

**Perspectives From
Nicole Furfaro, MSN, ARNP**

What are some of the barriers to early diagnosis of PsA?

The single most important and modifiable barrier to early diagnosis is improving disease



awareness. A dermatologist I was following while in nurse practitioner school pointed out a patient with psoriasis who had significant dactylitis in 2 fingers and said to the patient, "Nicole is a rheumatology nurse; this is arthritis, isn't it?" and that was the beginning and end of the conversation.

Although care has improved since then, symptoms of PsA often are overlooked by patients, their primary care providers, and sometimes even specialists. Many patients are not referred for a rheumatology consult until they have suffered with symptoms of inflammatory skin and joint disease for years. By then, many have irreversible damage to joints and their self-esteem.

Many patients do not receive early and aggressive treatment because they present with pauciarticular arthritis (ie, few symptomatic joints) coupled with vague back pain and stiffness or fatigue. In addition, PsA joints tend to have more tendon or enthesial inflammation and a relative lack of synovitis compared to RA, thus making the obvious signs difficult to evaluate.

Other factors are the lack of genetic markers and the lack of a disease-specific

(continued on page 3)

Psoriatic Arthritis: Biologic Treatment Advances and Guideline Interpretation

Martin J. Bergman, MD, Senior Editor

Psoriatic arthritis (PsA) is a complex progressive disease that affects the skin and joints. The inflammatory nature of PsA provides insights into pathogenic mechanisms as well as therapeutic targets. Conventional treatment for PsA, primarily nonsteroidal anti-inflammatory drugs (NSAIDs) and disease-modifying antirheumatic drugs (DMARDs), does not always provide relief nor prevent disease progression in many patients and is associated with potentially treatment-limiting adverse effects. This issue of PCE Updates in Rheumatology provides an overview of current knowledge of the pathogenesis of PsA, features of the disease that facilitate diagnosis, and use of tumor necrosis factor-alpha (TNF- α) agents to reduce symptoms of PsA and prevent disease progression.

Key Factors of PsA: Inflammation and Bone Erosion

In PsA, T cells initially infiltrate skin lesions and later proliferate in synovial fluid and tissue.¹ A key factor in the immune-mediated inflammatory reaction is the increased presence of activated T-lymphocyte-released chemokines and cytokines. TNF- α , in particular, appears to play a major role in the inflammatory manifestations of PsA and erosive bone damage in later stages of the disease.¹⁻⁶ A pro-inflammatory cytokine, TNF- α has been found in the skin and synovial fluid and tissues from patients with PsA.¹

Emerging evidence indicates that TNF- α is involved in multiple pathogenic pathways, including enhancement of cellular adhesion and trafficking and T-cell infiltration, as well as stimulation of keratinocyte proliferation in psoriatic plaques.^{1,2} Additionally, TNF- α has been shown to increase proliferation and activation of synovial and epidermal fibroblasts, which over time results in fibrosis, a feature of advanced disease.^{3,4} Along with interleukin 1 (IL-1), TNF- α regulates metalloproteinases, which may be involved in erosion of cartilage in inflammatory arthritis.⁶

(continued on page 4)

Understanding Psoriatic Arthritis: Fast Facts

- Among the 1% to 3% of the general population with psoriasis, up to 34% have associated arthritis
- PsA is an inflammatory disorder characterized by articular and extra-articular features
- Psoriatic manifestations of PsA are variable. Most patients experience psoriasis vulgaris; pustular psoriasis, flexural psoriasis, and guttate lesions also may develop. Nail lesions are common, occurring in nearly two thirds of patients
- Arthritic complications of PsA affect peripheral joints and the axial skeleton
- Early in the disease, 1 of 5 clinical patterns may be identifiable (Table); however, during the course of disease progression, the pattern of the articular manifestations of PsA often changes. In addition to psoriasis, extra-articular expressions of the disease include conjunctivitis and iritis, which may occur in as many as 1 of 3 patients, and, less commonly, aortic incompetence
- Individuals with PsA experience progressive joint damage accompanied by increasing disability. As many as 20% of people with PsA have severe, debilitating arthritis
- Factors predictive of progressive damage include the presence of certain human leukocyte antigens (HLAs), at least 5 swollen joints at presentation, and a high level of medication usage
- Each actively inflamed joint, as indicated by stress pain, joint line tenderness, and/or swelling, is associated with a 4% increase in risk of further damage within 6 months
- Risk for mortality may be increased in individuals suffering from PsA
- The disease affects men and women equally, and while most people experience onset of PsA during mid-adulthood (mean age, 36-40 years), children and older individuals also may be affected
- As many as 40% of patients with PsA report a family history of psoriasis and PsA
- HLAs have been associated with PsA, as well as its prognosis
 - HLA-B27 is present in 40% of patients with PsA
 - Support for non-HLA gene involvement comes from evidence suggesting that CARD15 is independently linked to risk for PsA
- Infections and trauma are other pathogenic factors that may be involved in PsA
 - Infections, such as those caused by streptococcus and viruses, may trigger an immune response that ultimately leads to PsA
 - Following trauma, psoriasis develops on irritated skin, the so-called Koebner's phenomenon. It may be that a trauma-activated neural response, in turn, stimulates an inflammatory reaction

