Learning Objectives

- Foot/wrist drop, +/- painful paraesthesia, can be a presenting sign of vasculitides.
- In clinically suspected HCV-MCV, rheumatoid factor is positive in 70-80% of cases and can be used as a quick screen for cryoglobulins.
- If concerned for latent HBV infection, must start entecavir prophylactically one week before treatment of HCV-MCV with rituximab.
- With all therapies, cutaneous and renal involvement respond more rapidly and more completely than peripheral neuropathy

Case Presentation

HPI:
Numerous histiocytes.

Path (cellular infiltrate.
Neutrophil fragments near vessels with extravasated erythrocytes and mixed

PE:
Buttocks (1A): symmetrically distributed, few 0.5-1.5cm pink-red, partially-blanching papules-plaques, few similarly sized pink-red partially-blanching macules, and several similarly sized brown macules.

Feet (1B): edematous; pink-purpuric retiform patch with central duskiness (L>R)

Neuro: R ankle 2/5 dorsiflexion, 4/5 plantar flexion; L ankle 4/5 dorsiflexion and plantar flexion

Feet DDx: Vasculitis (Skin-limited small vessel vasculitis, mixed cryoglobulinemic vasculitis (MCV) type II or III, ANCA-associated vasculitis), Other (Althropic assault)

Buttocks DDx: Vasculitis (Skin-limited small vessel vasculitis, mixed cryoglobulinemic vasculitis (MCV) type II or III, ANCA-associated vasculitis)

History Continued:
PMH: Benign prostatic hyperplasia, IVDU c/b hepatitis C virus infection
Allergies: NKDA
Meds: tamsulosin, suboxone, gabapentin (Rx’d 1 week prior)
Family Hx: No family history of autoimmune disease or cancer
Social Hx: Cocaine use in past month, IVDU in college; quit tobacco 25 years ago and drinking 10 years ago

Labs/Imaging/Path

| C4 | 6.1 (H) |
| HCV Ab: positive |
| 123: 100 (wnl) |
| ALT/AST: 39/61 |
| HBV: negative |
| CRP: 207.6 (H) |
| HBV+ antigen: negative |
| ESR: 59 (H) |
| HBV+ antibody: positive |
| WBC: 15.1 (H) |
| HBV core Ab: positive |

Imaging: X-ray of b/l feet and US venous duplex of LEs: findings unremarkable.

Path (FD): Leukocytoclastic vasculitides, demonstrated by fibrin, neutrophils, and neutrophil fragments near vessels with extravasated erythrocytes and mixed cellular infiltrate.

Path (FE): Hemorrhage and fibrosis with reparative features, without small or medium vessel involvement, patchy chronic inflammatory infiltrate including numerous histiocytes.

Hospital Course

Day 1: 4:35 PM Dermatology consult seen

Rheumatoid Factor: 118.2 (H)
500mg of Methylprednisolone: 10:33pm
1g of Methylprednisolone x 3 days, followed by 60mg prednisone daily
Rheumatoid factor: 205.8 (H)

Day 4: C4 < 2 (H) (L) on 10/15

Day 5: Skin much improved; motor function improving but pain persisting in feet

Day 7: Cryoglobulins: Positive

Plasmapheresis started Day 8

Day 11: Entecavir ppx started

Prevalence of vasculitic neuropathy

Incidence of neuropathy within each condition

HCV-MCV

Overall incidence of vasculitic neuropathy by condition

Cryoglobulinemia

Cryoglobulins = cold-precipitable circulating immune complexes

Pathogenesis: B-cell stimulation and expansion -> immune complex formation and deposition in vessel walls, activating complement

Epidemiology: Half of HCV patients have circulating cryoglobulins;

- 15% develop vasculitis (<2%, 5%, 10%)
- MCV also seen in 1.2 – 4% of HBV-infected patients

Presentation: Meltzer’s Triad: arthralgia, weakness, and purpura

Management

1) Pulse dose steroids (1g methylprednisolone) — acute setting

2) Rituximab complete remission 68%; partial remission 14%; no response 10% (Median values from 440 patients across 16 trials)

3) Direct anti-viral agents (e.g. sofosbuvir)

- 90%, cure rate for HCV

78% complete responders for HCV-MCV (45 patients; 1.5 yr follow-up)

Cryoglobulins remained detectable in 42%; B-cell clones detected in 40%

No correlation of persistent cryoglobulins or clones with vasculitis response

4) Plasmapheresis for refractory/urgent cases

References

8. Meltzer, M. et al. Cryoglobulinemia: a clinical and laboratory study. II. Cryoglobulins remained detectable in 42%; B-cell clones detected in 40%

Overall incidence of vasculitic neuropathy by condition

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4) Plasmapheresis for refractory/urgent cases