The multiple comorbidities of psoriasis

The importance of a holistic approach

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Background
Psoriasis is a common immune-mediated skin condition that affects at least 2% of the Australian population. Though psoriasis was often considered a cutaneous condition alone, more recent literature has shown other organ involvement. These comorbidities may be missed unless specifically looked for.

Objective
The aim of this article is to outline the well-recognised comorbidities associated with psoriasis to facilitate a discussion for general practitioners (GPs) to have with their patients about lifestyle changes, the need to screen for other diseases and management of comorbidities.

Discussion
GPs are in a prime position to screen, diagnose and manage comorbidities in a patient with psoriasis. GPs have a broad understanding of and exposure to general medicine and are in a privileged position of seeing many patients with psoriasis within the spectrum of the disease.

Psoriatic arthritis
Psoriatic arthritis (PsA) is a chronic inflammatory spondyloarthropathy that affects up to 42% of patients with psoriasis¹ and up to 1% of the general population.² Moll et al described five types of PsA, namely oligoarticular asymmetrical arthritis, symmetrical polyarthritis, distal arthritis, arthritis mutilans and spondyloarthropathy (which can affect the spine and sacroiliac joints).¹

PsA affects men and women equally; in contrast, rheumatoid arthritis has a female preponderance.³ In the majority of cases, psoriasis precedes PsA; however, PsA can occur concomitantly or precede the cutaneous signs. PsA is often underdiagnosed, with a delay in therapy resulting in morbidity and impaired quality of life (QoL). Joint damage starts early in the disease, manifesting in dactylitis, enthesitis and spondylitis.³ Tendons, ligaments, joints, synovium and bone can all be inflamed in PsA.³

PsA typically starts as a mild oligoarticular disease, although for 20% of affected patients it progresses to a severe form that comprises polyarticular disease and joint destruction.² It is more asymmetrical than rheumatoid arthritis.² Symptoms include pain and stiffness at rest that improve with movement, and morning stiffness that lasts for longer than 30 minutes.³ Enthesitis represents inflammation around the insertion of the tendon or ligament into the bone. Dactylitis, which is inflammation of the entire digit, can present as a ‘sausage finger’ because of inflammation of the joints and tendons.²,⁴ Both enthesitis and dactylitis are common in PsA.

Serum rheumatoid factor is elevated in 13% of patients with PsA, compared with 80% of those with rheumatoid arthritis.²
Radiographic changes include pencil-in-cup deformity, with digit shortening and bone lysis. These changes can occur within two years of disease onset.

PsA is considered a spondyloarthropathy because of the extra-articular features and spondylitis that occur in up to 40% of patients. It is also associated with HLA-B27. Nail involvement affects approximately 87% of patients with PsA. Typical changes include pitting, crumbling, onycholysis, leukonychia, subungual hyperkeratosis and splinter haemorrhages.

Because psoriasis precedes PsA by approximately 12 years, there is ample time to ask patients about symptoms of PsA and investigate and treat early in the disease process before permanent joint destruction occurs. This primary prevention is not undertaken in almost 60% of patients with PsA, who do not have their joints treated. When assessing a patient with psoriasis, no matter how severe, it is important to examine their nails and joints, ask about symptoms of PsA and provide analgesia and early referral to a rheumatologist.

Metabolic syndrome
Patients with psoriasis typically have a large habitus, an unhealthy diet and risk factors for cardiovascular disease (CVD). In patients with psoriasis, the prevalence of hyperlipidaemia is 46%, hypertension 42%, type 2 diabetes (T2D) 17% and obesity 14%. The more severe the psoriasis, the greater the risk and severity of metabolic syndrome. Therefore, it is critical that patients with psoriasis are evaluated for the risk factors for metabolic syndrome.

The development of hypertension is 1.3 times more likely in patients with mild psoriasis than in patients without psoriasis. This increases to 1.49 times in patients with severe disease. The risk of T2D is almost two times greater in patients with psoriasis when compared with patients without psoriasis. Proinflammatory cytokines and systemic inflammation compounded by lifestyle and social circumstances are thought to be responsible for the increased risk. Obesity alone with inflammatory cytokines increases the risk of developing and worsening psoriasis. Weight loss can therefore improve psoriasis and the effect of therapies. Patients with psoriasis are more likely to have cardiovascular mortality than patients without psoriasis, so it is important that risk factors are screened for and treated. Newer systemic therapies aimed at reducing inflammation have been shown to reduce the risk of developing CVD.

Psoriasis has also been reported to occur with peripheral vascular disease, uveitis, fatty liver and renal disease.

