FO93 – Granulomatous Disorders of the Adult Skin
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Disclaimer:

• Conflict of Interest
  – None

• Financial Associations
  – None

• Off-label drug usage may be discussed
Practice Gap:

Granulomatous disorders represent a unique group of diseases, both noninfectious and infectious, that require the utmost clinical pathologic correlation combined with a keen sense of inquiry for underlying systemic disease and immunosuppression.

Dermatologists need to be able to differentiate these entities, evaluate patients for specific underlying systemic disease (i.e. from diabetes to cancer), and treat them with a wide range of immunosuppressant to anti-infectious medications.

By being aware of the skin manifestations of these abnormal physiologic responses dermatologists can improve patient safety, outcome and health care costs.
Objectives:

• Differentiate the Non-infectious granulomatous diseases (NIGD) and Infectious granulomatous diseases (IGD) of adult skin.
• Recognize the cutaneous clinical, histological and systemic manifestations of NIGD and IGD.
• Determine the best evidence based therapeutic modalities for the treatment of NIGD and IGD.
Granulomatous Disorders of the Skin

Non-infectious GD

Palisading Granulomas:
- GA
- EGCG
- NL
- RN
- Reactive GD

Epithelioid Granulomas:
- Sarcoidosis
- Cutaneous Crohns
- Orofacial Gran
- Gr. Rosacea/POD

Xanthomatous Granulomas
- Adult onset XG
- Adult onset APXG
- NXG
- MC Reticulohistiocytosis
- Rosai-Dorfman
- Xanthoma Disseminatum

Other:
- Gr. Vasculitis
- Gr. Lymphoproliferative
- Foreign Body Reactions
- Gr. Drug Reactions

Infectious GD

Caseating Granulomas
- Tuberculosis
- Leprosy
- Atyp. Mycobacterium
- Leishmaniasis

Suppurative Granulomas
- Deep Fungal
- Pyodermas
- Gr. STD
Granuloma Annulare

- **Pathogenesis**
  - Th1 lymphocytes activate macrophage expression of TNF-alpha and matrix metalloproteinases 2,9 leading to granuloma formation to unknown antigen.
  - Drug reaction
- **Clinical**
  - Localized, Generalized, Atypical
- **Histological**
  - Palisaded or Interstitial histiocytic infiltrates. MUCIN!!!!!!
- **Systemic Manifestations**
  - Generalized or Atypical forms and >60
  - DM/Autoimmune thyroiditis/HIV, Hep B +C/Elevated Lipids/Lymphoproliferative and visceral malignancy
- **Treatment Options**
  - Topical/IL/oral steroids/cryotherapy/phototherapy/laser
  - Oral agents: Hydroxychloroquine, Methotrexate, Mycopenolate mofetil, Acitretin, TNF inhibitors, Oral antibiotics
Elastolytic Giant Cell Granuloma

**Pathogenesis**
- Presumed severe actinic degeneration of skin elastic tissue modifying it to an antigenic form

**Clinical**
- Annular plaque with central clearing to polymorphic

**Histological**
- Granuloma formation distributed peripherally to a central zone of dermal atrophy and loss of elastic tissue. Elastophagocytosis. No necrobiosis of collagen
- NO MUCIN!!!!!!
- Elastophagocytosis is not specific – other granulomatous diseases can have it too

**Systemic Manifestations**
- DM
- Malignancy: lymphoproliferative (AML, Peripheral T cell lymphoma, MGUS)
  solid (prostate)

**Treatment Options**
- Steroids, Calcineurin inhibitors
- Hydroxychloroquine, Dapsone, Cyclosporine
Necrobiosis Lipoidica

- Pathogenesis
  - T-cell mediated hypersensitivity reaction to altered collagen production with immunologically mediated vascular disease and trauma

- Clinical
  - Early/Middle/Late Stages (85% on the lower legs)

- Histological
  - Multiple layers of hyalinized and necrotic collagen, surround by histiocytes and lymphocytes.
  - NO MUCIN