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Target Audience

Nurse practitioners (NPs), physician assistants (PAs), and physicians in the practice of rheumatology

Goal

To provide clinicians with insights into the presentation and pathogenesis of psoriatic arthritis (PsA) and review currently available therapies with a focus on tumor necrosis factor-alpha (TNF- α) inhibitors.

Learning Objectives

After completing this activity, the participant should be better able to:

- Describe the dermal, articular, and extra-articular manifestations of psoriatic arthritis (PsA).
- List criteria from the CLASSification criteria of Psoriatic ARthritis (CASPAR) that may serve as a diagnostic guide for patients presenting with symptoms of PsA.
- Review results from clinical trials assessing the efficacy, safety, and inhibition of disease progression associated with anti-tumor necrosis factor-alpha (TNF- α) therapy.

Accreditation Information



This activity has been planned and implemented in accordance with the Essential Areas and Policies of the Accreditation Council for Continuing Medical Education (ACCME) through the joint sponsorship of Continuing Education Alliance and the University of Nebraska Medical Center, Center for Continuing Education.

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Table.
Five Patterns of Psoriatic Arthritis

Symmetric arthritis	Affects multiple symmetric pairs of joints, occurring in same joints bilaterally; can be disabling; generally milder; associated with less deformity than RA
Asymmetric arthritis	Can affect any joint (ie, knee, hip, ankle, wrist); may involve a few or several joints; does not occur in same joints bilaterally; hands and feet may have enlarged "sausage" digits; joints may be warm, tender, and red; episodic pain may occur that is responsive to medical therapy; in more severe cases, disabling disease can develop
Distal interphalangeal predominant (DIP)	Involves primarily distal joints of fingers and toes; affects ~5% of patients with PsA; may be differentiated from osteoarthritis by presence of nail changes
Spondylitis	Inflammation with stiffness of neck, lower back, sacroiliac, or spinal vertebrae, hindering motion and causing pain; peripheral arthritis may be present in hands, arms, hips, legs, and feet; affects ~5% of people with PsA
Arthritis mutilans	Affects primarily small joints of hands and feet; may also be associated with neck or lower back pain; severe, deforming, and destructive type of arthritis; affects ~5% of people with PsA

RA = rheumatoid arthritis.

National Psoriasis Foundation.¹⁷

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1. Read the newsletter.
2. Relate the content material to the learning objectives.
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Perspectives From Nicole Furfaro, MSN, ARNP

(continued from page 1)

laboratory marker, such as the RF or anti-CCP used to diagnose RA. In addition, only about half of the patients with PsA have elevated ESR. There is also a tendency in primary care to dismiss PsA as osteoarthritis, which is more common.

With ongoing education, awareness, disease classification, and the growing recognition of the importance of early treatment, hopefully there will be fewer barriers to early diagnosis.

What is the impact of biologics on the management of PsA?

Biologic DMARD treatment has a significant impact on the severity of PsA in the skin and joints and reduction of disease progression. I have witnessed the advent of anti-TNF- α use in PsA and the life-altering changes patients have enjoyed with such efficacious medications. Aside from the benefit in physical functioning, lack of radiographic progression, and relative lack of side effects, these medications have allowed patients with severe skin disease to lead more normal lives.

Rheumatology professionals often are unaware of the dramatic statistics of how a "visible" disease such as PsA affects patients' lives, with many patients acknowledging thoughts of suicide in relation to living with psoriasis. For example, I remember a patient involved in early clinical trials who would come to the office for evaluation and leave an outline of his body on the chair from skin flaking. To see that person with an exuberant smile on his face because of improvement in his joint pain and stiffness and virtual clearing of his skin after a few months of therapy says it all. For that person to say that he can now go out in public without fear of people staring at him speaks volumes about the impact of biologics on psoriasis and PsA.