Inflammatory bowel disease
Patients with psoriasis are at higher risk of having inflammatory bowel disease (IBD) than the general population. The prevalence of psoriasis in patients with IBD can be up to 10%. IBD occurs in 0.4% of the general population, compared with 1.6% of patients with psoriasis. The risk of developing psoriasis in patients with Crohn’s disease has been reported to be five times greater than the risk for controls. Crohn’s disease and psoriasis have similar peak ages of onset, findings of intestinal permeability, immunopathogenesis and responses to therapies. IBD occurs more commonly in patients with both psoriasis and PsA when compared with patients with psoriasis alone.

This is important to consider when choosing therapies, as TNF-inhibitors and IL-17 inhibitors have been reported to induce IBD in patients with psoriasis.

Psychiatric illness: Depression, anxiety
Social stigmatisation and cosmetic and financial impacts, in addition to the psychological distress of a chronic disease, result in psychiatric and mental health issues with psoriasis. The location and duration of psoriasis – as well as patient factors such as age, sex and occupational and relationship status – contribute to the impact on QoL. The impact of psoriasis on QoL is reported as similar to, if not worse than, the impact of cancer or diabetes.

Avoiding intimacy and close relationships because of stigmatisation and social isolation can worsen psychiatric conditions. While psychiatric conditions can be the result of psoriasis, it has recently been shown that they can also induce or worsen the disease. The pathophysiology of depression and psoriasis may be similar, with elevation of proinflammatory cytokines interleukin (IL)-1 and IL-6 suggesting biochemical and physiological interdependence rather than physical consequence.

The prevalence of depression in patients with psoriasis has been reported as high as 18% in some studies, although anxiety has been reported in up to 30% of patients. Anxiety does not correlate with the severity of the skin disease. The economic burden of psoriasis is accentuated by the presence of psychiatric disorders when taking into account emergency department and outpatient visits, time off work and prescription costs.

Suicidal ideation occurs in 7–17% of patients with psoriasis. Patients with severe psoriasis were more likely to have suicidal ideation, suicide attempts and completed suicide than the general population. Clinical trials evaluating the efficacy of newer medications for psoriasis typically incorporate QoL and depression questionnaires to assess the impact on psychiatric health. It is therefore important to identify patients with psoriasis at risk of mental health issues and monitor them for anxiety, seclusion, depression and suicidal ideation.

Dementia
Patients with dementia are more likely to have had psoriasis than patients without dementia. A case control study found that after accounting for confounders (eg cardiovascular risk factors including hypertension, hyperlipidaemia and income status), patients with dementia had an odds ratio of 1.46 of having previous psoriasis when compared with the control group. Other studies have implied cognitive decline, poor QoL and earlier death for patients with psoriasis.

Harmful behaviours
Alcohol consumption may be elevated in patients with psoriasis. Harmful,
hazardous and dependent drinking can lead to increased morbidity and mortality. Alcohol intake is an independent risk factor for the development of psoriasis and PsA.17 One study found that high-risk drinking occurred in 24% of the study population, compared with 14% of the general population. Alcohol dependency was four times as likely in patients with psoriasis.18

Alcohol consumption in young male patients with psoriasis is associated with depression and anxiety.17 Although alcohol and drug intake might be a response to the impaired QoL associated with psoriasis, it also promotes a cytokine inflammatory response that worsens psoriasis, with evidence showing that alcohol abstinence improves psoriasis.17

Gambling is also more likely to occur in patients with psoriasis.18 Patients with psoriasis are more than 30 times likely to gamble than the general population.18

Smoking and exposure to tobacco smoke is associated with the development of psoriasis.19 Patients with psoriasis are also more likely to be smokers, which adds to the increased risk of cardiovascular disease and metabolic syndrome.20 One study showed that 49% of patients with psoriasis were smokers, compared with 30% of the general population.18

Malignancies
There is a higher incidence of lymphoproliferative malignancies and non-melanoma skin cancers (NMSCs) in patients with psoriasis when compared with the general population. The risk of lymphoma – in particular, Hodgkin’s lymphoma and cutaneous T-cell lymphoma – is at least three times greater in patients with severe psoriasis than the general population.21 The relative risk of any lymphoma in patients with mild psoriasis is 1.34.

The risk of cutaneous malignancies in psoriasis is difficult to measure given treatments and immunosuppressive medications may increase the risk. Despite treatment-attributable risk, there seems to be a moderately increased risk of NMSCs but not melanomas,22,23 so regular skin checks and vigilance are prudent, especially for patients who have had immunosuppressive therapy or phototherapy.

