Psoriasis Pearls: What to do when the joints respond but the skin does not

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Conflict of Interest Declaration

- Clinical Trials:
  » Abbvie, Novartis

- Speaker’s Bureau:
  » Janssen-Ortho, Abbvie, Amgen, Leo Pharma, Celgene, Novartis

- Consultant / Ad board:
  » Janssen-Ortho, Abbvie, Amgen, Leo Pharma, Celgene, Lilly, Novartis, Cipher
Learning objectives

- Describe the clinical classification
- Recognize mimics
- Therapy for mild-to-moderate psoriasis
  - Canadian Guidelines for the Management of Plaque Psoriasis
- Strategies for challenging body areas – e.g. scalp
- Select treatment strategies appropriate for TNFi resistant skin disease
Agenda

- Types of psoriasis
- Clinical features of scalp and body psoriasis
- Management of psoriasis
- TNFi and psoriasis - Special considerations
- Cases
## Psoriasis: Different forms, different areas

<table>
<thead>
<tr>
<th>Lesion types</th>
<th>Areas affected</th>
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<tbody>
<tr>
<td>Plaque psoriasis (psoriasis vulgaris)</td>
<td>Body psoriasis</td>
</tr>
<tr>
<td>Guttate psoriasis</td>
<td>Scalp psoriasis</td>
</tr>
<tr>
<td>Pustular psoriasis</td>
<td>Palmoplantar psoriasis</td>
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<tr>
<td>Erythrodermic psoriasis</td>
<td>- Plaque type</td>
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<tr>
<td></td>
<td>- Palmoplantar pustulosis</td>
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<tr>
<td></td>
<td>Nail psoriasis</td>
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<tr>
<td></td>
<td>Flexural (inverse) psoriasis</td>
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</tbody>
</table>

Canadian Guidelines for the Management of Plaque Psoriasis, Chapter 3. [1]
Plaque psoriasis

- 90% of all psoriasis cases
- Red, well-defined plaques, silver scales
- Symmetrical
- Common on: elbows, knees, lumbosacral area
- Seen in areas of physical trauma (Koebner reaction)
- Bleed when scale removed (Auspitz’s sign)

Guttate psoriasis

- Acute eruption of scaly, drop-like pink papules on trunk, limbs or face
- Typically in children or young adults

- Onset within 1 to 2 weeks of:
  - Streptococcal pharyngitis
  - Perianal streptococcal cellulitis
- May resolve spontaneously

Mallbris L et al., 2005. [32]
Pustular psoriasis

- Small, uniform sterile pustules
- Can occur as flare - With plaque type
- Pustules sometimes seen on edges of expanding plaques
- Severe form: generalized pustular (von Zumbusch) psoriasis

Erythroderma

- Diffuse, widespread psoriatic patches
- Dermatological emergency:
  - Acute loss of skin’s normal barrier function
  - Risk of dehydration, infection, electrolyte imbalance
  - Potential cardiac and renal complications

Canadian Guidelines for the Management of Plaque Psoriasis, Chapters 3,4. [1]
Scalp psoriasis

- Scalp lesions common along hairline, on face or retro-auricular areas

- Itchy & Visible:
  - Patients report feeling embarrassed, frustrated, depressed

van de Kerkhof PCM and Franssen MEJ, 2001 [28]
Papp K et al., 2007. [14]
Palmoplantar psoriasis

- May be debilitating if it interferes with working or mobility
- Two major forms:
  - Plaque-type psoriasis
  - Palmoplantar pustular psoriasis
- Both poorly responsive to topical therapy

Canadian Guidelines for the Management of Plaque Psoriasis, Chapter 12. [1]
Nail psoriasis

- Disfiguring
- May also be painful or debilitating
- Common alongside psoriatic arthritis
- Resistant to most therapies

Canadian Guidelines for the Management of Plaque Psoriasis, Chapter 10. [1]
Flexural psoriasis

- Well-defined plaques confined to skin folds (inframammary, groin, axillary, genital or natal cleft regions)

