Psoriasis

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Abbreviation used:

HLA	: human leucocyte antigen
Th1	: type I helper T cell
IL	: interleukin
TNF	: tumour necrosis factor
PASI	: psoriasis area and severity index
BSA	: body surface area
DLQI	: dermatology life quality index
UV	: ultraviolet light
PUVA	: ultraviolet A with psoralen therapy

Introduction

Definition

Psoriasis is one of the prototypic papulosquamous skin diseases characterised by erythematous papules or plaques with silvery scales. It is a chronic inflammatory skin disease with increased epidermal proliferation related to dysregulation of the immune system.

Epidemiology

Psoriasis is said to affect 2% of the world population. The prevalence is up to 5% in selected Western population. The prevalence in Chinese is estimated to be 0.3% to slightly more than 1%, the variation in estimation is accounted for by the methodological differences in these surveys.

Psoriasis has a bimodal age of disease onset. The first peak is around 20 and the second peak is around 60. People with disease onset around 20 year old have stronger genetic predisposition. They have a higher prevalence of having HLA-Cw6. The linkage to genetic factor is lower for the group with late onset disease.

Pathology and Pathogenesis

Pathology

The pathology of an established lesion of psoriasis is characterised by epidermal hyperplasia with squared-off rete ridges, parakeratosis, elongation of dermal papillae with thinning of the supra-papillary epidermis, dilated tortuous capillaries and perivascular lymphohistiocytic infiltration of the superficial dermis. In some of these lesions, collection of polymorphonuclear cells in the stratum corneum (known as Munro microabscess) and between keratinocytes (known as spongiform abscess of Kogoj) may be found.

Pathogenesis

The cell cycles of the epidermal cells in psoriatic lesions are greatly accelerated. Turnover of the basal cells, which divide every 1.5 days, in psoriatic skin is as fast as the rapidly growing cells of the small intestinal mucosa. The epidermal transit time is shortened from the normal 28 days to as short as 3-4 days. Such a change in epidermal cell cycle is thought to be related to the inflammatory cytokine released in the inflammatory process. Psoriasis is considered to be a prototypic Th1 disease. Increased amounts of Th1 cytokines viz interferon γ and IL-2 are observed. Early interventional researches adopted drugs such as cyclosporine A with pharmacological effects on this pathway, rendered proof of concept evidence to this observation. Studies have also demonstrated that keratinocytes and dendritic cells play an important role in innate and adaptive immune response of the skin. The innate immune response cytokines IL-1, 6 and TNFα are up-regulated in psoriatic skin. Biologic approaches to reduce the activity of TNFα are found to be useful in psoriasis. Recent studies show that Th17 cells, a novel subset of T cells, play a pivotal role in the pathogenesis of psoriasis. Recognition of the early dendritic cell-T cell interaction through IL-12 and IL-23 provides the new insight for the latest biological treatment, the monoclonal antibody against IL-12/IL-23, which results in a breakthrough in the management of psoriasis[1].

Clinical Features

Prototypic lesion

The typical lesion of psoriasis is a well-demarcated erythematous plaque with silvery scales on top of the plaque (figure 1). The affected patient may experience itchiness. The plaques may affect anywhere of the skin surface but the mucosa is normally spared. The scales may only be loosely attached and easily fall off from the skin. The disease may wax and wane, and not uncommonly is aggravated by trauma and irritation, infections, various drugs, seasonal changes and psychogenic stress.

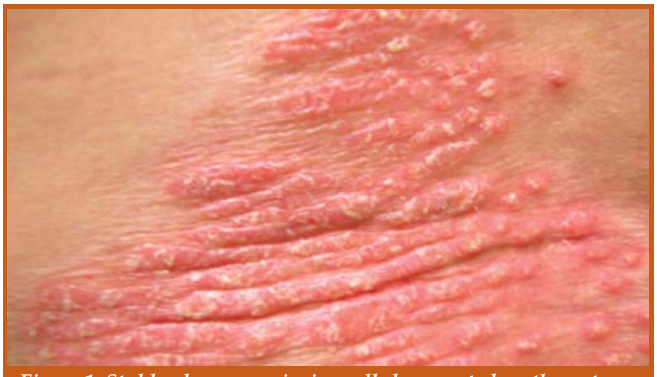

Figure 1. Stable plaque psoriasis: well-demarcated erythematous plaque with a silvery scale on top.

