Psoriatic Arthritis: An Update on Classification, Clinical Features and Therapies

Ying-Ying Leung, Lai-Shan Tam, Emily Wai-Lin Kun, Edmund Kwok-Ming Li

Abstract: Psoriatic arthritis (PsA) is a chronic systemic inflammatory disease characterized by joint inflammation and cutaneous psoriasis. With advances in knowledge of genetics, immunohistology and pathogenesis, PsA is now recognized as a distinct disease entity. Unique clinical features include distal interphalangeal joint (DIPJ) involvement, dactylitis, enthesitis, axial involvement, specific radiographic features, and specific skin and nail changes. PsA affects young adults and is progressive and destructive, causing deformities, impaired physical function, reduced quality of life and lost of productivity. We now focus on more aggressive treatment in patients with progressive disease. With both conventional disease modifying anti-rheumatic drugs (DMARDs) and emerging biological agents, the outlook for patients with PsA has improved.

Keywords: Classification, Diagnosis, Drug therapy, Epidemiology, Pathology, Psoriatic arthritis

Introduction

Psoriatic arthritis (PsA) is a chronic inflammatory arthritis occurring in individuals with psoriasis. Both the joint and skin lesions have deleterious effect on affected individuals causing impaired physical function and quality of life. Distinction between PsA and rheumatoid arthritis (RA) is now recognized clinically, genetically and immunohistologically. The key pathophysiology and cellular processes are being elucidated. Along with advances in the development of a number of targeted biological therapies, substantial progress in the targeted therapies has been made. The clinical profile of 127 PsA patients in Hong Kong has been described. The mean age of onset was in the third decade. Men and women were equally affected. Predominant axial disease occurred in 11% and over 70% of patients were treated with disease modifying anti-rheumatic drugs (DMARDs). Impairment in physical function and quality of life was prominent and 33% of patients reported loss of employment due to the disease.

Classification

Historically, the Moll and Wright criteria have been used to classify PsA. PsA can be classified when a patient with psoriasis has inflammatory arthritis and negative rheumatoid factor. Under these criteria, five subgroups were described: 1) asymmetrical oligoarthritis (<5 joints), 2) symmetrical polyarthritis, 3) distal interphalangeal joint (DIPJ) predominant, 4) spondylitis predominant, and 5) arthritis mutilans. Considerable overlaps between subgroups have been recognized, and asymmetrical oligoarthritis and symmetrical polyarthritis was noted to be changing with time and with treatment. Some authors advocated classification into two broad subgroups: peripheral disease (PD) and axial disease (AD). The Classification of Psoriatic Arthritis study group (CASPAR) criteria were recently developed as a agreed and validated classification for PsA. They give a sensitivity and specificity of 0.914 and 0.987 to classify PsA from other arthropathies (Table 1).
Psoriatic Arthritis

Clinical Manifestations

PsA is classified as subtype of spondyloarthropathy based on common HLA association and characteristic clinical and immunopathological features. As compared to RA, PsA has greater tendency towards asymmetry and oligoarticular involvement. The DIPJs are more frequently involved. Severe DIPJ involvement and digital tuft resorption could give rise to telescoping of finger or arthritis mutilans. Enthesitis and dactylitis are more common. Rheumatoid factor, which is detected in 80% of patients with RA, may only present in 3% of PsA. Rheumatoid nodules are typically absent in PsA.1

Spondylitis

PsA is classified as a subtype of spondyloarthopathy based on common HLA association and characteristic inflammatory clinical and immunopathological features. The prevalence of axial disease varies from 25% to 70% depending on the criteria used.8,9 High prevalence of asymptomatic radiological sacroiliitis and spondylitis have been reported.2,10-12 The distribution of sacroiliitis and syndesmophytes tends to be asymmetrical. The occurrence of extraarticular manifestation is common, including mucous membrane lesion, iritis, and urethritis. The association with HLA-B27 however is only weak. The prevalence of HLA-B27 was only around 20% in various cohort. It had no associated with MRI sacroiliitis11 and did not influence disease progression in long term follow up.13

