral source is likely when bleeding occurs only at the beginning or the end of micturition (Whelan, 2013), urinary urgency and frequency is associated with infections. Clots would differentiate a glomerular source from an extra-glomerular source (Middleton, n.d.) and bright red blood is more likely an anatomical problem such as urolithiasis (Welch, 2012).
- Were you treated for a strep infection two weeks ago? What antibiotic were you prescribed? Did you take the entire course of antibiotics? Were you hospitalized for this condition? If

patient confirms a streptococcus infection without a full course of antibiotics, this would increase suspicion for post streptococcal glomerulonephritis (PSGN). If patient had a staph infection or was hospitalized, this would increase my suspicion for Staphylococcus aureus infection-associated glomerulonephritis (SAAGN)

- Do you smoke? Smoking is the most important risk factor for bladder cancer.
- Do you have any rashes or new joint pain? Considerations for Lupus, vasculitis and Henoch-Schonlein purpura (Middleton, n.d.).
- Have you traveled outside the country? Considerations for schistosomiasis or extra-pulmonary tuberculosis (Middleton, n.d.).
- Do you have a history of high blood pressure? This helps to differentiate primary from secondary hypertension and whether the HTN is an acute or chronic finding.
- Is there anyone in your family that has renal failure (history of dialysis or kidney transplant) or autoimmune diseases? This information helps to differentiate autoimmune causes of hematuria from Alport Syndrome, a genetic disorder (Welch, 2012).
- Do you have a history of immunosuppression, diabetes, or alcohol abuse? According to one study up to 50% of adults in developed countries who developed post-staph GN were found to be immunocompromised (Nasir, Radhakrishnan, & D-Agati, 2013). Post-staph GN has poorer clinical outcomes than post-strep, especially in older and immunocompromised patients.

2. Name The Top Five Diagnoses In Your List Of Differentials From Most To Least Likely.

a) Post-infectious glomerulonephritis - likely post-streptococcal or post-staphylococcal glomerulonephritis

b) Acute nephrotic syndrome

c) IgA Nephropathy

d) Membranoproliferative glomerulonephritis

e) Acute Kidney Injury

Post-infectious GN is the most likely diagnosis, based on the presentation of hematuria, edema, and HTN in the presence and timing of an "upper respiratory infection" several weeks ago (Niaudet, 2012). Determining whether a strep test was positive at the previous visit would certainly help narrow the differentials. Post-staphylococcus GN is becoming more common than post-streptococcal as a source of post-infectious GN, and both are being seen more commonly in adults (Nasr, Radhakrishnan, & D'Agati, 2013). According to Nadasdy and Hebert (2011), staphylococcus associated glomerulonephritis (SAAGN) is on the rise in developed countries due to the increased incidence of MRSA. Interesting to note is that SAAGN mimics IgA nephritis, so it must be ruled-out should heavy IgA deposits be found in the glomeruli (Nadasdy & Hebert, 2011). IgA Nephropathy and Membranoproliferative GN can also present after an upper respiratory infection, but IgA nephropathy typically has a shorter duration (less than 5 days) between infection and symptoms (Niaudet, 2012). Membranoproliferative GN usually lasts longer (4-6 weeks) than post-strep GN. Acute nephrotic syndrome and acute kidney injury are also potential causes of hematuria, HTN, and edema (Niaudet, 2012). Other less likely differentials include UTI, urethritis, cancer, and renal calculi. However, the presence of edema and HTN would not be as consistent with these diagnoses.

3. What Initial Tests Would You Perform To Help You Narrow Down Your Diagnosis?

Initial labs I would perform include a UA, complements, CBC, throat and skin cultures for streptococcal and/or staphylococcus infections, and a renal function panel (Hollier &

Hensley, 2011; Niaudet, 2012). The UA is to look for proteinuria, hematuria, pyuria, low specific gravity, and RBC casts associated with post-infectious glomerulonephritis. The degree of hematuria and proteinuria will indicate if this patient's condition falls into a nephritic or nephrotic spectrum (Watnick & Dirkx, 2013). The UA is also used to confirm or rule out a UTI, which is indicated by the presence of WBCs, positive leukocyte esterases, and positive nitrites. A renal function panel is to assess the kidneys and detect an increased BUN and creatinine ratio (which would be >20:1 in post-infectious glomerulonephritis) and a CBC is to assess for both anemia and an increase in WBC's for initial indication of whether or not an infection is still present. No serology is indicated to aid in the diagnosis of IgA Nephropathy (Watnick & Dirkx, 2013).

A complement study is to look for depressed C3, CH50, C4, and C2. Plasma/serum levels of C3 are low in the majority of post-infectious glomerulonephritis cases due to a streptococcal infection (Nadasdy & Hebert, 2011). Positive serology indicating elevated antistreptolysin O (ASO) titers of antibodies to extracellular streptococcal products will confirm a recent group A streptococcal infection (GAS) infection (Niaudet, 2012) unless the immune response was blunted by previous antibiotic treatment (Watnick & Dirkx, 2013). The streptozyme test measures five different streptococcal antibodies and is positive in more than 95% of patients due to pharyngitis. It includes the antibodies of: anti-streptolysin (ASO), anti-hyaluronidase (AHase), anti-streptokinase (ASKase), anti-nicotinamide-adenine dinucleotidase (anti-NAD), and anti-DNAse B antibodies (Niaudet, 2012). After a pharyngeal infection, the ASO, anti-DNAse B, anti-NAD, and AHase titers are commonly elevated (Niaudet, 2012).

