Non-Streptococcal Post-Infectious Glomerulonephritis

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H.G. is a 77 year old male with severe O2 dependant COPD. He had been admitted one
month prior with left sided pneumonia and NSTEMI. The pneumonia had clinically and
radiographically resolved upon discharge. Nine days later he was readmitted to Grayling
Mercy Hospital for right sided pneumonia, which was classified as healthcare acquired
pneumonia, and acute renal failure. He was transferred to Munson Medical Center two days
later with a creatinine of 4.5 and BUN of 110.

A nephrology consult was requested and patient was hemodialyzed upon admission. A full
workup for precipitating factors of acute renal failure ensued. No definitive cause was found,
and a renal biopsy was not appropriate as the patient had multiple comorbidities. Post-
infectious glomerulonephritis was considered the most likely diagnosis.

The patient’s pneumonia resolved a few days after admission. He continued to need dialysis
indefinitely, and was discharged 19 days later on an outpatient hemodialysis program.

Acute renal failure is common among hospitalized patients, and initiating a workup to
decipher the underlying cause can be daunting. This case presents the workup in a logical
manner.

Poststreptococcal glomerulonephritis is a diagnosis many providers would consider in a
patient with the above presenting features, but without evidence of a recent streptococcal
infection, this diagnosis may be disregarded. It is important to remember that while a rare
occurrence, other non-strep infectious processes can precipitate an immune-complex
phenomenon resulting in acute glomerulonephritis. It is vital to monitor renal function tests
and urine output in any hospitalized patient with infection, as early hemodialysis may be
required if acute renal failure develops.

H.G. is a 77 year old male with O2 dependant COPD, and no history of renal impairment. He
had been recently hospitalized (2/5/09-2/10/09) for LLL pneumonia and NSTEMI. Cardiac
catheterization on 2/5/09 revealed significant CAD, and as he was not a good surgical
candidate this was treated medically. The pneumonia was treated with Levaquin and Flagyl
initially then Avelox per ID recommendations, which clinically and radiographically resolved.
Renal function remained normal throughout his first admission. At the time of his discharge
on 2/10/09 the patient was back at his baseline health, with a creatinine of 1.2 and of BUN
22. He had received contrast material for the catheterization and for a CT of the abdomen
done 1/31/09.

On 2/19/09, the patient was using a snow rake to shovel his roof. He began to get shaking
chills and SOB. He was admitted to Grayling Mercy Hospital with RLL pneumonia. At
admission, creatinine was 3.7 and BUN was 90. Empiric treatment for nosocomial
pneumonia was initiated with renally dosed vancomycin, Levaquin, Fortaz, and meropenam.
During the first 24 hours of his stay, his urine output was only 300 mL with a total intake of 2.1 L. Creatinine increased to 4.5 and BUN reached 110. On 2/21/09 he was transferred to Munson Medical Center for further care.

**Past Medical History:**
1: O2 dependant COPD
2: Nonspecific inflammatory arthritis, currently being treated with Arava
3: Nonoperable triple vessel CAD
4: Status post LLL pneumonia, resolved.
5: Diverticulitis
6: Diabetes Mellitus type II

**Past Surgical History:**
1: Cardiac catheterization 2/5/09
2: Colon resection secondary to diverticulitis
3: Cholecystectomy

**Medications prior to admission to Grayling Mercy 2/20/09**
1: Spirivia 1 puff qd
2: Lotrel 10/20 qd
3: Flovent 1 puff bid
4: Januvia 100 mg qd
5: Aspirin 81 mg qd
6: Simvistatin 10 mg qd
7: Lopressor 50 mg qd
8: SL nitro PRN
9: Ventolin inhaler PRN
10: Arava, dosing unknown

**Medications added at Grayling Mercy prior to arrival at Munson:**
1: Novolog Sliding scale
2: Levaquin 500 mg q 48 hrs
3: Meropenem 250 mg q 12 hrs
4: Fortaz, 2000 mg, unknown interval
5: Lovenox 30 mg subQ qd
6: Solu-medrol 60 mg q 6 hrs
7: Vancomycin 1.25 grams given once
8: Bumex drip 0.5 mg q 1 hr.

