An approach to psoriasis in general practice

Motswaledi MH, MBChB, MMedDerm, FCDerm(SA), Head
Nkosi L, MBChB, FCDerm(SA), Specialist
Department of Dermatology, University of Limpopo (Medunsa Campus)
Correspondence to: Mojakgomo Motswaledi, e-mail: motswaledi1@webmail.co.za
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Abstract

Psoriasis is a genetically determined inflammatory and proliferative disease of the skin, presenting with sharply demarcated scaly plaques, especially on the extensor prominences and the scalp. Although it is a clinical diagnosis, biopsy can help to confirm the diagnosis. Treatment modalities include topical corticosteroids, tar preparations, vitamin D analogues, systemic retinoids, immunosuppressive drugs, phototherapy, and recently, biologicals.

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Introduction

Psoriasis is a genetically determined chronic disfiguring disease of the skin, characterised by well demarcated, indurated, red, scaly plaques, which may be limited or widespread in extent.[1] Prevalence of the disease is 2-3% of the world population.[2] It is uncommon in West Africans and African Americans.[3] It occurs in both children and adults, with no gender predilection. Precipitating factors are skin trauma, infections, drugs, alcohol, smoking, and immunosuppression. It is a chronic disease, characterised by relapses and remissions.

Clinical presentation

There are several clinical types.

Plaque psoriasis

Plaque psoriasis is the most common type, and is also called psoriasis vulgaris. It presents with well circumscribed plaques, with silvery-white scaling lesions on the skin. The scalp is often affected (Figure 1, Figure 2).

When scaling is not evident, it may be induced by scratching. This is a useful sign in diagnostically uncertain cases.[3] Lesions of psoriasis may extend along areas of trauma, and this is referred to as the Koebner phenomenon.

Guttate psoriasis

The name, guttate psoriasis, is derived from the Latin word *gutta* (meaning drop).

It occurs commonly in children and young adults.[4] In children, it often appears abruptly following an infection, such as streptococcal pharyngitis, otitis media, urinary tract infection, or dental caries. Lesions are smaller than plaques of psoriasis vulgaris (Figure 3).