4. What, If Any, Treatments Or Referrals Would You Initiate Today For This Patient?

First of all, I need more of his medical history and then might able to narrow down his DD based on his course of illness and will confirm diagnosis with lab work. Diagnosis can be made presumptively based on history of infection, clinical symptoms (hematuria, HTN, edema, proteinuria, etc), and serum complement levels (decreased C3). Based on the history we do have, I believe either post-streptococcal or post-staphylococcal glomerulonephritis (PSGN) are our most likely diagnoses. Both of these diseases are treated in a similar manner. Post-staph GN has poorer outcomes, often leading to chronic renal dysfunction (8-54% of patients), especially in the elderly and immuno-compromised (Nasr et al., 2013). A kidney biopsy may be required for definitive diagnosis (Niaudet, 2012).

PSGN is a rare complication that may develop one to two weeks after an untreated throat infection, or three to four weeks after a skin infection. There is no specific treatment for post-streptococcal GN, and it is focused on relieving symptoms (PubMed Health, n.d.). The treatment includes treatment of infection and management of complications of nephritis. Treatment of symptoms includes antihypertensive drugs (ACEI or ARB), diuretics, and dietary salt restriction (Nasir et al., 2013). The role of immunosuppressive therapy in the treatment of sporadic bacterial infection related glomerulonephritis (IRGN) in adults has not been tested in a randomized prospective clinical trial (Nasr et al., 2013). Despite the frequent use of steroids for the treatment of adult IRGN (“used in 22–48% of patients in various studies for renal insufficiency with or without crescentic disease”), none of the studies in which statistical analysis was performed found a beneficial effect of steroids on outcome (Nasr et al., 2013). So, the basis of the absence of proven benefit and the potential risks in this population (DM, or other immunosuppressive diseases), steroid therapy not include for this patient. I would draw some labs to check if he has any anemia from hematuria and check his renal function and basic electrolytes (CBC, BMP).

The severity of illness and patient co-morbidities will determine if hospitalization is required. In more severe illness, the patient may require IV antibiotics to resolve concurrent infection (particularly staph) as well as IV diuresis with Lasix.

Referral to nephrology is indicated, particularly for post-staph GN to monitor for long term kidney dysfunction. Serial BUN/creatinine/GFR will need to be followed to monitor for long term sequelae. Serum complement (C3, C4) can also be monitored and all values should be monitored for return to baseline over several weeks to several months (Nasr et al., 2013).

PICOT Questions

Beatty: In adult patients with post-strep glomerulonephritis, how does treatment with Lasix, compared to supportive care alone, affect renal function measures (Serum Creatinine, GFR) at one, three, six, and 12 months post nephritis?

Corey: For adult patients with post-streptococcal glomerulonephritis (GN), does the use of steroids reduce the future risk of chronic kidney disease compared with standard treatment?

Kim: In adult patients with post-streptococcal glomerulonephritis (GN), how does treatment with steroids, compared to standard treatment, impact renal function at one, three, six, and 12 months post nephritis?

Negard: In patients with post-infectious glomerulonephritis, is a pneumococcal infection more likely to lead to an increase in the complement level when compared to a streptococcal infection?

Torres: In patients with acute glomerulonephritis, how often does presence of WBCs in the urinalysis, compared with no WBCs in the urinalysis, lead to misdiagnosis of a UTI?

References

Hollier, A., & Hensley, R. (2011). Urologic disorders: Poststreptococcal glomerulonephritis. In A. Hollier, & R. Hensley (Eds.), *Clinical guidelines in primary care: A reference and review book* (p. 707). Lafayette, LA: Advanced Practice Education Association.

Kelepouris, E. K., & Rovin, B. H. (2013). Overview of heavy proteinuria and the nephrotic syndrome. Retrieved from http://www.uptodate.com

Middleton, T. O. (n.d.). Hematuria. Retrieved from http://www.unboundmedicine.com.lrc1.usuhs.edu/ucentral/view/5-Minute-Clinical-Consult/116258/all/Hematuria

Nadasdy, T., & Hebert, L. A. (2011). Infection-related glomerulonephritis: Understanding mechanisms. *Seminars in Nephrology*, *31*(4), 369-375. doi:10.1016/j.semnephrol.2011.06.008

Nasr, H. N., Radhakrishnan, J., & D'Agati, V. D. (2013). Bacterial infection related glomerulonephritis in adults. *Kidney International*, *83*(5), 792-803. doi:10.1038/ki.2012.407

Niaudet, P. (2012). Post-streptococcal glomerulonephritis. Retrieved from http://www.uptodate.com

PubMed Health. (n.d.). Post-streptococcal glomerulonephritis (GN). Retrieved from http://www.ncbi.nlm.nih.gov/pubmedhealth/PMH0001532/

Watnick, S., & Dirkx, T. (2013). Kidney disease. In M. A. Papadakis, & J. McPhee (Eds.), *Current medical diagnosis & treatment* (52nd ed.) (pp. 898-937). New York, NY: McGraw-Hill.

Welch, T. R. (2012). An approach to the child with acute glomerulonephritis. *International Journal of Pediatrics, 1*(3). doi:10.1155/2012/426192

Whelan, C. A. (2013). Proteinuria and hematuria. In T. M. Buttaro, J. Trybulski, P. P. Bailey, & J. Sandberg-Cook (Eds.), *Primary care: A collaborative practice* (4th ed.) (pp. 758-764). St. Louis, MO: Elsevier Mosby.