PHOTO ROUNDS

A young girl with scaly skin plaques

The patient had numerous thick red plaques on her back and the extensor surfaces of elbows, knees, and forearms

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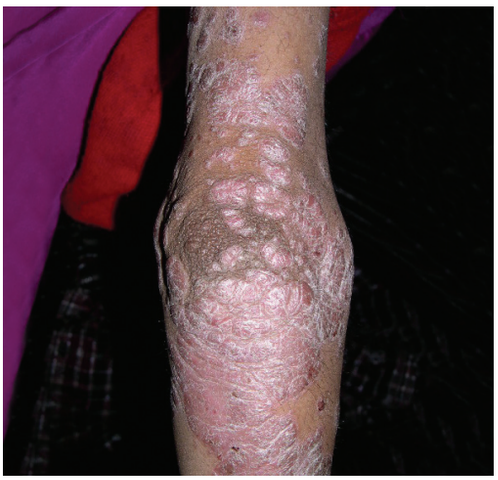
An otherwise healthy 12-year-old girl came to the office with a 1-year history of a symmetric, generalized scaly eruption. These skin plaques did not itch; she had no recent history of sore throat. She also had no personal or family history of atopy or any similar eruption. She mentioned that the appearance of her skin and the "flaking" was making her very self-conscious and she wanted to have some intervention to make the skin clear.

The patient had multiple red, scaly, thick plaques on her back and the extensor surfaces of her elbows, knees, legs, and forearms (**FIGURES 1 AND 2**). There were no scalp, mucosal, or nail involvements. Rheumatologic examination and review of systems were unremarkable.

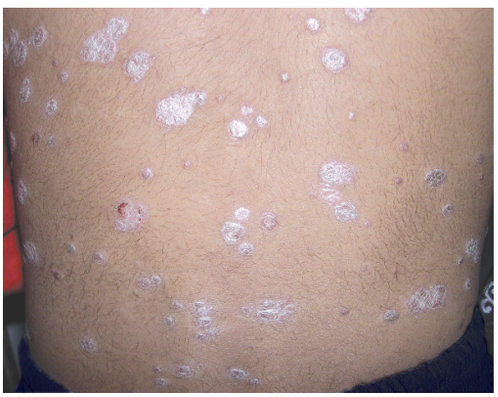
- **What is your diagnosis?**
- **How would you manage this case?**

FIGURE 1 **Plaques on the arm...**



Scaly eruptions on the patient's arm. Similar plaques were on her legs.

FIGURE 2 **...and on the back**



Well-demarcated scaly plaques on the patient's back.

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TABLE 1

Classification of psoriasis

Chronic plaque psoriasis	Symmetrical plaques up to 20 cm in diameter, with a predilection for the elbows, knees, presacrum, scalp, hands, and feet 5%–30% of patients develop a seronegative arthropathy
Guttate psoriasis	Numerous small papules and plaques over the upper trunk and proximal extremities Most common form of psoriasis in children, and may be triggered by any streptococcal infection including streptococcal perianal dermatitis Spontaneous remission is the rule
Generalized pustular and erythrodermic psoriasis	Uncommon variants associated with high morbidity that may be fatal

FAST TRACK

Triggering factors for psoriasis include reactions to certain drugs and streptococcal antigens

Diagnosis: Chronic plaque psoriasis

Psoriasis is a noninfectious inflammatory skin disorder characterized by well-defined erythematous plaques that bear large, adherent silvery scales. It can appear at any age, but 75% of patients have an onset before the age of 40 years.[1]

Psoriasis was once considered a hyperproliferative disorder, but is now recognized as an autoimmune phenomenon involving activation of T-cells. As a result, new immunosuppressive agents have been added to the list of traditional therapies, opening a new chapter of immunomodulatory therapy.