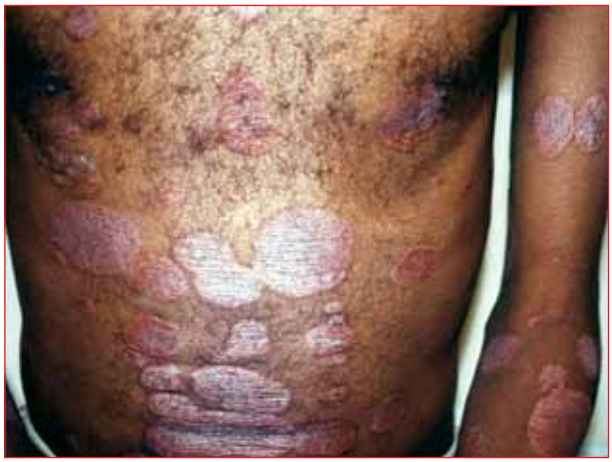

Figure 1: Plaque psoriasis on the trunk and arms

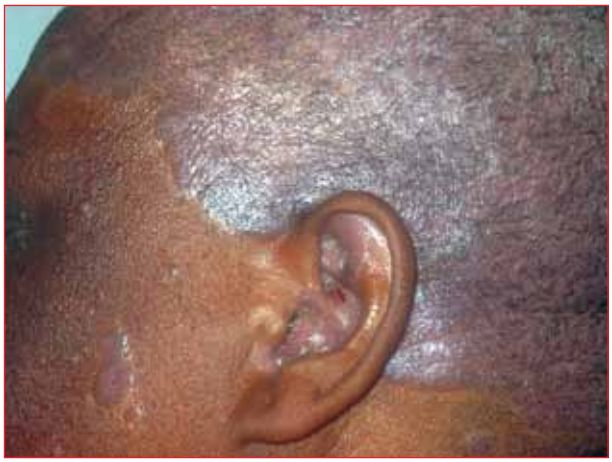

Figure 2: Psoriasis that has affected the scalp

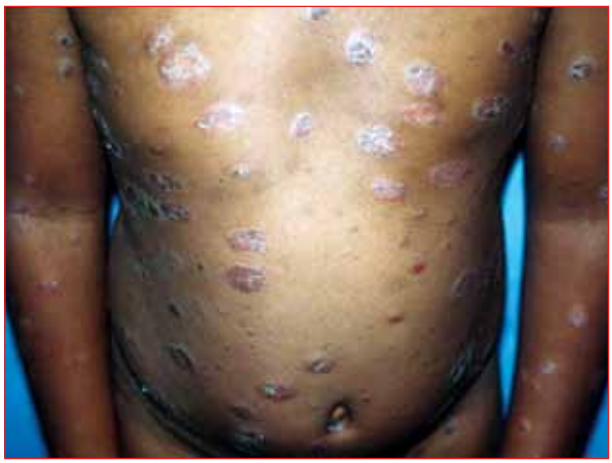

Figure 3: Guttate psoriasis in a child

Inverse psoriasis

This occurs on major skin folds, such as the groin, axillae, inframammary folds in females, the vulva, intergluteal area, and flexural aspects of limbs (Figure 4a and 4b). Due to moisture and friction in these areas, scaling is greatly reduced, and the typical silvery-white scaling may not be clinically evident.[3]

Pustular psoriasis

Pustular psoriasis presents with extensive pustular lesions on the skin. This may be localised or generalised (Figure 5). Pustular psoriasis can be triggered by infections, pregnancy,

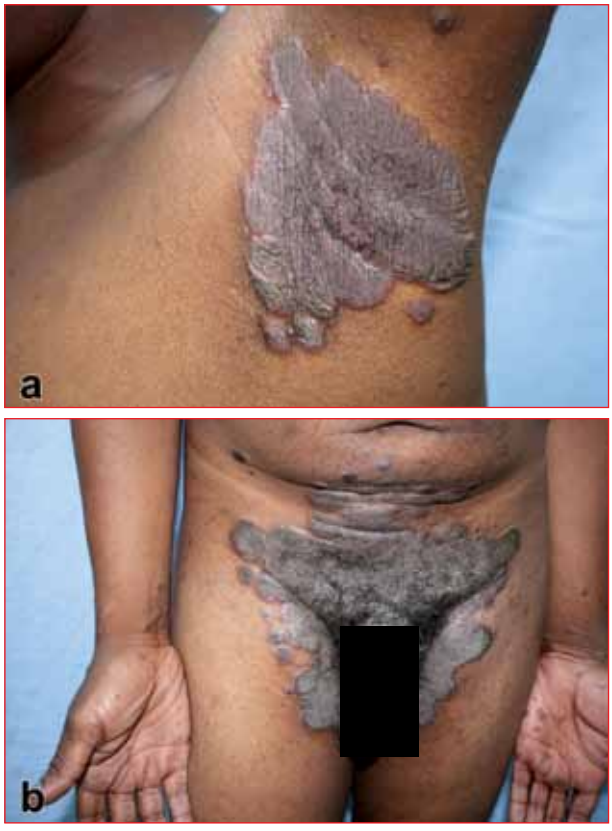

Figure 4a, 4b: Inverse psoriasis in the axillae and inguinal areas

Figure 5: Localised pustular psoriasis affecting the fingertips and nails

and the withdrawal of oral corticosteroids. The affected patient is usually febrile and ill-looking. There is appreciable mortality in severe cases.

Erythrodermic psoriasis

Erythrodermic psoriasis is a complication of psoriasis, often precipitated by infections and loss of disease control. The disease is generalised, and the entire body becomes red, with scaling. Typical features of psoriasis are often lost in erythrodermic psoriasis. The normal thermoregulatory function of the skin is impaired, and the patient shivers. This may lead to hypothermia.

