Case Conference

Stephen Anesi, MD
September 24, 2010
MD – Emergency consult

- Called to evaluate patient with eye pain and periocular erythema
67WF admitted to Mt. Auburn for necrotic ulceration of left leg x 5 days
- Treated with IV Zosyn
- C/o bilateral burning eye pain x 2 days
- Edematous erythematous eyelids with “discharge”
- Vision unaffected, no diplopia, no pain with eye movement; patient had been rubbing eyes
- Diffuse purpuric lesions, many over lower limbs, with early necrotic appearing areas; one with large necrotic ulceration
MD – Background

**PMH**
- Poorly controlled IDDM
- CRF on hemodialysis
- Morbidly obese
- Diabetic neuropathy
- Hypertension
- Hypercholesterolemia

**SH**
- No history of tobacco or EtOH abuse
- Lives in nursing facility

**NKDA**
- Insulin, Zosyn, anti-hypertensives, neurontin, heparin
<table>
<thead>
<tr>
<th>MD - Exam</th>
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<tbody>
<tr>
<td><strong>VA cc</strong> 20/40 OU</td>
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<tr>
<td><strong>IOP</strong> wnl tactile OU</td>
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<td><strong>EOM full OU</strong></td>
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<tr>
<td><strong>CVF full OU</strong></td>
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<tr>
<td><strong>LLL</strong> – epidermal necrosis</td>
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<td>lower lids OU with exposed dermis and</td>
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<td>surrounding erythema; mild mucous</td>
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<td>discharge</td>
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<tr>
<td><strong>Normal conjunctiva,</strong></td>
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<tr>
<td>sclera, cornea, AC, iris</td>
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<td><strong>No injection or chemosis</strong></td>
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<td><strong>Mild cataract OU</strong></td>
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<td><strong>DFE</strong> – 0.3 OU, sharp disc,</td>
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<td>normal foveal reflex, no heme, MAs,</td>
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<td>ischemia</td>
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Differential?
Differential?

- Infectious cellulitis
  - Necrotizing fasciitis
- Vascular insufficiency
- Hypercoagulable states
- Vasculitis with cutaneous manifestations
  - Wegener’s, hypersensitivity
- Cutaneous hypersensitivity
  - Erythema nodosum, Lichen planus, Erythema multiforme
- Pyoderma gangrenosum
  - Neutrophilic dysregulation involving cutaneous necrosis, mainly limbs
- Calciphylaxis
  - Usually seen in the setting of ESRD and hemodialysis
Calciphylaxis  
(Calcific Uremic Arteriolopathy)  

- Vascular and subcutaneous calcification with cutaneous necrosis  
- First described in 1898 in association with uremia by Bryant and White  
- In 1962 Selye constructed an animal model similar to clinical presentation in humans  
  - Coined the term  
- 1976 Gipstein et al. presented 11 patient case series of vascular calcification and skin necrosis in humans with renal failure  
- Also described in patients without ESRD … obesity, RA, breast cancer, primary hyperparathyroidism, cirrhosis, Crohn’s disease
Epidemiology

- Very rare, even with existing vascular calcification
- Some reported incidence of 1-4% in ESRD
- More common in Caucasians
- Women > men (3:1 in reports)
- Any age group
- May be more prevalent with longer history of dialysis
- Mortality reported ~ 50 to 80%
  - Mainly from ulceration and sepsis
Pathophysiology

- Poorly understood
- Commonly occurs in ESRD
- Calcium deposition in media of small- and medium-sized arterioles as well as subcutaneous areas $\rightarrow$ cutaneous necrosis
- Selye – hypothesis of sequence of events leading to calcinosis
  - “Sensitizing” agents – PTH, vitamin D, nephrectomy
  - “Challenging” agents – egg albumin, metallic salts (Al), tissue injury
  - Many suspected triggers
- Molecular mechanisms which regulate mineralization may be altered by ESRD, use of corticosteroids, hyperparathyroidism, cirrhosis, Coumadin use
- Not quite dystrophic or metastatic calcification
History

- Lesions develop and grow fast
- Most often appear on the lower limbs or trunk
- Can be very painful
- Associations may include obesity, malnutrition, IDDM, cirrhosis, corticosteroid or IMT use, Coumadin use, elevated aluminum, iron dextran
- May involve sepsis, non-healing ulcers
Exam

- Erythematous papules/nodules
- Stellate purpuric lesions
  - Cutaneous mottling
  - Livedo reticularis
- Cutaneous necrosis and ulcers with eschar
- Nodules are very tender and firm
- Ocular involvement in lids, conjunctiva
Work Up

- Complete metabolic panel
  - include Ca, Ph, BUN, Cr
- CBC with differential
- PTH level
- Amylase, lipase
- ESR, CRP
- ANA, ANCA
- PT, PTT, INR
- Coagulation work up

- Biopsy
  - Calcification in arteriolar media and subcutaneous tissue with fibrosis
  - Mixed inflammatory infiltrate
  - Microthrombi
  - Necrosis
Management

- **Medical**
  - Sodium thiosulfate
    - Increase Ca solubility
  - Avoid triggers (Ca, vitD)
  - Lower serum Ca, Ph
  - More frequent HD?
  - Calcimimetics
    - Help lower PTH
  - Bisphosphonates

- **Surgical**
  - Parathyroidectomy
  - Wound care
    - Debridement of necrotic tissue
    - Antibiotics/dressing
    - Pain management

- **Wound care**
  - Debridement of necrotic tissue
  - Antibiotics/dressing
  - Pain management
5 cases of cutaneous calciphylaxis

- Parenchymal involvement in only 1 case
- All had ESRD on HD, different etiologies
- No correlational trend in serum Ca, Ph
- 4 of 5 had high normal or elevated PTH
- Time from start of dialysis to appearance of lesions ranged from 1 week to 3 years


- Proposed a role in tissue devitalization after loss of fluid in HD in development of ocular calcification
- 38 ESRD pre/post HD vs healthy controls
- No relation between serum Ca, Ph, PTH and limboconjunctival calcification
- Pre-dialysis vs control
  - TBUT shorter, Lissamine green score higher; Schirmer not significant
- Pre- vs post-dialysis
  - Overall TBUT shorter, Lissamine green higher, Schirmer shorter
- Decrease in limbal calcification after successful transplant compared to matched controls