- Systemic Manifestations
  - DM/Retinopathy and nephropathy/Ocular inflammation (Retinal vasculitis in Non-DM) /Joint immobility

- Treatment Options:
  - Steroids
  - Hydroxychloroquine, Pentoxyfylline, Cyclosporine, Mycophenolate mofetil, Thalidomide, Biologics (IL-infliximab), Retinoids
  - Pulse Dye, PDT, Hyperbaric oxygen, topical PUVA, UVA-1
Rheumatoid Nodules

• **Pathogenesis**
  – Presumed complement-mediated process following RF immune complex deposition in small vessels that leads to immunologically-mediated vessel injury with fibrin deposition and subsequent monocyte induced granuloma formation.
  – Drug reaction

• **Clinical**
  – Classical RN/ Rheumatoid nodulosis/Accelerated rheumatoid nodulosis

• **Histological**
  – Granuloma formation with evidence of necrotic collagen rimmed by eosinophilic fibrin and palisading mononuclear cell infiltrate. NO MUCIN

• **Systemic Manifestations**
  – Rheumatoid arthritis (high titer RF, anti-CCP) with internal nodules can develop in the lung, liver, and heart
  – The presence of RN at baseline is a marker of extra-articular involvement and severe disease, and a predictor of subsequent joint damage

• **Treatment Options**
  • Asymptomatic
    – Leave alone
  • Symptomatic
    – Intralesional injections, surgical excision
Accelerated Rheumatoid Nodulosis:

- Reported with:
  MTX/Azathioprine/Biologics
  Aromatase Inhibitors
  - Joint Bone Spine 2011 Jan;78(1):62-4

Key Point: Letrozole (Femara) and Anastrozole (Arimidex)

- HLA DRB-1 or polymorphism of the methionine synthetase reductase gene
- May also occur in lungs
  J Clin Rheumatol 2009 (Feb) 15(1):29-30

-Treatment:
  D/C offending agent
  Trial of Plaquenil, Colchicine, Penicillamine, Sulfasalazine, Biologics
Reactive Granulomatous Dermatitis

- **Pathogenesis**
  - Unknown: ?immune complex deposition reaction?
  - Drug reaction
- **Clinical**
  - IGD-like (Rope sign)/GA-like (Polycyclic)/PNGD-like (Papulo-nodular)
  - Drug induced RGD (any of above patterns) vs IGDR
- **Histology**
  - IGD/GA-Like
    - Sparse palisaded and interstitial histocytic inflammation, degenerated collagen and variable PMNs
  - PNGD
    - Palisading granuloma with degenerated collagen, intense neutrophilic inflammation with LCV
  - IGDR
    - Similar but with vacuolar interface change and atypical lymphocytes
      [*All with no increase mucin]*
- **Systemic Manifestations**
  - RA, SLE, Other autoimmune: Sjogren’s, Scleroderma, Autoimmune thyroiditis/hepatitis. IBD
  - MDS/ Lymphoproliferative disorders
- **Treatment Options:**
  - Steroids
  - Hydroxychloroquine, Dapsone, MTX, Mycophenolate mofetil, Biologics
Sarcoidosis

• Pathogenesis
  – Presumed over exuberant Th-1/Th-17 mediated T cell inflammation to unknown agent
  – Drug reaction

• Clinical:
  – Specific (+underlying granuloma) or Non-specific (No underlying granuloma)

• Histological
  – Non-caseating granulomas

• Systemic Manifestations
  – Internal organ involvement: Ocular/Pulmonary/Cardiac/Neurologic
  – Associations: Testicular cancer/Lymphoma

• Treatment Options:
  – Steroids
  – Minocycline, Hydroxychloroquine, Methotrexate, Azathioprine, Biologics,Apremilast
Cutaneous Crohn’s

