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Diagnosis and Management of Psoriatic Arthritis

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Abstract

Psoriatic arthritis (PsA) is considered to be one of the spondyloarthritides, and as such has both spinal and peripheral joint involvement. In 80% of patients, psoriasis usually precedes the development of arthritis.

Although there are no widely accepted diagnostic criteria, a number of distinct clinical features allow it to be distinguished from other forms of inflammatory arthritis. It affects both sexes equally, and the pattern of joint involvement is characteristic with distal interphalangeal joint involvement, asymmetry, dactylitis, flail or ankylotic deformities of digits, and the frequent presence of enthesitis and spinal involvement. It may have a pattern of joint involvement similar to rheumatoid arthritis (RA) but in these patients rheumatoid factor and the other

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systemic features of RA are usually absent. Radiographs frequently reveal evidence of asymmetric sacroiliitis and spinal disease, and peripheral joints, as well as showing erosions, may also demonstrate profuse new bone formation and ankylosis. Profound osteolysis producing the pencil-in-cup deformity can also occur in the same individual. It is now recognised that PsA can be a destructive arthritis with an increased morbidity and mortality.

Studies of standard disease-modifying therapies have been small and frequently inconclusive because of a high placebo response rate. This may be as a result of heterogeneity in patient selection, poor assessment tools, or the difference in underlying pathogenesis and subsequent response to therapy. In meta-analyses, sulfasalazine and methotrexate have been shown to be effective. Treating the skin alone seems to have little impact on joint disease, and the relationship between skin and joints is still unclear. However, recent studies with anti-tumour necrosis factor agents, such as etanercept and infliximab, have shown considerable significant clinical benefit and provided the hope that we will at last have effective therapies for this disease.

Psoriasis and psoriatic arthritis (PsA) are not new diseases but making the correct diagnosis seems to have always caused problems. Archaeological remains from Judea suggest that in the 5th century individuals with PsA were considered to have 'biblical leprosy' and sent to monasteries for care.[1] In fact, even into the 19th century psoriasis was still considered by some to be a form of leprosy. Our knowledge has improved somewhat since that time but it is only in the last century, or indeed the last forty years, that PsA has been recognised as a disease in its own right. Nevertheless, exactly what PsA is, or what it encompasses, is still under heated debate. There is no single clinical feature or diagnostic test to identify individuals with PsA; even psoriasis is not present in all patients. With lack of good diagnostic criteria, it is understandable that there are few good tools for assessing disease, and subsequently few good or meaningful therapeutic studies. Fortunately, the fascinating range of musculoskeletal disease in these patients is starting to receive more attention, and we are slowly gaining some insights into its pathology and relationship to psoriasis. Hopefully, this will result in therapies directed specifically at PsA, instead of simply putting our faith in 'hand-me-down' treatments for rheumatoid arthritis (RA).

1. Diagnosis of Psoriatic Arthritis (PsA)

1.1 An Historical Perspective

An arthritis associated with psoriasis was first recognised in the mid-nineteenth century and in 1860 Paul Bazin coined the term 'psoriasis arthritique'.[2] Interest waned until early this century, when it was simply defined by Hench as 'arthritis following psoriasis'.[3] Understandably, this definition received a lot of criticism as it encompassed a multitude of arthropathies, and debate raged during the 1930s as to whether it was indeed a single entity or merely the co-incidental co-existence of two independent conditions.[4] Epidemiological work in the 1950s and 1960s in Europe showed that there was an excess of arthritis in patients with psoriasis and a similar excess of psoriasis amongst those with arthritis,[5,6] and in 1964 the American Rheumatism Association recognised it as a separate entity. The work of Wright lead to a slightly more precise definition of 'psoriasis associated with erosive polyarthritis and usually rheumatoid factor (RF) negative'.[7] However, it became clear that PsA was not just confined to the peripheral skeleton but that it also had features of spondylitis. In 1973, Moll and Wright published their seminal paper on PsA and its subclassification, now defin-

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Table I. Moll & Wright subtypes of psoriatic arthritis