Chronic Stable Plaque Psoriasis

Sites of predilection of the characteristic plaques include the extensor surfaces of the elbows, knees, lower back and scalp. The genitalia and nails may also be affected. The plaques vary in size (figure 2). New lesions may be induced at traumatised skin such as surgical scar, or even scratch marks (known as Köbner phenomenon).

Figure 2. Diffuse involvement of the back in this patient. If more than 90% of the body surface is affected, it is referred as erythrodermic psoriasis.

Differential Diagnosis

Common conditions that may present as erythematous plaque include discoid eczema, lichen simplex chronicus, hypertrophic lichen planus and Bowen's disease.

Guttate Psoriasis

It is a variant characterised by small coins or even punctate lesions with less amount of scale affecting mostly young people. The disease may be precipitated by upper respiratory tract infection. Over half of these patients have some evidence of preceding streptococcal infection. A few may have prolonged disease remission after the acute episode.

Differential Diagnosis

Common conditions that may present as guttate papulosquamous lesions include pityriasis rosea, secondary syphilis and pityriasis lichenoides.

Unstable Psoriasis

Lesions are angry looking with more intense inflammation. These may be redder in colour with less scaling. Lesions may be less well-demarcated and occasionally exudation and crust are found[2]. Patients may experience more itchiness, irritation and even pain. Further progression to erythrodermic or pustular psoriasis can happen. Inappropriate use of corticosteroids, excessive irritation, sunburn are some of the factors not uncommonly associated with unstable psoriasis.

Differential Diagnosis

Common conditions that may present like unstable psoriasis include eczema and tinea incognito.

Erythrodermic Psoriasis

When more than 90% of the body is involved by psoriasis, it is defined as erythrodermic psoriasis. An affected patient is characterised by having generalised redness of skin and scaling. The colour may sometimes be described as dusky red. The face may occasionally be relatively spared. Individual plaques may not be obvious. Pustules may sometimes be found. Triggering factors are not uncommonly unidentified. Affected patients may have systemic symptoms.

Differential Diagnosis

Conditions that may present as erythroderma include eczema/dermatitis, cutaneous T cell lymphoma, drug reaction, pityriasis rubra pilaris and pemphigus foliaceus.

Pustular Psoriasis

Tiny superficial pustules with a background of erythema may occur. The roof of the pustules is easily broken. These pustules can be distributed throughout the whole skin surface or more localised especially in and around the unstable lesions. Some patients may have lesions with matted scales with a yellowish hue and if biopsy of these lesions is performed, the histology shows sheets of subcorneal polymorphs. Though very discrete pustules may not be seen clinically, these lesions may be described as pustular psoriasis by some clinicians. Steroid withdrawal* is the commonest precipitating factor encountered by the author as the cause of pustular psoriasis. Localised pustular psoriasis on the palms and soles is reported to be associated with smoking.

Differential Diagnosis

Conditions that may present as generalised pustulosis include infections, acute generalised exanthematous pustulosis and subcorneal pustular dermatosis.

*Not only when systemic steroids are given and tapered, but also when the patient has used super potent topical steroids for a long time, therefore, save for a few exceptional clinical situations, systemic steroids are contraindicated in psoriasis.

Psoriasis in Specific Body Locations

Scalp and face: The scalp is one of the most common sites affected by psoriasis. The typical plaques may extend slightly beyond the hairline (figure 3). Patients may present as recalcitrant dandruff. Some may involve the glabella region, eyebrows, and nasolabial fold, and in this situation it merges with seborrhoeic dermatitis. The term sebopsoriasis is coined to describe these cases. The external auditory canal is not uncommonly affected. Psoriatic lesions on the face may not be very well-demarcated nor is the silvery scale easily discernible.