Bone erosion is a well-recognized feature of PsA, which is demonstrated on radiographs as significant joint-space narrowing, large eccentric bone lesions, pencil-in-cup erosions, and extensive resorption of the distal phalanges, or acrolysis.⁷⁻⁹ Osteoclasts are the main cells responsible for bone erosion in inflammatory arthritis.^{5,6} Increased levels of circulating osteoclast precursors have been found in the peripheral blood of individuals with diseases featuring bone erosion, as well as in those with PsA.^{6,10,11} TNF- α may contribute to the process of bone erosion through osteoclastogenesis.^{5,6} One pathway might be through TNF- α increased production of circulating osteoclast precursors, and a second might occur in the joint via TNF- α -mediated upregulation of receptor activator of NF- κ B ligand (RANKL) expression.⁶ Wingless proteins (Wnt), which regulate bone formation, and the Dickkopf protein, DKK-1, which inhibits Wnt signaling, also appear to be involved in the pathogenesis of bony erosions in patients with PsA.¹² In the mouse model, normalization of DKK-1 eliminated bone erosions and led to increased bone growth. Interestingly, initiation of anti-TNF- α therapy in patients with rheumatoid arthritis (RA) results in normalization of elevated DKK-1 levels. Although the pathogenesis of PsA is not completely understood, insights into the probable role of TNF- α has stimulated interest in the cytokine as a possible therapeutic target for PsA.

Diagnosing PsA

There are no criteria for the diagnosis of PsA. Instead, the diagnosis has been based on the presence of inflammatory arthritis (peripheral

Table 1. CLASSification criteria for Psoriatic ARthritis (CASPAR) Criteria

Presence of inflammatory articular disease (joint, spine, or enthesal) with at least 3 points from the following 5 categories*:

1. Evidence of current psoriasis, personal history of psoriasis, or family history of psoriasis**
2. Typical psoriatic nail dystrophy, including onycholysis, pitting, and hyperkeratosis on examination
3. Negative test result for presence of rheumatoid factor by any method except latex, but preferably by enzyme-linked immunosorbent assay or nephelometry, according to local laboratory reference range
4. Current dactylitis, defined as swelling of an entire digit, or history of dactylitis recorded by a rheumatologist
5. Radiographic evidence of juxta-articular new bone formation, appearing as ill-defined ossification near joint margins (but excluding osteophyte formation) on plain radiographs of hand or foot

*Current psoriasis is assigned a score of 2; all other features are assigned a score of 1.

**Current psoriasis = psoriatic skin or scalp disease at time of examination as judged by a rheumatologist or dermatologist; personal history of psoriasis = history obtained from patient, family physician, dermatologist, rheumatologist, or other qualified healthcare provider; family history of psoriasis = history of the disease in first- or second-degree relative, according to patient report.

Taylor W et al.¹⁵

arthritis and/or sacroiliitis or spondylitis) and psoriasis and the absence of positive serologic tests for rheumatoid factor.¹³ While the erythrocyte sedimentation rate is elevated in 40% to 60% of patients, no laboratory test is diagnostic of PsA.¹⁴ Radiologic findings may be absent in early stages of the disease. In addition, a patient may have concurrent psoriasis and RA, psoriasis and osteoarthritis, or no known psoriasis, which complicates the diagnosis of PsA. The CLASSification criteria for Psoriatic ARthritis (CASPAR) criteria, which are derived from a large prospective database, may provide a guide for confirming a diagnosis of PsA (Table 1).¹⁵ Specificity of the criteria is high—98.7%, but the sensitivity of 91.4% is similar to or lower than that for other previously published criteria. Nonetheless, the system is easy to implement and recommended for use in clinical trials.¹⁵

Treatment should target skin and joint manifestations of the disease simultaneously.¹⁴ Successful treatment of PsA with conventional therapies is limited by several factors, including failure to effectively manage skin and joint aspects of the disease, risk of potentially serious adverse effects, and poor tolerability. For example, while initial treatment with NSAIDs may control PsA, some patients may experience an exacerbation of psoriasis and others may not respond adequately. In addition, NSAIDs do not affect the course of the disease or prevent development or progression of erosions.² Psoralen plus ultraviolet light (PUVA) and other medications may be effective therapies for psoriasis, but they do not halt progressive joint damage in patients with PsA. Data from clinical trials support the use of sulfasalazine; yet, in clinical practice, this therapy is intolerable in >4 of 10 patients.¹⁴ Methotrexate (MTX) may be a useful drug in PsA

patients; yet, risk for treatment-related hepatotoxicity complicates treatment.¹⁶ In addition to periodic (every 4 to 8 weeks) liver function tests, a complete blood cell count and renal function tests should be obtained during therapy. The risk for liver complications suggests the need for liver biopsy, but patient selection for biopsy is controversial. Although it is recognized that patients with psoriasis receiving MTX are at higher risk for advanced liver changes than patients with RA who take the drug, consensus recommendations for performing liver biopsy focus on cumulative MTX dose and patient risk factors, as well as individualized decision making.¹⁶ Similarly, cyclosporine A may provide efficacy, but serious toxic effects, including nephrotoxicity and hypertension, restrict its use.¹⁴ The limitations of conventional therapies underscore the need for effective treatment that manages joint and skin aspects of PsA.

