HAWOCC 2019
Atypical Wounds: Calciphylaxis, Pyoderma Gangrenosum, HIT Syndrome, Coumadin Necrosis, Necrobiosis Lipoidica

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Greetings From School of Nursing Rutgers University, Camden New Jersey
Greetings From Eagles Territory: Center of the Super Bowl Universe (2017)
Greetings from NCAA Championship Land (2017)
Objectives

Attendees will:

• 1) Differentiate among Pyoderma Gangrenosum, Calciphylaxis, HIT Syndrome, Coumadin Necrosis, and Necrobiosis Lipoidica.

• 2) Recommend topical/systemic pharmacologic/nonpharmacologic interventions to manage the patient with Calciphylaxis, Pyoderma Gangrenosum, HIT Syndrome, Coumadin Necrosis, and Necrobiosis Lipoidica wounds.
Atypical Wound

• One that is not “typical” chronic wound (not classic pressure, arterial, venous or neuropathic)
• Can be recalcitrant to healing
• Can be abrupt in onset or slowly occurring
• Often associated with systemic disorders/conditions
  – Vasculitic or pseudo-vasculitic conditions
  – Disorders in coagulation
  – Associated with an immune-mediated response to a trigger with antibody formation
• Can be difficult to diagnose and to treat effectively
Terminology

• Calciphylaxis

  – More formally called calcemic uremic arteriolopathy (CUA) (EWMA, 2019)
  – Also called cutaneous calcemic necrosis, soft tissue calcification, uremic gangrene syndrome, metastatic calcification.
  – If seen without ESRD called non-uremic calciphylaxis (NUC) (Altman et al, 2019)
Calciphylaxis (Definition)

• Syndrome of calcium deposition in small and intermediate dermal blood vessels
• Has been likened to an “MI” of the skin (Bilac et al, 2009)
• First case of CUA associated with CKD described in 1898 by Bryant and White (Anderson, 2013; Nunley, 2019) so NOT a new disorder
• Characterized by skin infarction and acral gangrene (EWMA, 2019)
• Small and medium sized blood vessels of dermis and subcutaneous fat become calcified (Young, 2019)
Pathomechanisms of Calciphylaxis (CUA)

- Pathogenesis is unclear and complex
- Many factors need to occur
- Selye proposed theory of calciphylaxis as “sensitizers” and “challengers”
- “Calci” (calcification) “phylaxis” (protection) – protect from calcium deposition (Chang, 2019)
Selye’s Theory of Calciphylyaxis

• “Sensitizers” are ESRD, secondary hyperparathyroidism, and hypophosphatemia

• “Challengers” are trauma, medications (iron, warfarin, vitamin D analogs, steroids, calcium-based phosphate binders)

• No real certainty which factor is a *cause* or *effect* (Anderson, 2013)
Epidemiology /Risk Factors

- Occurs in up to 4% of renal failure patients (Beitz 2003)
- Translates to 35/10,000 ESRD patients on dialysis (EWMA, 2019)
- Incidence is 1% per year (Beitz, 2003)
- Maybe as high as 5% in hemodialysis patients (Vedvyas et al, 2011)
- Associated heavily with chronic kidney disease (CKD) (ESRD)
- Prevalence of DM II and CKD has increased substantially (20-25% over past decade) (Feeser, 2011)
Epidemiology/Risk Factors

- Higher in women than men (3:1) (Bilac et al, 2009)
- Also seen in multiple other disorders
- Sepsis is leading cause of death
- Mortality rate of 80% (Anderson, 2013; Nunley 2019)
- One year mortality rate in central calciphylaxis is 50% in ESRD patients (EWMA, 2019)
- Patients with proximal lesions on trunk and upper thighs (central) do worse prognostically (Bilac et al, 2009)
- Calciphylaxis without ESRD is most common in morbid obesity with T2DM and hypertension (EWMA, 2019)
Risk Factors