Clinical presentations of psoriasis

In its classic presentation, psoriasis does not pose a diagnosis challenge to most clinicians—it presents as a sharply demarcated erythematous plaques with silvery white scales. Although many classification systems exist, a concise classification is included in **TABLE 1**. Skin conditions to be considered for differential diagnosis are summarized in **TABLE 2**. The US Food and Drug Administration defines "severe" psoriasis as involving more than 20% of body surface area.[2]

Pathogenesis of psoriasis

Psoriasis is a polygenic disorder. Susceptibility is determined by a large number of genes, each with a low penetrance. Important genetic associations are with HLA-Cw6, HLA-B27, and the genes PSOR-S1 and PSOR-S2 on chromosome 6 and 17, respectively.

Several triggering factors are identified, of which streptococcal antigens and certain drugs seem important, but the specific antigens are still unknown. The end result is activation of T-cells, overexpression of cytokines, and an inflammatory response.

Review of the classic treatments for psoriasis

Topical therapy

Topical therapy is indicated when psoriasis is limited to less than 20% of the body surface. Potent class I and II topical corticosteroids are the most widely used treatment for mild disease. After plaque clearance they can be given intermittently for maintenance.

The vitamin D3 derivative calcipotriene (Dovonex) is another first-line agent. Tazarotene (Tazorac), a topical retinoid prodrug, is a second-line agent used as monotherapy or in combination. Many combined regimens use topical corticosteroids, calcipotriene, and tazarotene. Coal tar—different concentrations in liquid form—is useful in treating extensive areas of the body and scalp psoriasis.

Phototherapy

Failure of topical therapy or extensive disease are indications for phototherapy or systemic medications. The trend is to use phototherapy in the form of narrowband UVB, which has proven more effective than broadband UVB and to have fewer adverse effects than psoralen UVA therapy (PUVA).[3] Other light sources for home use are being developed.

Systemic agents

Methotrexate, given as a single weekly dose or in divided doses, has been used for more than 30 years; it inhibits the enzyme dihydrofolate reductase. An alternative immunosuppressive agent is cyclosporine. These 2 agents have high efficacy, but due to potential adverse effects they require careful patient selection and close follow-up.

Acitretin (Soriatane), an oral retinoid, is the treatment of choice for generalized pustular and erythrodermic psoriasis. It is also used in chronic plaque psoriasis, often in combination with phototherapy, which has a synergistic effect.

New treatments

Our understanding of the immunopathogenesis of psoriasis has led to the development of therapies designed specifically to interfere with T-cell activation and effector functions. Three new immunomodulatory biologics are FDA-approved for the treatment of moderate to severe psoriasis. Typical cost of this therapy is more than $1000/month.

Anti-TNF-α strategies

Etanercept (Enbrel) is an antibody against the cytokine tumor necrosis factor alpha (TNF-α). It is self-administered at 25 mg to 50 mg subcutaneously twice weekly. Studies with 50-mg injections have shown a 75% clinical improvement in 49% of patients at 12 weeks and 59% of patients at 24 weeks.[4]

The most common side effect is reaction at the injection site. It was reported to produce dramatic remission of psoriatic arthritis and prevent radiographic progression of the disease.[4–5] Due to raised concern about the risk of opportunistic infections, a purified protein derivative (PPD) test is advised before initiation of therapy to detect potential latent tuberculosis. Other risks include sepsis, pancytopenia, and worsening of multiple sclerosis.

TABLE 2

Differential diagnosis

Fungal infections
Squamous cell carcinoma in situ
Cutaneous T-cell lymphoma
Discoid eczema
Seborrhoeic eczema
Pityriasis rosea
Secondary syphilis
Hypertrophic lichen planus
Nummular dermatitis

Antibodies against T-lymphocyte surface molecules

Alefacept (Amevive) is a fusion protein that blocks T-cell activation and triggers apoptosis of activated T-cells. It is given as 15-mg weekly intramuscular injections. Thirty-three percent of patients reported a 75% clinical improvement in their psoriasis within 12 weeks.[6] Alefacept also decreases synovial tissue T-cell count, and may have a future role in psoriatic arthritis.

