Editorial

Towards International Guidelines for the Management of Psoriatic Arthritis

Psoriatic arthritis (PsA) is an inflammatory arthritis associated with psoriasis. PsA was recognized as an entity distinct from rheumatoid arthritis, the prototype inflammatory arthritis, following discovery of the rheumatoid factor in 1948 and the recognition that the majority of patients with PsA were seronegative[1]. PsA affects men and women equally, and has a worldwide distribution. PsA is classified among the spondyloarthropathies because of the presence of spinal involvement in about 50% of patients and presence of extraarticular features common to spondyloarthropathies, as well as the association with HLA-B*27.

Until recent decades PsA was considered a rare and mild disease. In fact, PsA develops in up to one-third of patients with psoriasis. With psoriasis occurring in up to 3% of the population, PsA may affect up to 1% of the population[1,2]. Over the past 2 decades evidence has accumulated that PsA is a severe disease in at least 20% of patients with progression of joint damage[3-6]. Predictors for disease progression include polyarticular presentation, as well as the degree of joint inflammation[7,8]. Radiographic progression has been noted within 2 years of onset of PsA[9]. Moreover, patients with PsA have an increased mortality rate compared to the general population, and the mortality risk is related to disease severity at presentation to clinic[10,11]. Patients with PsA suffer from reduced quality of life and function[12]. Thus it is clear that joint inflammation in PsA must be treated appropriately to control patients' symptoms as well as to prevent progression of damage.

Therapies for PsA have been unsatisfactory until the last few years. Nonsteroidal antiinflammatory medications may control symptoms, but they have no effect on joint damage progression. Traditional disease modifying drugs commonly used in rheumatoid arthritis have been used in PsA[13]. The response rates have been small, and there is no evidence that any of these drugs actually prevented disease progression[14,15]. However, it could be argued that the lack of demonstrable efficacy in clinical trials by conventional drugs may have resulted from methodological issues, including small sample size, inadequate response criteria, and omission of radiographic assessment. An alternative explanation may be that these medications were given too late in the course of the disease and thus were unable to modify disease course.

Recently a more rigorous scientific approach has been applied to clinical trials in PsA with the ability to demonstrate efficacy with the antimetabolite leflunomide[16]. Reports of efficacy of etanercept for PsA in 2000[17] opened new horizons for patients. Subsequent trials with other antitumor necrosis factor (TNF) agents including infliximab and adalimumab, as well as the T cell directed agent alefacept, have also shown remarkable improvement[18-21]. In addition to controlling signs and symptoms of joint inflammation, the anti-TNF agents have shown a potential to prevent progression of radiological damage[20,22]. It has been suggested that treatment earlier in the course of the disease may provide better response and protection from disease progression. The availability of effective medications for PsA has generated renewed interest in the disease.

Because the new, effective agents for PsA are very expensive, they are not readily available to all patients. This is an issue for individuals who depend on a national health system for their medications, as well as those dependent on private insurance. Many national healthcare authorities as well as insurance companies have approached national rheumatology associations to help set guidelines for the use of these expensive therapies.

Physicians in several countries have developed treatment guidelines for PsA, primarily for the use of anti-TNF agents. In 2003, the Canadian Rheumatology Association provided their first set of guidelines for use of anti-TNF agents in spondyloarthritis, including a section on PsA. Following a systematic literature review they recommend-

See Systematic review of treatments for PsA: an evidence based approach and basis for treatment guidelines, *pages 1417 to 1456*

ed that anti-TNF use be based on the decision of the physician and patient, taking into consideration the degree of inflammation and stage of disease[23]. The British Society of Rheumatology also developed guidelines for use of anti-TNF therapy[24]. After completing a systematic review of literature on the treatment of PsA, they produced an algorithm for anti-TNF agents in PsA. These agents are recommended only after trials with nonsteroidal antiinflammatory medications, and at least 2 of 4 "disease modifying" medications including methotrexate, sulfasalazine, cyclosporin A, and leflunomide. While acknowledging that evidence to support use of these first 3 drugs is weak, this group favors a prudent approach. They further recommend that continued use be based on evidence for improvement within 3 months. The Italian Rheumatology Society also introduced anti-TNF guidelines[25]. Several other national rheumatology associations are still working towards publication of their own PsA guidelines. While each country may require its own version, there is also a need to develop guidelines that would be applicable worldwide. Efforts to date have concentrated on the musculoskeletal manifestations of PsA and have not specifically addressed the skin manifestations.

