CLINICAL VIGNETTE

Psoriasis: an update for the Internist

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Introduction

Psoriasis is a chronic, inflammatory disorder most commonly manifest by erythematous, scaly plaques of the skin[1], and pain, stiffness, and swelling of the joints[2]. The latest prevalence data show that psoriasis affects approximately 3% of the United States population, an estimated 7.4 million Americans[3]. With such a prevalence, psoriasis is likely to be commonly encountered by internists and primary care physicians in their every-day practices.

Depending on severity, numerous treatments for psoriasis exist: topical agents (steroids, Vitamin D analogue calcipotriene, and Vitamin A analogue tazarotene); oral systemic agents (methotrexate, acitretin, or cyclosporine); and phototherapy (narrowband ultraviolet B (NB-UVB) phototherapy, or less commonly, psoralens plus ultraviolet A (PUVA) photochemotherapy)[4]. In recent years, biologic agents have emerged as highly effective, but expensive, therapies for moderate-to-severe psoriasis[5]. We will review the basics of current biologic therapies, as well as aspects of phototherapy, discuss the growing evidence for cardiovascular risk associated with psoriasis, and address when to refer a psoriasis patient to a dermatologist.

Psoriasis Pathogenesis

In a simplified view, the pathogenesis of psoriasis is initiated by the activation of specialized dendritic cells in the epidermis and dermis (due to genetic factors, with environmental factors, infections, or autoimmune triggers contributing)[6], leading to the production of tumor necrosis factor (TNF)-α**,** interleukin (IL)-12, and interleukin (IL)-23.[7] These mediators promote the differentiation of CD4+ T lymphocytes into T helper (Th)-1 and T helper (Th)-17 cells. Further production of TNF-α, interferon (IFN)-γ, and interleukin (IL)-17 promote the inflammatory response, endothelial cell neovascularization, and keratinocyte hyper-proliferation characteristic of psoriatic lesions[6].

Biologic agents for psoriasis

The biologic agents are monoclonal antibodies that inhibit specific targets in the immune pathways of psoriasis. We review the current FDA-approved biologic therapies for psoriasis: etanercept, adalimumab, infliximab, and ustekinumab[8].

Comorbidities that may preclude use of biologic agents include congestive heart failure, demyelinating disorders, lymphoproliferative disease, hematologic disorders, malignancies, and infections (e.g. tuberculosis, HIV, hepatitis B or C). Patients should be screened with a baseline metabolic panel, complete blood count (CBC) with platelets, liver function tests, hepatitis B and C serologies, and a pregnancy test for women of child-bearing potential[13].

Consensus guidelines published in 2008 by the National Psoriasis Foundation recommended that all patients be screened with a tuberculin skin test (TST) prior to initiating immunosuppressive therapy. Patients with latent tuberculosis (TB) can be given biologics preferably after a 9 months course of isoniazid prophylaxis. However, some evidence showed immunosuppressive therapy could be initiated after 1 to 2 months of isoniazid therapy if necessary[14].

Phototherapy for psoriasis

Prior to the administration of biologic agents or oral systemic medications, many patients with moderate-to-severe psoriasis pursue treatment with phototherapy. Certainly, for patients with health problems prohibiting systemic immunosuppressants; pregnancy; or in pediatric or geriatric patients, phototherapy may be the first-line treatment option. Currently, the two main phototherapeutic modalities are NB-UVB and PUVA[15].

Ultraviolet B radiation exerts its effects on psoriasis by inducing pyrimidine dimer formation of nuclear DNA as well as up-regulation of the p53 tumor

suppressor gene. These effects ultimately lead to inhibition of proliferating keratinocytes and lymphocytes. In PUVA, the psoralen molecule is administered orally or topically, followed by ultraviolet A (UVA) radiation. Psoralen intercalates into DNA molecules, binding to a thymidine base upon UVA radiation. This DNA-psoralen cross-linking leads to inhibition of psoriatic keratinocyte proliferation[15].

Cardiovascular risk associated with psoriasis

Psoriasis has been linked with traditional cardiovascular risk factors, including the metabolic syndrome[18]. One prospective cohort study found that psoriasis was associated with an elevated risk of diabetes and hypertension[19]. Numerous studies, however, have shown that patients with psoriasis have an elevated risk of myocardial infarction[20] (MI) and stroke[21], independent of these cardiovascular risk factors. In a prospective cohort study of psoriasis patients in the United Kingdom, Gelfand et al[20]. found an increased risk of MI in psoriasis patients of varying severity and age, with the greatest adjusted relative risk of 3.10 (95% CI, 1.98-4.86) in younger patients with severe psoriasis. In another study, Gelfand et al[21]. showed an independently elevated risk of stroke in severe psoriasis patients (hazard ratio (HR) 1.43, 95% CI, 1.1-1.9).