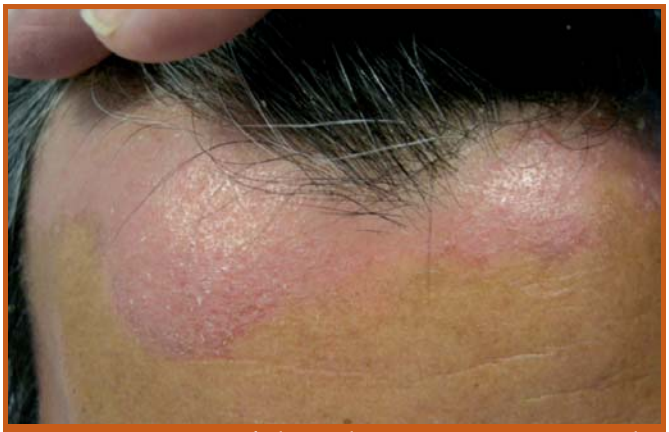

Figure 3. Psoriasis of the scalp. Lesion not uncommonly extends beyond the hairline. Psoriatic lesion on the face may not be very well-demarcated nor is the silvery scale easily discernible.

Differential Diagnosis
Conditions that may mimic psoriasis on the face or scalp include seborrhoeic dermatitis, lichen simplex chronicus (plaques on scalp) and tinea capitis.

Flexural regions: Lesions located at the axillae, inframammary folds, groins, intergluteal cleft and prepuce of the uncircumcised may present as shiny pink to red thin plaques or even patches. Fissure may sometimes be present. The scale is not discernible. Itchiness and irritation are not uncommon. The term inverse psoriasis is coined to describe these lesions.

Differential Diagnosis
Conditions that may mimic psoriasis in the intertriginous areas include seborrhoeic dermatitis, candida infection, intertrigo and extramammary Paget's disease.

Nail: Nail involvement has been reported in 10 - 80% of patients with psoriasis (figure 4). Features include onycholysis with or without the oil drop phenomenon, distal subungual hyperkeratosis, thimble pitting, crumbly poorly adherent nail, loss of lustre among other changes. The finger and toe nails can be affected. Patients with nail involvement may have a higher incidence of arthropathy. Psoriatic nails may also predispose to fungal infection. Nail disease can cause much concern to those affected because it can be symptomatic, have functional disability, cosmetically unacceptable but otherwise recalcitrant to all forms of treatment.

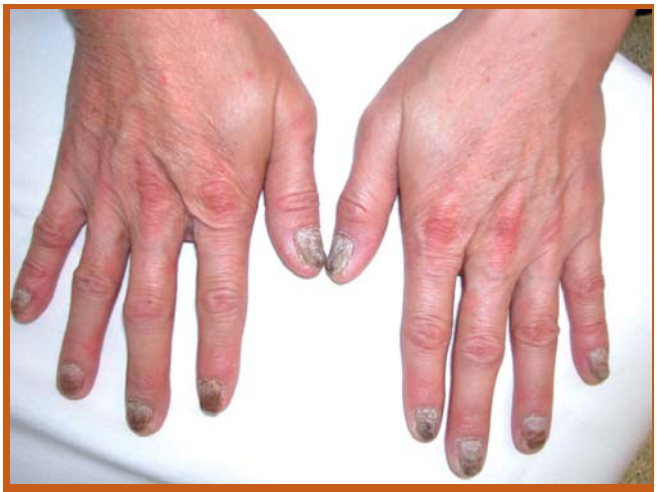

Figure 4. Nail psoriasis. Onychomycosis seldom presents as symmetrical involvement of the finger nails especially when all ten nails are involved. The unhealthy nails are more prone to secondary fungal infection and therefore should be excluded as appropriately.

Differential Diagnosis
Conditions that may mimic changes in nail psoriasis include fungal infection and various forms of idiopathic nail dystrophy.

Clues to differentiate these conditions are summarised in table 1. Psoriatic arthropathy is discussed in another article of this issue.