Subtype	Percent Moll & Wright (1973)[8]	Percent Gladman (1987)[17]a
Distal interphalangeal predominant	<5	12
Arthritis mutilans (severe joint destruction)	5	16
Symmetrical polyarthritis (similar to rheumatoid arthritis)	15	40
Asymmetrical/oligo-articular	70	16
Spinal predominant	5	2

a Does not total 100% because some patients did not fit the categories as they had symmetric oligoarthritis or asymmetric polyarthritis.

ing it as 'psoriasis associated with inflammatory arthritis or spondylitis and usually RF negative'.[8]

With their paper and attempts at sub-classification, they highlighted some of the distinctive diagnostic features.[8] The different groups were based solely on clinical phenotype (table I). Other authors have since attempted to re-classify subtypes into peripheral and spinal or those patients with a large extra-articular component (such as Synovitis Acne, Pustulosis Hyperostosis Osteitis - SAPHO), but none has usefully replaced the original sub-classification.[9,10] Recently, a French group has produced a set of nine diagnostic criteria incorporating both clinical, radiological and serological tests which in their cohort is 95% sensitive and 98% specific for PsA when compared with RA and ankylosing spondylitis (AS).[11] However, this has yet to be applied to other populations. With the benefit of long-term follow-up there is much greater appreciation of the heterogeneity of patients, and that a single patient may possibly pass through all these groups during the course of their disease. Although many (approximately 40%) of patients start with an oligo-articular pattern of disease, the vast majority develop further joint involvement to become poly-articular and even progress to the mutilating form of the arthritis.[12-14] Similarly, the longer the follow-up the greater the proportion of patients with spinal disease. Presentation with solely distal joint involvement occurs in approximately 10% of patients; however, by 5 years only 2% still have disease confined to these joints. The most useful distinction prognostically is the presence of polyarticular disease (>4 swollen joints) as this predicts a worse outcome, whether found at diagnosis or later during the course of the illness.[15,16]

As can be seen from the above sub-classification, the pattern of arthritis alone is not necessarily specific to PsA and there is no specific test to identify patients. Indeed, even psoriasis is absent in up to 20% of patients. Many patients could simultaneously fulfil criteria for PsA, RA or indeed AS. The distinguishing clinical features of PsA, RA and the other spondyloarthritides are listed in table II.

1.2 Comparison with Rheumatoid Arthritis (RA)

To begin with, compared with RA, PsA affects both sexes equally[4] and in RA the rheumatoid factor is more commonly positive. Rheumatoid factor may be detected in up to 30% of the general population and so of its own does not exclude a diagnosis of PsA but has to be placed in the context of the clinical picture.[8] Looking at the distribution of joint involvement, involvement of the distal interphalangeal (DIP) joint is uncommon in RA but is frequently found in PsA (up to 50%), particularly in patients with associated psoriatic nail involvement. There is frequently less symmetry in joint involvement, and often a 'ray' distribution – whereby all the joints in a single digit will be affected.[18] Looking at the joint swelling itself, it may have a mild violaceous discolouration, and is usually not as effusive or prolific as that seen in RA, being more fibrous and also less tender.[19] Unfortunately, these are features that can only be readily appreciated with experience. Dactylitis (the swelling of an entire digit) is a common occurrence (up to 48% of patients with PsA in the Toronto clinic have at least one episode), but far rarer in RA. It can also be seen in other spondy-

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Table II. Distinguishing clinical features of psoriatic arthritis (PsA), rheumatoid arthritis (RA) and the other spondyloarthritides

Clinical feature	PsA	RA	AS	Reactive	IBD
Gender	M = F	F > M	M > F	M > F	M = F
Peripheral joint pattern	Oligo/poly, asymmetric	Poly-articular, symmetric	Oligo-articular, lower limb	Oligo-articular, lower limb	Oligo-articular, lower limb
DIP joint	+++	+	–	–	–
Dactylitis	+++	–	+	++	+
Enthesitis	++	–	++	+++	++
Spondylitis	++	–	+++	+	++
Sacroiliitis	Asymmetric	–	Symmetric	Asymmetric	Symmetric
Eye involvement	+	++	++	+++	+
Nodules/Sjögren's	–	+++	–	–	–
Skin/nail lesions	+++	–	–	++	–
Rheumatoid factor positive	–	+++	–	–	–