• Pathogenesis
  • Presumed a Th-1 driven delayed-type hypersensitivity reaction

• Clinical:
  – Metastatic/Perigenital + Peristomal/Oral

• Histological
  – Non-caseating granulomas with MNGC’s and granulomatous perivascular inflammation

• Systemic Manifestations
  – Inflammatory Bowel Disease
  – MCD is in temporal discordance with gastrointestinal involvement and removal of affected bowel doesn’t modify MCD course

• Treatment Options:
  – Steroids
  – Metronidazole, Azathioprine. Biologics (Adalimumab)
Orofacial Granulomatosis

- **Pathogenesis**
  - Presumed reactive inflammation to an unknown allergen.
  - Common sensitivities: Cinnamon-related compounds/Benzoic Acids
- **Clinical**:
  - Cheilitis granulomatosis/Angular cheilitis/Labial swelling + fissuring/Gingival enlargement/Facial erythema + edema/ Mucosal ulceration + tags or cobblestoning
  - Anogential granulomatosis
- **Histological**
  - Non-caseating epitheliod granulomas that are paralymphatic and intralymphatic +/- Dermal edema and Dilated lymphatics
- **Systemic Manifestations**
  - Melkerson-Rosenthal Syndrome (facial paralysis)
  - Gustatory defects and Regional adenopathy
  - Assoc: Psoriasis and Crohn's (in children)
- **Treatment Options**:
  - Steroids, Diet modification
  - Doxycycline, Azithromycin
  - HCQ, MTX, AZA, Biologics (Infliximab/Adalimumab)

Epitheloid Granuloma
Granulomatous Rosacea and POD

Gr. Rosacea

- Pathogenesis
  - Cathelicidin antimicrobial peptides, Demodex
- Clinical
  - Red brown papules/rhinophyma/LMDF
- Histology
  - Lymphohistiocytic inflammation and non-caseating epithelioid granulomas that are folliculocentric
  - Necrosis in Lupus miliaris disseminata facei variant
- Systemic
  - Ocular involvement
- Treatment
  - Metronidazole
  - Tetracyclines
  - Dapsone
  - Isotretinoin
  - Ivermectin
  - Azelaic acid

Gr. Periorificial Dermatitis

- Pathogenesis
  - Presumed granulomatous inflammation due to a non-specific reaction to unknown allergen with focal disruption of the follicular epithelium
- Clinical
  - Yellow-brown monomorphic papules in a periorificial distribution
- Histology
  - Granulomatous perifollicular inflammation
- Systemic
  - None
- Treatment
  - Tetracyclines or macrolides
  - Calcineurin inhibitors, Azelaic Acid
  - Topical antibiotics
    - Erythromycin
    - Metronidazole
    - Sulfacetamide
    - Clindamycin
Adult Onset XG

- **Pathogenesis**
  - Reaction to trauma, infection, malignancy

- **Clinical**
  - Isolated/Multiple

- **Histological**
  - Non-LCH histiocytosis [CD68 (+), S100 and CD1a (-)]

- **Systemic Manifestations**
  - Isolated: None
  - Multiple:
    - Cervical spine and Intracardiac infiltration
    - Lymphoproliferative malignancy (Essential thrombocytosis/CLL/Large B cell Lymphoma/MGUS to MM)

- **Treatment Options**:
  - Isolated: excision
  - Multiple: Spontaneous resolution / Treat underlying malignancy
Adult Onset Asthma with Periocular XG

- **Pathogenesis**
  - Systemic immunologic derangement with concurrent bronchiolar and ocular adnexal dysfunction.