Table 1. Differential diagnosis and clinical clues to guide differentiation

Psoriasis presentation	Differential diagnosis	Clinical differentiation
Stable plaque	• Eczema (discoid and chronic lichenified) • Hypertrophic lichen planus • Bowen's disease	• Weeping in active discoid eczema; lichenification in lichen simplex, scales in lichen simplex are not as loosely attached and silvery as in psoriasis • Violaceous plaques mostly located on the shins, scales are not as loosely attached and silvery • Long standing solitary thin plaque without the characteristic silvery scale in psoriasis
Guttate	• Pityriasis rosea • Secondary syphilis • Pityriasis lichenoides chronicus (PLC)	• Oval papulosquamous plaques with long axis of lesions aligned in a fir tree distribution mostly on the trunk • Palm and sole involvement, mucosal lesions, systemic symptom, lymphadenopathy • More polymorphic in PLC, mica scale and Oblaten sign
Unstable	• Eczema • Tinea incognito	• Among the unstable psoriatic lesions, some may have otherwise typical morphology of psoriasis; history of using potent topical steroid or systemic steroid • Less plaque like and angry looking in tinea incognito
Erythrodermic	• Other causes of erythroderma such as eczema/dermatitis, cutaneous T cell lymphoma, drug reaction, pityriasis rubra pilaris (PRP), pemphigus foliaceus.	• History of psoriasis; nail changes of psoriasis; history of eczema or exposure to allergens; painful keratoderma, diffuse alopecia and leonine face in T cell lymphoma; starts as morbilliform rash in drug reaction; island of sparing, perifollicular erythema and orange hue in PRP; impetigo-like blisters and erosions followed by collarettes of scale or scale-like crusts in pemphigus foliaceus
Pustular	• Generalised: acute generalised exanthematous pustulosis • Subcorneal pustular dermatosis • Localised palmoplantar pompholyx; tinea pedis	• Sudden onset after taking drug; no past history of skin diseases; self limited • Predilection for axillae and around the groins • Vesicular lesions instead of pustular lesions
Scalp	• Seborrhoeic dermatitis • Tinea capitis	• Discernible plaque or patch in psoriasis • Bald patches in tinea with broken hair stump
Inverse	• Candidiasis • Tinea • Extramammary Paget's disease	• Satellite lesions with scalloped scale in candida intertrigo • Faintly discernible active margin in tinea • More wet looking and with erosion in extramammary Paget's disease
Nail	• Onychomycosis	• Chalky white subungual hyperkeratosis or superficial or proximal subungual whitish discolouration; the oil drop sign and thimble pitting in nail psoriasis

Disease Assessment

Clinician Based
The British guidelines define "severe" disease as PASI score of 10 or more (or a BSA of 10% or greater where PASI is not applicable) and a DLQI > 10, i.e. the rule of ten proposed by Finlay[3]. PASI and BSA are regarded as clinician-based assessment of severity. In recent years, patient reported outcome such as health related quality of life assessment by various tools is required by the

regulatory agencies for drug registration. DLQI and SF-36 are two of such instruments commonly used in clinical trials in psoriasis. PASI 75, which refers to a reduction of PASI score by 75% of the baseline, is employed as an endpoint assessment in modern clinical trials involving biologics. PASI is calculated as follows:

$\sum$[area score of the region X extent indicator of the region X (sum of severity indicator of the region)]
= 0.1 $Å_{Head}$ (E + S+ T) + 0.2 $Å_{Upper\ limbs}$ (E + S+ T) + 0.3 $Å_{Trunk}$ (E + S+ T) + 0.4 $Å_{Lower\ limbs}$ (E + S+ T) wherein Å refers to area of the suffix region according to a 7-point scale (0-6), E, S, T refers to the degree of erythema, scaling and thickness respectively according to a 5-point scale (0-4). The maximum score is 72.

Severity assessment of joint disease is discussed in the other chapter of the same issue.

Other Assessment

The occupation history is also important as this will give an idea of the social and functional disability associated with the skin condition of the index patient. Treatment and drug history will provide further information guiding the choice of various therapeutic modalities for a particular patient.

As a routine, the author also asks the patient how he/she feels about his/her skin disease and what his/her major concern is before the discussion of the various treatment options.