AS = ankylosing spondylitis; **DIP** = distal interphalangeal; **F** = female; **IBD** = inflammatory bowel disease; **M** = male; + indicates low frequency of occurence; ++ indicates medium frequency of occurence; +++ indicates very high frequency of occurence; – indicates feature did not occur.

loarthropathies, sarcoidosis, sickle cell disease and tuberculosis. A gout-like presentation of arthritis can occur, and PsA should be considered in any one with psoriasis who has a podagra-like episode, particularly if young or female, although joint aspiration for crystals is the gold standard.[8]

With long-standing disease further differences may be found. The classical deformities of RA such as swan necking or boutonniere may be found but are not so common in PsA. Instead different deformities are often seen; rigid ankylosis of joints is frequently observed, and the classical telescoping flail digit or 'doigt en lorgnette' may be seen if marked osteolysis occurs. Spinal involvement occurs in 40% of patients with PsA and up to 70% may have sacroiliac involvement in contra-distinction to RA.[20] Atlantoaxial subluxation with neck disease does occur, although to a lesser degree than in RA. Enthesitis is a frequent feature of PsA, however, true inflammatory heel pain (plantar fasciitis or Achilles tendonitis) is very uncommon in RA.

Fortunately, the systemic manifestations of RA are absent. Rheumatoid nodules or vasculitis are not seen, and Sjögren's syndrome or scleral disease are similarly absent. Patients may develop iritis or conjunctivitis but not as frequently as that seen in ankylosing spondylitis or reactive arthritis.

If we compare radiographs between the two groups, erosive disease of the DIP joints, ankylosis, new bone formation or periostitis, enthesopathic spurs (often with erosions), tuft resorption or the marked osteolysis of the 'pencil in cup' deformity should all direct the physician to a diagnosis of PsA, particularly in the presence of spinal changes.[21]

1.3 Comparison with the Other Spondyloarthropathies

Fortunately in most patients, the spinal disease of PsA tends to be mild, often with minimal symptoms, and disease may only be detected if looked for carefully either clinically or on radiograph.[22] Sacroiliitis is often asymmetrical but can progress to full ankylosis. Unlike AS, which tends to progress in a caudo-cranial fashion, the first radiographic changes may be seen in the thoracic or cervical spine. These may be simple classical syndesmophytes but large chunky paramarginal syndesmophytes that are more reminiscent of diffuse idiopathic skeletal hyperostosis (DISH) maybe seen.[22,23]

Distinguishing PsA from enteropathic or inflammatory bowel disease associated arthropathy can be more difficult at presentation as psoriasis can be associated with Crohn's disease and an oligoarticular disease is often seen as well as sacroiliac involvement. In recent years there has been a move to describe PsA as an enthesopathy,

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with the arthritis being due to an overflow of inflammation from local enthesopathic sites.[24] Enthesitis is certainly found more frequently amongst PsA patients and indeed all spondyloarthropathy patients. The European Spondyloarthropathy Study Group (ESSG) found inflammatory heel pain to be 90% specific for spondyloarthritis.[25] It has even been proposed that psoriatic enthesopathy should be a distinct subset of PsA.[26] Interestingly, enthesitis was not even mentioned as a clinical manifestation in Moll & Wright's original description.[8] However, it is commonly seen in Reiter's syndrome/reactive arthritis, which can also present with sacroiliitis, oligoarthritis, dactylitis and a palmoplantar rash (Keratoderma Blenorrhagica). This could be confused with palmoplantar pustular psoriasis and it is these patients who probably present the greatest opportunity for diagnostic confusion. In such patients a careful history, examination and search for an infective aetiology is necessary.

