PSORIASIS AND OTHER PAPULOSEQUAMOUS SKIN DISEASES

Overview

Papulosequamous Skin Diseases: papules or small red bumps and scaling on the surrounding skin surface. It also includes other disorders such as Pityriasis rosea, parapsoriasis and lichen planus ----ect.

PSORIASIS

it is a common, chronic inflammatory and proliferative disorder of the skin, clinically manifested as well-circumscribed, erythematous papules and plaques covered with silvery scales typically located over the extensor surfaces and scalp.

Prevalence: World-wide occurrence; **0.1 % to 3 %**

Age of Onset: may begin at any age (15 and 30 years mostly)

Bimodal peaks: *Early onset. Late onset*

Sex: males = females.


very low incidence or absence: in North and South American Indians.

AETIOLOGY AND PATHOGENESIS:

Cause of psoriasis is not fully understood, but it is believed to have a **genetic component** and local psoriatic changes can be triggered by an injury to the skin known as the Koebner phenomenon.

Various environmental factors have been suggested as aggravating psoriasis, including stress, withdrawal of systemic corticosteroid, But few have shown statistical significance

Genetic factors:

thought polygenic.

twin studies and analysis of pedigrees.

HLA system: psoriasis significantly associated with.: HLA Cw6, B13, B16, and B27.

Proventing factors:

1. Trauma
2. Infection
3. Drugs.
4. Sunlight .
5. Stress .
6. Smoking
7. Alcohol
8. Endocrine .

PATHOGENESIS

The most obvious abnormalities in psoriasis are

(1) **an alteration of the cell kinetics of keratinocytes** with a shortening of the cell cycle from 311 to 36 h, resulting in 28 times the normal production of epidermal cells
Psoriasis is a T cell–driven disease. There are many CD8 + T cells present in psoriatic lesions surrounding the upper dermal blood vessels, and the cytokine spectrum is that of a TH1 response.

Clinical Features
Skin Lesions
- Sharply demarcated papules and plaques
- Non-coherent silvery scales
- Auspitz sign → bleeding upon removal of scale
- Koebnerization seen in 20%
- Woronoff Ring: Area of blanching around psoriatic plaques.

CLINICAL VARIANTS
Psoriasis Vulgaris /Chronic Stationary plaque
Most frequent. Red, scaly lesions persist for years.
Little alteration in shape/distribution of plaques.
Areas of predilection: elbows, knees, scalp, retroauricular region, lumbar, umbilicus
**Guttate (Eruptive) Psoriasis:** Is commoner in childhood. Acute eruption of drop-shaped lesions distributed widely over the body. Streptococcal throat infection frequently precedes eruption.

**Flexural psoriasis:** Lesions are present over the flexors and intertriginous areas (axilla, groin, umbilical region, inframammary folds) the lesions may be moist and lack the typical scaling.

**Pustular psoriasis.** May be **localized** or **generalized**.

Localized pustular: Persistent pustular eruptions of the hands and feet. Systemic symptoms absent

Generalized pustular: Von Zumbusch type; acute variant.

Psoriasis may occur as an explosive eruption of generalized pustules with systemic disturbances. This may follow withdrawal of systemic steroid therapy or application of irritants.

**Arthropathic psoriasis.** Arthritis may accompany any variety of psoriasis in about 10% of patients.

Psoriatic arthritis may take several forms. The commonest type is **asymmetrical oligoarthritis**.

Other types are: symmetrical seronegative rheumatoid-like disease, distal interphalangeal involvement (most characteristic, but relatively rare), axial skeletal involvement, and a destructive mutilating form (arthritis mutilans)

**Erythrodermic psoriasis.** Psoriasis may present with erythroderma (exfoliative dermatitis) There is generalized inflammatory erythema with profuse scaling

**PSORIATIC NAIL DISEASE**

- May be of nail matrix or nail bed origin
- Fingernails > toenails
- Nail changes more frequent (80-90%) in patients with arthritis
- Psoriatic nail changes of **matrix → pits**
- Psoriatic nails changes of nail bed origin include:
  1. “oil spots,”
  2. onycholysis,
  3. subungual hyperkeratosis,

**PATHOLOGY:**

**Epidermis:**

Hyperkeratosis with parakeratosis (nuclei retained in the st. cor.) of st. corneum. Reduced or absent granular layer.

Acanthosis with elongation of rete ridges and a corresponding upward elongation of dermal papillae.