The Presence of Skin Psoriasis

The presence of psoriasis is the most distinguished feature of PsA. Psoriasis is an itchy skin lesion characterized by well-demarcated erythematous and scaly plaques, distributed over extensor body surfaces and scalp. Psoriasis is of two main types: psoriasis vulgaris (plaque psoriasis) and pustular psoriasis. Different types of psoriasis can be divided into subgroups according to severity, location on body and morphological appearance of the lesion. Psoriasis usually precedes arthritis in 70% of patients and occurs concomitantly in 15%. Arthritis however, may precede psoriasis in 15% of cases and make diagnosis of PsA difficult.14 In the Hong Kong cohort, psoriasis preceded PsA in 60.4% of the patients by 5.4 (± 4.8) years. Psoriasis occurred concurrently with PsA in 18.9%; psoriasis occurred after arthritis in 20.7%.2

Psoriasis may also present in ‘hidden’ sites like around the umbilicus, under the hairline, or even natal cleft. Psoriasis may only be evident in the nails. Nail dystrophies includes pitting, subungual hyperkeratosis, discoloration and onycholysis. The association of nail lesions with DIPJ was well recognized.15 PsA is associated with higher rate of nail dystrophy than psoriasis alone. One study reported nail lesions in 40-45% of patients with psoriasis and up to 80% of patients with PsA.16 In true absence of psoriasis, positive family history in the first-degree relative might be of equal importance.

The course of psoriasis is influenced by various environmental factors. Many patients experience worsening of symptoms with weather change. The classical Koebner’s phenomenon which describe the worsening of psoriasis lesion at site of physical injury, is possibly mediated through the unmasking of autoantigens and release of proinflammatory cytokines.17 Infection like streptococcal infections and human immunodeficiency virus infection have long been recognized as triggers for psoriasis.18,19

Dactylitis

Dactylitis is one of the hallmarks of PsA. It occurs in one third of patients with PsA. It appears as swelling and sausaging

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Table 1. The Classification of Psoriatic Arthritis (CASPAR) criteria for classification of PsA7

<table>
<thead>
<tr>
<th>Inflammatory articular disease (joint, spine or enthesal)</th>
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<tr>
<td>With 3 or more points from the following:</td>
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<tr>
<td>1. Current psoriasis (sores 2 points)</td>
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<tr>
<td>2. Personal history of psoriasis (if current psoriasis not present)</td>
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<tr>
<td>3. Family history of psoriasis (if personal history of psoriasis or current psoriasis not present)</td>
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<tr>
<td>4. Psoriatic nail dystrophy</td>
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<tr>
<td>5. A negative test for rheumatoid factor</td>
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<tr>
<td>6. Current dactylitis</td>
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<tr>
<td>7. History of dactylitis (if current dactylitis not present)</td>
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<tr>
<td>8. Radiological evidence of juxta-articular new bone formation</td>
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Predominant flexor tenosynovitis was demonstrated in magnetic resonance imaging (MRI) and ultrasonography studies. Dactylitis may also extend beyond the digits to involve other structures like the palmer tendon sheath and bursa. Soft tissue edema was also a common feature. Acute dactylitis is a marker of active disease of PsA. It was shown to be associated with a greater degree of radiological damage than digits without dactylitis.

**Enthesitis**

Enthesitis is the inflammation at the site of attachment of a tendon or ligament to the joint capsule. With the emerging knowledge from anatomical and MRI studies, the concept of "enthesis organ" has emerged. In this concept, the enthesis and its adjacent fibrocartilage, periosteum, synovium should be viewed as an "unique" organ. PsA was proposed to be a primarily enthesis disease as compared to synovial disease of RA. Clinical features that are supporting this enthesis pathology include peripheral enthesitis, dactylitis, DIPJ involvement, spinal inflammation, and specific periostitis and osteolysis. For example, the typical "pencil-in-cup" deformity of the DIPJ can be explained by enthesitis. While the DIPJ has too little synovium to be inflamed, the distal tuft exhibits capsule calcification and central erosion at the site of tendon insertion. The fluffy periostitis and bone erosion adjacent to the capsule are also suggestive of enthesitis.

**SAPHO Syndrome**

The SAPHO syndrome (Synovitis, Acne, Pustulosis, Hyperostosis and Osteitis) was reported in 2% of patients with PsA. The occurrence of musculoskeletal manifestations (including synovitis, chest wall arthro-osteoitis and multifocal aseptic osteomyelitis) in association with severe acne, palmoplantar pustulosis and psoriasis was also related to inflammatory bowel disease and other spondyloarthopathies. The psoriatic variety is typically HLA-B27 negative.