Psoriatic arthritis

This is an association of psoriasis of the skin with peripheral and/or spinal arthropathy. It is classified as a spondyloarthropathy, and is characterised by synovitis, enthesitis, dactylitis, and spondylitis. Usually, it manifests in a person having skin and nail psoriasis.[5] Current estimates are that approximately 20-30% of patients with psoriasis will develop psoriatic arthritis.[5] Skin lesions often precede the arthritis in the majority of cases. As the disease progresses, there is joint destruction, associated with cartilage and bone damage, leading to joint deformities and fusion that result in impairment of function and poor quality of life.[5] Psoriatic arthritis also occurs in children. Unfortunately, the differentiation of psoriatic arthritis and non-psoriatic arthritis in children is challenging. This is because in half of them, the classic skin lesions present after the onset of arthritis, with a lag time that may be 10 years or longer.[6] Also, psoriatic lesions in a young child may be atypical and non-specific.

Psoriasis and cardiovascular disease

There are several reports on the association between psoriasis and cardiovascular disease risk factors. Psoriasis serves as an independent risk factor for the development of diabetes and other components of metabolic syndrome, and indirectly for cardiovascular disease.[7] Psoriasis is also associated with atherosclerosis. Angiogenesis and oxidative stress were found to be common mechanisms linking

psoriasis and atherosclerosis. Psoriasis and atherosclerosis also share common enzymatic sources of reactive oxygen species, and these influence several cellular signalling pathways that are implicated in the pathogenesis of both diseases.[8]To assist in preventing cardiovascular disease, the association between psoriasis and cardiovascular disease must be taken into consideration when treating patients with psoriasis.[7]

Psoriasis and HIV infection

Psoriasis is observed in all stages of human immunodeficiency virus (HIV) infection, and in some patients, may be the initial presentation of HIV infection. The severity of psoriasis in patients with HIV ranges from mild to severe. The severe forms of psoriasis in these patients seem to correlate with the worsening immunosuppression.[9]

Patients with pre-existing psoriasis experience exacerbation of their disease status when HIV infection occurs. This is attributed to the elevated tumour necrosis factor-alpha (TNF-α) cytokine which corresponds to the HIV viral replication. The TNF-α is a key inflammatory mediator in the pathogenesis of psoriasis. It is for this reason that TNF-α inhibitors (biologic agents) are advocated to treat severe psoriasis in patients with HIV infection. A notable improvement of psoriasis lesions or arthropathy occurs when these patients commence antiretroviral therapy to decrease the viral load.

Although all clinical subtypes of psoriasis may occur in patients with HIV infection, a high tendency of the erythrodermic, guttate, and inverse variants, is observed. Often, more than one form of psoriasis may coexist in a single patient. Psoriatic arthropathy also tends to be more common and severe, with a progressive clinical course. Typically, it is refractory to conventional forms of therapy.[9]

Management

As a chronic recurrent disease, management of psoriasis can be both satisfying and frustrating. The clinician bears the responsibility of taking into consideration the various factors that impact on the choice of treatment. All these factors are dictated by both the patient profile and the disease profile.[10]

Patient profile includes age, gender, occupation, personality, socio-economic status and co-morbidities. The disease profile includes the type of psoriasis, extent of the disease, symptoms, presence or absence of arthropathy, duration of the disease, natural history of the disease process, treatments used previously, and subsequent clinical responses to those treatments.[10]

Topical therapies

Various agents are available to treat psoriasis. These contain either supportive, or therapeutic, properties. These topical agents can be used as monotherapy, or concurrently in combination for maximum benefit, as some have synergistic mechanisms of action. It is equally important to be aware of aspects of incompatibility in certain agents to avoid possible adverse effects or drug interactions. Topical therapies include corticosteroids, vitamin D analogues, tar preparations, as well as calcineurin inhibitors.

