Scratch That Itch in HIV

Scabies, Psoriasis, Eosinophilic Folliculitis and Atopic Dermatitis

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Scratch That Itch in HIV
Scabies, Psoriasis, Eosinophilic Folliculitis and Atopic Dermatitis: Goals

- Review structure of the skin
- Review how to examine the skin
- Review causes for itchy skin especially in HIV
- Illustrate clinical cases
- Share important pearls for care for these common skin conditions

Skin Anatomy

- Three layers:
  - The epidermis
  - The dermis
  - The subcutaneous tissues
- Four primary adnexal structures
  - hair follicles
  - sebaceous glands
  - apocrine glands
  - eccrine glands
- Mucous membranes

What is Skin?

- Largest organ of the body
- Helps keep out chemical /toxins/microorganisms
- Helps retain moisture and chemicals
- Diffuses excess heat
- Protects from harmful effects of sun
- Permits sensations (touch, pain, temperature)
- Complex organ - social, sexual, and political significance
- Produces vitamin D

Skin Examination

- Important to be organized
- Make patient comfortable
  (drapes and curtains)
- Good lighting in room
- Get lots of lights on the subject
- Have both doctor and patient in comfortable position
- Practice universal precautions

Routine Skin Examination

- Head and scalp including hair
- Skin of face, neck, arms, legs, back, chest, stomach
- Moist lining of eyes, nose, mouth and genital area
- Nails

Pitfalls of the Skin Examination

- If you don't look, you can't see it
- If it is covered, it can't be seen
  - Undress the patient, remove shoes, remove appliances
- Moisture alters the appearance (water, creams, oils)
- Minor trauma alters primary morphology
- Limited reaction patterns
- Tests (KOH, bacterial, fungal and viral studies, biopsies, x-rays serologic test…)

Classic Scabies

- Highly contagious
- Intense nighttime itching
- An erythematous papular eruption, serpiginous burrows hives, tiny bites, knots, or pimples
- May resemble eczema or sores

Scabies

- Parasitic mite infection; *Sarcoptes scabiei var. hominis*
- >300 million cases world-wide
- Transmitted via close intimate or personal contact
- Vesicle at end of fine wavy lines (represent the excreta-soiled burrows in stratum corneum)

Scabies

- Diagnosis: clinically or made by demonstration of mite or scybala
- May take one month to present
- Sites of predilection: finger webs, volar wrists, lateral fingers, extensor surfaces of, knees, waist, navel, abdomen, buttock or belt line, nipple and genitals
- Clinical variants: Classic, crusted scabies, nodular scabies, and bullous scabies

Norwegian (Crusted) Scabies

- Massive infestation
- *Sarcoptes scabiei* var *hominis*
- Inadequate host response
- Millions of parasites colonize the epidermis inducing a hyperplastic response
- Immunocompromised hosts face, scalp neck and trunk can be affected
- Many mites burrows in the skin, the rash and itch become severe

Treatment of *Sarcoptes scabiei*

- Permethrin 5% cream (Elimite®)
  - apply from the neck down, under nails and foreskin
  - and washed off the next day; repeat in 7-10 days;
  - retreat all recurrences
  - safe for infants and pregnant women
- Lindane (gamma benzene hexachloride) (Kwell®)
  - apply as for Permethrin; neurotoxic _→ seizures in infants, small children and pregnant or nursing women
- Precipitated sulfur in petrolatum (hs x 3)
- Ivermectin 3 mg x 3 tabs repeat 1-2 weeks
- Use concomitant topical steroids x 2 weeks
  and systemic antihistamines x 1 month

Crusted Scabies - Treatment

- Combined repeated treatment is necessary
- Permethrin cream daily x 1 week then twice weekly till healing
- Ivermectin 3 mg x 3 tabs on days 1, 2, 8, 9, 15 and possibly 22, and 29
- Urea, salicylic acid or mechanical debridement

Scabies: Adjunctive Therapy

- Simultaneous treatment of all close contacts
  - Family members, caregivers
- Decontamination
  - Machine wash all textiles in warm to hot water x 35 min
  - Store remaining clothing, shoes, stuffed animals x 3-4 days at room temperature or freezing temperature x 5 hours
  - Clean all contact surfaces
  - Vacuum upholstered furniture, cushions, beds mattresses, carpets, floors and car seats
  -

Scabies: Treatment Failures

- Permethrin resistance - controversial
- Errors in application - common
- Inadequate or lack of repeated therapy
- Imperfect compliance
- Reinfestation (incomplete decontamination)
- Lack of simultaneous treatment of contacts