**Specific Radiographical Features**

The specific radiographical features of PsA are grouped into erosion and proliferation. Erosions typically begin at the joint margins and progress towards the center. Erosions can be very extensive leading to the characteristic pencil-in-cup deformity (Figure 1a) with a blunted osseous surface on the proximal bone, protruding into an expanded surface of the distal bone. Marked osteolysis may occur such that the whole phalanx may be resorbed (Figure 1b). The DIPJs are often the first to be affected. Proliferative changes with new bone formation may occur along the shaft of the bones, causing metacarpal or metatarsal shaft periostitis. Osteoperiostitis of the distal phalanx of big toe is frequent in PsA and is reported to be associated with nail dystrophy. Typically, osteolysis (erosive change) and ankylosis (proliferative change) may occur in the same hand and even the same finger. Joint involvement in PsA is often asymmetrical. A ray pattern involving the same finger is contrasted with the mirror pattern in RA. Periarticular osteoporosis is less commonly observed than in RA. Spondylitis may be similar to that of AS. However, unilateral sacroiliitis, asymmetry of syndesmophytes, and...
non-marginal syndesmophytes distinguish PsA from AS. Non-marginal syndesmophytes describes vertebral ossification from vertebral body-to-body as compared to those from corner-to-corner in AS. PsA spondylitis can be less symptomatic and even asymptomatic.\textsuperscript{2,10,12} Nonetheless, radiological spinal disease also predict increased mortality.\textsuperscript{29}

**Burden of Disease and Increased Atherosclerosis**

PsA typically affects young adults aged 35-55 years. The spectrum of severity of PsA is broad, ranging from mild degree of joint pain to severe deformities. PsA is not benign, there is substantial social and financial implications to the society including impact on medical burden and inability to work.\textsuperscript{30,31} PsA is well recognized as a cause of progressive joint damage,\textsuperscript{32,33} increased disability,\textsuperscript{31,34} impairment of quality of life,\textsuperscript{35,36} and increased mortality.\textsuperscript{29} The commonest cause of death is cardiovascular diseases. The risk of premature death is related to previous active and severe joint disease, presence of erosions and high erythrocyte sedimentation rate at presentation. Interestingly, PsA patients have higher incidence of metabolic syndrome including obesity, insulin resistance, dyslipidemia, hypertension possibly related to the common inflammatory pathway.\textsuperscript{37,38} Subclinical atherosclerosis has also been reported in PsA cohorts.\textsuperscript{39-41}

**Outcome Measures**

PsA outcome measures have been adapted from that of RA. Many of these measures were shown to be effective in assessment of peripheral joint and skin diseases, physical functioning, quality of life and X-ray structural damages. Methods to evaluate enthesis, dactylitis and spinal involvement are still under development (Table 2). The Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) is a consortium of international investigators. It is involved in developing, refining and validating these existing outcome measures as well as those under development.\textsuperscript{42}

<table>
<thead>
<tr>
<th>Table 2. Psoriatic arthritis outcome measures\textsuperscript{50,57}</th>
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<tr>
<td><strong>Arthritis Response</strong></td>
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<tr>
<td>• ACR Response Criteria (including DIPJ and CMCJ)</td>
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<tr>
<td>• Psoriatic Arthritis Response Criteria (PsARC)</td>
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<td>• Disease Activity Score (DAS)</td>
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<td><strong>Enthesitis</strong></td>
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<td>• Mander Enthesitis Index (MEI)</td>
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<td>• Maastricht Ankylosing Spondylitis Enthesitis Score (MASES)</td>
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<td>• Leeds Enthesitis Index (LEI)</td>
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<tr>
<td><strong>Dactylitis</strong></td>
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<tr>
<td>• Dactylitis Count</td>
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<tr>
<td>• Leeds Dactylitis Index (LDI)</td>
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<td><strong>Radiological Assessments</strong></td>
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<td>• Modified Sharp</td>
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<td>• Modified van der Heijde</td>
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<td><strong>Skin Response</strong></td>
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<td>• Psoriasis Area and Severity Index (PASI)</td>
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<tr>
<td>• Dermatologist Static Global</td>
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<td>• Physician Global Assessment of Psoriasis (PGA)</td>
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<tr>
<td><strong>QoL/ Physical Functioning</strong></td>
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<td>• Medical Outcome Short Form 36 (SF-36)</td>
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<tr>
<td>• Health Assessment Questionnaire Disability Index (HAQ-DI)</td>
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<tr>
<td>• Psoriatic Arthritis Quality of Life (PsAQoL)</td>
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<tr>
<td>• Dermatology Life Quality Index (DLQI)</td>
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<tr>
<td>• Dermatology Quality of Life Scale (DQoLs)</td>
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PsA has been the focus of the Outcome Measures in Rheumatology Clinical Trials (OMERACT) group in the past few years. Consensus has been achieved on a core set of 6 domains (peripheral joint activity, skin activity, patient global assessment, pain assessment, physical functioning, and health related quality of life HRQOL) to be assessed in clinical trials.43