- **Clinical**
  - Periorbital yellow-orange plaques, nodules to masses (bilateral)
  - Extends to anterior orbital fat, extraocular muscles and/or the lacrimal gland(s)
  - No optic nerve damage may cause obstruction

- **Histological**
  - Non-LCH histiocytosis [CD68 (+) S100 and CD1a (-)]

- **Systemic Manifestations:**
  - Adult onset asthma /Lymphadenopathy
  - Hematologic malignancies reported : CLL/SLL, multiple myeloma, non-Hodgkin’s lymphoma.
  - Associations: Diabetes /Lymphoplasmacytic sclerosing pancreatitis/Rosai- Dorfman

- **Treatment Options:**
  - Surgery
  - Corticosteroids and radiotherapy
Necrobiotic xanthogranuloma

• Pathogenesis
  – Paraprotein triggering an immune complex formation and inflammation with subsequent granuloma formation
  – Reactive inflammation No presence of monoclonal plasma cells
  – TCR-PCR clonality can distinguish reactive NXG from malignant granulomatous MF

• Clinical
  – Erythematous yellow-orange plaques that develop telangiectasia and may ulcerate
  – Periorbital location common with secondary eye inflammation (episcleritis)

• Histologic
  - Non-LCH histiocytosis [CD68 (+), S100 and CD1a (-)]
    – Prominent palisading granulomas with bizarre-appearing foreign body giant cells around cholesterol cleft

• Systemic
  – Multiple myeloma IgG kappa > IgG lambda > IgA
  – CTCL, Lymphoma, Leukemia
  – Infiltration of internal organs } heart, lungs, eyes

• Treatment Options:
  – No curative therapy – consider treating paraprotein
  – Topical / intralesional corticosteroids, IFN, nitrogen mustard
  – Chlorambucil, Melphalan, Steriods, Interferon alpha 2b, Azathioprine, Cyclophosphamide, Methotrexate therapy, Plasmapheresis, IVIG, Thalidomide/Lenalidomide
  – Surgical excision, radiation

Xanthomatous Granulomas
Multicentric Reticulohistiocytosis

• Pathogenesis
  – Unknown

• Clinical
  – Solitary/Multicentric (Periungual Coral beading)

• Histologic
  – Non-LCH histiocytosis [CD68 (+) S100 and CD1a (-)]
  – Histiocytes demonstrate a “ground glass appearance” - i.e. copious eosinophilic, granular cytoplasm.

• Systemic
  – Solitary: None
  – Multicentric:
    • Weight loss/anorexia / dysphagia/ pruritus/weakness/myalgia/fever/malaise
    • Systemic erosive arthritis and lymphadenopathy
    • Associations:
      – Autoimmunity (PBC, SS, SLE, DMM, Sjorgens)
      – Malignancy (solid/lymphoproliferative)
      – Pregnancy (solitary and multicentric)

• Treatment
  – hydroxychloroquine, methotrexate, leflunomide, mycophenolate mofetil, azathioprine, cyclophosphamide, cyclosporine, chlorambucil, dapsone, TNF-alpha inhibitors (etanercept, infliximab, adalimumab), bisphosphonates
Xanthomatous Granulomas

Rosai Dorfman

* Pathogenesis
  - Unknown reactive process
  - Mutations in SLC29A3, the gene that encodes the equilibrative nucleoside transporter hENT3, have been found in 2 families with familial Rosai-Dorfman disease.

• Clinical
  – Painless bilateral cervical adenopathy and red to red-brown papules or nodules in skin
  – Nodular inflammatory infiltrate by large foamy histiocytes (dermis and lymphatics)

• Histological
  – S100 (+) no beirbeck granules with nodular inflammatory infiltrate by large foamy histiocytes (dermis and lymphatics) + Emperiploisis [CD68 (+) S100 (+) and CD1a (-)]

• Systemic:
  – Lymphadenopathy, fever, elevated ESR, leukocytosis, anemia, MGUS, organ infiltration
  – Associations: Crohns/Bloodline malignancies

• Treatment Options:
  – Surgery or Radiation for vital organ involvement/ Corticosteroids/ MTX/Chemotherapy Interferon
Xanthomatous Granulomas

Xanthoma Disseminatum

• Pathogenesis:
  – Remains elusive

• Clinical:
  – Orange-red papulo-nodules to plaques (inverse location)