• More common in females, diabetics, dialysis dependence
• More common in obesity, Caucasian race, hypoalbuminemia, elevated alkaline phosphatase
• Vitamin K deficiency or drugs affecting Vitamin K
• Also associated with hypercoagulable states: protein C and protein S deficiencies
• Also associated with calcium and phosphorus disorders (high calcium, high phosphorus), hyperparathyroidism, malignancy, liver disease) (Burnie et al, 2013; Chang, 2019; EWMA, 2019; Nigwekar et al, 2008; Nunley, 2019; Young, 2019)
Risk Factors for Non-Uremic Calciphylaxis (NUC)

- Hyperparathyroidism
- Malignant neoplasms
- Alcoholic liver disease
- Autoimmune disorders
- Medication use: Corticosteroids (Altman et al, 2019; Dado et al, 2019)
Calciphylaxis Registries

- Goal is to record as many cases of CUA as possible to get “real picture”
- Country – USA – KU Medical Center, University of Kansas  
  (http://www2.kumc.edu/calciphylaxisregistry)
- Also in Germany and United Kingdom
Diagnosis/Differential Diagnosis

- No specific diagnostic tests
- Diagnosis of exclusion
- Most significant criteria:
  - Clinical appearance of painful skin lesions
  - Intact peripheral pulses
  - Absence of neuropathy
  - Presence of one or more risk factors
  - Biopsy may worsen; recommend CT scan or ultrasound (Feeser, 2011)

- Classic calciphylaxis is laterodorsal legs, medial thighs abdominal fat apron, female breasts, lateral upper arms (EWMA, 2019)
Differential Diagnoses
(Chang, 2019; Young, 2019)

- Hyperparathyroidism
- Peripheral arterial disease
- Warfarin necrosis
- Necrotizing fasciitis
- Pyoderma gangrenosum
- HIT Syndrome purpura

- Vasculitis
- Anti-phospholipid syndrome
- Diabetic neuropathy
- Chronic venous insufficiency
- Protein C or Protein S deficiencies
Clinical Manifestations

- Often starts with dull deep dermal pain and neuritic-type dysesthesias (Anderson, 2013)
- Develop dermal changes including erythema, violet mottling and livedo reticularis (network like changes)
- Progress to indurated plaques and nodules
Calciphylaxis
Calciphylaxis
Clinical Manifestations

• Finally develop severe necrotic foci and deep excruciatingly painful non-healing ulcerations
• May get calcification of surrounding fat tissue
• **Excruciating pain** is most consistent element of clinical presentation (likely ischemic and neuropathic) (Chang, 2019)
• Lesions in two distinct patterns:
  1) Distal with lesions on the lower extremities
  2) Proximal – abdomen, inner thigh, buttocks (Hayashi, 2013)
• Can involve organs: heart, lungs, pancreas, GI tract and penis (Burnie et al, 2013 EWMA, 2019)
• Quickly develop; prove to infection (Todhunster, 2019)
Calciphylaxis
Traditional Treatment Options

- Avoiding foods rich in phosphate (colas) (Chang, 2019)
- Avoidance of calcium containing phosphate binders
- Avoidance of vitamin D analogues
- Low calcium dialysate
- Cinacalcet (Helps suppress PTH)
- Parathyroidectomy
- Avoidance of warfarin
- Meticulous wound care
- Judicious use of antibiotics
- Avoid surgical debridement/trauma
- Adequate anesthesia
- Optimize nutrition
- Do skin biopsy only if clinically essential in CUA (Burnie et al, 2013; Chang, 2019; EWMA, 2019)
- Skin biopsy less risky than CUA (Chang, 2019)
Not So Novel Treatment Options

• Sodium thiosulfate (25 gms in 100ml IV at end of dialysis)
• Bisphosphonates
• Hyperbaric oxygen (Burnie et al, 2013)
• Maggot therapy (Vedvyas et al, 2011)
Pharmacological Management

• Sodium Thiosulfate (Calcium chelator)
  – Originally used as an antidote to cyanide toxicity
  – Has anti-oxidant activity (Reduces inflammation)
  – Acts as a reducing agent by forming water soluble complexes (Hayashi, 2013)
  – Improves solubility of calcium and phosphate (Burnie et al, 2013)
  – Reverses endothelial dysfunction (EWMA, 2019)
  – Helps decalcify calcified blood vessels (Chang, 2019)
Pharmacological Management