Laboratory investigations are not required in an otherwise simple and mild case of psoriasis. Skin biopsy is not usually required to establish the diagnosis of psoriasis unless in doubt. Skin scraping, hair plugging or nail clipping for fungal study may be performed as appropriate. If systemic therapy or phototherapy is contemplated, baseline investigations include complete blood picture, liver and renal biochemistry, hepatitis serology, anti-nuclear antigen, fasting sugar and lipid, and chest X-ray should be performed to guide choosing a preferred modality from the various possible options.

Table 2. Prevalence of diseases associated with metabolic syndrome (WHO case definition) in patients with psoriasis (Cohen et al. 2008)

Category	Prevalence		
	Psoriasis n = 16 850	Control n = 48 677	OR (95% CI)
Mean age, years (SD)	42.7 (20.3)	51.0 (19.1)	
Ischaemic heart disease % (n)	14.2 (2 387)	7.1 (3 479)	2.1 (2.0-2.3)
Diabetes mellitus % (n)	13.8 (2 324)	7.3 (3 556)	2.0 (1.9-2.1)
Hypertension % (n)	27.5 (4 627)	14.4 (7 017)	2.2 (2.2-2.3)
Obesity % (n)	8.4 (1 419)	3.6 (1 768)	2.4 (2.3-2.6)

SD = standard deviation; CI = confidence interval; OR = odds ratio

Recent epidemiological studies also reveal that people with psoriasis are associated with risk factors for cardiovascular diseases, table 2[4]. Although standard guidelines for screening of cardiovascular risk factors have not arrived, to take a good history covering these risk factors such as smoking habit, personal and family history of diabetes, hypertension, hyperlipidaemia and cardiovascular diseases may be contributory to the holistic management of a person with psoriasis. The affiliated service of the author also recommends routine measurement of the body mass index and blood pressure in patients newly presented with psoriasis.

Management

The Principle of Management

To understand the expectation of the patient is the most important first step in management. To communicate and educate the index case is the next important step. Appropriate skin care, avoidance of aggravating factors, the importance of keeping a good treatment history, cessation of smoking, avoidance of excessive alcohol drinking, reinforcement of the non-contagious nature and chronicity of the condition and conveying the message that psoriasis is amenable to very good control are the important contents in communication, especially in the first few encounters. Instruction on using especially the perplexing large number of topical drugs should be simple and clear. Printed information is invaluable.

Treatment Options

Treatment for psoriasis can be classified as:

1. **Topical drugs:** topical steroids, vitamin D analogues, tar, dithranol (which may have been withdrawn from the local market), keratolytics, calcineurin inhibitors, tazarotene (vitamin A analogue which is not available in the local market)
2. **UV light therapy:** UVB including nBUVB, PUVA, targeted phototherapy such as UVB delivered with the laser system (Excimer® 308 nm)
3. **Traditional systemic therapy:** methotrexate, systemic retinoid, cyclosporine A, (others include hydroxyurea, 6-thioguanine, mycophenolate mofetil, fumaric acid esters, these are less extensively used and their use is regarded off-label by the manufacturers, fumaric acid esters are not available in the local market)
4. **Biologic therapy:** etanercept, infliximab, adalimumab which target TNFα; ustekinumab which targets IL-12 & 23

Management Hierarchy

A combination of topical therapies is usually used as the first line treatment in patients with limited area involvement i.e. <10-20% BSA. If the condition is not under satisfactory control by topical therapy or the disease is too extensive, phototherapy or systemic therapies may be considered. Poor adherence to topical therapy is not uncommon. Therefore, before considering systemic treatment, skillful counselling is almost a must not only to confirm poor adherence, but also to know the expectation and concern of the patient. In a patient who has severe disease (c.f. the aforementioned rule of ten) which fails phototherapy and systemic therapy, or who is intolerant to these therapies, or who has significant, coexisting comorbidity (e.g. significant impairment of renal or liver function and unable to attend 2x/week for phototherapy in a designated dermatology clinic) which precludes the use of these treatments, biologic therapy can be considered[5].

As the adverse effects of these treatments differ or overlap one another, and some of these treatments have

recommended ceiling cumulative exposure such as not more than 150 to 200 treatment sessions in PUVA, treatment rotation is not uncommonly adopted. For recalcitrant cases, a combination of systemic including biologic therapies may be used. A failure of treatment with one biologic does not necessarily mean knocking out the whole group of biologics. The strength and weakness is summarised in table 3.

