Renal Failure and Muscle Disease

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Case Presentation

- A 20-year-old previously healthy African American female:
  - Acute onset of muscle weakness proximal>distal
  - Can't ambulate
  - CK 23,000
  - No overt infectious or toxic injury
  - No other symptoms
  - Did not improve with hydration

Case Presentation—muscle biopsy

- **A significant degree of myonecrosis with partial invasion of non-necrotic myofiber by inflammatory cells.**
- **Patchy upregulation of MHC1 in the sarcolemma and within the sarcoplasm of myofibers.**

Case Presentation—Pauci-immune necrotizing myopathy

- **Notable serologies**
  - **Negative HMG-CoA reductase antibody and anti-SRP**
  - **ANA 1:5120**
  - **Anti-SSA>8**
  - **Anti-SSB>8**
  - **U1 RNP >8**
  - **Anti-Smith 7.3**
- **No clinical features of a connective tissue disease (rashes, mucocutaneous ulcers, alopecia, arthritis, Raynaud's, serositis, proteinuria, etc)**

Case Presentation—Treatment

- **Responded to treatment with IV steroids and IVIG**
- **Subsequently treated with prednisone, hydroxychloroquine, and mycophenolate**

Case Presentation—Renal failure

- A year later, she presented in acute renal failure (creatinine 7.0) with hypertensive emergency after having being out of medications for several months.
- Proximal muscle weakness with CK 10,000
- 2g of proteinuria, no RBCs but + blood
- Normal C3, C4, negative dsDNA

Case Presentation—Renal biopsy

- Diffuse sclerosing glomerulonephritis with diffuse glomerular capillary wall and mesangial staining for IgG, IgM, C1q, C3, kappa, and lambda (i.e. consistent with lupus nephritis class IV)
- Severe interstitial fibrosis and tubular atrophy (80%)
- Thrombotic microangiopathy: multiple arterioles have fibrin thrombi. Thrombotic microangiopathy has many causes including SLE, scleroderma, and malignant (accelerated) hypertension

Case Presentation—SLE dx

- **Anti-cardiolipin IgM+, anti-beta-2 glycoprotein IgG+ and IgA+**
- **Dx with SLE (lupus nephritis IV; ANA/Smith/APS Abs)**
- Started on peritoneal dialysis

Case Presentation—Renal failure

- Further testing was notable for **a positive RNA polymerase III antibody**
- Developed Raynaud's phenomenon, and 'salt and pepper' skin changes to her skin.

Case Presentation—Renal failure with myositis

- CK at 10,000
- Treated with steroids, azathioprine then mycophenolate/IVIG
- Responding with CK declining and being worked up for renal transplant when…

Case Presentation—A year later Myocarditis

- Chest pain
- Troponin 3500 ng/L (normal <50)
- Negative left heart cath
- Endomyocardial biopsy
  - Rare scattered foci of inflammatory cells without active myocyte injury most consistent with a prior/resolving myocarditis.
  - CD68: highlights scattered interstitial macrophages
    CD3: highlights scattered interstitial T lymphocytes
  - No evidence of Plaquenil toxicity on electron microscopy.
- Possibly from influenza; possibly related to CTD

Case summary

- Young African American woman presents:
  - Auto-immune necrotizing myopathy with positive serologies (ANA/Smith/SSA/SSB/anti-U1RNP) but no clinical features of SLE
  - Then developed renal failure with accelerated hypertension with kidney biopsy notable for lupus nephritis class IV and thrombotic microangiopathy
  - Lab testing notable for + RNA-pol III (specific for scleroderma and associated with scleroderma renal crisis)
  - Active myositis treated with immunosuppression
  - Did develop myocarditis (viral vs auto-immune)
- Thus she has NAIM, SLE, and possible features/antibody of scleroderma renal crisis

Take Home Points

- Inflammatory myositis can be the presenting feature of a connective tissue disease such as lupus or scleroderma
- Auto-immune necrotizing myopathy can be seen in the setting of systemic auto-immune disease such as SLE or systemic sclerosis