• Sodium thiosulfate
  – Given IV
  – Up to 80 grams a day (higher dosing)
  – Some sources say 5-25 grams IV three times weekly (EWMA, 2019; Vedvyas et al, 2011)
  – Exact mechanism of why sodium thiosulfate works is still elusive (Salmhofer et al, 2013)
  – Given after (or at end of) dialysis and is usually used for two months
Pharmacological Management

• Cinacalcet (Calcimimetic Agent)
  – Approved to treat secondary hyperparathyroidism
  – Helps control hyperparathyroid effects
  – Acts to increase sensitivity of calcium-sensing receptors to suppress PTH secretion
  – Commonly 30 mg/day for five months
  – Australian study on 228 dialysis patients with cinacalcet withdrawal; experienced increased PTH, calcium and alkaline phosphatase levels (Ruderman et al, 2019)
Pharmacologic Care

- **Sevelamer (Renagel)**
  - Replaces aluminum and calcium containing phosphate binders
  - Acts to bind excess phosphorus in blood usually related to CKD
  - 800 mg or 400 mg tablets
Pharmacological Management

• Bisphosphonates
  – Usually treat osteoporosis, bone metastasis etc.
  – Bisphosphonates decrease inflammation and decrease cytokine response (lower inflammation)
  – Pamidronate, ibandronate (IV), oral etidronate have been used – usually 6-8 weeks (EWMA, 2019)
Vitamin K therapy

- Investigational
- Vitamin K deficiency promotes vascular calcification
- Clinical trial currently testing Vitamin K 10mg orally three times weekly (Chang, 2019)
Calciphylaxis: Local Care

• Good basic wound care
• Pain management (Fentanyl preferred)
• Treatment of local and systemic infections
• Good nutrition (support)
• Likely to have surgical debridement
• HBOT for recalcitrant wounds (Chang, 2019)
Switching Gears
Pyoderma Gangrenosum

- Rare inflammatory neutrophilic skin disorder
- Unknown patho-mechanism
- Not infection primarily
- Not gangrenous in origin
- Association with systemic diseases suggests underlying immune abnormality
- Sometimes called PG vs. PPG (Peristomal Pyoderma Gangrenosum)
- Cutaneous manifestation of generalized inflammatory response (Associated with T Cells) (EWMA, 2019)
Pyoderma Gangrenosum

• Several forms of disorder:
  – Classic (ulcerative): on lower extremities or trunk
  – Pustular (painful pustules on exterior limbs)
  – Bullous (painful superficial blistering) (Ratnagobal et al, 2013)

• Known to be exacerbated by skin trauma (Pathergy) (Hanley, 2011)

• Incidence of 0.3 to 1.0/100,000 people; called an “orphan” disease (EWMA, 2019)
Pyoderma Gangrenosum

Risk factors
• Up to 70% of patients have underlying systemic disease
  – Inflammatory bowel disease
  – Arthritis, Behcet’s disease
  – Hematologic disease (e.g., Polycythemia vera)
  – Malignancy (e.g., Leukemia, multiple myeloma)
• Can also be associated with HIV infection
• Some cases are idiopathic
Pyoderma Gangrenosum

Differential Diagnosis
- Vasculitis
- Occlusive vasculopathy
- Infection-related ulceration
- Neoplasia

Skin biopsy rules out other disorders but is not definitive for PG
## Diagnostic Criteria: Paracelsus Score

<table>
<thead>
<tr>
<th>Diagnostic criteria of PG according to the Paracelsus score</th>
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<tr>
<td>Evaluation: ≥ 10 points = PG highly likely; &lt; 10 points PG unlikely</td>
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### Major criteria (3 points)
- Progressive disease course
- Assessment (absence) of relevant differential diagnosis
- Reddish-violaceous wound border