In general, it is recommended that the more potent agents are used on a short-term basis to allow for rapid response, and thereafter on an intermittent basis, according to the waxing and waning of the disease. Usually, milder agents are used for disease maintenance on a long term basis.[11]

Corticosteroids

Topical corticosteroids are the mainstay of treatment in psoriasis. Their mechanism of action includes anti-inflammatory, anti-proliferative, immunosuppressive and vasoconstrictive effects. They are available in many strengths and formulations, allowing for versatility of use. When determining appropriate choice of potency and its vehicle, significant consideration should be given to disease activity, location of the treated lesion, age of the patient, and duration of treatment. The lower-potency corticosteroids are recommended for intertrigenous areas, thin skin, and in infants, whilst the highest potency is best suited to thick chronic plaques in adults. A once-daily application is shown to be just as effective as a twice-daily application. Long-term remissions can be maintained by applications on alternate days.[12] The additional advantage of using topical corticosteroids includes their tolerance at sites where other topical agents might induce irritation.

Tachyphylaxis is loss of effectiveness with continued use of topical corticosteroids, and may affect the long-term results that have been achieved in a given patient.[11] Another concern with the use of corticosteroids is the rebound phenomenon. This is when the topical corticosteroids are discontinued and the disease gets worse than it ever was before treatment.[11] Side-effects of topical corticosteroids include skin atrophy, purpura, telangiectasia, striae distensae, acneform eruptions and folliculitis. Systemic absorption and subsequent effects are possible following prolonged treatment of high-potency topical corticosteroids, and especially in young children.

Vitamin D_3 analogues

Calcipotriol is a synthetic vitamin D analogue, and is available commercially as a topical treatment for psoriasis.

Its vitamin D receptors are on the skin cells (keratinocytes), and calcipotriol inhibits proliferation of these receptors. Calcipotriol has also been observed to enhance keratinocyte differentiation. Its anti-inflammatory properties are derived from its ability to inhibit neutrophil function.[12]

Vitamin D analogues have an important advantage, namely their potential to function as steroid-sparing agents. Recently, they have become first-line topical therapy for psoriasis, due to their therapeutic efficacy and limited toxicity.[12]

They are mainly indicated for mild-to-moderate disease. However, they are poorly tolerated on the face and flexures as they tend to induce a burning sensation or irritation.

Calcineurin inhibitors

Calcineurin inhibitors, such as tacrolimus and pimecrolimus, act on the inflammatory lymphocytes by suppressing their ability to produce pro-inflammatory cytokines that play an important role in the pathogenesis of psoriasis. Generally, they are also used to treat atopic dermatitis. They are available in ointment and cream formulations, with varying concentrations. When applied under occlusion dressings, they can improve lesional penetration into thick psoriatic plaques. Increasingly, they are being chosen as second-line agents for the maintenance of clinical remission on thin skin, as they are not associated with skin atrophy that is sometimes caused by other topical corticosteroids, when applied to those areas.[11]

Tar preparations

Coal tar has a range of anti-inflammatory properties, and is effective as an antipruritic agent. It is used widely in inflammatory dermatoses, especially when associated with pruritus. Its mechanism of action is poorly understood. However, it is known to inhibit deoxyribonucleic acid (DNA) synthesis by decreasing the mitotic index of proliferating keratinocytes.

It is available as a crude coal tar formulation, which is most effective for psoriasis, and also as a distilled product, liquor carbonis detergens (LCD). Many formulations of coal tar exist at varying concentrations. It can be effective as monotherapy, or in combination with topical corticosteroids, salicylic acid, or phototherapy [ultraviolet B (UVB)].[12]

The use of tar preparations is limited by patient concerns regarding the unpleasant odour, and staining of clothes and bathroom equipment. Potential side-effects include irritant contact dermatitis, folliculitis, and photosensitivity, especially with ultraviolet A (UVA).