1.4 Laboratory Findings in PsA

Serological tests have little role in the diagnosis of PsA and act more as confirmation, although the presence of high titre RF with symmetrical polyarticular arthritis would be more indicative of RA. Antinuclear antibody may be elevated in up to 10% of patients, usually at low levels. Inflammatory markers such as erythrocyte sedimentation rate (ESR) or C reactive protein (CRP) may be elevated but are not necessarily so, and have not been shown consistently to follow disease activity as closely as in RA.[27] However, the presence of an elevated ESR does predict a poorer prognosis.[28] Arthroscopy and biopsy of inflamed joints is still in its infancy as a diagnostic tool and reveals only quantitative differences between RA or spondyloarthropathy joints. The synovium of patients with PsA tends to be more vascular both macro- and microscopically than in patients with RA. There is less inflammatory infiltrate, with a shift towards a CD8+ population of T cells as opposed to a CD4+ predominance in RA.[29,30] Measuring cytokines within joint fluid also reveals a less inflammatory profile.[31] Tumour necrosis factor (TNF)-α and interleukin (IL)-1 are elevated above normal but at far lower levels than in RA.[32] There is clearly a difference in pathogenesis but at the moment its implications for therapy or diagnosis are not clear.

2. Treatment of PsA

When the concept of PsA was first developed it was thought to be a comparatively mild disease, affecting only a few joints and causing little long-term damage. Indeed, patients with psoriatic arthritis have less painful joints and complain less than patients with RA with similar disease.[19] However, with long-term follow up it has become apparent that a large proportion develop a polyarticular pattern of disease, progress to radiological joint damage and may also have an increased mortality.[13,28,33]

Unfortunately, placebo-controlled therapeutic studies in the past have been few, often with limited numbers of patients and of short follow-up. There have been no prospective, controlled studies looking at radiological progression, which is not surprising when, until recently, no 'disease-modifying' therapy has convincingly shown an improvement in symptoms above placebo. In fact, most studies show a high placebo response rate of up to 50%, some two to three times greater than that usually found in studies on RA.[34] This could be due to poor initial case selection through lack of good diagnostic criteria.

We also have no established tools to measure disease activity, particularly when we need to take account of not only peripheral joint disease, but also spinal involvement, enthesopathy and of course skin disease. Ideally, any drug for treating joint disease should also improve the skin or at least make it no worse. Recently the PsARC (Psoriatic Arthritis Response Criteria), a scoring system based on a combination of joint and skin disease, has been proposed and used in clinical trials, although it has not been validated.[35,36] An alternative, and more interesting, explanation for the apparent lack of response may be the different pathogenic mechanisms involved in PsA and RA.

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2.1 Non-Steroidal Anti-Inflammatory Drugs

Non-steroidal anti-inflammatory drugs (NSAIDs) have been the cornerstone of symptomatic control of inflammatory arthritis for many years. Studies in the English literature on their use in PsA are scarce but in clinical practice they appear to be effective in easing symptoms, with similar individual differences in efficacy as seen in other conditions. In patients with spinal disease (where no second-line agent has been shown efficacious), or with minimal peripheral joint disease and a good prognosis, they may be sufficient to control symptoms while waiting for a remission of disease activity. The newer cyclo-oxygenase (COX)-2 specific NSAIDs (celecoxib and rofecoxib) appear to work as well as the less-specific agents in practice. No formal studies of efficacy or safety have been performed in patients with PsA. Rarely, in some individuals the introduction of NSAIDs is associated with a flare in skin disease.

2.2 Methotrexate

Methotrexate (an anti-folate) has been used extensively for the management of psoriasis and PsA since the 1950s. Although there is good evidence for its efficacy in psoriasis and also for RA, where it not only improves symptoms but also slows progression of joint damage, placebo-controlled studies in patients with PsA are sadly lacking. Studies have been small and of brief duration. In 1960, Black et al. found a significant benefit with intravenous methotrexate 2–3mg/kg given every 10 days in ten patients over 80 days.[37] In 1984, Wilkens et al. examined 37 patients over 12 weeks (7.5–15 mg/week, orally), but found only an improvement in physician global assessment and skin disease.[38] In uncontrolled studies, a good response has been reported with associated fall in the ESR[39,40] but comparing radiological outcome over time with other therapies showed no additional benefit.[41]

When it was first used at high doses significant liver disease was seen but with lower dose, once weekly therapy, severe liver disease is now rare. A high rate of alcohol-related morbidity is seen in psoriatic patients and caution must be exercised.[42] Regular monitoring of both blood count and liver function is recommended.

In spite of lack of good evidence to support its use, methotrexate is still probably the initial drug of choice in view of its good affect on the skin and proven success in RA. Empirically, in the clinic setting, it also seems to be of benefit.