### Minor criteria (2 points)
- Amelioration (Alleviation in response to immune suppression)
- Bizarre shape of ulcer
- Extreme pain (>4/10 VAS)
- Localized pathergy phenomenon

### Additional criteria (1 point)
- Suppurative inflammation in histopathology
- Undermined wound border
- Systemic disease associated
## PG Diagnostic Criteria
(Mavarakakis et al, 2018)

<table>
<thead>
<tr>
<th>Major Criterion</th>
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<tr>
<td>Biopsy of ulcer edge with neutrophilic infiltrate</td>
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<table>
<thead>
<tr>
<th>Minor criteria</th>
<th></th>
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<tbody>
<tr>
<td><strong>Exclusion of Infection</strong></td>
<td><strong>Peripheral erythema, undermining border, and tenderness at ulcer site</strong></td>
</tr>
<tr>
<td>Pathergy phenomenon</td>
<td>Multiple ulcerations at least one on an anterior lower leg</td>
</tr>
<tr>
<td>History of IBD or Inflammatory arthritis</td>
<td>Cribiform or “wrinkled paper” scar at healed ulcer site(s)</td>
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<tr>
<td>History of papule, pustule, or vesicle ulcerating within 4 days of appearing</td>
<td>Decreased ulcer size within one month of immunosuppressive medications</td>
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For diagnosis of PG, major criterion is obligatory; at least **four** of minor criteria
PG – Clinical Manifestations

• Painful pustule or papule or nodule
• Painful ulceration
• Bluish-reddish (violaceous) ulcer edges
• Ragged ulcer edges
• Deep ulcers
• 70% of PG on lower legs; secondary site around stomas (EWMA, 2019)
• N.B. PG can also have extracutaneous involvement:
  Cavitary lung lesions, pulmonary infiltrates, episcleritis, psoas muscle, and splenic abscesses
PPG

- Similar clinical appearance
- Occurs near diversion (ostomy)
Stepwise Approach
(Ratnagobal and Singh, 2013)

Initial Suspectiom
Wound Swab
Biopsy

Topical Therapy
Steroids
Tacrolimus
Cyclosporine
HBOT

Systemic Therapy
Steroids
Methotrexate
Cyclosporine
Infliximab
IV Immune Globulin

Surgery
Skin Graft
Possible Amputation
Overview of Treatments for PPG (Gray and Catanzaro, 2004)

• The D’s of Treatment
  – Debridement: local debridement *may* help
  – Dressings: topical wound therapy
  – Drugs: Intra-lesional steroids: may be effective
  – Drugs: Systemic: antimicrobials, monoclonal antibodies, steroids, cyclosporine
  – Drugs: Topical: steroids-can be used with systemic therapy
  – Displacement: stoma relocation: ineffective
Interesting Research

• Stomal and Peristomal Complications Management Study (Beitz and Colwell, 2014)
• TOP Three Recommended Practices for PPG
  1. Decrease inflammatory response using topical steroids (spray, paste)
  2. Use of biopsy to confirm PG diagnosis
  3. Administration of systemic therapy (prednisone, cyclosporine, dapsone, infliximab)
PPG – Clinical Manifestations

- Purulent discharge
- Localized erythema and edema
- Necrosis in ulcer bed
- Presence of satellite lesions possible
- Located around stoma site
Pharmacologic Management (EWMA, 2019)

- Corticosteroids
- Cyclosporine
- Methotrexate
- Azathioprine

- Mycophenolate mofetil
- Tacrolimus
- Infliximab
- Thalidomide
- Dapsone
- Interferon alfa
- Etanercept
Pharmacologic Management

• No RCTs directing treatment (no optimal approach)

• Best documented approaches are high dose oral steroids (>60mg/day) or cyclosporine (5mg/kg/day)

• Neither are good for long-term therapy due to side effects (Panuncialman et al, 2010)
Pharmacologic Management