Conclusion

Psoriasis is a chronic inflammatory skin disease which causes significant functional impairment to those affected. A constellation of treatments is now available which can achieve disease control in most people with psoriasis. The best available evidence in management should, however, be applied on an individual basis.

References

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Table 3. Highlights and comparison of treatments for psoriasis

Treatment	Short notes for Practical use	Strength	Weakness
Topical			
Steroids	• Still the mainstay of topical treatment • A wide variety of choice with respect to potency and formulations; the most potent is more than 600 times the least one • No more than twice daily use recommended • Co-formulated with other active ingredients such as calcipotriol, salicylic acid	• Effective & user friendly	• Tachyphylaxis dissociated with adverse effects • Systemic effects after prolonged use of potent topical steroids • Caution: use on the face and intertriginous regions; use of super potent topical steroid in unstable psoriasis
Vit D analogues	• Calcipotriol; calcitriol • Calcipotriol is co-formulated with betamethasone dipropionate • May be used during the steroid drug holiday	• The main non- steroidal topical preparation • No evidence for tachyphylaxis	• Not all patients like vit D analogues because of irritation and less quick in action compared to topical steroids • Caution: maximum weekly amount 100 gm for calcipotriol (210 gm for calcitriol)
Tar	• Commonly used for bathing, though gel formulation for direct application is available • Combined with phototherapy in the classic Goeckerman regime	• Non-steroidal topical preparation	• Not user friendly because of its smell and appearance • Caution: use in unstable psoriasis
Others	• Dithranol is not available in the local market • Calcineurin inhibitors can be used to treat facial and flexural psoriasis • Sulphur and salicylic acid are commonly used as de-scaling agents but seldom used alone		
Phototherapy			
	• These include UVB (broad or narrow band); PUVA; targeted phototherapy	• Treatments do not have substantial systemic adverse effects • PUVA is a very effective treatment • UVB therapy can be use in pregnancy	• Patient needs to present personally to the clinic for treatment 2-3x weekly • Patient needs to wear glasses that filter UV light for the whole day after PUVA • Less than 150-200 lifetime cumulative exposure is recommended for PUVA • Not suitable for unstable, erythrodermic, or pustular psoriasis
Systemic			
Methotrexate	• Weekly dosing with dose ranges from 5 mg to 25 mg • Commonly dosed together with folate supplement	• Convenient, user friendly • Effective, inexpensive traditional systemic treatment • Long experience • Can be used in a variety of psoriatic state	• Idiosyncratic reaction leading to pancytopaenia, paradoxic skin necrosis, hence,slow incremental dosing is commonly adopted • Teratogenicity and effect on male fertility • In real life situation it may be difficult to use as so many people may have deranged liver function such as fatty liver
Systemic retinoid	• Acitretin is the retinoid of choice in psoriasis • Dose seldom exceeds 1 mg/kg/day	• Long experience • Very effective when combined with PUVA • Severe acute adverse event uncommon	• Seldom achieves very satisfactory disease control • Fair patient acceptability because of constellation of minor adverse effects • One of the most potent teratogen known; in female, written consent is required by the manufacturer
Cyclosporine A	• 2.5 to 5.0 mg/kg/day;	• Not usually hepatotoxic • May be effective in arthritis	• Extensive drug interaction with a variety of drugs • Seldom used for more than 2 years because of its nephrotoxicity • Relapse is common upon treatment cessation
Biologics	• Etanercept, infliximab and adalimumab target TNFα • Ustekinumab targets IL 12 & 23 • Available in the local market • Apart from infliximab which is delivered by intravenous route, the others can be given subcutaneously	• Neither toxic to the liver nor to the kidney in contrast to the conventional systemic drugs • Dosing can be spaced out e.g. quarterly dose of ustekinumab is required after the initial induction • Effective in arthropathy	• Apart from adverse effects such as demyelinating disease, proneness to infections of which TB is of most concern • Induction of ANA positivity • Long term adverse effects are unknown

NB. Readers are encouraged to refer to the insert and standard textbook for details of the adverse effects of these treatments.