2.3 Sulfasalazine

Sulfasalazine has been studied the most of the anti-rheumatic drugs, and in meta-analyses has been shown to be of small but significant benefit over placebo.[34] A number of small studies of short duration have shown a trend towards improvement with a reduction in the ESR.[43-45] Even the large Veterans affairs study of 221 patients over 36 weeks showed no significant benefit over placebo with response to sulfasalazine 2g. In the sulfasalazine group 57.8% had a positive response compared to 44.6% in the placebo group. Looking at individual components of response, only the ESR showed a significant reduction with sulfasalazine ($p < 0.0001$).[35]

Adverse effects in all the studies were surprisingly mild and not significantly higher than placebo. They tended to involve primarily the gastrointestinal tract. The skin did not deteriorate and in some patients improved. A review of the use of sulfasalazine in the clinical setting did not confirm its superiority to other medications neither in the short nor long-term, and toxicity was a major issue.[46]

2.4 Cyclosporin

Cyclosporin (a selective T cell immunosuppressant) has been used successfully in placebo-controlled studies to treat both plaque and palmo-pustular forms of psoriasis. However, adverse effects, particularly renal, have limited its use and lead to a pulse regimen being used in skin treatment.[47] For arthritis, continued use is usually required and so far there have been no placebo-controlled studies. Study dosages have ranged from 2–6

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mg/kg/day, and there have been a number of open studies with less than ten patients. In a larger study of 55 patients over 6 months on a mean dosage of 2.7mg/kg/day, skin disease tends to respond well within 5–6 weeks, while a similar improvement in joint symptoms did not tend to occur until after much longer periods of treatment (24 weeks).[48] Relapse occurs rapidly within 4 weeks after stopping treatment.[49] In comparison with methotrexate, over 1 year it had similar efficacy but the withdrawal rate was higher with cyclosporin.[50]

2.5 Gold

Gold has been used for many years in the management of RA, and would appear to be effective and able to induce remission. Large, placebo-controlled studies in PsA of both intramuscular and oral gold have failed to show any significant improvement over placebo.[51,52] Drop out rates and adverse effects were no greater than those seen in studies in RA. A few patients reported the onset of psoriasis with gold use.

2.6 Other Standard Disease Modifying Anti-Rheumatic Drugs

Studies on other disease modifying anti-rheumatic drugs (DMARDs) are even fewer. Azathioprine has been reported in abstract form to be effective.[53] Excellent experience was reported in individual patients in a nested case control study which did not reveal an overall advantage of azathioprine over other medications in PsA.[54] The antimalarial chloroquine has been studied retrospectively and not found to be more effective than placebo. Anecdotal reports suggest an increased risk of flare of psoriasis or exfoliative dermatitis but this has not been born out in practice.[55]

2.7 Corticosteroids

In our practice, we use few oral corticosteroids because of their potential long-term adverse effects, risk of rebound flare of pustular psoriasis on withdrawal and possibly reduced efficacy from that seen in RA. There are no controlled or open studies on their use in PsA. Corticosteroid injections either intra-articular or at the site of an enthesis can be rapidly effective in controlling inflammation and may be a good treatment approach in those with an oligo-articular pattern of disease. We frequently use digital flexor sheath injections to manage acute dactylitis. Again there are no studies confirming efficacy intra-articularly or in soft tissues.

2.8 Newer Therapies for Psoriatic Arthritis

2.8.1 Bisphosphonates

Bisphosphonates have been shown in animal models to inhibit the development of chronic inflammation and erosion. Pamidronate has been investigated in pilot studies in patients with spondyloarthropathy (though not PsA) and found to be effective in improving both spinal and peripheral joint symptoms. An associated improvement in ESR, CRP and decreased gadolinium uptake on magnetic resonance imaging was also seen.[56] Clinical experience in our centre suggests it may also be useful in patients with PsA.