- Thin plaques with little scaling and shiny surface
- Can have secondary fissuring/maceration
- Responds to topical CS and TCI (tacrolimus 0.1%)

*Canadian Guidelines for the Management of Plaque Psoriasis, Chapters 3,9.*
Plaque psoriasis varies in appearance

Relatively consistent features:
- Well-defined plaque borders
- Erythematous base
- Silver-white scale
- Symmetric distribution

◆ Variable degree of:
- Scaling
- Erythema
- Induration

Canadian Guidelines for the Management of Plaque Psoriasis, Chapter 1 [1]; Luba KM and Stulberg DL, 2006 [39]; Naldi L and Gambini D, 2007. [38]
DDX  Plaque psoriasis

- Most likely confounders:
  - Nummular (discoid) eczema
  - Cutaneous T cell lymphoma (CTCL)
  - Tinea corporis

- Also consider:
  - Seborrheic dermatitis
  - Pityriasis rubra pilaris
  - Discoid cutaneous lupus
  - Cutaneous lupus erythematosus

Nummular (discoid) eczema

- Well-defined, coin-sized plaques
- Etiology unclear; diverse triggers
- May respond to topical emollients and corticosteroids

Cutaneous T cell lymphoma

- Class of T cell malignancies with diverse presentations & prognosis
- May present with lightly scaly erythematous patches
  - Also nodules or tumours
- Requires biopsy and dermatologist referral

Weenig et al., 2009 [16]
Tinea corporis

- Causal agent: any of several fungi
  - Some identifiable microscopically (skin scraping)
  - Positive ID may require fungal culture
- Topical antifungal treatment

Andrews MD and Burns M, 2008. [17]
Pityriasis rubra pilaris

- Symmetric, salmon-coloured plaques: sharply defined “islands of sparing”
  - Adults: typically starts on scalp or face, spreading caudally
  - Children: may start in lower half of body
- Pruritus/burning in 20% of cases

Discoid lupus erythematosus

- Typically heal with scarring/pigmentary changes
- May progress to systemic lupus

Miettunen PMH et al., 2009. [21] ; Vera-Recabarren MA et al., 2009. [46]
Scalp psoriasis - DDX

Most likely confounders:

- Seborrheic dermatitis
- Tinea capitis
- Lichen simplex chronicus
- Lupus erythematosus
- Contact dermatitis

van de Kerkhof PCM and Franssen MEJ, 2001. [28]
Papp K et al, 2007. [14]
Seborrheic scalp dermatitis

- Erythematous plaques, greasy scale
- Also affects: eyebrows, forehead, nasolabial folds, chest
- Itchy when present on the scalp

Johnson BA and Nunley JR, 2000. [29]
Tinea capitis

- Scaly patches on scalp with localized hair loss
  - May see crusting
  - Pruritus
- Requires systemic antifungals to clear infected hair shafts

Lichen simplex chronicus

- Thickened lesions with distinct border
  - Lichenification caused by chronic rubbing
  - Itchy; may see excoriation
- Found on neck as well as ankles, wrists, forearms, genitalia, scalp

Lotti T et al., 2008. [23]
Does the skin in psoriatic disease matter to Rheumatologists?

- Most patients with psoriatic arthritis have only mild to moderate skin disease based upon surface area.
Most patients with psoriatic arthritis have only mild to moderate skin disease based upon surface area.

Mease Arth Rheumat 52:3279 (2005)
Clinical predictors of PsA

- Population based study - Olmstead County
  - 1633 PsO patients - 57 developed PsA within 10 years

- Higher risk
  - Scalp psoriasis (HR 3.89)
  - Nail disease (HR 2.93)
  - Intergluteal/perianal disease (HR 2.35)

Does the skin in psoriatic disease matter to Rheumatologists?

- Most patients with psoriatic arthritis have significant skin disease in the following areas
  - Scalp
  - Intertriginous (skin folds)
  - Nails
Does the skin in psoriatic disease matter to Rheumatologists?

- Is mild-moderate psoriasis impactful?
- Population-based survey of PsO in US
- Many individuals with little psoriasis at the time of interview considered the disease to be a large problem in everyday life
Is genital psoriasis impactful?