Aggressive treatment of psoriasis was also found to be associated with a significant reduction in the risk of MI, as demonstrated by Wu et al[22], who found that psoriasis patients treated with TNF-inhibitors had a decreased risk of MI compared to topically treated patients (HR 0.50, 95% CI, 0.32-0.79). Despite this growing evidence, a survey from 2010 to 2011 found most primary care physicians and cardiologists did not routinely screen for cardiovascular risk factors in psoriasis patients[23]. Although further prospective studies need to be performed, a recent article published in the *Journal of the American Heart Association* states that psoriasis patients should be educated on the elevated risk of cardiovascular disease and aggressively managed for modifiable cardiovascular risk factors[24].

Referral to a dermatologist

One practical method of analyzing psoriasis severity is based on body surface area (BSA) involvement. Generally, primary care physicians can manage mild psoriasis with topical modalities[7]. If patients progress to moderate or severe psoriasis requiring higher doses of high-potency steroids or alternative systemic therapies, referral to dermatology is warranted. Other recommended criteria for referral include failed or poorly tolerated topical therapy, involvement of difficult-to-treat sites (e.g. palmoplantar, facial, genital), generalized pustular psoriasis, acute unstable psoriasis, or acute erythroderma[26].

Special consideration should be given to pediatric and geriatric populations with psoriasis. In children, streptococcal throat infection can trigger guttate psoriasis, characterized by scaly, pink or salmon-colored papules mostly on the trunk. In geriatric patients, treatment of psoriasis can be challenging due to the high prevalence of comorbidities, polypharmacy, and risk of infection. Even topical agents must be used with heightened caution to avoid skin atrophy, fragility, purpura, and skin infections[27]. Elderly patients, therefore, may be appropriately referred to a dermatologist sooner in the management of their psoriasis.

Conclusion

In this brief update, we have provided an overview of advancements in psoriasis since the turn of the 21st century. Biologic agents have emerged as highly effective therapies, providing significant relief from moderate-to-severe psoriasis. However, phototherapy still remains as a safe and effective alternative to systemic immunosuppressive medications. Moreover, numerous studies have found an elevated risk of cardiovascular events in psoriasis patients, independent of traditional risk factors. Although certain situations necessitate dermatology referral, psoriasis is a common disorder with systemic manifestations requiring the attention of internists and dermatologists alike.

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Table I. FDA-approved biologic therapies for psoriasis

	Immune target	Indications	Dosing	Clinical efficacy for psoriasis
Etanercept (Enbrel®)	TNF-α	Psoriasis, PsA, RA, JRA, AS	Twice weekly	In a phase III, randomized, controlled trial, 49% of etanercept-treated patients with moderate-to-severe plaque psoriasis achieved PASI 75 at week 12[9]
Adalimumab (Humira®)	TNF-α	Psoriasis, PsA, AS, RA	Every other week	In a phase III, randomized, controlled trial, 71% of adalimumab-treated patients with moderate-to-severe plaque psoriasis achieved PASI 75 at week 16[10]
Infliximab (Remicade®)	TNF-α	Psoriasis, PsA, RA, UC, CD, AS	Weeks 0, 2, and 6, followed by every 8 weeks	In a phase III, randomized, controlled trial, 80% of infliximab-treated patients with moderate-to-severe plaque psoriasis achieved PASI 75 at week 10[11]
Ustekinumab (Stelara®)	IL-12/ IL-23	Plaque psoriasis, PsA	Weeks 0 and 4, followed by every 12 weeks	In a phase III, randomized, controlled trial, 67.1% of ustekinumab-treated patients with moderate-to-severe plaque psoriasis achieved PASI 75 at week 12[12]

Abbreviations: PsA: psoriatic arthritis, RA: rheumatoid arthritis, AS: ankylosing spondylitis, JRA: juvenile rheumatoid arthritis, UC: ulcerative colitis, CD: Crohn's disease

PASI 75: Achievement of 75% reduction in the Psoriasis Area and Severity Index (PASI) as measured by body surface area involvement (BSA) and degree of erythema, induration, and scaling.

Table II. Phototherapeutic modalities for psoriasis

	Efficacy	**Advantages**	**Disadvantages**
NB-UVB	NB-UVB was shown to reduce PASI by a mean of 84.1% after 12 weeks of treatment[16]	Safe for almost any patient, including children and pregnant women[4]	Phototoxicity
PUVA	PUVA demonstrated a PASI 90 and PASI 75 of 69% and 86% after 12 weeks of treatment[17]	Deeper tissue penetration with UVA, increasing efficacy for thick plaques, palms, soles, and nail involvement[4]	Phototoxicity; Long-term elevated risk of cutaneous malignancy[4]

PASI: Psoriasis Area and Severity Index as measured by body surface area involvement (BSA) and degree of erythema, induration, and scaling.

Table III. Assessment of psoriasis severity via BSA

	BSA
Mild	<3%
Moderate-to-Severe	3-10%
Severe	>10%

Patient's palmar surface area approximates 1% BSA[25]