Deconditioning or Disease?

VSR 2022 Thieves Market

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Introduction

- 88yoM presents to the emergency room with global weakness and loss of functional status two months following a brief hospital stay for pneumonia, was previously independent; could walk two miles slowly and mow his large lawn without difficulty
- Medical Hx:
  - Atrial fibrillation s/p pacemaker two years prior
  - Essential hypertension
- Social Hx:
  - Distant smoker >30 pack-years
- Meds:
  - Amiodarone, Atorvastatin, Lasix, Hydralazine, Metoprolol, Xarelto

Case Presentation

- 2 months ago: OSH admission for CAP
  - Respiratory symptoms resolved but energy level never returned to normal
- Past 2 weeks: dependent on rolling walker & assistance to stand from sitting
- 1 week ago re-admitted to OSH for weakness
  - Leukocytosis & elevated CRP
  - Infectious & neoplastic w/u negative
  - Presumed to have PMR, discharged on prednisone 20mg
  - Patient & family denied benefit; drove him from outside hospital straight to our emergency department!

Case Presentation (continued)

- Physical examination:
  - **VS** unremarkable, weight 98kg
  - **Constitutional**: Elderly, somnolent but easily rousable
  - **ENT**: Oral thrush present
  - **Cardiac**: Regular rhythm, no murmurs, 2+ radial pulses, 1+ DP/PT pulses, 2+ b/l pitting lower leg edema
  - **Musculoskeletal**: No obvious joint effusions, tenderness, or warmth
  - **Neurologic**: Strength 4+/5 proximal UE, 5/5 distal UE, 2/5 proximal LE, 4+/5 distal LE, globally reduced reflexes, at baseline per family aside from somnolence
  - **Skin**: Mild periungual erythema of fingers, lower legs and feet with faint scattered non-blanchable flat erythematous lesions

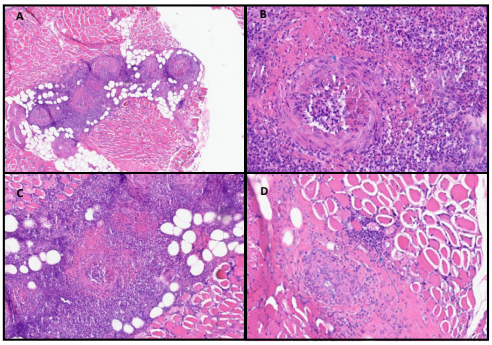
Case Investigation

Test	Level (range)
WBC	**32** (4.5 – 11.0 10^9/L)
Hgb	12 (13.3 – 17.2 g/dL)
Plt	398 (179 – 373 10^9/L)
Na	133 (135 – 145 mmol/L)
K	**5.5** (3.6 – 5.1 mmol/L)
BUN	**60** (8 – 23 mg/dL)
Cr	**1.26** (0.6 – 1.2 mg/dL)
AST	63 (0 – 50 U/L)
ALT	91 (0 – 60 U/L)
Albumin	**1.9** (3.7 – 5.2 g/dL)
ESR	**70** (0 – 15 mm/hr)
CRP	**12** (0 – 0.5 mg/dL)

Test	Level (range)
ANA	**1:160** atypical speckled
Anti-Histone	2.4 units (**moderate positive**)
C3	93 (80 – 200 mg/dL)
C4	15 (10 – 50 mg/dL)
CK	**8** (40 – 350 U/L)
LDH	221 (0 – 250 U/L)
p-ANCA	**1:320** (<1:20)
c-ANCA	<1:20 (<1:20)
MPO	**17.2** (0 – 9 U/mL)
PR3	Negative (0 – 3.5 U/mL)
HMG-CoA R.	Negative (<20 Units)
Ur Protein:Cr	**0.8** (<0.2 mg/mg)

Case Investigation (continued)

- **PET CT**:
  - No obvious neoplasm
- **Renal biopsy**:
  - Focal/segmental glomerulosclerosis and active tubulointerstitial inflammation (+IgM, C3) with mesangial electron dense deposits and endothelial swelling
- **MRI hips & lumbar spine**:
  - Severe L4-L5 spinal stenosis
  - Mild edema & enhancement of paraspinal musculature & psoas muscles
- **EMG/NCS** (of right lower & right upper extremities):
  - Myopathic changes in rectus femoris without insertional activity; vastus medialis with mild chronic neurogenic changes; deltoid/biceps normal
- **Muscle biopsy (left thigh)**:
  - Skeletal muscle with focal vessels showing transmural inflammation



Our patient:
H&E stained sections of skeletal muscle biopsy (A-D). Sections of skeletal muscle show significant inflammatory infiltrate surrounding & involving the vessels in the adjacent soft tissue & intramuscular vessels, consistent with vasculitis.

Audience Participation ☺

- How would you manage this patient?
  - Medication changes?
  - Steroid plan?
  - Steroid-sparing therapy?
    - Long term plan?

Case Management

- Stop hydralazine!
  - Stop statin?
- Steroids:
  - Pulse dose Methylprednisolone x3 days followed by slow prednisone taper (traditional vs PEXIVAS reduced-dose)
- Steroid-sparing:
  - Rituximab 1g x2 doses two weeks apart
  - Re-dose in 4 - 6 months?

Case Discussion

- Final diagnosis:
  - Hydralazine-induced ANCA-vasculitis
    - Majority of cases >12 months hydralazine exposure
    - Usually high positive pANCA/MPO
    - Often anti-histone, hypocomplementemia
    - Often has renal involvement
      - Not always pauci-immune (mesangial expansion, electron dense deposits, tubuloreticular inclusions)
    - Extra-renal involvement uncommon
    - Similar long term outcomes to primary ANCA-vasculitis glomerulonephritis
    - May not need long-term maintenance therapy
    - Other well-described causative agents: minocycline, propylthiouracil, cocaine (levimasole)

Case Discussion

- Lessons learned:
  - Vasculitis can mimic myositis by causing a CK-negative myopathy
  - Hydralazine can cause more just than well-described drug-induced lupus
    - Often involves kidneys as opposed to drug-induced lupus
    - Not always typical glomerulonephritis
  - Drug-induced vasculitis may have unusual presentation
  - Drug-induced vasculitis may not warrant long-term maintenance therapy
  - Avoid anchoring on simple explanation of deconditioning in elderly patients

References

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