**Allergies:**
NKDA

**Family History:**
Father died of suicide, mother died in her 70s of “old age.” Specific medical history unknown.

**Immunizations:**
Influenza up to date, Pneumovax >5 years

**Social History:**
Retired from GM, married. No ETOH. 30 pack year hx smoking, quit 20 yrs ago.

**Review of Systems:**
General: -F/C/S since 2/19. -weight loss/gain
HEENT: -H/A, -ST. No recent URI.
Cardiorespiratory: no increase in cough or sputum from baseline. Increased dyspnea. -CP, -palpitations. Edematous ankles.
GI: -N/V/D/C. Decreased oral intake but eating and drinking satisfactorily.
GU: decreased urine output. No difficulties with urination, no burning, urgency, frequency, hesitancy or dribbling. No hx BPH or prostate ca. Foley catheter in place.
Rest unremarkable
Physical Exam on admission:
Vitals: Temp 37.1, P 80, RR 25, BP 148/77, PO2 98% on 6L O2 via NC
Integument: -rash, -splinter hemorrhage, -Janeway lesion
HEENT: normocephalic, atraumatic. PEERLA, EOMI, TM clear, nares patent, oropharynx clear without enlarged tonsils, exudates, or erythema.
Neck: supple, -LN, -JVD, -thyromegally, trachea midline
Lungs: very diminished throughout, but CTAB.
Heart: RRR without M/R/G
Abd: soft, NT, ND, -HSM, BSx4
Extremities: 1+ pretibial edema and 2+ pitting edema over both ankles.

INVESTIGATIONS If relevant

Laboratory:
WBC: 15,400, no left shift
Hgb: 10.7
Na: 135
K+: 6.0
Cl: 107
Bicarb: 19
BUN: 124
Creatinine: 4.5
Albumin: 3.2
ABG: pH 7.24, pCO2 46, pO2 80, bicarb 21.
BNP: 585
UA: 5-10 WBC, 50-100 RBC, 2-5 granular casts, 0-2 waxy casts, 300 mg/dl protein.
ANA: normal
Complement: C3 73.4 (RR 73-156), C4 18.1 (RR 13-39)
ANCA: normal
ASO titer: <100
24 hour urine for protein: >6 grams
Serum protein electrophoresis: normal

Imaging:
EKG: peaked T waves
CXR: RLL pneumonia
Renal US: no hydronephrosis or other abnormalities

DIFFERENTIAL DIAGNOSIS If relevant

**Prerenal causes of ARF** were quickly ruled out. Patients BUN:creatinine ratio was >20:1, however steroids can increase BUN. Patient did not clinically appear dehydrated or septic, and there was no evidence to suggest blood loss. A recent echocardiogram had revealed a normal ejection fraction. His BNP was 585, which appeared to be his baseline.

**Postrenal causes of ARF** were also ruled out. A foley catheter had been placed at Grayling Mercy. This would have negated any urethral obstruction. Renal US showed no hydronephrosis or abnormalities. Patient had no history of BPH or prostate cancer.

**Intrinsic ARF** was considered to be the cause. Interstitial nephritis was considered with the contrast history, but the patient had no signs such as rash, fever, eosinophilia or urine eosinophils. With patient's presenting signs and symptoms of HTN, edema, hematuria, granular casts (which can be the breakdown product of RBC casts), and proteinuria, the source was identified as glomerular with nephritic features. Differential diagnosis of glomerulonephritis:
- IgA nephropathy: serum IgA elevated in 50% of cases (patient’s was normal). Requires biopsy for definitive diagnosis.
• Systemic lupus erythematosus: ANA was negative.
• Systemic vasculitis: ANCA panel was negative.
• Henoch-Schoenlein Purpura: palpable purpura not present.
• Postinfective glomerulonephritis: low normal complement levels with other diagnoses ruled out brought the diagnosis of PIGN.

TREATMENT If relevant

ARF:
• Patient was hemodialyzed within hours of admission due to hyperkalemia, and continued to be dialyzed about every other day through his 19 day hospital course.
• Januvia and Lotrel were discontinued due to renal failure.
• Phos-Lo was added for hyperphosphetemia.
• Steroids were given for COPD/pneumonia, and this is sometimes indicated in PIGN.

The rest of the patient’s co-morbidities were treated according to protocol.

OUTCOME AND FOLLOW-UP

The patient’s pneumonia did clinically and radiographically resolve during his hospital stay. BUN and creatinine did improve through the hospital course but he continued to need dialysis and was scheduled for OP dialysis upon discharge. A causative agent was never identified from sputum or blood cultures.

The patient’s dialysis port was removed on April 16th, 2009, a month after discharge. Sadly, he was readmitted to Grayling Mercy for LLL pneumonia later that day. He progressed to severe respiratory failure and his renal function worsened. He was made comfort measures only on April 18th and passed away later that evening.