Survey of PsO pts.


<table>
<thead>
<tr>
<th>Table II. Patient characteristics predisposing to genital involvement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Disease characteristics</td>
</tr>
<tr>
<td>Younger age of onset of psoriasis</td>
</tr>
<tr>
<td>Type 1 (onset ≤40 years of age) vs type 2 psoriasis (onset &gt;40 years of age)</td>
</tr>
<tr>
<td>Younger current age</td>
</tr>
<tr>
<td>Male sex</td>
</tr>
<tr>
<td>Circumcision</td>
</tr>
<tr>
<td>Disease severity: % body surface area and PASI score</td>
</tr>
<tr>
<td>Scalp involvement</td>
</tr>
<tr>
<td>Nail involvement</td>
</tr>
<tr>
<td>Axillary involvement</td>
</tr>
<tr>
<td>Infra mammary involvement in women</td>
</tr>
<tr>
<td>Joint involvement</td>
</tr>
<tr>
<td>Body mass index; obesity (BMI &gt;30 kg/m²)</td>
</tr>
<tr>
<td>History of smoking (current or previous); current smoking</td>
</tr>
<tr>
<td>Current systemic therapy (n = 170)</td>
</tr>
<tr>
<td>Current anti-TNF-α therapy (n = 164)</td>
</tr>
<tr>
<td>Current ustekinumab (n = 16)</td>
</tr>
</tbody>
</table>

BMI, Body mass index; PASI, Psoriasis Area and Severity Index; TNF, tumor necrosis factor.
*Statistically significant difference.
Table III. Comparison of quality of life measurements in patients with psoriasis with and without genital involvement

<table>
<thead>
<tr>
<th></th>
<th>Genital involvement</th>
<th>No genital involvement</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>DLQI, mean ± SD</td>
<td>8.7 ± 6.5</td>
<td>4.0 ± 5.5</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>CES-D, mean ± SD</td>
<td>13.8 ± 10.7</td>
<td>11.0 ± 9.2</td>
<td>.01</td>
</tr>
<tr>
<td>RLSS, mean ± SD</td>
<td>26.0 ± 6.4</td>
<td>22.9 ± 5.0</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Sexual function component</td>
<td>13.1 ± 2.7</td>
<td>12.0 ± 2.0</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Frequency component</td>
<td>8.9 ± 3.5</td>
<td>8.0 ± 3.2</td>
<td>.02</td>
</tr>
<tr>
<td>Fear component</td>
<td>3.8 ± 2.0</td>
<td>2.9 ± 1.7</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

CES-D, Center for Epidemiological Studies Depression Scale; DLQI, Dermatology Life Quality Index; RLSS, Relationship and Sexuality Scale.
Nail psoriasis is often debilitating

- Dutch survey respondents with psoriasis (N=1728), 79% reported nail disease.
  - 93% cosmetic problem
  - 52% experienced pain

<table>
<thead>
<tr>
<th>Difficulty</th>
<th>Proportion reporting</th>
</tr>
</thead>
<tbody>
<tr>
<td>Difficulty in daily life</td>
<td>59%</td>
</tr>
<tr>
<td>Professional difficulties</td>
<td>56%</td>
</tr>
<tr>
<td>Difficulty with housekeeping</td>
<td>48%</td>
</tr>
</tbody>
</table>

de Jong EM et al., 1996; Gupta AK and Cooper EA, 2009.
Distribution of psoriasis severity

- Severe: 8%
- Moderate: 25%
- Mild: 65%

Source: National Psoriasis Foundation (random sample of 278 adults with psoriasis)
Topical corticosteroids: First line option for psoriasis

- Many products available for body and scalp psoriasis
  - Differ in dosage, potency, formulation

Canadian Guidelines for the Management of Plaque Psoriasis, Chapter 5. [1]
Ference JD and Last AR, 2009. [18]
Psoriasis - Topicals

- Topical treatments are first line if BSA<5% = 2/3 psoriasis patients
- Potent and ultra-potent CS have good efficacy
  - use is limited by local SE to 2 wks
- Calcipotriol
  - as effective as potent CS
  - less effective than ultrapotent CS
Higher-potency corticosteroids formulated for body and scalp use