Sunderkotter C et al. Dtsch Arztebl Int 2021; 118:695-704

Eosinophilic Folliculitis

- Chronic, pruritic recurrent dermatosis
- No known etiology
- Folliculotropic inflammatory infiltrates with eosinophils in the dermis
- Seborrheic areas
  - Women -excoriated papules on face
  - Men - trunk

Eosinophilic Folliculitis
Clinical Presentation

- Classical
- Infantile
- Immuno-suppression associated with HIV or malignancies
- HIV-EF → unremitting pruritus, palms and soles are spared and leucopenia

Eosinophilic Folliculitis
Treatment

- **Treatment is unsatisfactory**
- Intiat combined antiretroviral therapy (HAART)
- Topical tacrolimus and steroids
- UVB radiation
- Topical ketoconazole, metronidazole, permethrin
- Systemic treatments: indomethacin, tetracyclines and itraconazole

Nomura T, et al. Eosinophilic pustular folliculitis: a proposal of diagnostic and therapeutic algorithms. *J Dermatol.* 2016;43(11):1301–1306.

Psoriasis
Clinical presentation

- Chronic, immune mediated, inflammatory dermatosis
- Sharply demarcated papules and plaques
- Red (inflammation) and silvery plaques (Accumulation of stratum corneum/keratin & scaling)
- Increased epidermal proliferation
- Multiple variants (chronic plaque, erythrodermic, guttate, pustular, inverse and nail)

Psoriasis

Epidemiology

- All races, Worldwide prevalence ~2%, but…
  - 4-5% US, Canada; 2% Europe
  - Lower in Africans, African-Americans, Asians
  - Extremely low in native American Indians
- Male = female
- Bimodal onset: 20-30 & 50-60 years old
- Genetic predisposition:
- 2 affected parents: 41%, 1 parent: 14%, 1 sibling: 6%
- Polygenic: over 10 genes linked to psoriasis

Psoriasis

Physical Examination

- Scalp, elbows, and knees are classic sites
- Intergluteal cleft is a common site
- Rarely entire skin surface is affected ➔ red man or erythrodermic

Psoriasis

Genetic Predisposition

- ~ 40% of individuals with psoriasis or psoriatic arthritis have + family history (HLA-B17 and HLA-Cw6)

Psoriasis
Typical Clinical Appearances

- Nail involvement ~ 50% of patients
  - Pitting, oil spot, onycholysis, hyperkeratosis

Psoriasis

Pathogenesis

- Genetic predisposition
- Unknown precipitating factors --> unmask
- An increased number of dividing cells in the epidermis
- Cellular turnover is increased sevenfold and decreased from the normal 28 days to 3 or 4 days
- Cells accumulate --> characteristic scale

Psoriasis

History

- May occur at any age from age of 1 to 80 years
- Onset is usually gradual
- Positive family history in one-third of patients
- Precipitated by infection (strep, HIV), pregnancy, trauma (Koebner (25%), smoking or stress (hard to document)
- Some drugs that aggravate psoriasis: lithium and Beta blockers, steroid withdrawal, NSAIDs, interferon, antimalarials*

*Cullen G, Kroshinsky D, Cheifetz AS, Korzenik JR. Psoriasis associated with anti-tumor necrosis factor therapy in inflammatory bowel disease: a new series and a review of 120 cases from the literature. *Aliment Pharmacol Ther*. 2011;34(11-12):1318-1327.

Clinical Signs of Chronic Plaque Psoriasis

- The Koebner phenomenon - the development of skin disease at sites of skin trauma; it can also be seen in other dermatologic disorders such as lichen planus and vitiligo
- Auspitz sign - visualization of pinpoint bleeding after the overlying scale is removed from a plaque

Psoriasis
Systemic Considerations

- Cardiovascular events: MI's, stroke, mortality
- Obesity
  - Increased risk of onset of psoriasis
  - Increased body surface area
  - Increased risk of psoriatic arthritis (PsA)
  - Increased risk of cardiovascular disease
- Depression
- Obstructive sleep apnea
- Uveitis
- NASH (nonalcoholic steatohepatitis)
- Metabolic syndrome (Hypertension, diabetes, dyslipidemia, obesity)

Psoriatic Arthritis

- Seronegative spondyloarthropathy
  - Synovial inflammation → degeneration of joint structures
  - Proinflammatory mediators (TNF-alpha, IL-1, IL-6, IL-17, and others)
- Clinical features
  - Joint pain, effusion, erythema and warmth
  - Joint stiffness (am > 45-60 min)
  - Presence of systemic symptoms (fatigue, fever…)