• Histological:
  – Non-LCH, xanthoma cells, Touton GC, mild inflammatory infiltrate
    [CD68 (+) S100 and CD1a (-)]

• Systemic Manifestations:
  – Diabetes insipidus, other hypopituitarism, dysphagia, dysphonea, ocular
    (corneal/conjunctiva), lipid abnl

• Treatment options
  – Cyclophosphamide, Azathioprine, Vinblastine, 2-chlorodeoxyadenosine
Other Granulomas

- Granulomatous Vasculitis
  - Granulomatosis with Polyangiitis (GPA)
  - EGPA
  - Microscopic Polyangiitis
  - PAN
Other Granulomas

- Granulomatous Lymphoproliferative Disorders
  - Gr. T cell Lymphoma
    - Gr MF
    - Gr Slack Skin
  - Lymphomatoid Granulomatosis
    - EBV driven
    - Large B cell Lymphoma (T-cell Rich)
Other Granulomas

• Foreign body reactions
  – Tattoo pigment
  – Cosmetic implants
  – Other
Other Granulomas

- Granulomatous Drug Reactions
  - Interstitial Granulomatous Drug Reaction
  - Reactive Granulomatous Dermatitis to Drugs
  - Drug-induced Accelerated Rheumatoid Nodulosis
  - Drug-induced GA
  - Drug-induced Sarcoidosis
Drugs that cause IGDR and Drug Induced RGD:
Calcium channel blockers
ACE inhibitors
Lipid Lower Medications
Anti- TNF α agents

Drugs that cause Accelerated Rheumatoid Nodulosis:
Methotrexate
Anti- TNF α agents
Aromatase inhibitors
Azathioprine
Leflunomide

Drugs that cause Granuloma annulare:
Anti- TNF α agents
Amlodipine
Allopurinol
Immunizations
PEG interferon  α
Topiramate
Drugs that cause Sarcoidosis:
Chemotherapy
Interferon α
Anti- TNF α agents
Other Biologics
- Pembrolizumab
- Ipilimumab
- Nivolumab


Tuberculosis

Infectious granulomatous diseases:

Caseating granulomas

- Pathogenesis
  - *Mycobacterium tuberculosis*

- Epidemiology
  - TB is the 2nd leading cause of death worldwide – 8.6 million people diagnosed, 1.3 million died in 2012
  - Skin involvement is rare: 1-2% of all cases

- Clinical
  - Tuberculosis verrucosa cutis – warty plaques on the extremities from direct inoculation (“prosector’s wart” or walking barefoot where pulmonary-TB infected patients have expectorated contaminated sputum)
  - Lupus vulgaris – red-brown papules coalesce to plaques with gelatinous quality
  - Scrofuloderma – suppurating nodule over affected lymph nodes with ulcerating fistulae
  - Miliary tuberculosis – discrete minute red-to-violaceous papulopustules
  - Rare forms: tuberculosis cutis orificialis, tuberculuous gumma, tuberculous chancre
  - Tuberculid reactions:
    - Lichen scrofulosorum: grouped lichenoid papules
    - Papulonecrotis tuberculid: dusky papules with central necrosis
    - Erythema induratum: painful ulcerated nodules on posterior legs
    - Nodular tuberculid: bluish-red nodules on legs
    - Nodular granulomatous phlebitis: subcutaneous nodules along leg veins

- Histologic
  - Tuberculoid granuloma with central histiocytes, giant cells, and rim of lymphocytes; usually with caseation necrosis (plus calcification and fibrosis)
  - Caseation necrosis should make one consider infectious causes of granulomatous inflammation

Treatment
  - Multiple drug treatment: refer to CDC – 8wks daily INH, rifampin, pyrazinamide, and ethambutol or streptomycin, then 16 weeks of INH and Rifampin
Leprosy

- **Pathogenesis**
  - *Mycobacterium leprae*

- **Epidemiology**
  - WHO estimate: 220,000 new cases per year, likely underreported. 200/year in the US (Travel, Gulf coast – armadillo)