<table>
<thead>
<tr>
<th>Corticosteroid</th>
<th>Potency</th>
<th>Brand name (for use on body)</th>
<th>Brand name (for use on scalp)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clobetasol propionate (0.05%)</td>
<td>Ultrahigh</td>
<td>Clobex™ lotion/spray D ermovate® cream/oointment*</td>
<td>Cl o bex® shampoo/spray D ermovate® scalp application</td>
</tr>
<tr>
<td>Betamethasone dipropionate (0.05%)</td>
<td>High</td>
<td>Diprolene® glycol cream/oointment* Diprosone® cream/oointment*</td>
<td>Dip rosone® lotion</td>
</tr>
<tr>
<td>Desoximetasone (0.05%)</td>
<td>High</td>
<td>Topicort® Mild cream/oointment</td>
<td>T o p icort® gel*</td>
</tr>
<tr>
<td>Fluocinonide (0.05%)</td>
<td>High</td>
<td>Lidex® cream/oointment* Ly derm cream/oointment* T i a mol cream* Topactin cream*</td>
<td>L y d e rm® gel T o psyn® gel</td>
</tr>
<tr>
<td>Betamethasone valerate (0.1%)</td>
<td>Mid-potent</td>
<td>Betaderm® cream/lotion/oointment Pre vex® cream Val isone® cream/oointment</td>
<td>R i v asone® scalp lotion* V a l isone® scalp lotion*</td>
</tr>
</tbody>
</table>
Topical corticosteroids

- Vehicles affect both efficacy and patient preference
- Once to twice daily application, depends on vehicle, potency & body site treated, rapid onset of action

- Chronic use, especially with the most potent forms, risks:
  - Tachyphylaxis (loss of efficacy)
  - Irreversible local changes to skin, including atrophy, telangiectasia and striae formation

Canadian Guidelines for the Management of Plaque Psoriasis, Chapter 5. [1]
FerenceJD, Last AR, 2009. [18]
Vitamin $D_3$ analogues

- Calcipotriol is among the first line options for:
  - Mild body psoriasis (cream and ointment)
  - Scalp psoriasis (scalp solution)

- Approved for pediatric use (ages 2 to 14)
  - Not used in combination with other anti-psoriatic therapies

*Canadian Guidelines for the Management of Plaque Psoriasis, Chapters 5, 11. [1]*
Calcipotriol

- Modulates keratinocyte differentiation, proliferation
- Inhibits T cell activity
- Twice daily application, slow onset of action
- Dosage limited by systemic effects on calcium metabolism
  - Can cause irritation; not recommended for facial use; use with caution in flexural psoriasis

Canadian Guidelines for the Management of Plaque Psoriasis, Chapters 5, 11. [1]
DOVONEX® (calcipotriol) Product Monograph [48]
Add emollients

- Restore barrier function to skin lesions, including psoriatic plaques
- Can be ‘steroid-sparing’
- Canadian Guidelines recommend emollient use in combination with medicinal agents
Salicylic acid

Keratolytic agent

- Increases corticosteroid penetration
- Marketed as combination product: Betamethasone dipropionate and salicylic acid (e.g., Diprosalic® and Nerisalic®)

Canadian Guidelines for the Management of Plaque Psoriasis, Chapter 5. [1]
Scalp Treatment

- May be the most difficult aspect of the disease for many patients.
- Treatments must be applied on scalp, not on the hair.
- Caution must be used with topical agents on lesions progressing down onto face.
- Cosmetic acceptability / ease of use important to patients.
Nail Psoriasis Treatment

- Treatment options for nail psoriasis are limited.
- Nail recovery is often refractory to traditional topical, intralesional and some systemic therapies.
- Although various topical and intralesional therapies have been advocated, the use of these therapies is not supported by level 1 evidence.
Moderate to severe psoriasis = Systemics