In this issue, *The Journal* reports a new approach undertaken by members of GRAPPA[26]. GRAPPA is not just the name of an after-dinner wine. It refers to the Group of Research and Assessment of Psoriasis and Psoriatic Arthritis, which was formed in New York, August 15-17, 2003, with the mission to:

1. Increase awareness and early diagnosis of psoriatic arthritis
2. Develop and validate assessment tools
3. Evaluate treatment modalities to promote clinical research with the ultimate goal of improving disease outcome
4. Promote basic research into disease pathophysiology
5. Foster interdisciplinary communication
6. Foster communication with the general public via patient service leagues, industry, regulatory agencies, and other concerned bodies.

GRAPPA is an international group of rheumatologists, dermatologists, and methodologists committed to achieving these goals[27]. Several of their objectives have already been addressed. Particularly with availability of new, effective therapies for both psoriasis and PsA, there is greater awareness of the condition and a push towards earlier diagnosis. Early recognition of the disease is a challenge, however, because of the lack of classification and diagnostic criteria. The recent development of the CASPAR classification criteria for PsA should help identify patients earlier in the course of the disease[28]. GRAPPA members have been involved in development and validation of assessment tools for PsA. This effort has benefitted from collaboration with OMERACT[29] and other spondyloarthritis working groups, such as the Ankylosing Spondylitis Assessment (ASAS) group, the SPondyloArthritis Research Consortium Canada (SPARCC), and the SPondyloARthritis Treatment Assessment Network (SPARTAN)[30].

Developing treatment guidelines has been one of the major goals of GRAPPA. A committee to develop treatment guidelines was formed at the first meeting of GRAPPA with Drs. Arthur Kavanaugh and Christopher Ritchlin as cochairs. Members of the committee, consisting of rheumatologists and dermatologists, have performed systematic reviews on all aspects of management of PsA, including skin and joint manifestations.

For joint manifestations, rheumatologists have undertaken review of treatments from nonsteroidal antiinflammatory medications through biologic therapies. This has been an important effort, since the musculoskeletal manifestations of PsA are diverse, including peripheral joint disease, axial disease, dactylitis, and enthesitis. Axial disease has not been assessed in clinical trials in PsA. Even dactylitis and enthesitis, which are typical features of the PsA, have only been assessed in a few studies.

For psoriasis, a review of treatment from simple topical moisturizers through biologic therapies was undertaken by dermatologists. Psoriasis may also have variable manifestations in the skin and nails. Most studies have looked at psoriasis vulgaris. Nail lesions have been ignored in most studies. Nonetheless, this is the first and an important step in developing guidelines for current management of the disease. The committee had to grapple with issues such as what to do when there is no evidence, as the lack of evidence does not mean evidence of lack of effect. They also had to determine, in situations where there is no evidence from studies in PsA, whether extrapolation from rheumatoid arthritis or ankylosing spondylitis could be accepted.

The articles in this series represent a thorough review of data on treatment of various aspects of PsA. Development of international guidelines for treatment will be based on this and newly emerging evidence. In preparing final recommendations, the committee must consider the appropriate management of the disease regardless of where the patient resides or the type of healthcare program available. It is expected that these international guidelines will be adapted within individual countries according to their specific needs and constraints.

The GRAPPA guidelines are intended not only to direct the use of anti-TNF therapy, but also for general management of patients with PsA. The committee should be congratulated on its work to date. This effort must continue with future participation and consensus among GRAPPA members, followed by dissemination to other interested parties and stakeholders, until the appropriate recommendations for the management of PsA are fully accepted.

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