- Tumor Necrosis Factor Inhibitors
- Most studied drug is infliximab: usually 5mg/kg at weeks, 0, 2, and 6
- Associated with allergic response and activation of latent infections (e.g., tuberculosis)
- Etanercept is also TNF Blocker: usually 25 to 50 mg weekly (Panuncialman & Falanga, 2010)
Pharmacologic Management (Topical)

- For patients with more superficial PG and PPG
- Topical or intralesional steroids (Clobetasol)
- Topical tacrolimus (0.1% ointment) (EWMA, 2019)
Unique Topical Approach

- Study by Fonseka et al, 2010 in *International Wound Journal*
- Done in Sri Lanka on 6 patients (had IRB approval)
- Innovation: Phenytoin sodium solution (2%) applied in wet gauze to wounds daily (were PG, not PPG)
- Discontinued systemic therapy
- Complete healing in 4/6 patients in 4 weeks
- Theorized that has anti-inflammatory effect
Novel Topical Approach

• Case report of three patients (DeMartyn, Faller, Miller, 2014) (*OWM*, June 2014)
• About PPG
• Topical prednisone protocol: crush 1 mg pill; mix with equal part of barrier powder
• Apply mixture to PPG ulcer, cover with calcium alginate or hydrofiber, secure with hydrocolloid
• Pouch over dressing; change q3 to 5 days
• No negative side effects with healing
PG

- Other interventions
- HBOT (Altunay et al, 2012)
- Apligraf (with systemic immunosuppressive agents) (Duchini et al, 2011)
- NPWT
Changing Direction
Heparin-Induced Thrombocytopenia (HIT) Syndrome

- Epidemiology
- Pathophysiology
- Risk factors
- Clinical presentation
- Medical/surgical Therapies
- Pharmacological Treatments
HIT Syndrome: The Disorder

- Heparin use can be associated with thrombocytopenia usually **within first 5-14 days** of treatment
- Two forms of HIT syndrome exist
  - **Type I**: Transient slight fall in platelet count within first two days and returns to normal with continued heparin use
  - **Type II**: Immune-mediated disorder formation of antibodies against heparin-platelet complex ***
HIT Syndrome Type II

Synonyms for this disorder include:

• Heparin-associated immune thrombocytopenia
• Heparin-associated thrombocytopenia and thrombosis (HITT)
• White clot syndrome
• Involves arterial thrombosis (EWMA, 2019)
HIT Syndrome Type II

- Immune mediated HIT noted to be incidence of 2.6 percent (meta-analysis done by Martel et al, Journal Blood, 2005, 106, 2710)
- Range of 0.2 to 5 percent (Coutre, 2019)
- Symptomatic HIT occurs in 1 to 5% of patients on UFH, LMH,
- Up to 30% of those with HIT develop thrombosis (Thornsberry et al, 2013)
- You do the math; Uncommon but not rare due to prevalence of use
Risk Factors: HIT Type II

• Use of Unfractionated (UFH) Heparin
• Surgical versus medical patients
• Female rather than male patients
• Analyzed through retrospective reviews
  (Warkentin et al, 2016)
Pathophysiology of HIT Type II

- IgG, IgM, IgA antibodies triggered by highly immunogenic complex of heparin and platelet factory
- Antibodies (heparin-Pfy antibody complex) bind to platelet surface and platelets undergo aggregation – removed prematurely from circulation
- Also generated are pro-coagulant platelet-derived micro-particles that generate thrombin and thrombosis
- Full pathophysiology – not understood-get significant disease variability (Coutre, 2019; EWMA, 2019)
Pathophysiology of HIT Type II

Disease variability – Why such a range of manifestations?