Despite its differences from RA, the adaptation of RA methodologies in radiological assessment was considered to be appropriate.44 Given its construct validity and sensitivity to change, there is adequate evidence in using the physical functioning of SF-36 in assessing physical functioning in PsA.45,46 A quality of life instrument specific to PsA (PsAQoL) has been developed recently.47 In addition to HAQ and SF-36, there is consensus to use this PsAQoL in future treatment trials to test its performance. Researches are underway aiming at incorporating the World Health Organization (WHO)'s International Classification of Functioning, Disability and Health (ICF) schema in the development of a comprehensive questionnaire that more comprehensively address physical functioning, quality of life and participation (i.e. the involvement in life situations) pertinent to patients with PsA.48

Genetic Basis for PsA

Psoriasis and PsA are complex genetic disorders resulting from interplay between genetic and environmental factors. The relative risk for PsA among first-degree relatives indicates a strong genetics association. The human leukocyte antigen (HLA) region on chromosome 6p is implicated as one of the candidate regions in PsA. Association with HLA-B13, B-17, B-27, B-39, HLA-Cw6 and HLADRB1*07 has been demonstrated.49

Immunopathogenesis of PsA

Immunohistology of various spondyloarthropathy subtypes including PsA is in synovial biopsy. It is distinct from that of RA. Angiogenesis is a prominent early event in both psoriasis skin and synovium. TNF-α up-regulates angiogenic growth factors including vascular endothelial growth factor (VEGF), transforming growth factor beta (TGFβ), platelet-derived growth factor and angiopoietins. The resultant neovascularization is an important component of the inflammatory and erosive nature of the disease.50

TNF-α plays a central role in the pathogenesis of PsA and psoriasis. High levels of TNF-α are found in synovial fluid, synovium, serum and psoriatic skin lesions of patients with PsA. Treatment with TNF-α inhibitors also leads to substantial benefit. The pathophysiology of PsA is summarized in Figure 2. Other key cytokines that are up regulated in PsA, and thus may be potential therapeutic targets include IL-1, IL-6, IL-12, IL-15, and IL-18. T cell activity is also up regulated and inhibition of T cell via blockade of "co-stimulatory" pathway may also be a therapeutic target.

PsA Therapy

Conventional DMARDs

A challenge of PsA therapy is to address the multiple domains of the disease: arthritis, enthesitis, dactylitis, spinal disease, skin disease, physical functioning and quality of life. In mild disease, nonsteroidal anti-inflammatory drugs (NSAIDs) or topical ointment (e.g. corticosteroid or vitamin D analogues) for skin disease may be appropriate. Moderate to severe manifestation often requires disease modifying anti-rheumatic drugs (DMARDs) Conventional DMARDs including methotrexate, sulphasalazine, leflunomide, anti-malarials and cyclosporin A have proven efficacy in PsA. Comprehensive reviews of therapy of PsA have been published.51,52 In the CASPAR cohort study involving 588 PsA patients across 13 countries (mean duration of illness, 12.5 ± 0.4 years), methotrexate was the most frequently used DAMRDs (39%) in which > 70% of patients were still taking the drug. Other drugs were used with the following frequencies respectively: sulphasalazine 22%, gold salts 7%, anti-malarials drugs 5%, corticosteroids 10% and anti-TNF drugs 6%.53 A summary of these treatment with ratings of level of evidence is outlined in Figure 3.

