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Chronic renal failure, but why?
A Case Report.

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Hackensack Meridian *Health*

INTRODUCTION

Renal failure, both acute and chronic, can present from many different etiologies and if diagnosed with diabetes mellitus, it is commonly assumed to be due to diabetic nephropathy. Monoclonal gammopathy of renal significance (MGRS) is a disorder that combines monoclonal gammopathy of undetermined significance with end stage renal disease. Monoclonal immunoglobulins are secreted by B or plasma cells leading to deposition in the kidney causing end organ damage. Several different subtypes fall under this category of renal diseases including, but not limited to, amyloidosis, C3 glomeruopathy, and light chain proximal tubulopathy, or better known as Fanconi syndrome[1]. Fanconi syndrome, which can be acquired or inherited, occurs due to toxicity of the proximal renal tubule in the kidney which leads to hypophosphatemia, hypokalemia, metabolic acidosis due to impaired bicarbonate absorption, impaired glucose and uric acid absorption, and proteinuria.

CASE PRESENTATION

84 year old Caucasian male presented to the emergency department with complaints of shortness of breath and weakness. He had c/o decreased appetite and urinary retention for a few days. He denied chest pain, hemoptysis, polyuria, and hematuria. His past medical history includes chronic renal disease secondary to type II diabetes mellitus (DM), perirenal lymphangiectasis, pulmonary fibrosis, hypertension, atrial fibrillation, hyperlipidemia, and anemia of chronic disease. He had a left radiocephalic AV fistula permacath placement 3 days prior to admission for dialysis and has had a left hip replacement. He reports no tobacco use, no alcohol use, no allergies, and no significant family history.

- Medications: insulin, doxazosin, carvedilol, sitagliptin, atorvastatin, epoetin alfa, torsemide, hydralazine
  * no recent heparin administration
- Initial vital signs: BP: 141/60, HR 56, RR:18, O2: 95%
- Positive exam signs: bilateral extremity swelling, generalized weakness, decreased breath sounds bilaterally at both lung bases

DIAGNOSTIC/TREATMENT MODALITIES

- Chest x-ray PA/Lateral
  - On admission: Left base opacification with patchy bilateral disease and pulmonary vascular congestion
  - Post-pericardiocentesis: moderate CHF and cardiomegaly
- Urinalysis = moderate hematuria, glucosuria, proteinuria
- Platelet transfusion and steroids for persistent thrombocytopenia
  - Heparin induced thrombocytopenia platelet factor-4 antibodies = not detected
- Echocardiogram = moderate to large pericardial effusion
  - Pericardiocentesis = 600 mL of straw-colored aspirated
- Serum protein electrophoresis (SPEP) = M-spike
- Immunofixation serum electrophoresis = IgG type kappa monoclonal protein
- Bone marrow biopsy = Monoclonal gammopathy of undetermined of significance (MGUS)
- Complement panel, ANA, c-ANCA and p-ANCA
- Renal Ultrasound = abnormal appearance of renal parenchyma with numerous cysts and septations; Indeterminate 4 mm right renal echogenic lesion