• Clinical variables in the patient
  ? Pro-thrombotic state in patient
  ? Severity of trauma (if any)
  ? Degree of surgery?
  ? Underlying genetic polymorphisms (Coutre, 2019)
HIT Type II Clinical Manifestations

• Fall in platelet count >50 percent – typically occurs within 5 to 10 days after heparin initiation

• Usually develop HIT antibodies within five to eight days after exposure

• Note: HIT Type II can have delayed onset (Range of 9-19 days) (Salter et al, 2016)
HIT Syndrome Type II Clinical Manifestations

- Can get thrombosis both arterial and venous
- May present as DVT, PE
- May develop venous limb gangrene and full-thickness skin necrosis
- Can get arterial thrombosis with consequent stroke, acute limb ischemia, organ infarction
- Skin necrosis – usually in fat-rich areas (abdomen, extremities, etc)
- **Erythema** followed by **purpura** followed by **necrosis** (EWMA, 2019)
Diagnostics

• Initially clinical diagnosis: Decrease in platelets, signs of thrombosis, skin lesions may progress to skin necrosis
• Suspect presence of syndrome and order tests
• Serotonin release assay – gold standard shows action of heparin on patient’s serum sample
• Heparin-induced platelet aggregation or immunoassay – show HIT antibodies
Probability of HIT ("4Ts"): Screening Instrument

- Thrombocytopenia
- Timing of platelet count fall
- Thrombosis or other sequelae
- Other causes for thrombocytopenia present? (each item scored 2 for yes; get score of 0-8; 6 to 8 → high probability)
HIT Syndrome Prevention

1) Low molecular weight heparins
   Heparin analogue (fondaparinux)
   Heparinoids (danaparoid)
   (All are associated with much lower rates of HIT syndrome)

2) If using UFH, limit to less than 5 days and switch to coumadin.
HIT Therapy or Treatment

• Stop heparin immediately in all exposures (not even flushes)
• No UFH or LMWH
• Patient should be considered as having a “heparin allergy”
• If no active bleeding, switch to alternate form of anticoagulation
• Options include: argatroban, bivalirudin (Angiomax), fondaparinux
• Bivalirudin is direct thrombin inhibitor
• Eventually transition to coumadin (Warfarin)
• Established process available
HIT Syndrome Lesions
HIT Syndrome Lesions
HIT Syndrome Lesions (Later)
HIT Necrosis
Onward and Upward
Coumadin Necrosis

- Epidemiology
- Pathophysiology
- Pathophysiology
- Risk Factors
- Clinical Presentation
- Medical/surgical Therapies
- Pharmacological Treatment
Coumadin Necrosis

• Rare, unusual and unpredictable integumentary complication of anticoagulant therapy
• Synonym is warfarin – induced skin necrosis
• Coumadin first introduced in 1941 so condition has been “around” for decades
• Has high associated morbidity and mortality
Coumadin Necrosis

- Coumadin is the standard oral anticoagulant used in a variety of clinical conditions
- 90% of cases occur between 3rd and 6th day of therapy
- Coumadin or warfarin takes 36 to 72 hours for peak effect
- Creates a window of possible problems for a transient hyper-coagulable state (Valentine & Hull, 2013)
- Reported frequency between 1:100 and 1:10,000 individuals (Bartholomew, 2005)
Coumadin Necrosis Pathophysiology

- Not entirely understood but thought to involve a profound imbalance in procoagulative/anticoagulative factors once coumadin administered
- Quantitative or functional deficiency of Protein C (less commonly Protein S)
- Congenital or acquired Protein C and Protein S deficiency (EWMA, 2019)
- Skin biopsy shows fibrin clots in dermal vessels without vasculitis and without inflammation (Wallace et al, 2010)
Coumadin Necrosis Risk Factors

• Typical/historical constellation of factors has been identified
• Female gender
• Obese body type
• Middle aged group
• In-patient hospital stay for acute illness
• Required anticoagulation for:
  – Deep vein thrombosis
  – Myocardial infarction
  – Prosthetic cardiac valve surgery
  – History of coagulation pathologies (Protein C deficiency)
  – High-loading doses of coumadin in history
Coumadin Necrosis Clinical Presentation

• Usually manifests as small lesions on breast, thigh, penis, buttocks, abdomen (fatty areas)
• Evolve from erythematous macules to edematous purpuric zones
• Ultimately proceeds to necrosis
• Can also progress from flushed areas to petechiae to hemorrhagic bullae to skin necrosis (Bartholomew, 2005)
Coumadin Necrosis Clinical Presentation