Role of TNF- α Inhibition in Managing Psoriatic Arthritis: The Basics

Psoriatic arthritis is characterized by flares and remissions.¹⁴ A challenging aspect of PsA therapy is the need to concurrently treat skin and arthritic manifestations. Conventional treatment, aimed at controlling the inflammatory process, consists of NSAIDs and DMARDs. In a substantial proportion of patients, conventional therapy fails to ameliorate the symptoms of both skin and joint manifestations, does not slow or prevent disease progression, is associated with potentially serious adverse effects, and offers limited patient satisfaction.¹⁷⁻²² A study assessing patient satisfaction with

treatment—acitretin, cyclosporine, MTX, or PUVA—found <40% of patients were very satisfied with their treatment.¹⁷ Notably, about 4 in 5 respondents who were dissatisfied did not have severe PsA.

The involvement of TNF- α in the pathogenesis of PsA makes it a rational therapeutic target. Used first to treat RA, anti-TNF- α therapy reduces signs and symptoms of the disease and offers the additional benefit

...limitations of conventional therapy underscore the need for effective treatment... for PsA.

of inhibition of disease progression.²³ Clinical trials assessing the efficacy and safety of this therapy in patients with PsA have led to Food and Drug Administration approval of 3 agents: infliximab (Remicade®), a human-mouse chimeric monoclonal antibody; etanercept (Enbrel®), a soluble TNF receptor antagonist; and adalimumab (Humira®), a human anti-TNF monoclonal antibody.²⁴⁻²⁹

Review of Infliximab, Etanercept, and Adalimumab for the Treatment of PsA

Infliximab: IMPACT 2 Study
Results of a double-blind, placebo-controlled, cross-over study evaluated disease progression in 200 subjects with active PsA who received infliximab through 54 weeks.²⁵

Methods. Infliximab (5 mg/kg) was infused at baseline and weeks 2 and 6, and then every 8 weeks thereafter. At week 24, subjects who had received placebo were crossed over

to infliximab therapy. Subjects in the placebo group who failed to achieve at least a 10% improvement from baseline in swollen joint count (SJC) and tender joint count (TJC) were crossed over to infliximab therapy at week 16. The dose of infliximab was increased to 10 mg/kg in subjects receiving the study drug who failed to achieve at least a 20% improvement in the same end points. Of note: subjects were not required to receive MTX to participate in the study and receive infliximab. Primary end points included changes from baseline in joint erosion, joint space narrowing (JSN), and the sum of these 2 scores, referred to as the total radiographic score. Baseline structural damage was similar among the 166 subjects who completed the study.²⁵

Results. At week 24 and week 54, subjects receiving infliximab experienced a significant reduction in total radiographic score, as well as in erosion and JSN scores. While these scores also declined in subjects who were crossed over to infliximab from placebo at week 16 or 24, the reduction was not as great as that observed in subjects who received infliximab throughout the 54-week study. The infliximab dose was increased to 10 mg/kg at week 38 in 15 of these subjects. The study results demonstrate the inhibitory effects of anti-TNF- α therapy on structural damage in patients with PsA.

Etanercept

A multicenter, placebo-controlled, double-blind investigation evaluated the safety and efficacy of etanercept in 205 subjects with PsA.²⁶ The primary end point was the proportion of subjects who achieved a 20%

improvement in the American College of Rheumatology criteria (ACR 20), as well as improvement in target psoriatic lesions, as assessed by dermatologists' static global assessment and a 50% or 75% improvement in the Psoriasis Area and Severity Index (PASI) (PASI 50 and PASI 75, respectively). The effect of anti-TNF- α therapy on disease progression was evaluated using

Investigators propose that findings from... studies indicate the benefits of early and continued anti-TNF- α therapy...

the total radiographic score, which is a composite of the joint erosion score and the JSN score. MTX therapy (≤ 25 mg/week) could be continued, but other DMARDs and phototherapy were discontinued before study onset. Corticosteroid therapy at a prednisone dosage ≤ 10 mg/day was permitted. Etanercept (25 mg) was administered subcutaneously twice weekly for 24 weeks.

