Case Conference

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MD – Emergency consult

- Called to evaluate patient with eye pain and periocular erythema

MD - History

- 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

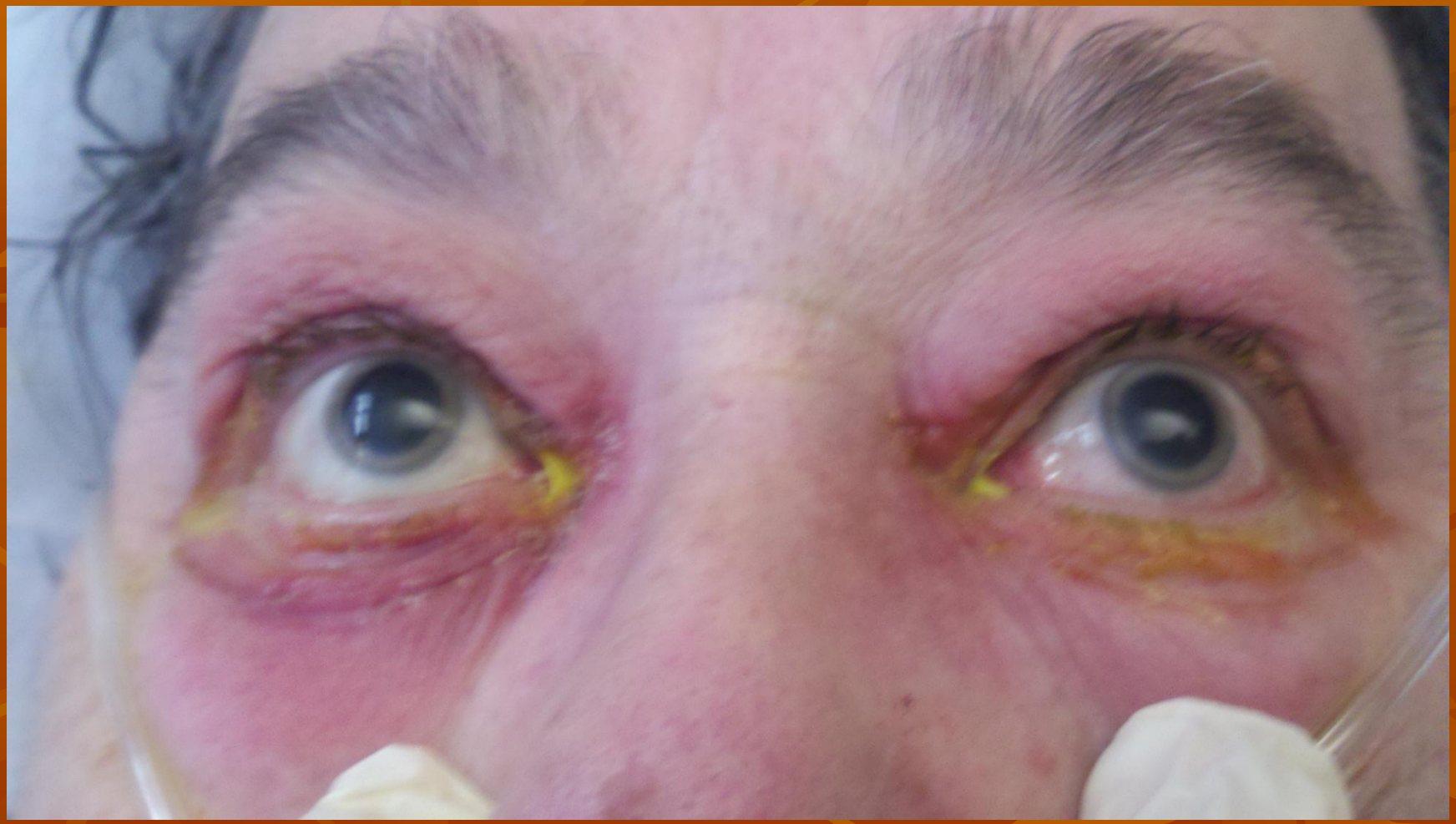
- Poorly controlled IDDM
- CRF on hemodialysis
- Morbidly obese
- Diabetic neuropathy
- Hypertension
- Hypercholesterolemia

SH

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

NKDA

Insulin, Zosyn, anti-hypertensives, neurontin, heparin



MD - Exam

Va cc 20/40 OU

IOP wnl tactile OU

EOM full OU

CVF full OU

LLL – epidermal necrosis lower lids OU with exposed dermis and surrounding erythema; mild mucous discharge

Normal conjunctiva, sclera, cornea, AC, iris

No injection or chemosis

Mild cataract OU

DFE – 0.3 OU, sharp disc, normal foveal reflex, no heme, MAs, ischemia

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 → 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

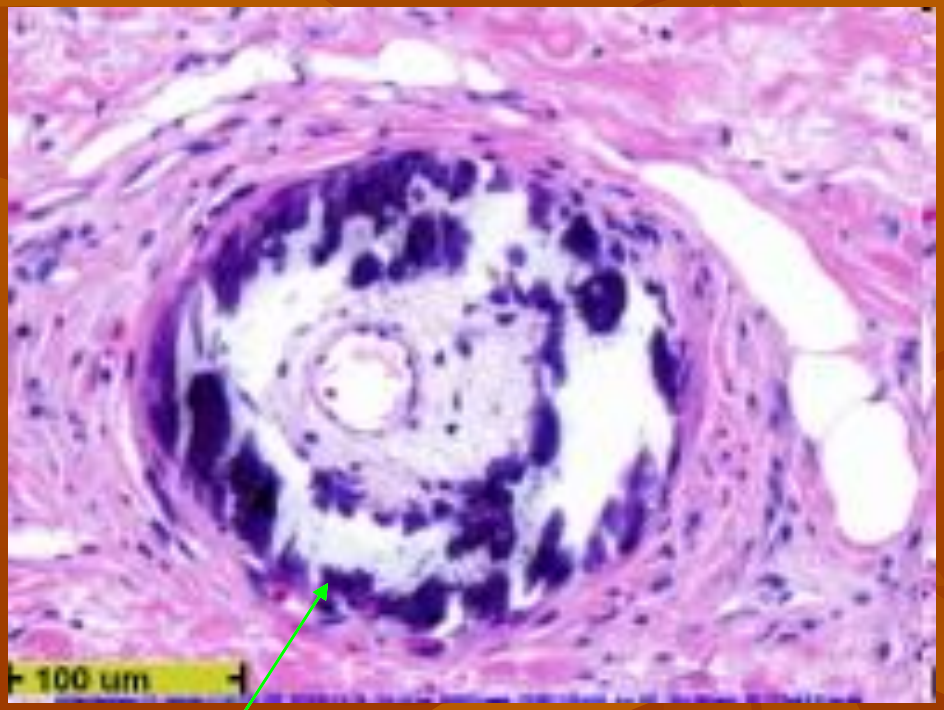
Exam

- 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


100 um

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

Oh, DH, et al. Five cases of calciphylaxis and a review of the literature. J Am Acad Derm. 40 (6), part 1: 979-87.

- 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

Klaassen-Broekema, N. and van Bijsterveld, OP. A local challenger of ocular calciphylaxis in patients with chronic renal failure: a hypothesis. Graefe's Arch Clin Exp Ophthal. 233: 717-20.

- 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