It has few side effects, but patients need weekly monitoring of their CD4+ count. Ongoing studies on combining it with ultraviolet light or extending the dose to 16 weeks are showing promise.[6]

Antibodies against adhesion molecules

Efalizumab (Raptiva) is a monoclonal antibody that blocks T-cell activation and migration. It is self-administered by the patient as a 1 mg/kg weekly subcutaneous injection. Forty-four percent of patients achieve a 75% clinical improvement in their psoriasis by 24 weeks.

FAST TRACK

New therapies for psoriasis are designed to interfere with T-cell activation and effector functions

TABLE 3

Future investigations

Photodynamic therapy	The use of a photosensitizing drug in combination with a light source is showing promise, and clinical studies are under way for the treatment of psoriasis
Excimer lasers	Deliver high-dose narrowband UVB to a localized area sparing uninvolved skin. Clear psoriasis faster than conventional phototherapy, and may become predominant in the future
CNTO-1275	Anti-interleukin-12 antibody that switches the immune response from a T-helper cell 1 cytokine reaction most commonly seen in psoriasis to a T-helper cell 2 cytokine response
T-cell receptor vaccines	Have been developed and are undergoing clinical trials in patients with psoriasis
Pimecrolimus	Used orally. It is a cytokine-release inhibitor with lesser immunosuppressive effects and side effects than tacrolimus and cyclosporin
Angiogenesis	Cutaneous blood vessels in psoriatic plaques are dilated, tortuous, and leaky Vascular endothelial growth factor (VEGF) is overexpressed, and VEGF or its receptors are potential therapeutic targets for psoriasis
Gene therapy	Chromosomes involved in psoriasis are being mapped Gene therapy promises to be one of the most important areas of treatment of psoriasis for the new millennium

FAST TRACK

Choose agents with synergistic effects without additive toxicities, such as a systemic agent combined with topical or phototherapy

The most common side effects are headache, fever, nausea, vomiting, and myalgia. A "rebound" phenomenon after discontinuation is observed in 14%, and it may worsen psoriasis in those unresponsive to treatment.[7]

Other anti-TNF medications such as infliximab (Remicade), adalimumab (Humira), and onercept are still in clinical trials.

Combination therapy: Achieving goals while reducing adverse effects

Some patients require therapy with several agents to maintain adequate clearing of their psoriasis. The ideal combination therapy should lead to enhanced clinical response with reduction of adverse effects.

It is important to choose agents with synergistic effects without additive toxicities. Examples are combination of a systemic agent with topical calcipotriene, topical steroids, or with phototherapy. PUVA should be used with care for patients taking immunosuppressive agents due to risk of squamous cell carcinoma.[8] A combination of 2 immunosuppressive agents is generally avoided due to risk of opportunistic infections, but has proven beneficial in a few therapy-resistant patients.[9] Further clinical experience is needed for the inclusion of the new biologics in combination therapy.

New directions in treating psoriasis

A summary of future directions and current investigations in the management of psoriasis is given in **TABLE 3**.

Our patient's treatment consisted of topical emollients, mid-potency topical corticosteroids, and tar shampoos/tar baths. She was responding well to the treatment. Introducing calcipotriene and reducing topical steroids is our next step.

Regular follow-up visits are scheduled every 4 to 6 weeks.

Conclusion

Patients with mild localized psoriasis can easily and effectively be managed by family physicians using topical treatments or combinations modalities as outlined above. Patients with extensive disease or resistant to treatment should be referred to a dermatologist in conjunction with a rheumatologist if psoriatic arthritis is suspected.

With improved understanding of the immunopathogenesis and genetics of psoriasis, advent of the biologic agents, and future strategies under investigation, our approach to treating psoriasis may be very different in the years to come. ■

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