A total of 72 placebo subjects and 93 etanercept subjects completed the study.²⁶ Of the 8 subjects in the etanercept group who discontinued therapy, only 1 did so due to an adverse event (elevated liver enzymes in a subject receiving concomitant MTX). A significantly higher proportion of subjects in the etanercept group achieved ACR 20 compared with those in the placebo group (59% vs 15%; $P < .0001$). Physician and patient global assessment of swollen and tender joints also was improved in the etanercept group versus the placebo group at weeks 12 and 24

(72% and 70% vs 31% and 23%). The proportion of subjects who achieved psoriasis end points at week 24 was also significantly greater in the etanercept group.²⁶ Similar to the findings from the infliximab study, the investigation showed the inhibitory effects of anti-TNF- α therapy on disease progression. While the mean annualized rate of change in the total radiographic score decreased 0.03 units in etanercept subjects, it increased 1.00 unit in the placebo subjects ($P = .0001$). The differences in joint erosion and JSN between the 2 groups also were significant. The only adverse event that occurred more frequently in etanercept subjects was injection-site reaction (9% of placebo subjects vs 36% of etanercept subjects; $P < .001$). No serious laboratory abnormality developed in any subject.

While this study was conducted for only 24 weeks, the results show significant improvement in skin and arthritic manifestations of

PsA and, importantly, inhibition of disease progression. To assess the long-term effects of etanercept, subjects completing the study were permitted to enroll in a 48-week, open-label extension period.²⁷ MTX, NSAID therapy, glucocorticoids, or topical therapies were allowed; dosages of concomitant therapy used during the first 12 weeks could be modified at the discretion of the investigator. Subjects self-administered subcutaneous etanercept 25 mg twice weekly during the open-label period. End points were similar to those of the initial 24-week study.

Radiographs from 71 subjects who received placebo and then crossed over to etanercept and continued the study drug in the open-label investigation and 70 subjects originally randomized to etanercept were available for evaluation at 2 years.²⁷ During the 48-week open-label extension period, all etanercept subjects maintained

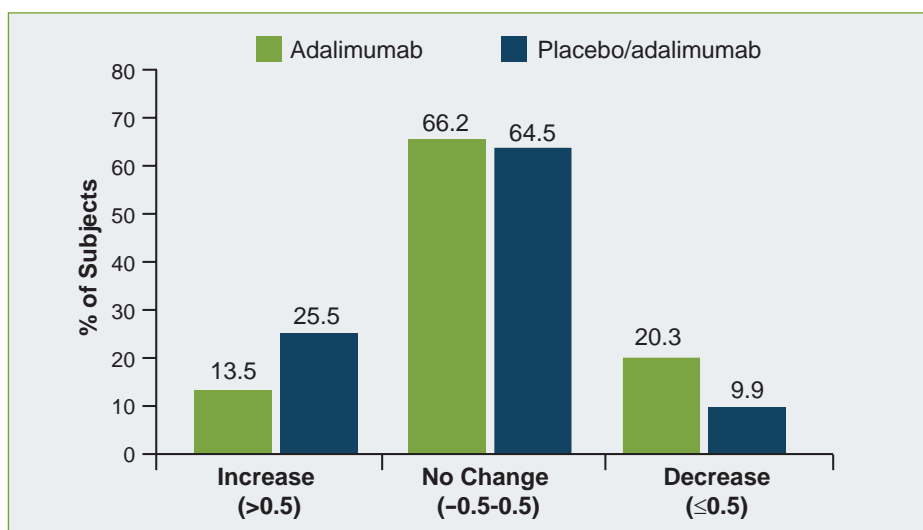


Figure 1. Adalimumab and inhibition of disease progression. Lack of radiographic progression as indicated by changes in Sharp score of -0.5 to 0.5 units was documented in a majority of subjects (66.2%) who received adalimumab ($n = 133$) over 48 weeks, as well as those who initially received placebo then switched to adalimumab ($n = 141$). As indicated by an increase in Sharp score of at least 0.5 units, radiographic progression was demonstrated in 13.5% of those who received adalimumab monotherapy for the duration of the study vs 25.5% of those who initially received placebo. Gladman DD et al.²⁸

their response to therapy in terms of arthritis and psoriasis end points. Those who initially received placebo reached parity with the etanercept subjects by week 12. Radiographic evaluation showed continued inhibition of disease progression in all subjects.²⁷ Adverse effects of therapy were generally mild or moderate in severity. Rates per patient-year of upper respiratory infection, sinusitis, urinary tract infection, flu syndrome, pharyngitis, and bronchitis were similar to those observed during the 24-week trial. These adverse effects are similar to those of the other biologic agents. The investigators propose that the findings from the 2 studies indicate the benefits of early and continued anti-TNF- α therapy in patients with PsA.

Adalimumab

Researchers reported findings from a trial assessing the long-term effectiveness of adalimumab in patients with PsA.²⁸ Subjects who completed the 24-week blinded phase of the Adalimumab Effectiveness in Psoriatic Arthritis Trial (ADEPT) were allowed to enter an open-label study and receive adalimumab 40 mg subcutaneously every other week for 48 weeks.