Psoriasis
Differential diagnosis

- Dermatophyte (tinea) infection
- Seborrheic dermatitis
- Eczema
- Secondary syphilis
- Pityriasis rosea

Psoriasis
Laboratory and Biopsy

- Characteristic changes
  - Hyperkeratosis
  - Epidermal hyperplasia
  - Dilated tortuous vessels in the papillary dermis
  - Inflammatory infiltrate with neutrophils extending into the epidermis

Psoriasis
Laboratory and Biopsy

- Hyperkeratosis
- Epidermal hyperplasia
- Dilated tortuous vessels in the papillary dermis
- Inflammatory infiltrate with neutrophils extending into the epidermis
- Resembles geographic tongue

Psoriasis
Goals of Therapy

- Decrease epidermal proliferation and dermal inflammation
- DOC are topical regimens especially corticosteroids (CS)
- Topical therapy used to treat moderate psoriasis; Used alone or in conjunction with phototherapy and systemic therapy
    - Ointments most effective; foams and sprays for large areas; alcohol base may burn

Psoriasis

Topical Therapy

- Corticosteroids – first line of treatment
- Vitamin D analogs
- Tazarotene
- Topical tars
- Risks – adrenal suppression - rare – increased with super potent steroids and large body surface
- Atrophy of epidermis and dermis, telangiectasias and irreversible striae – prolonged periods or under occlusion; large quantities or on face or intertriginous areas
- Responds to systemic steroids however disease may rebound badly

Psoriasis

Topical Therapy

- Calcipotriene – synthetic vitamin D_3 analog
  - As effective as mid strength corticosteroid
  - Well tolerated; burning and itching; hypercalcemia rare; Pregnancy category C (fetotoxicity in animals; no adequate studies in women) for use in pregnancy
- Calcipotriene/Betamethasone/Dipropionate ointment
  - More effective than either alone; Well tolerated
  - Suspension formulation for scalp
- Tazarotene – an acetylated retinoid
  - Therapy may continue after treatment is stopped
  - Synergistic effect with topical corticosteroids
  - Erythema, burning, pruritus, peeling, increased sunburn
  - Cream better tolerated than gel

Psoriasis

Systemic Therapy

- Moderate to severe disease
  - Phototherapy (ultraviolet light)
  - Methotrexate, cyclosporine and acitretin*
  - Etretinate (Vitamin A derivative)
  - PUVA (Psoralen plus ultraviolet light A (UVA)

  - Gastric Bypass reduced inflammation and reduced obesity

  - * Relative lack of efficacy and side effect profile (falling out of favor)

Psoriasis

Systemic Treatments

- Ustekinumab (Stelara) blocks interleukin IL-12 and IL-23 which help activate certain T-cells
- Apremilast (Otezla) - oral PD-4 inhibitor
- Other targets include TNF alpha, IL-17
- Many indicated to treat psoriatic arthritis

- Newer therapies
  - >10 biologic agents indicated for psoriasis
  - Favorable safety profile and better efficacy
  - All require an annual tuberculosis evaluation
  - All with variable efficacy (but > traditional therapies

Seborrheic Dermatitis

Definition

- Common (5% of adults) inflammatory papulosquamous condition
- Waxing and waning course
- Bilateral and symmetrical
- Superficial, greasy scale on erythematous base
- Demographics
  - Infants: self-limited eruption
  - Adults: chronic eruption
  - In patients with darker skin, hypopigmentation is common
  - Associated with Parkinson's disease and AIDS/HIV

Seborrheic Dermatitis

- Infants and adults
- Presentation differs
- “cradle cap” in infants

Seborrheic Dermatitis

Pathophysiology

- Etiology is complex but may be related to Pityrosporum ovale, a lipophilic yeast that makes up part of the normal adult cutaneous flora. It is commonly a saprophyte but rarely can be an opportunistic pathogen
- Some cases may overlap with psoriasis

Seborrheic Dermatitis

Dandruff (pityriasis sicca)

- Prevalence: 46-83% of HIV + patients vs 3-14% in controls (exc Parkinson)
- Recurrent symmetric scaling eruption
- Overgrowth of *Pityrosporum ovale*
- Treatment, topical antifungals and low potency steroids
- D/dx: atopic dermatitis, mycosis fungoides, tinea capitis

Seborrheic Dermatitis Clinical Involvement

- Scalp, mid face/eyebrows/ nasolabial creases, central chest and upper trunk, groin and intertriginous areas (axilla, groin, buttocks, inframammary folds)

Seborrheic Dermatitis

Therapy

- Antiseborrheic shampoos are the mainstay of treatment for scalp involvement
  - Salicylic acid selenium sulfide, tar, pyrithione zinc, ketoconazole
- Topical steroid lotion for hairy areas; cream for non hairy skin
- Antifungal creams or oral antifungals in conjunction with steroids