Methotrexate is effective for both skin and joint disease in PsA. Its efficacy has been demonstrated but in small randomized controlled trials.54,55 Its liver toxicity has elicited concerns regarding its long-term use. There is an apparent yet unexplained increase in proclivity for hepatotoxicity in psoriasis patients verse RA patients.56 A discord still exists among dermatologists and rheumatologists regarding methotrexate monitoring. The American College of Dermatology recommends pretreatment liver biopsies and repeat biopsies after 1.5 gram accumulated dose,57 whereas the American College of Rheumatology (ACR) guideline recommends pretreatment liver biopsies only in patients with
persistently elevated liver enzymes, chronic hepatitis B or C infection, or significant alcohol intake; and with repeat biopsies only as indicated by results of liver enzymes. In a retrospective study of 104 PsA patients followed over two decades, there was no suggestion of increased liver toxicity.

Sulphasalazine has proven efficacy for peripheral arthritis in PsA from several randomized controlled trials. In the largest trial that evaluated 221 patients treated with sulphasalazine 2 g/day for 36 weeks, 57.8% of sulphasalazine patients vs. 44.6% of placebo patients (p=0.05) achieved the PsA Response Criteria (PsARC). The efficacy of sulphasalazine however, is confined to peripheral joints. It is not effective for axial disease or skin disease.

Leflunomide is a selective pyrimidine synthesis inhibitor targeting activated T cells lacking a salvage pathway. Its efficacy in PsA and psoriasis was demonstrated in one randomized controlled trial in 188 patients with active PsA. More than half of them had been inadequately controlled by other DMARD. After 6 months, 59% of leflunomide-treated vs. 30% placebo-treated patients achieved the PsARC respond; 24% had significant PASI score improvement (compared with 0% in placebo group). Leflunomide is generally well tolerated, with the commonest adverse event being diarrhea.

The use of anti-malarials is limited by the concern of their exacerbation of psoriasis skin lesions. More frequent reactions were observed in early trials that primarily used regimens with quinacrine. Chloroquine or hydroxychloroquine seems to have less toxicity. In a case-control study, 6 out of 32 chloroquine-treated patients experienced a psoriasis flare, only one required discontinuation of therapy. There was no case of exfoliative
dermatitis. Six of the 24 control patients had an exacerbation of psoriasis as well. 75% of the chloroquine-treated patients (compared with 58% of control) had a 30% reduction in active joint inflammation over a 6-month period. Prospective controlled trials are required to establish the efficacy and safety of these agents.

Cyclosporin A has been used with success in psoriasis and PsA. Toxic effects, most notably hypertension and renal toxicity, limit its use. A prospective controlled trial comparing cyclosporin A (3 mg/kg/day) with methotrexate (7.5 mg/week) for one year has demonstrated equivalent efficacy in 35 patients with PsA. The efficacy of cyclosporin A with methotrexate on arthritis and PASI has been demonstrated.

**TNFα Inhibitors**

Anti-TNFα agents, including infliximab, etanercept and adalimumab have shown the greater efficacy over any conventional DMARDs in various clinical aspect of PsA. They may have minor difference in efficacy in the skin and enthesium, but all have excellent effects in these domains.

A phase 3 double blind placebo-controlled trial evaluated the efficacy of 5 mg/kg infliximab in 200 patients with PsA unresponsive to previous treatment (IMPACT 2). ACR criteria and PsARC response were achieved by 58% and 77% of infliximab patients as compared to 11% and 27% of placebo patients at week 14. Fewer infliximab patients than placebo...
Psoriatic Arthritis patients had dactylitis (12% vs. 34%; p<0.001) and active enthesopathy (20% vs. 37%; p = 0.002) at week 24. Significant beneficial effect to skin lesions was demonstrated, 64% of infliximab patients achieved 75% PASI improvement (PASI 75) compared to 2% of placebo patients. A high degree of clinical response in peripheral arthritis, dactylitis, enthesopathy and psoriasis were maintained at end of 2 years.70 Infliximab was shown to inhibit radiographic progression. At week 54, the change of modified Sharp/van der Heijde score in infliximab patients were -0.7 ± 2.53 compared to 0.82 ± 2.62 in placebo patients (p<0.001).71 Over 2 years, the average estimated annual radiographic progression with infliximab treatment was significantly reduced versus the estimated baseline rate of progression.70 At week 14, a higher proportion of infliximab patients achieved a minimal clinical change in HAQ score [i.e. more than 0.3 decrease] (59% vs. 19%; p < 0.001). The physical and mental components of SF-36 scores also improved in infliximab group.72 Infliximab was well tolerated with similar incidence of adverse events compared to placebo group.