A majority of subjects (56%) who received adalimumab for 48 weeks achieved ACR 20, experiencing a 20% improvement in ACR criteria.²⁸ Similarly, 67% of the subjects had at least a 50% reduction in the PASI. The total radiographic score in the randomized 24-week study in the adalimumab group declined 0.2 versus a 1.0 increase in the placebo group. No radiographic progression was observed in 91% of adalimumab subjects at week 24. The inhibitory effect of adalimumab on disease progression was sustained at week 48. The radiographic

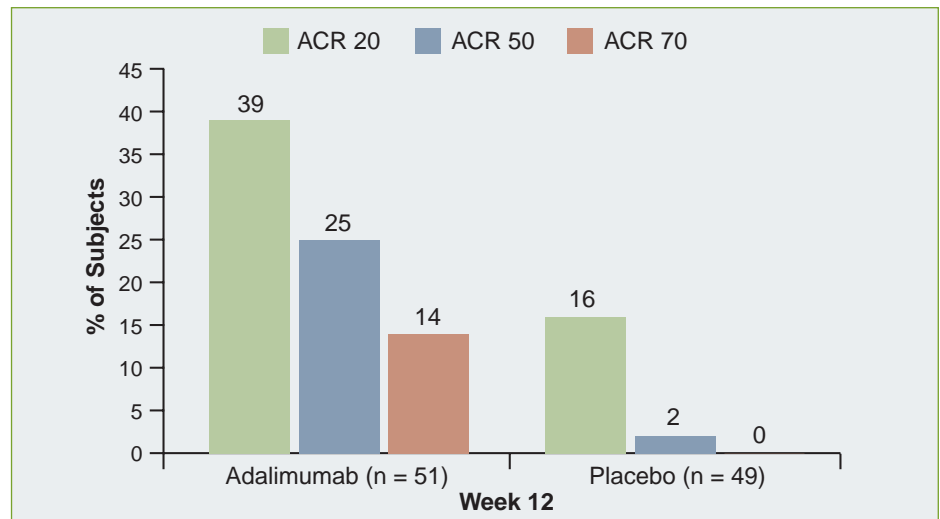


Figure 2. Subjects receiving adalimumab experience greater improvement in (ACR) criteria at 12 weeks compared with placebo. Significantly more subjects with PsA receiving adalimumab for 24 weeks experienced a 20%, 50%, and 70% improvement ($P < .05$, $P \leq .001$, and $P < .05$, respectively) in ACR criteria (ACR 20, ACR 50, and ACR 70, respectively) vs those subjects in the placebo group. Genovese MC et al.²⁹

score increased 13.5% from baseline to week 48 in subjects who received adalimumab, in contrast to 25.5% of subjects who received placebo through week 24 then crossed over to adalimumab (Figure 1).²⁸ Concomitant baseline use of MTX had no effect on radiographic effects.

In another clinical trial, the safety and efficacy of adalimumab were assessed in 100 subjects with PsA who failed to respond to DMARD therapy.²⁹ Subjects received subcutaneous adalimumab 40 mg or placebo every other week for 12 weeks. All subjects who completed the blinded phase could enter a 12-week, open-label extension during which placebo subjects were switched to adalimumab therapy. A total of 50 subjects in the adalimumab group and 46 in the placebo group completed the 12-week study; 92 of 97 subjects who enrolled in the open-label study received 12 weeks of adalimumab. The primary outcome was the ACR 20 response rate. Other measurements were used to assess psoriatic response to therapy, as well as effects of treatment on

pain and physicians' and patients' global assessment of disease activity.

Significantly more subjects in the adalimumab group achieved ACR criteria for a 20%, 50%, and 70% improvement in arthritis compared with placebo at week 12 (Figure 2).²⁹ After week 12, open-label adalimumab provided continued improvement and initiated rapid improvement in those patients who had previously been receiving placebo, with ACR 20 response rates of 65% and 57%, respectively, observed at week 24. These data confirm the durability of response through 24 weeks in patients who failed to respond to DMARDs.

Safety and Tolerability

The aforementioned studies provide a snapshot of the efficacy of anti-TNF- α therapy. Patients with active PsA who receive anti-TNF- α therapy experience a reduction in the skin and arthritic symptoms of their disease and inhibition of disease progression. These benefits have been shown to extend

(continued on page 10)

Case Study in PsA

Nicole Furfaro, MSN, ARNP

Present Illness

40-year-old man presents with history of mild scalp psoriasis, which was diagnosed in his early 20s.