• Can also present as “purple toe” syndrome
• Not as common presentation
• Most coumadin necrosis presents between day 3 and 6
• Can present unilaterally but 30% of cases present bilaterally
Coumadin Necrosis
Coumadin Necrosis
Coumadin Necrosis
Coumadin Necrosis Prevention

• Initial doses of warfarin should **not** exceed 5mg/day
• Be aware of risk factors
• **Stop** coumadin if any suspicion
Coumadin Necrosis Pharmacological Care

• Immediately stop coumadin
• Reverse effects with Vitamin K and/or fresh frozen plasma
• Common to switch to heparin therapy (LMWH) or more commonly IV Heparin (EWMA, 2019)
Coumadin Necrosis Medical/Surgical Therapies

• No consensus – treatment is empirical
• Topical therapy – antibiotics, silver sulfadiazine
• Surgery – may be needed for removal of necrosis
Disease Complication

- Diabetes mellitus
- Genetic
- Congenital defects
- Blood
- Insulin
- Metabolic
- Deficiency
- Resistance
- Weight
- Transplants
- Sugar
- Metabolic
- Symptons
- Treatment
- Healthy
- Suffer
Necrobiosis Lipoidica

- Epidemiology
- Pathophysiology
- Risk Factors
- Clinical Presentation
- Medical/surgical Therapies
- Pharmacological Treatments
Necrobiosis Lipoidica

- Disorder of collagen degeneration with a granulomatous response, thickened blood vessel walls and fat deposition
- Major complication is ulceration
- First called necrobiosis lipoidica diabeticorum in 1932 by Urbach (no longer include diabeticorum)
- Rarely resolves spontaneously
- Up to 25% of NL sufferers are diagnosed with lesions before their diabetes has been diagnosed (Dissemond, 2012)
Necrobiosis Lipoidica Epidemiology

• Average age of onset is 30 years but can occur at any age
• Develops at earlier age in diabetics; more likely in Type I (Fore, 2007)
• Three times more common in women
• Occurs in about 0.3 to 2% of diabetic patients (Type I and Type II) (EWMA, 2019)
• Progression of NL does not correlate with diabetes control
• 75% of NL cases are associated with diabetes (Barouti et al, 2014)
• In 25% of patients who are not diabetic, they often have a family history of DM or Impaired Glucose Tolerance (Duncan et al, 2005)
Necrobiosis Lipoidica Pathophysiology

• Etiology of NL still uncertain

• Several theories:
  a) Diabetic micro-angiopathy affects blood vessels (get glycoprotein deposition)
  b) Theorized that immune globulins are deposited in blood vessel walls due to vasculitis
  c) Defective collagen fibrils – get increased cross linking and basement membrane thickening
Necrobiosis Lipoidica Pathophysiology

- NL cause is unknown but smoking, proteinuria, and retinopathy are more prevalent in subset of diabetic patients who have NL (Hoffman, 2013)
- Role of genetics is unclear
Necrobiosis Lipoidica Risk Factors

- Diabetes mellitus
- Female gender
- Not degree of glycemic control in diabetic
- Impaired Glucose Tolerance/family history of Diabetes Mellitus
Necrobiosis Lipoidica Clinical Presentation

- May start looking like a “bruised” area
- Present with shiny, asymptomatic patches that slowly enlarge over months to years
- Patches are red-brown and progress to yellow, depressed atropic waxy plaques
- Thinning of epidermis and dermis makes subcutaneous fat visible
- Ulcerations occur typically after trauma
- Telangiectasia and scaling may be present (Hawryluk et al, 2010)
- Ulceration occurs in 15% of NL patients related to trauma (EWMA, 2019)
Necrobiosis Lipoidica Clinical Presentation

• Lesions most commonly occur on pretibial area of lower extremities
• Has been reported on upper extremities, trunk, and face
• Lesions may be painless (75% of cases) (Barnes & Davis, 2012)
• Lesions are usually multiple and bilateral
• Lesions can be associated with hypohidrosis, decreased sensation, and alopecia (Binamer et al, 2012)
Necrobiosis Lipoidica
Necrobiosis Lipoidica
Necrobiosis Lipoidica
Necrobiosis Lipoidica
Necrobiosis Lipoidica