- Methotrexate:
  - Inhibits DNA replication, suppressing keratinocyte proliferation
  - Modulates T cell function
- Cyclosporin:
  - Immunomodulator; acts on T cells
- Acitretin:
  - Retinoid; regulates keratinocyte differentiation and proliferation

Canadian Guidelines for the Management of Plaque Psoriasis, Chapter 6. [1]
Phototherapy for moderate to severe psoriasis uses – UVB light – Ultraviolet A light (lower energy) with psoralen (PUVA)

Several phototherapy sessions needed per week – Maintain schedule until adequate control – Then discontinue, rely on topical agents

Ultraviolet (UV) light: Effective as monotherapy

Canadian Guidelines for the Management of Plaque Psoriasis, Chapter 6. [1]
UV action spectrum for psoriasis

Reciprocal MED values

Reciprocal lowest effective daily psoriasis healing dose

UVB

- Narrow band UV 311nm emission
- Decreased sunburn cell formation
- Decreased carcinogenesis
- Decreased redness
- Effective for psoriasis
UVB kills lymphocytes in the skin

UVB kills lymphocytes in the skin

Combination treatment

- Canadian Guidelines suggest combining therapies with distinct targets or complementary mechanisms of action:
  - Different topicals
  - Phototherapy plus topical or systemic (photochemotherapy)
  - Biologics plus other therapies
IL-17 in CD8 T cells in psoriasis


2 EPITOPES – AUTOANTIGENS

ADAMTS15
LL37
IL17 in “mild” psoriasis

Mild psoriasis (n = 34, PASI 5.5)

VS

Severe psoriasis (n = 23, PASI 23.2)
IL17 in “mild” psoriasis

More inflammation in mild psoriasis

2016 Nov;136(11):2173-2182
IL17 in “mild” psoriasis

Less regulatory molecules in severe psoriasis

2016 Nov;136(11):2173-2182
IL17 in “mild” psoriasis
Case 1

- 30 YO M
- Long history of scalp scale and itch
Scalp Psoriasis

- Involvement in 50-100% of psoriasis patients
- May be first area of involvement
- Inflammation is inter-follicular and like Ps on skin
- Some differences notes – Incr IFN gamma
Case 1 (scalp psoriasis)

- Clobex shampoo (Clobetasol 0.05% Foam)
  - Applied nightly 15 min
  - No HPA suppression (cw gel)
Case 2

- 45 YO F
- Pruritic feet
Case 2 (Plantar psoriasis)

- Rule out dermatophyte
  - KOH
  - Culture
- Potent topical CS
Case 3

- Palmoplantar pustulosis
  - Chronic sterile pustules
  - Associations
    » Female
    » Smoking
Case 3

- Palmoplantar pustulosis
  - No association with PSOR1 (HLACw6)
  - Pathology is in acrosyringium
    - ↑ IL-17 in sweat duct
    - ↑ MxA (IFNα) in sweat duct
    - Sweat-associated antimicrobial peptides in pustules

Hagforsen, Br J Dermatol 2010 163:572
Murakami J Invest Dermatol 2010 130:2010
Palmoplantar pustulosis – Not simple psoriasis

- Palmar plantar pustulosis (PPP) and Pustular palmoplantar psoriasis (PPPP) are similar and different from psoriasis vulgaris
- Increased TH17 and Th1 but not IL12/23
- Up-regulation of IL36

Bissonnette R PLOS ONE DOI:10.1371/journal.pone.0155215
Case 4

- Nail dystrophy - 1 yr
- KOH/culture Neg
Case 4 (Nail psoriasis)

- Topicals minimally helpful
- IL CS painful
- Biologics can improve nails
Case 5

- 55 YO F
- 20 Y Hx of arthritis
- On etanercept for 2 years
- New eruption
Case 5  (TNF alpha inhibitor induced psoriasis)

- Topical CS therapy
- Addition of acitretin
Conclusions

- Recognize psoriasis
  - Variants
  - Mimics

- Multiple approaches to manage skin
  - Topical treatment
  - Traditional and biologic systemic agents
  - Phototherapies
  - Combination approaches

- Manage skin along with joint disease – TNFi, ustekinumab Th17i