Atopic Dermatitis (eczema, atopic eczema)

- Common chronic relapsing and remitting
- Pruritic inflammatory skin disease
- 10% lifetime prevalence
- Begins in childhood 10-20% of children and most clear 70-80% resolve by adolescence
- High association with food/environmental allergies, asthma and allergic rhinitis
- Twice as likely to develop ear infections, streptococcal pharyngitis and UTI's

Atopic Dermatitis
Pathogenesis

- Multifactorial
  - Genetic, immunologic and environmental factors
  - Family history of atopy and mutations in filaggrin gene (monomers compromise the epidermal barrier→ allergens, irritants and bacteria trigger a hyperimmune response; increased IL-4 and Interleukin 13 drives the T-helper 2 immune response –Skin barrier impairment

Atopic Dermatitis

Pathophysiology

- Filaggrin mutation in AD → Impaired skin barrier function
  - Loss of function mutation in filaggrin → impaired skin adhesion, elevated pH, disorganization of s. corneum, increased transepidermal water loss and increased skin permeability
- Upregulation of T helper cell 2 (Th2) type immune responses
  - Overproduction of IL-4 and IL-13 and increased IgE antibody production are key components of Th2-mediated inflammation

Atopic Dermatitis

Physical Examination

- Infantile --> Acute to subacute eczema with papules, vesicles, oozing and crusting the head, the diaper area, and the extensor surfaces of the extremities
- School age --> chronic dermatitis with lichenification and scaling
- Adult --> neck, face, upper chest and the antecubital and popliteal fossae
- Generally dry skin, an infraorbital fold, and increased linear markings on the palms

Atopic Dermatitis

Therapy

- Daily to BID emollient (fragrance free) use
  - Retain and replenish epidermal moisture;
  - Reduce severity; prolong intervals % flares
  - Ointments > creams > lotions
- Regular bathing with tepid or lukewarm water
- Limit to 5-10 minutes
- Soap free, dye free and fragrance free
- Pat to dry and seal in moisture
- Dilute Bleach baths ½ c per 40 gal
- Room humidifier

Atopic Dermatitis
Therapy

- Topical corticosteroids (CS) BID → inflammatory immune response
  - Tailor to sites and extent of involvement
- Topical calcineurin inhibitors
  - Second line alone or in conjunction with CS
  - Steroid sparing immune modulators (face and flexures)
  - Tacrolimus (Protopic)and pimecrolimus (Elidel)
  - not skin atrophy; burning on application; black box warning

Atopic Dermatitis

Therapy

- Ultraviolet light and phototherapy (NBUVB
  - Reduces inflammation with limited side effects
- Systemic immunomodulators (cyclosporine (Sandimmune) and azathioprine (Imuran) off label for severe flare-ups
  - Antibiotics – oral not recommended
  - Oral antihistamines - short term severe sleep disturbances
  - Benadryl or hydroxyzine
  - Integrative medicine* - lack evidence
  - *Evening primrose oil, oral borage oil, probiotics and St Johns wort

Atopic Dermatitis
Therapy

- Crisaborole (Eucrisa) topical steroid sparing PD-4 inhibitor BID; costly
- Dupilumab (Duprixent) injectable monoclonal ab decreases inflammatory response and skin barrier impairment by blocking iL-4 and IL-13 expression

Atopic Dermatitis
Therapy

- Psychosocial comorbidities
  - Disrupted sleep
  - Attention deficit hyperactivity
  - Depression
  - Suicidal ideation
- Severe antibiotic-resistant infection
- Important to incorporate shared decision-making practices into patient care
- Infants and children with severe AD are more likely to develop BCC's and SCC's; almost 50% reduction in risk of melanoma

Atopic Dermatitis
Complications

- Infections
  - Bacterial - *staphylococcus aureus* and beta-hemolytic streptococcus
  - HSV- eczema herpeticum - highly morbid meningitis and even death
- Postinflammatory scars
- Lichenification

Kaposi Varicelliform Eruption
Eczema Herpeticum

- high morbidity c
- In patients with preexisting dermatitis (usually atopic dermatitis)
- Co-infection with (HSV > Coxsackie > others)
- Presents as vesicular or ulcerated eruption
- Eruption can be severe, progressive and may result in disseminated infection and death if unrecognized or untreated!!

In Summary

- Reviewed disorders of importance when caring for HIV positive patients
- Presented clinical and histologic findings
- Discussed diagnostic features
- Shared some treatment options
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