Medical/Surgical Therapies

• No lab findings specific to Necrobiosis Lipoidica
• Do check blood sugar
• Do check for glucose intolerance
• Biopsy findings however have a classic appearance
• **No specific therapy is curative in all people**
Necrobiosis Lipoidica

Medical/Surgical Therapies

• Surgery – not commonly used – but if done, usually ulcer excision and skin grafting done
• Not many proven approaches
• Some reports of using laser therapy to stabilize lesions (Barnes, 2013)
• HBOT
• Protect legs from trauma –
  – Leg rest and elevation
  – Elastic support stockings
Necrobiosis Lipoidica

Topical Therapy

• Wound healing enhancers – (Oxidized Regenerated Cellulose)
• Topical oil emulsion dressings
• Silicone foam dressings (non-adherent)
• Bilayers skin equivalent (Fore, 2007)
• (Removed trade names but they were used in published studies: see bibliography)
Necrobiosis Lipoidica

Pharmacological Therapies

Since exact etiology is unknown, treatment is not very effective

• Pharmacotherapy includes:
  • Topical (Triamcinolone (0.1%) TID) and intralesional (Triamcinolone 5-10mg/ml) steroids good with early active lesions (not with open lesions)
Necrobiosis Lipoidica

- Cyclosporine 2.5mg/kg/day
- IV Infliximab
- Topical bovine collagen
- Many other drugs tried off label
- Topical psoralen and ultraviolet (PUVA)
- Oral aspirin, dipyridamole, pentoxifylline (Trental), ticlodipine to enhance blood flow and prolong platelet survival (best evidence)
Necrobiosis Lipoidica

Pharmacological Approaches: Individual Reports

• Intravenous Immune Globulin IVIG at 0.4g/kg/day for five days (Bapouti, 2013)
• Intravenous immune globulin (2G/KG/Day and methylprednisolone (IV) (500mg, I gram) (Batchelor & Todd, 2012)
Necrobiosis Lipoidica

Final Caution

• Chronicity of NL ulceration may predispose to development of squamous cell cancer

• At least 8 cases of SCC have been reported in NL ulcer (Hoffman, 2013)
Case Study

Heparin-Induced Thrombocytopenia Syndrome

70-year-old obese woman is admitted to the surgical ICU following repair of an aortic valve and coronary artery bypass (x2). The intraoperative course was uneventful. Patient had multiple co-morbidities including hyperlipidemia, diabetes, hypothyroidism. On day three the patient began to develop bruises (ecchymoses) and sero-sanguinious blisters on the arms, legs, and trunk. Lab testing revealed heparin antibodies. What should be done?
Case Study

Coumadin Necrosis

• 80-year-old man is in a MVA and suffered multiple injuries. He develops asystole on way to hospital where CPR is initiated. He has a cardiac tamponade and requires a pericardiocentesis. He has fractures of the sternum, left scapula, and multiple RIB fractures.
Case Study

Coumadin Necrosis

• He develops atrial fibrillation and is started on heparin and warfarin. He requires a ventilator to breathe. As he is being transferred to step down unit, he develops petechiae of feet and purpura of legs. What needs to happen?
Case Study

Necrobiosis Lipoidica

• A 43-year-old white woman with a 30-year history of Type I diabetes is referred to a wound clinic with well-demarcated lesions on both lower extremities with a brownish-yellowish hue tone of the lesions on the right leg has recently ulcerated and has enlarged. The patient smokes 2 PPD and has well controlled D.M. Hemoglobin AIC of 7%. What would be the workup? What would be the approach?
Summary

• Atypical Wounds are Challenging
• Discussed Five Interesting Conditions
• Critical for WOC Nurse to Understand Pathophysiology and Therapeutics in Addition to Topical Therapy Approaches
Summary

• Thanks for joining in and caring to learn more!!
• Any questions?
• Comments?
References

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