Medical History

He was treated for several years by his primary care physician (PCP) and managed with a topical steroid liquid applied to the scalp. As the plaque psoriasis worsened, he tried several different over-the-counter (OTC) shampoo treatments, including tar, but discontinued these because of the “smell and mess.” He used Dovonex and topical steroids prescribed by his PCP until 2 years ago when he developed plaque psoriasis on both elbows, bilateral knees, and 50% of his scalp. He was seen by a dermatologist and given ultraviolet light B (UVB) therapy because of difficulty controlling symptoms. There was an improvement in the thickness of scale, but itching and skin tightness continued with increasing areas of involvement. He then received PUVA therapy for 1 year, but concern over a family history of melanoma and potential for risks related to light therapy resulted in discontinuation. Cyclosporine was then started, resulting in a 50% improvement in PASI and physician global assessment of skin.

At a 6-month follow-up for medication check, he related that at the same time he experienced a skin flare, he began experiencing unilateral low back pain with radiation to the buttock. He noticed that some mornings he felt like he was “the tin man in need of oil” and the bottom of his feet felt like he was “walking on broken glass.” He neglected to tell his dermatologist about it because he thought it was related to age and his participation in a bowling league 2 nights per week.

He has been experiencing progressive joint stiffness. It takes an hour to get moving in the morning; and after sitting for 45 minutes at work, “the stiffness starts all over again.” The back pain returns in the evening. He was concerned that he may have PsA because his toes “look like little sausages,” similar to a condition his uncle has who does have PsA. NSAIDs OTC have relieved the pain by only 20% and have had no impact on joint swelling.

The dermatologist suspected PsA and changed the prescription from cyclosporin to MTX 15 mg QW to treat PsA and referred him to rheumatology for confirmatory diagnosis and management.

Family History

Father with psoriasis; uncle with PsA

Physical Examination (rheumatology)

Toes: dactylitis, 2nd and 3rd toes bilaterally; toenail pitting

Fingers: nail pitting

Tenderness in all MTPs, bilaterally, ad tarsi

Hip range of motion: normal

Spine: normal, except right SI joint tenderness

Right knee: tenderness without swelling

Tender joint count: 15; swollen joint count: 4

Current Medications

MTX, 15 mg QW for 3 months

Folic acid, 1 mg QD

Ibuprofen, 600 mg BID to TID, PRN

Radiographic Evaluation

Single pelvis: evidence for unilateral sacroiliitis on the right

Feet: diffuse soft tissue swelling in 2nd and 3rd toes right foot without obvious erosion or joint space narrowing

Hands: normal

Laboratory Values

WBC	10.0	H	(4.5-10.5)
RBC	5.4	L	(4.2-6.2)
Hgb	11.7	WNL	
HCT	40.8	WNL	
ESR	32 MM/hr	H	(0-20)
CRP	1.12	H	(<0.8)
RF		NEG	
Hep B and C		NEG	
HLA-B27		NEG	

Clinical Commentary

Nicole Furfaro, MSN, ARNP

What is the diagnosis based on these findings?

Based on the finding of dactylitis, arthritis, nail pitting, elevated inflammatory markers (negative RF), hour of morning stiffness, and positive family and personal history for psoriasis and PsA, the diagnosis is PsA (see CASPAR criteria, Table 1, page 4).

What is the management decision at this point?

The patient is educated regarding the diagnosis of PsA. He is frustrated that he was not diagnosed earlier and saved the worry of whether or not he would be able to continue working and bowling, given the worsening of his joint pain and stiffness. His PCP recommended NSAIDs because of pain, and the dermatologist focused on the skin. The patient would like to maximize therapy. NSAIDs have not helped the pain, and although the skin is better on MTX 15 mg QW, he is mildly nauseated.

At the initial visit, he was educated on the nature of PsA, an inflammatory disease that occurs in some people with psoriasis. We discussed his clinical risk factors and that MTX has been effective for the skin lesions but not adequate treatment for the joints, as evidenced by sacroiliitis, and a number of swollen and tender joints. In addition, studies indicate that early treatment to prevent erosions is important and that a combination of MTX plus a biologic DMARD affords the best control of radiographic progression.

The patient was given handouts on medication options; a PPD was placed to be read in 72 hours. He will return for ongoing discussion and education regarding the potential benefits and side effects of anti-TNF- α therapy.

What are the findings at follow-up?

At follow-up, the patient and his healthcare professional decide the best option for treating his worsening and likely progressive PsA is to add an anti-TNF- α agent. Based on his busy life style, he prefers to self-inject. He was taught the self-injection technique and given education handouts regarding

the management of injection site reactions, how to monitor for infections, and the importance of follow-up at regularly scheduled times to assess for side effects and monitor disease progression.

What are the findings after 3 months of anti-TNF- α therapy?

At 3-month follow-up the patient rates his pain at zero on most days with only episodic back stiffness. He feels like he did 2 years prior to the onset of symptoms. Laboratory values show normalization of ESR and CRP levels. He has been able to discontinue ibuprofen, tolerates MTX better, and feels more hopeful that he will be able to continue working and bowling.