Of most concern to many subjects is the association of occupational coal tar exposure with increased risk of lung, scrotal, and skin cancer. However, patients with inflammatory dermatoses, who are treated with topical coal tar, do not exhibit this risk factor. To date, there have not been any convincing data or epidemiologic studies that have proved carcinogenicity in humans following its therapeutic use topically.[11]

Salicylic acid preparations

Salicylic acid is a topical keratolytic agent, recommended in the treatment of chronic thick plaques of psoriasis. It is thought to reduce keratinocyte-to-keratinocyte binding, and also lowers the pH of the stratum corneum. These effects result in softening of the psoriatic plaques, and less scaling subsequently.

Keratolytic effects are achieved at concentrations of more than five per cent. Its combination with other topical treatments is advantageous, as salicylic acid provides easy lesional penetration. However, concurrent use with calcipotriol should be avoided, as it neutralises the pH base of the calcipotriol.[11]

Topical salicylic acid also decreases the efficacy of UVB phototherapy due to its filtering effect. Therefore, it should be avoided prior to UVB phototherapy. Systemic absorption is possible when applied over a large body surface area of more than 20%, resulting in salicylism. It should be avoided in the treatment of children.[11]

Phototherapy

Phototherapy refers to the use of ultraviolet rays emitted by a special source, with the ability to select specific wavelength ranges. This is achieved using controlled strength, intensity and exposure periods. Its benefits are derived from the ancient observation of natural sunlight inducing remission of various skin ailments, including psoriasis.

The therapeutic effects of phototherapy are noted with UVA and UVB rays. Both have clinical responses when used as monotherapy, or in combination with other therapeutic modalities, for moderate-to-severe psoriasis. The best results are observed with at least three-times-weekly treatment sessions on alternate days. This limits it as a therapeutic modality of choice, as most patients find it impractical or inconvenient to visit the treatment site that often.[13]

Both psoralen and UVA (PUVA) and UVB phototherapy affect inflammatory cytokine production by the epidermal keratinocytes and lymphocytes. The added psoralen to the UVA crosslinks with the cellular DNA, thereby inhibiting DNA replication, and subsequent cell cycle arrest.

Systemic therapies

The conventional systemic agents for psoriasis are mainly methotrexate, cyclosporine and acitretin. Other systemic agents have been used, with variable clinical responses. These include sulfasalazine, azathioprine, hydroxyurea, leflunomide, mycophenolate mofetil and fumaric acid esters.[12]

Generally, these agents are recommended when there are extensive cutaneous lesions, or the disease is severe and responding poorly to topical forms of therapy. Due to the complexity and side-effects associated with these drugs, it is preferable that such patients are referred for specialist attention.

Biological agents

Biological agents are proteins that can be extracted from animal tissue, or produced by recombinant DNA technology. They possess pharmacological activity.[14]

In recent years, biological agents have changed the treatment of psoriasis by providing additional therapeutic options that are potentially less toxic to the liver, kidneys and bone marrow, and are also not teratogenic.

However, they are associated with high costs and a long-term safety profile. It is for these reasons that they are a subject of interest currently, regarding the comparison of their data with those of conventional systemic agents, in terms of their safety profile and clinical efficacy in the treatment of psoriasis, as well as various other immunological conditions.[14]

Several biological agents have been approved for the treatment of psoriasis.[12,14,15] They are etanercept, alefacept, adalimumab, infliximab and efalizumab. Efalizumab has been withdrawn by the US Food and Drug Administration due to safety concerns.[16] TNF-α inhibitors, such as adalimumab, infliximab and etanercept, are associated with adverse effects, including demyelinating disease, opportunistic infections, and most importantly, reactivation of latent tuberculosis.[16] This is particularly more important in South Africa because of the burden of tuberculosis. Screening for tuberculosis must be carried out in patients scheduled for TNF-α inhibitors.[16] Extreme caution has to be exercised when selecting patients for these treatment modalities.

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