Infections
Infections can induce psoriasis or be associated with or caused by medications that treat psoriasis.24 Chronic plaque psoriasis and guttate psoriasis are both associated with Streptococcus pyogenes infection activating T cells through superantigens. The pathogenesis occurs via a dysfunction of the skin microbiome and impaired tolerance, resulting in abnormal immune activation.25

Beta-haemolytic streptococcus is known to trigger and exacerbate psoriasis. There are reports of perianal streptococcus with psoriasis, and streptococcal infections with palmoplantar psoriasis.24 Other microorganisms that have been linked with psoriatic lesions include Staphylococcus spp., Corynebacterium spp. and Cutibacterium spp., though there are some conflicting reports.25 Staphylococcus aureus colonises psoriasis in approximately 60% of cases, with the majority secreting staphylococcal toxins. These toxins are associated with a more severe type of psoriasis.25 There is no evidence to date to support tonsillectomies to reduce the incidence of guttate psoriasis.

Malassezia spp., a common yeast, is associated with scalp psoriasis, seborrhoeic dermatitis and sebopsoriasis. It is part of the normal skin flora and is found in areas with a high density of sebaceous glands.26 Treatment of Malassezia spp. is associated with a reduction in scalp psoriasis, but to date there is no correlation with the severity of psoriasis.

Periodontitis a common Gram-negative bacterial infection affecting the teeth that is more common in patients with psoriasis than in the general population.26 It is difficult to determine whether the presence of infections causes psoriasis or is a result of immune changes that make the lesions more susceptible to infectious colonisation. Patients with human immunodeficiency virus (HIV) tend to have more severe psoriasis. Hepatitis C virus and Candida albicans are known triggers of psoriasis. Candida superimposed on flexural psoriasis makes treatment difficult, resulting in persistent and severe plaques. Hepatitis C infection typically occurs before the development of psoriasis, possibly due to upregulation of cytokines.24

Immune modifiers, immunosuppressive agents and biological therapies predispose patients to develop infections or exacerbate existing infections. Therefore, it is important to screen for conditions such as tuberculosis, hepatitis B and C, HIV, syphilis and strongyloidiasis before commencing and, if at high risk, during such therapies. Live vaccines must also be avoided given the risk of dissemination. There is an increased risk of herpes zoster with tumour necrosis factor-α inhibitors and Candida spp. infections with secukinumab and ixekizumab.24

Disease activity scores and quality of life scores
The Psoriasis Area and Severity Index (PASI) is the most commonly used tool in Australia for the assessment of psoriasis.
It calculates a score between 0 and 72 on the basis of the erythema (redness), induration (thickness) and desquamation (scaling) on the various locations of the body. It is a criterion for the initiation and continuation of biological therapy. Patient Global Assessment (PGA) and Body Surface Area (BSA) are also used.

QoL scores such as the Dermatology Life Quality Index (DLQI), Health-related quality of life (HRQOL), Psoriasis Disability Index (PDI) and Skindex can be used to assess the impact of psoriasis. PsA questionnaires include but are not limited to Psoriatic Arthritis Quality of Life (PsAQoL) and Psoriatic Arthritis Impact of Disease (PsAID). Depression scoring systems also exist.

Although these QoL tools are time consuming to complete and analyse, they provide important current and evolving information about the impact that psoriasis has on a patient.

**Conclusion**

In addition to treating the skin, it is important to assess patients for psoriasis-related comorbidities by taking a simple history (eg asking about arthralgia and arthritis, alcohol and drug intake/abuse, sexual dysfunction), performing clinical examinations (eg measuring waist circumference, weight, body mass index), performing QoL scales (eg depression and anxiety scales) and ordering laboratory investigations (eg lipid profile, blood sugar levels, liver and renal function). A multidisciplinary team approach to patients with psoriasis may include non-GP specialists such as dermatologists, rheumatologists, cardiologists, endocrinologists, gastroenterologists and psychiatrists as well as allied health practitioners (eg psychologists and dietitians).

Treating a patient with psoriasis should encompass education about lifestyle changes and evaluating their risk of other comorbidities. It is speculated that reducing the amount of circulating cytokines will improve the systemic manifestations and complications associated with psoriasis.

With the advent of newer biological and immunosuppressive agents in the armamentarium to treat psoriasis, it is essential to monitor for other infections, malignancies and side effects. A holistic approach to a patient with psoriasis that includes evaluating and assessing comorbidities and risk of morbidity is essential, as psoriasis should be considered a systemic disease rather than cutaneous condition alone.

**References**