- **Clinical**
  - Manifestations vary by immune response
    - Polar tuberculoid (TT) – few macules/patch, sharp margin, usually reduced sensation
    - Borderline tuberculoid (BT) – many macules/patches, sharp margin, reduced sensation
    - Mid-borderline (BB) – macules plaques, both sharp margins and diffuse, reduced sensation
    - Borderline lepromatous (BL) – multiple plaques and nodules, widespread, sensory loss in some
    - Lepromatous leprosy (LL) – plaques, papules, nodules, thickening, widespread, sensory loss in some

- **Histologic**
  - Varies by immunologic response from well-organized epithelioid granulomas involving nerves with rare necrosis, to disorganized aggregates of lymphocytes and histiocytes or sheets of histiocytes; neurotropism is a key feature in all

- **Treatment**
  - Varies by disease type – dapsone, rifampin, and clofazimine are mainstays; often 1-2 years of treatment

**Caseating Granulomas:**
Atypical mycobacteria

• Pathogenesis
  – Nontuberculous mycobacteria (NTM) include over 170 species, can often cause skin and soft tissue infections (SSTI)
  – Divided into rapidly growing and slow growing mycobacteria
  – RGM: *M. fortuitum*, *M. chelonae/abscessus*, *M. mucogenicum*, *M. smegmatis*, and early pigmenting RGM
  – SGM: *M. marinum*, *M. ulcersans*, *M. kansasii*, *M. haemophilum*, *M. avium complex* and more

• Epidemiology
  – NTM are ubiquitous – water, soil, plants, animals; tap water is a major reservoir, can contaminate hospital equipment – pedicure/nail salon outbreaks

• Clinical
  – Varies by species – generally for dermatologists can be disseminated disease (skin seeding in severely immunocompromised patients) or primary skin and soft tissue infection (in suppressed or normal hosts)
  – Disseminated disease (HIV, organ transplant, iatrogenic suppression, leukemia): red, draining nodules, ulcerations, abscesses
  – SSTI: sporotrichoid nodules, “fish-tank” granuloma, Buruli ulcer, abscesses, cellulitis, sinus tracts, panniculitis, etc

• Histologic
  – May vary somewhat by organism and clinical morphology; generally intense granulomatous inflammation with neutrophils and necrosis; organisms may be seen on special stains, but cultures and sometimes PCR is necessary to ID

• Treatment
  – Varies by organism type; most require multidrug therapy and can develop resistance rapidly to single agents.
  – Cultures may be slow to grow but should be performed for antibiotic sensitivities (although educated guesses can be made once speciation is available)
  – Most cases should be co-managed with an infectious disease doctor
  – Local surgical treatment is indicated in some cases
Leishmaniasis

• Pathogenesis
  – Leishmania infection – multiple species, divided into “New World” (Western) and “Old World” (Eastern Hemisphere)
  – Transmitted through bite of female sandfly
  – 4 types: cutaneous leish, diffuse cutaneous leish, mucocutaneous leish, and visceral leish

• Epidemiology
  – 12 million infected, 2 million new cases per year, 20-30,000 deaths annually

• Clinical
  – Subclinical, self-healing disease is common
  – Cutaneous lesions: solitary papules at bite site, enlarge into nodules/plaques, often ulcerate (painless); may have satellite lesions, multiple primary lesions, or sporotrichoid spread
  – Patients can have persistent leish in healed scars and lymph nodes, and can get delayed mucocutaneous disease depending on the organism and immune response

• Histologic
  – Ulceration, intense dermal inflammation with variable granulomas and histiocytes; histiocytes with small organisms
  – Confirmatory PCR testing is available through the CDC and speciation can impact follow-up and treatment