DISCUSSION including very brief review of similar published cases (how many similar cases have been published?)

1. What is the epidemiology and pathophysiology of nonstreptococcal PIGN?
Nonstreptococcal PIGN is more common in adults than children, but is still considered a rare entity. The mean age of diagnosis is 56 years, with a male to female ratio of 2:1. Interestingly, 38.4% are immunocompromised. The patient in this case had been on Arava, an immunosuppressant agent.

Streptococcal pyogenes is the most common cause of postinfectious glomerulonephritis, however, similar syndromes have been seen with a variety of other pathogens. The pathophysiological process that occurs with strep pyogenes is believed to be similar with other antigens. The process involves an immune mediated response with activation of the complement pathway. IgG and the antigen bind to complement and form complexes that deposit in the glomeruli, causing inflammation and damage. The RAS system is also activated, causing hypertension, water and sodium retention and edema. The glomerulus then leaks blood and protein, leading to the clinical syndrome of nephritis.

After the glomerulus is damaged it can no longer filter effectively and GFR decreases. Nitrogenous wastes cannot be secreted and build up in the blood, and fluid and electrolyte balance cannot be maintained. BUN and creatinine rise, leading to the syndrome of acute renal failure. Acute renal failure is defined as an increase in serum creatinine to 0.5 mg/dL above baseline, a 50% decrease in baseline GFR, or the need for acute kidney replacement therapy.

2. How do you evaluate a patient for PIGN?
Any patient with ARF must be worked up. If pre-renal and post-renal causes are ruled out, an investigation for the cause of intrinsic renal failure must ensue. The findings of hypertension, hematuria with casts, proteinuria (often in the nephrotic range of >3 g/24 hr), and edema indicate a glomerular cause, all of which the patient in this case report had. A nephrology consult may be warranted at this point.

Differential diagnoses of PIGN must be ruled out. ASO titers should be obtained, and if positive, the cause is PSGN. If negative, and another source of recent infection can be identified such as pneumonia in this case report, nonstreptococcal PIGN can be considered the diagnosis. Complement levels should be checked, as hypocomplementemia is found in 73.9% of cases. Often, C3 is low, and C4 is normal, which this patient displayed. Definitive diagnosis is found by renal biopsy.

3. **What is the management and prognosis of nonstreptococcal PIGN?**

**Treatment is supportive.** Eradication of underlying infection is indicated. Diuretics and antihypertensive agents can be used to control hypertension and fluid overload. Electrolyte imbalances and acidosis must be managed. Hemodialysis may be required in severe cases of ARF. The use of high dose corticosteroids has not been found to decrease the length of renal impairment, however can be used if indicated to treat comorbidities, such as pneumonia and COPD in the patient in this case study.

The prognosis of nonstreptococcal PIGN is significantly worse than PSGN. In a retrospective study done of 36 adult patients with PIGN, all 7 cases of poststreptococcal GN had excellent outcomes, while 25% of non-strep PIGN progressed to end stage renal disease. Another retrospective study of 86 patients found that in adult patients without diabetes, 17.1% progressed to end stage renal disease, while a large majority, 81.8%, with underlying diabetic glomerulosclerosis progressed to end stage renal disease. The patient in this case report did not have a history of diabetic kidney disease, however he did have DM II and a minimal degree of diabetic nephropathy may have been previously undiscovered.

4. **Have similar cases been reported?**

Nonstreptococcal postinfectious glomerulonephritis is not common, and studies of postinfectious GN usually involve a streptococcal pathogen. However, in the retrospective study of 36 adults with PIGN, 28 cases were identified as being non-strep in origin, and in 24 of those 28 cases, the causative pathogen was never identified as in this case report.

In the retrospective study of 86 adults with PIGN, pneumonia was considered the source of infection in 17.4%. As discussed above, similar cases involving diabetes and immunosuppression have occurred, both of which could have been contributing factors in this case report.

**LEARNING POINTS/TAKE HOME MESSAGES 3 to 5 bullet points**

- Acute renal failure can be easy to diagnose if done in a stepwise manner through the causes of pre-renal disease, intrinsic renal disease, and post-renal disease.
- Infectious processes other than strep can cause PIGN, and these often have a worse prognosis.
- Renal function should be monitored in all hospitalized patients with infection as early treatment/hemodialysis may be required as acute renal failure can quickly progress.
REFERENCES


8 Brady, H., O’Meara, Y., Brenner, B. Harrison’s Principles of Internal Medicine. Glomerular disease. McGraw-Hill. pg 1681

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