2.8.2 Leflunomide

Leflunomide, or more precisely its active metabolite teriflunomide (A-771726), selectively inhibits dihydro-orotate dehydrogenase thus blocking *de novo* synthesis of pyrimidines and so suppressing activated lymphocyte DNA production. It may have also have other contributory anti-inflammatory effects by altering cell signalling.[57] It has proven efficacy in placebo-controlled trials for the treatment of RA and is a true disease modifying agent, delaying progression of radiological damage.[58] However, when it comes to PsA there is scant evidence of its efficacy. A multi-national, placebo-controlled study is in progress.

2.8.3 Mycophenolate Mofetil

Mycophenolate mofetil is an immunosuppressive that is now being extensively used to prevent rejection post organ transplant and is starting to be used in other autoimmune diseases. Initial small, short-term (10 weeks), pilot studies in severe psoriasis and PsA have shown doses of 2 g/day pro-

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duce some benefit, although the study size and short duration may have precluded a meaningful response.[59]

2.8.4 Anti-Tumour Necrosis Factor Agents

The anti-TNF agents etanercept and infliximab are now licensed in most countries for use in the management of RA (and for Crohn's disease in the case of infliximab). They have been shown to not only produce a rapid response in symptoms but also to delay disease progression when compared with placebo.[60,61] Again, what is used in RA, is eventually tried in PsA. A flurry of papers has appeared in press recently describing their use in patients with PsA. The results so far appear to be encouraging and for the first time show a significantly improved response above placebo.

Etanercept

Etanercept is a soluble fusion protein comprising a TNFα type II receptor and immunoglobulin (Ig)G1 heavy chain. It is usually administered twice weekly subcutaneously at a dose of 25mg. There has been one randomised, placebo-controlled study in 60 patients with PsA.[36] Initial 12-week data have been published that show a highly significant improvement in PsARC (87 vs 23%), and American College of Rheumatology (ACR) improvement criteria (ACR20) [73 vs 13%] and ACR50 (50 vs 3%) over placebo, with minimally significant adverse effects. Further long-term data to 9 months was presented in abstract form.[62] Efficacy in the treatment group appeared to be maintained and other therapies such as methotrexate or corticosteroids could be reduced or discontinued in many patients. The original placebo-control group of 30 patients was commenced on etanercept at the end of the original 12-week period. Interestingly, the response in this group was far less impressive, achieving an ACR20 of 61% as opposed to 87% in the treatment group by the end of the study. However, the Psoriasis Area and Severity Index (PASI) score improved consistently in both groups by 62% compared with only a 9% improvement on placebo to 12 weeks. In general, adverse effects continued to be minimal, although significantly a multiple sclerosis like disease was diagnosed in one patient receiving etanercept.

Infliximab

Infliximab is a mouse-human chimeric protein containing a human Ig Fc component and a murine monoclonal antibody to TNFα. It has to be administered intravenously but can be given at longer time intervals than etanercept. There are as yet no placebo-controlled studies in patients with PsA, although one will soon be underway. The only published data comes from a Belgian study on its use in a group of 21 patients with spondyloarthropathy, which included nine patients with PsA.[63] Patients received three loading doses of infliximab 5 mg/kg at weeks 0, 2 and 6. Unfortunately, specific data for the PsA patients was not available, although it was reported that peripheral and axial disease improved significantly across the whole group and that this continued out to 20 weeks. Skin disease, as measured by PASI, also showed a marked improvement. One case of pyelonephritis was noted. Results from another study of ten patients has also been presented in abstract.[64] At 1 year, six of the original ten patients had no tender or swollen joints, and three patients had managed to stop therapy, while four were on a lower baseline therapy. One patient experienced an infusion reaction and the drug was stopped. One patient required increased dose and frequency to every 4 weeks. Unfortunately we have no information on their disease at baseline.

We have had the opportunity to use infliximab in 15 of our refractory patients attending the PsA clinic in Toronto Western Hospital. Seven patients have improved their joint counts by 50% and nearly all have shown significant skin improvement. However, this has not been without cost as some patients have deteriorated, and a number of severe adverse events have occurred. Infliximab has had to be stopped in five patients as result of significant adverse effects. Once therapy was halted patients have tended to relapse rapidly.[65]

2.8.5 Efalizumab (Anti-CD11a)

CD11a comprises part of the lymphocyte function-associated antigen and is important in T-cell

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trafficking into tissues. Blockade of this receptor has been seen as a possible means to prevent lymphocyte accumulation in psoriatic skin and so treat psoriasis.[66] In phase III studies, a monoclonal antibody to CD11a efalizumab has been anecdotally reported to improve psoriatic arthritis.