• Treatment
  – High cost, toxicity, drug resistance, access issues, paucity of high quality data all complicate treatment
  – Drugs are available through the CDC and patients should be treated in conjunction with an ID doctor
  – Stibogluconate, amphotericin, liposomal ampho, or miltefosine
  – Pentamidine, other agents pending intolerance/response
  – Need long-term follow up of all patients
Deep fungal infections

• Pathogenesis
  – Generally due to Blastomycosis, coccidioidomycosis, Cryptococcus, histoplasmosis, and sporotrichosis

• Epidemiology
  – Most are acquired through inhalation and secondary spread to the skin; direct inoculation can occur
  – Blastomyces: Ohio/Mississippi river valleys
  – Coccidioidomycosis: San Joaquin Valley, SW US (incidence and area increasing due to climate change)
  – Cryptococcus: Pigeon droppings/soil, widespread, seen usually in immunocompromised hosts
  – Histoplasmosis: Contaminated soil/bat-bird droppings, caves, often seen in immunocompromised hosts
  – Sporotrichosis: Rose thorns, moss, other contaminants, causes infection from direct inoculation

• Clinical
  – Varies by infectious agent; many can cause nodules, papules, ulcerated, and/or verrucous/crusted lesions
  – Characteristic lymphocutaneous spread seen in sporotrichosis

• Histologic
  – Often a dense mixed infiltrate with neutrophils, histiocytes, giant cells and acute granulomas with overlying pseudoepitheliomatous hyperplasia
    – Blastomycosis – large yeast with broad based, single bud
    – Coccidioidomycosis – thick-walled spherule with endospores
    – Cryptococcus – small narrow-based budding yeast forms
    – Histoplasmosis – very small narrow-based budding, intracellular
    – Sporotrichosis – round/cigar-shaped yeast, rarely visualized (may need EM)
Deep fungal infections

- Treatment
  - Varies by organism
  - All patients should be evaluated for potential immunosuppression, and in most cases skin findings represent likely secondary seeding from a systemic process (particularly for cryptococcus)
  - Treatment should be conducted in consultation with an infectious disease physician and tailored towards the individual infection
  - Itraconazole, amphotericin, voriconazole, posaconazole, debridement all have a role
Blastomycoses like-pyoderma

- Pathogenesis: Abnormal rxn to bacteria, often Staph, in immunosuppressed pts
  *Must exclude: SCC, Deep fungal, Atypical Mycobromoderma, iododerma*
- Clinical: Verrucous to vegetative plaques with pustules and elevated border
- Histology: PEH and abscesses
- Treatment:
  1. Cultures to determine cause & guide antibiotic Tx
  2. Other: acitretin, CO2 laser, cryotherapy, curettage

Bacterial causes:

- S. aureus/Beta-hemolytic streptococci
- E.coli/Proteus/Pseudomonas
- Clostridium perfringens/Prevotella
Granuloma inguinale

• Pathogenesis: STI from *Klebsiella granulomatis*
• Epidemiology: Rare in US, more Tropical areas
• Clinical: Beefy to velvety red papules/plaques
• Histology: Dense infiltrate of lymphocytes, neutrophils, plasma cells and histiocytes (with Donovan bodies)
• Treatment:
  – Doxycycline
  – Azithromycin
  – Erythromycin
Suppurative Granulomas

Lymphogranuloma venereum

- Pathogenesis: STI from *Chlamydia trachomatis* (*serovars L1,2,3*)
- Epidemiology: Tropical areas
- Clinical: Rarely seen painless ulceration, f/b painful inquinal adenopathy
- Histology: Lymph node – stellate central necrosis with neuts and palisading granulomatou srxn. + MNGC
- Treatment:
  - Doxycyline
  - Azithromycin
  - Erythromycin
Reference of Choice:

Granulomatous Disorders of the Skin
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Selected Other References:

- **GA**

- **EGCG**

- **NL**

- **RN**
• RGD

• Sarcoidosis

• Cutaneous Crohn’s

• OFG
• Gr R and POD
• XG
• AOAPXG
• NXG
• MR
• RD

• XD
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• Leishmaniasis