Infl. Cells (PMNs) in the upper epidermis forming collections called ‘microabscess of Munro’.

**Dermis:**

Infl. Cells in the dermis (lymphocytes + monocytes)

Upper dermal vasculature shows dilatation and tortuosity
DIAGNOSIS AND DIFFERENTIAL DIAGNOSIS

Diagnosis is made on clinical grounds.

**Acute Guttate Psoriasis:**

Any maculopapular drug eruption, secondary syphilis, pityriasis rosea.

**Small Scaling Plaques:**

1. Seborrheic dermatitis
2. Lichen simplex chronicus —may complicate psoriasis as a result of pruritus.
4. Tinea corporis —KOH examination is mandatory, particularly in single lesions.
5. Mycosis fungoides —scaling plaques can be an initial stage of mycosis fungoides.

**Large Geographic Plaques:**

Tinea corporis, mycosis fungoides.

**Scalp Psoriasis:**

Seborrhieic dermatitis, tinea capitis.

**Inverse Psoriasis:**

Tinea, candidiasis, intertrigo, extramammary Paget disease.

**Nails:**

Onychomycosis. KOH is mandatory

**TREATMENT**

**Topical**

**Phototherapy**

**Systemic agents.**

These are used either alone or in combinations.

**TOPICAL TREATMENT**

**Topical Glucocorticoids**

**Anthralin (topical)**

- Possesses antiproliferative activity on human keratinocytes
- Also, strong anti-inflammatory effects by inhibiting PMNs and monocytes
- Irritant reactions, especially after increasing concentration too fast
- Can stain hair to purple
- Brownish discoloration of surrounding skin—reversible

**Vitamin D3 Analogues**

- Calcipotriol, calcitriol
- Inhibit keratinocyte proliferation and induce terminal differentiation
- Anti-inflammatory
- Used for plaque-type psoriasis
- Calcipotriol inactivated by salicylic acid or lactic acid
- Should be used after UV-light (calcipotriol absorbs UV)
- Local irritation
Tazarotene

- Retinoid
- Reduces scaling and plaque thickness, with little effectiveness on erythema
- May be beneficial in combination with phototherapy

Tar:
- Unknown activity
- 2-5% tar in various bases effective in chronic plaque-type ps

PHOTOTHERAPY

Phototherapy is used in the cases of extensive, widespread disease resistant to topical treatment.

1. UVB – Ultraviolet irradiation (290-320 nm wavelength)
   - Broadband UVB (BB-UVB), it is used alone or combined with one or more topical treatments. The Goeckerman regimen uses coal tar followed by UVB exposure.
   - The Ingram method is based on anthralin application following a tar bath and UVB treatment.

Narrowband UVB (NB-UVB; 310-331 NM): is now increasingly used for its effectiveness and low potential for photodamage.

2. PUVA = psoralen + UVA (320-400 nm)
   - Psoralen a photosensitizing drug (8-methoxypsoralens) is given orally, followed by UVA to treat patients with more extensive disease.
   - Mode of action: PUVA, decreases cellular proliferation by interfering with DNA synthesis, and also induces a localized immunosuppression by its action on T lymphocytes.
   - DOSE: usually is given 2-3 times per week on an outpatient basis.

Side effects of PUVA therapy include:
- acute SE: include, nausea, pruritus, and burning.
- long-term complications: include increased risks of photo damage and skin cancer.

PUVA has been combined with oral retinoid derivatives to decrease the cumulative dose of UVA radiation to the skin.

3. EXCIMER LASER (308 NM)

SYSTEMIC TREATMENT

Methotrexate

Synthetic analog of folic acid that competitively inhibits dihydrofolate reductase enzyme
- Inhibiting S-phase of cell cycle (like hydroxyurea) leading to inhibition of purine and pyrimidine synthesis. Also anti-inflammatory
- Start with a test dose of 2.5 mg (average range, 10-15 mg weekly; maximum, 25-30 mg weekly)
- Hepatotoxicity, chronic use may lead to hepatic fibrosis. Fetal abnormalities or death, myelosuppression, pulmonary fibrosis, severe skin reactions.
- Rarely, severe opportunistic infections
- Baseline CBC and LFTs. Monitor CBC and LFTs weekly until target dose is achieved, then every 4-8 wk
- Liver biopsy every 1.5 g of cumulative dose or use procollagen III assay.
- Also effective in treating psoriatic arthritis