The efficacy of subcutaneous etanercept 25 mg administered twice-weekly was demonstrated in a phase 3 randomized placebo-controlled trial (n=205).73 ACR 20 response was achieved in 59% of etanercept patients as compared to 15% of placebo patients at the end of 12 weeks (p<0.001), and the results were sustained at 24 and 48 weeks. Psoriasis response was significant, 23% of etanercept patients achieved PASI 75 verse 3% of placebo patients (p<0.001). Radiographic progression was inhibited in etanercept group at 12 months, the change of modified Sharp score (mTSS) was -0.03 units, compared with +1.00 unit in placebo patients (p=0.001). Sustained respond with arthritis, radiographic damage suppression, physical function and quality of life were demonstrated in the extension trail at the end of 2 years.74

The efficacy of adalimumab, given at 40 mg subcutaneous every other week was studied in a large (n=313) phase 3 study, the Adalimumab Effectiveness in Psoriatic Arthritis Trial (ADEPT).75 At week 12, 58% of adalimumab patients achieved ACR20 response compared to 14% of placebo patients (p<0.001). No difference in response rate was noted between patients taking adalimumab alone or in combination with methotrexate (50% of patients). There were greater mean improvement in dactylitis and enthesitis in the treatment group, but the results were not statistically significant. PASI 75 was achieved in 59% of adalimumab patients compared to 1% of placebo patients (p=0.01). Radiographic progression as assessed by modified Sharp score was significantly inhibited in the treatment group. Mean change in HAQ score was significant and clinically meaningful (-0.4 vs. -0.1; p<0.001). Improvement in SF-36 in the treatment group was noted. These clinical response were sustained at end of 2 year with a good drug safety profile.76

The Risks and Benefits of TNFα inhibitors in PsA were evaluated in a metaanalysis. Six randomized controlled trials with 982 patients were included. All 3 TNFα inhibitors were shown to be more effective than placebo as measured by PsARC, ACR20, 50 and 70 ratings. There were no important added risks associated with their short-term use.77 Spine disease however, was not studied in these trials. As significant efficacy of TNFα inhibitors has been demonstrated in AS,78 extrapolation of this experience to PsA seems reasonable. Although with limited data, cost effectiveness of TNFα inhibitors in the management of PsA seems promizing.79,80

**Other Biologic Agents**

Alefacept is a fusion protein that blocks interaction between leukocyte-function-associated antigen-3 (LFA-3) on antigen presenting cells and CD2 on T cells. It binds to CD2 on activated T cells and impairs the co-stimulatory signals delivered by LFA-3 and thus induces apoptosis in circulating memory T cells. It efficacy in combination with methotrexate for both joint and skin diseases was demonstrated in a phase 2 trial (n=185). However, its efficacy for joint disease was very limited.81

Efalizumab is a humanized monoclonal antibody targeting at CD11 subunit of LFA-1 on T cells. It interferes with T cell coupling with ICAM-1 on endothelial cells. Activation of T cells and migration of cells to the site of inflammation is then inhibited. It is approved for use in psoriasis. A phase 2 trial (n=107) failed to demonstrate significant difference in ACR20 response as compared to placebo.82 It is therefore not recommended for treatment of arthritis.

Abatacept (CTLA4-Ig) is a recombinant fusion protein binding to the CD80/86 receptor on antigen presenting cells. It blocks the second-signal activation of CD28 on T cells. It has been approved for use in RA. A phase 2 trial for use in psoriasis has been conducted.83 It may have beneficial effects on peripheral arthritis in PsA.

**Conclusion**

PsA is a chronic systemic inflammatory disease involving skin, peripheral joints, spine and enthesis. It affects young adults
and is progressive and destructive, causing deformities, impaired functional status and quality of life. It is now recognized as a distinct disease entity clinically, radiographically, genetically, immunohistologically and has unique pathogenesis. Numerous studies have increased our understanding of pathophysiology of PsA, which provided support for targeted therapy. The effectiveness of these agents has also helped to elucidate the pathogenesis of PsA and psoriasis, which may lead to more novel and effective targeted therapies. Anti-TNF therapy has achieved encouraging efficacy in alleviating skin and joint disease and various domain. The benefit of anti-TNF therapy should be balanced against the adverse events and cost. The risk of serious infection, in particular tuberculosis is a definite challenge in Southeast Asian countries. Further comprehensive and long term health economic analyses are required to aid our ability to see the full impact of these new targeted therapies on patient function, quality of life, employment and productivity in the context of the society.

References