At every visit, each patient requires assessment of educational needs. Some patients have no prior knowledge of PsA, and clinicians have to slowly educate them. The patient in this case study had an uncle with the disease so he suspected something more than “overuse and age” regarding his joint symptoms.

Those of us who practice in the subspecialty of rheumatology need to continually strive to educate, not only our patients, but other providers on the need to diagnose and treat early. The use of validated disease activity tools in PsA lags behind RA, although measures are “borrowed” from RA in clinical practice and research. The DAS28, ACR 20, 50, 70, the HAQ (modified to include skin), and other objective measures are being developed or are currently in use. Until there is a consensus regarding the best objective disease activity measure, we need to become familiar with and begin to use a validated tool that measures disease activity and response to therapy.

over a long duration. While no direct comparative studies have been conducted, the anti-TNF- α agents appear to be safer and better tolerated than DMARDs,²³ however, caution should be exercised when prescribing these medications.^{23,30}

Contraindications for the 3 anti-TNF- α drugs include hypersensitivity to any specific agent and sepsis.³⁰ These medications should be avoided in patients with a history of multiple sclerosis, active infection, or malignancy. Live vaccines should not be given to patients receiving anti-TNF- α therapy, and attenuated vaccines may not provide full protection. Patients who are going to start treatment with biologic agents should have appropriate screening for tuberculosis.

Drug-drug interactions between anti-TNF- α agents and DMARDs have not been observed.³⁰ Etanercept, infliximab, and adalimumab

can be used concomitantly with MTX, as well as other combinations, to treat PsA.

Goals of Management of PsA

The onset of PsA is variable, characterized by mild symptoms and slow progression in some patients and severe manifestations of the disease and rapid progression in others.¹⁷ In all patients, early recognition and timely diagnosis, followed by implementation of therapy, are necessary to limit or prevent extensive joint damage and consequent disability. While NSAIDs and corticosteroids may help suppress joint, tendon, and enthesal inflammation and are important components of treatment, the British Society for Rheumatology recommends early use of potential DMARDs to provide persistent suppression of inflammation.³¹ Patients with active disease who fail to respond to a trial of

DMARD therapy or must discontinue use of these agents due to toxicity should be considered candidates for anti-TNF- α medication.¹

Summary

Psoriatic arthritis, which affects 1% to 3% of the general population, is characterized by dermal, articular, and extra-articular manifestations. The disease is progressive, resulting in substantial disability in as many as 1 of 5 affected persons. To prevent disease progression, it is important to recognize the features of PsA, diagnose early, and institute effective therapy. The role of the pro-inflammatory cytokine, TNF- α , in the pathogenesis of the disease has led to the use of anti-TNF- α therapy in patients with PSA. Findings from clinical trials confirm the efficacy of these medications in reducing or eliminating dermal and articular signs and symptoms and in preventing disease progression.

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About PCE Updates in Rheumatology...

Welcome to the fourth of 4 issues of *PCE Updates in Rheumatology*, developed for those rheumatologists, NPs, and PAs who serve patients in rheumatology practices throughout the country. "The demands for rheumatologic services are increasing exponentially with the aging population, while the number of physicians entering the rheumatology specialty is shrinking," according to the Society of Physician Assistants in Rheumatology (SPAR). Rheumatologists treating patients with rheumatoid diseases increasingly rely on specialist NPs and PAs to take an active management role in the frequent clinical contacts these patients require.

As healthcare professionals, NPs and PAs collectively provide a vital and increasing role in the diagnosis and management of acute and chronic illness. As clinicians, you spend more time with patients than most physicians, with your emphasis being patient disease state counseling and preventive care. Most importantly, NPs and PAs report that their roles have evolved from assisting physicians to treating and following their own patients. This increased role includes writing prescriptions, monitoring patient progress, and seeing patients in your own examination rooms. As NPs and PAs, you are rapidly emerging as key providers of patient care. You practice with greater autonomy and prescribe more medication than ever before.

Approximately 286 NPs and 188 PAs see patients in rheumatology practices that provide ongoing care for patients with rheumatoid diseases. Therefore, you need to be thoroughly familiar with innovative and complex biologic therapies: how and why such agents are useful, how to identify patients who are likely to benefit from biologic therapy, how to administer biologic treatments to ensure the greatest clinical advantage, and which clinical markers to monitor in balancing benefit versus risk. As prescribers, some NPs and PAs require information regarding the clinical features and drug properties of the specific biologics approved for similar indications. This issue of *PCE Updates in Rheumatology* focuses on the advances of biologic therapy for the management of psoriatic arthritis.

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