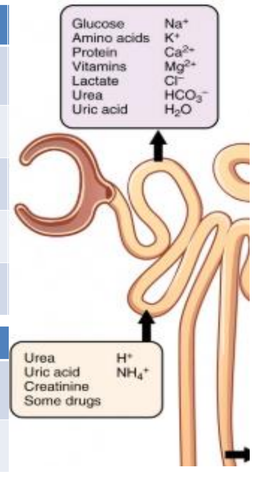
LABORATORY DATA

Lab (Normal Range)	Day 0	Day 5	Day 16	Day 19
WBC (4.5-11 K/uL)	6.8	6.4	20.1	18.3
Neutrophil (50-70%)	81.7	72	92.5	90.2
CO2 (24-31 mmol/L)	17			
Anion Gap (5-13)	16			
BUN (5-25 mg/dL)	63	36	35	90
Uric acid (4.0-8.0 mg/dL)			2.8	
Creatinine (0.44-1.0 mg/dL)	4.21	3.00	1.71	2.99
Hemoglobin (12-16 gm/dL)	10.1	9.8	10.4	8.9
Hematocrit (36-53%)	32.3%	30.1	30.6	27.0
Platelet Count* (140-450 K/uL)	157	33	89[a]	81
Albumin (3.5-5.0 mg/dL)	2.6		2.5	2.4
Cr-clearance (91-137 mL/min)	11	24	24	7
Protein (6.0-8.0 g/dL)	7.0		5.7	5.0
Glucose (70-99 mg/dl)	134	158	238	191
Potassium (3.5-5.2 mmol/L)	5.0	4.7	3.2	3.1
Phosphorus (2.5-4.6 mg/dL)	6.2	1.6	1.3	1.8
BNP (<100 pg/mL)		1772		

[a.] 1 day post-platelet transfusion – levels decreased from 176K to 89K

SPEP	Day 5	Day 12
Kappa QT (3.3-19.4)	197.75	
Lambda QT (5.71-26.3)	86.40	
Kappa/Lambda ratio (0.26-1.65)	2.29	
Beta Protein (0.6-1.3)	1.64	
Beta-2 Microglobulin (1.1-2.4 mg/L)		11.4

Complement Levels	Day 14	Day 23
C3 (85-170 mg/dL)	62.6	46.4
C4 (16-40 mg/dL)	14.3	11.7



DISCUSSION

A combined team effort from general internal medicine, nephrology, hematology/oncology, cardiology, pulmonary, vascular, infectious disease, radiology, and pathology was made to investigate the patients' present illness and provide a diagnosis that would be causing his many symptoms. Over the course of the patient's one-month stay, a series of blood tests, imaging, and procedures were ordered to diagnose the etiology of his acute on chronic renal failure:

1. ANA and ds DNA IgG to rule out lupus
   1. Normal level = 0.64
2. Negative c-ANCA and p-ANCA to rule out vasculitidies
3. Negative glomerular basement membrane IgG to rule out Goodpasture syndrome
4. Negative Cryo quant screen to rule out mixed cryoglobulinemia
5. Negative ASO titer
6. Negative hepatitis panel
7. Significantly low C3 and mildly low C4 levels
   - Possible C3 Glomerulopathy[2] = monoclonal gammopathy-associated proliferative glomerulonephritis
     - Requires a kidney biopsy
8. Pericardial effusion secondary to uremia from renal failure
9. Anion gap metabolic acidosis secondary to uremia

A bone marrow biopsy lead to the finding of monoclonal gammopathy of undetermined significance (MGUS) with end-organ damage = MONOCLONAL GAMMOPATHY OF RENAL SIGNIFICANCE (MGRS)

1. Monoclonal spike on SPEP
2. Increased kappa Ig, lambda Ig, and Kappa/Lambda ratio
3. Immunofixation electrophoresis = IgG monoclonal protein
4. Can cause proximal light chain tubulopathy (isolated proximal renal tubular acidosis) = FANCONI SYNDROME
   - Immunoglobulin light chains can lead to proximal renal toxicity due to the inability of lysosomal proteases to break them down[3].
   - Hypophosphotemia, hypouricemia, hypokalemia, metabolic acidosis, elevated kappa and lambda immunoglobulin chains

Though type II DM played a role in the development of this patient's chronic kidney disease, MGRS is a significant causal factor of the progression to end stage renal disease. Currently, treatment with chemotherapy that targets plasma or B cells can be used for MGRS. Several case studies reported improvement or stabilization of renal function in those treated with chemotherapeutic agents vs. no therapy[4,5]. Though renal transplantation can be done, recurrence post-transplantation is common[6]. The main goal in managing MGRS with Fanconi syndrome is slowing the progression of renal disease and preventing associated extra-renal complications[7].

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