Contraindications: Absolute: Pregnancy, lactation. Relative: Hepatic dysfunction, hepatitis, renal insufficiency
**Cyclosporine**

- Inhibits release of cytokines, specifically IL-2, by binding and deactivating calcineurin
- Use: Effective in erythrodermic and generalized pustular psoriasis
- Start at 2.5 to 4 mg/kg per day.
- Renal impairment (often reversible) $\rightarrow$ reduce dosage by 25% if creatinine increases to 30% or greater of baseline.
- Hypertension (Treat with ACE-inhibitors)
- Elevated triglycerides
- Hyperkalemia
- Hepatotoxicity
- Hypertrichosis (common), gingival hyperplasia, trichomegaly, nausea, vomiting, diarrhea, arthralgia, myalgia, tremor, acne, sebaceous hyperplasia, and fatigue may occur
- Long-term risk of malignancy
- Metabolized by P450, thus erythromycin or ketoconazole will increase drug levels

**Retinoids $\rightarrow$ Acitretin**

- Vitamin A derivatives
- Effective in pustular and palmoplantar forms of psoriasis
- Acitretin is most commonly used, given at 25 mg per day initially

- **Restrict use in women of childbearing age**
  - Regulate growth and terminal differentiation of keratinocytes; modulate transcription of specific genes through retinoid response elements
  - Show lower response rates than other systemic modalities for treatment of plaque-type psoriasis $\rightarrow$ often ineffective as monotherapy for plaque-type psoriasis
  - Effective when combined with ultraviolet phototherapy (either UVB or PUVA)
  - Treatment over 3-4 months necessary
  - Dose related adverse effects: cheilitis, sicca symptoms of eyes and mouth, generalized pruritus, dry skin, loss of stratum corneum of palms and soles, hair loss
  - Muscle and joint pain
  - Elevation in serum lipids, and also LFTs
  - Monitor liver and kidney function, blood glucose, lipid profile
Biologic Agents
Like: • Etanercept, • Efalizumab, • Alefacept
• Infliximab

Combination Therapies
Often desirable, as combinations can limit the toxicities of individual therapies; examples:
– Topical steroids with UVB or PUVA
– Retinoids with PUVA or narrow band UVB
– Vitamin D analogues with UVB
– Ingram method: coal tar baths, UVB, anthralin
– Methotrexate with UVB
– Methotrexate with cyclosporine
– Etanercept with methotrexate

COMPLICATIONS
Complications are relatively uncommon.
Many of the complications (pustular psoriasis, erythroderma) are commonly due to inappropriate and aggressive therapy.
Psoriatic arthritis.
Pustular psoriasis.
Erythroderma and its metabolic complications.
Infection, particularly Staph. infections of the patches.
Eczematization due to topical agents.
Amyloidosis, rare sequel to arthropathic of pustular psoriasis.
Psychological consequences: depression, anxiety, lack of self-esteem.
Potential complications of systemic therapy should not be overlooked.

PROGNOSIS
The course of plaque psoriasis is unpredictable.
Acute guttate psoriasis appears rapidly, a generalized “rash.”
S.T. this type of psoriasis disappears spontaneously in a few weeks without any treatment.
More often, guttate psoriasis evolves into chronic plaque psoriasis.
The disease rarely is life threatening, but often is intractable to treatment with relapses occurring in the majority of patients.
Both early onset and family history of disease are considered poor prognostic indicators.
Some suggest that stress also is associated with an unfavorable prognosis.
Chronic generalized psoriasis may undergo remission after months or years, recur, and be a lifelong companion.
Chronic generalized psoriasis is one of the causing of embarrassment and a compromised lifestyle.
PITYRIASIS ROSEA (PR)

Age of Onset:
mainly affect children and young adults, but rare in infants and old persons.

Etiology: unknown, but there is good evidence that PR is associated with reactivation of HHV-7 or HHV-6, two closely related β-herpesviruses

Clinically: common, particularly during winter,
Most patients develop one plaque or patch (Herald or Mother patch). It is larger (2-5cm) than later lesions, that will appear after several days, as oval scaly salmon red plaques on the neck, trunk and extremities in “Christmas tree distribution”.

COURSE:
Spontaneous remission in 6–12 weeks or less. Recurrences are uncommon.

MANAGEMENT: Symptomatic:
Oral antihistamines and/or topical antipruritic lotions for relief of pruritus.
Topical glucocorticoids.
UVB phototherapy or natural sunlight exposure.
Short course of systemic glucocorticoids.