2.8.6 Cytotoxic T Lymphocyte-Associated Antigen 4 Immunoglobulin (CTLA4-Ig)

For activation, T cells require two signals one through the major histocompatibility complex (MHC)/antigen complex and a co-signal via CD80/86 (B7-1/B7-2) and CD28 interaction. Cytotoxic T lymphocyte-associated antigen (CTLA)-4 (CD152) binding to CD80/86, however, strongly inhibits activation. A CTLA4-Ig hybrid has been developed which binds with great affinity to CD80/86, so inhibiting the CD28 dependent co-stimulatory pathway necessary for T-cell activation. In animals studies CTLA4-Ig can ameliorate collagen-induced arthritis and in human studies in patients with psoriasis it has been found to be effective, producing 50% or greater improvement in skin disease, particularly in those receiving the higher doses.[67] It has yet to be studied in patients with PsA but studies are underway in those with RA.

2.9 Treating the Skin

Skin disease is not always present in patients with PsA, indeed some studies suggest that skin disease is milder in patients with arthritis.[68] In those patients with synchronous onset of psoriasis and arthritis, skin and joint activity may correlate.[69] Treating the skin alone with topical therapy does not seem to have much impact on underlying joint disease. However, clearing severe skin disease can still greatly improve the quality of life of the patient. Etretinate therapy, although effective for skin, probably has only a minor role in treating PsA because of its high adverse events rate.[70] In an open study, photochemotherapy has been shown to produce improvement in patients with peripheral joint disease but, interestingly, arthritis response was inversely proportional to the extent of skin disease.[71] However, the potential risk of skin cancers limits its widespread use. Heliotherapy (4 weeks in the Canaries) was found to be an effective treatment for skin and joints in Finnish patients with PsA in an uncontrolled study.[72] Dead sea therapy (balneotherapy) has been shown to be effective in uncontrolled studies.[73] A recent placebo-controlled study of infliximab as monotherapy in severe psoriasis (5% body surface) demonstrated its efficacy.[74] Eighty-two percent of patients receiving infliximab 5 mg/kg and 91% of patients receiving infliximab 10 mg/kg demonstrated good, excellent or clearing of psoriasis as opposed to only 18% of patients receiving placebo. Therefore, this agent also has a potential role in treating both the joint and skin manifestations of PsA.

2.10 A Therapeutic Strategy for Psoriatic Arthritis

For those patients with spinal disease or very minimal joint symptoms, NSAIDs and simple exercises to maintain mobility and reduce stiffness may be sufficient. Corticosteroid injections can be a useful adjunct in controlling disease in those patients with oligo-articular disease. In those patients with poly-articular disease where a poorer outcome has been demonstrated,[15,16,19] second-line therapy is clearly indicated. Initially we would use methotrexate up to 25mg subcutaneously for its added beneficial effect on the skin, or enteric-coated sulfasalazine up to 4 g/day. With more resistant disease we use combination therapy with other standard DMARDs, such as azathioprine, cyclosporin, hydroxychloroquine and leflunomide. Increasingly we are using the newer anti-TNF agents early after unsuccessful treatment with methotrexate and sulfasalazine alone or in combination, especially in those patients with very severe skin disease, where they can be particularly effective in controlling both aspects of the condition. Any treatment for the arthritis must not neglect the skin, which can prove to be just as socially disabling, and we encourage our patients to also seek dermatological advice.

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3. Conclusions

PsA is now proven as a distinct disease with a number of characteristic features, which should enable its diagnosis in the clinic setting. However, a formal classification system or set of accepted diagnostic features are not yet available. We have learnt in the last few decades that PsA is not necessarily a benign disease, but can be associated with significant morbidity and aggressive therapy, particularly in those with polyarticular disease, is necessary. What this treatment should be remains a moot point. Therapeutic studies of standard DMARDs have, in general, not shown significant benefit of any agent over placebo, although the newer biological agents are showing great promise and may eventually allow us to successfully treat PsA.

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