Meeting Report

GRAPPA at the European League Against Rheumatism (EULAR) 2008

DAFNA D. GLADMAN, MD, FRCPC, Professor of Medicine, University of Toronto, Senior Scientist, Toronto Western Research Institute, Toronto, Ontario, Canada, and President; PHILIP S. HELLIWELL, DM, PhD, Senior Lecturer in Rheumatology, Academic Unit of Musculoskeletal and Rehabilitation Medicine, University of Leeds, Leeds, UK, and Treasurer; PHILIP J. MEASE, MD, Professor, Division of Rheumatology, University of Washington School of Medicine, Seattle, Washington, USA, and Vice-President, on behalf of the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA). Address reprint requests to Dr. D. Gladman, Toronto Western Hospital, University Health Network, 399 Bathurst Street, 1E410B, Toronto, Ontario M5T 2S8, Canada. E-mail: dafna.gladman@utoronto.ca. J Rheumatol 2009;36:656-8;doi:10.3899/jrheum.081023

Supported by GRAPPA.

Launched in the summer of 2003, the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) is a nonprofit organization committed to advancing research and understanding of the assessment and treatment of psoriasis and psoriatic arthritis (PsA). This effort meets the need of helping rheumatologists recognize skin symptoms and helping dermatologists recognize joint symptoms for earlier diagnosis and more appropriate treatment of this disease, which affects millions of people throughout the world.

GRAPPA members meet several times a year to discuss issues relevant to the organization's objectives. There are 2 meetings a year adjacent to major rheumatology meetings: the American College of Rheumatology (ACR), which takes place in North America, and the European League Against Rheumatism (EULAR), which takes place in Europe; and adjacent to major dermatology meetings: the American Academy of Dermatology (AAD) in North America and the European Academy for Dermatology and Venereology (EADV) in Europe.

Our report summarizes the recent GRAPPA meeting at EULAR, June 11, 2008, at the Paris Convention Center.

This meeting was dedicated to defining psoriatic spondylitis. The prevalence of spinal involvement in patients with PsA has varied from 25% to 70%[1]. The wide variation is due to the lack of a common definition for psoriatic spondylitis. The agenda included presentations by a number of GRAPPA members followed by breakout groups and discussion.

Plenary presentations. Philip Helliwell, of Leeds, UK, presented the background and issues to be addressed by the group. He pointed out that there have been 2 general approaches to the diagnosis of psoriatic spondylitis. One uses the criteria for ankylosing spondylitis (AS), which rely on the presence of signs and symptoms of inflammatory back pain and limitation of lumbar mobility as well as the presence of either bilateral grade 2 or unilateral grade 3 or 4 sacroiliitis. The other uses the symptoms and signs of unilateral sacroiliitis. The first method is highly specific but not very sensitive, whereas the second is more sensitive, but not very specific. Both methods may be improved by use of magnetic resonance imaging (MRI), but this is costly. The question arises: Are there 2 entities? One consisting of classical AS, and the other psoriatic spondylitis, where spondylitis may be present in absence of sacroiliac changes, with different syndesmophyte morphology and paravertebral ossification and, sometimes, with asymptomatic spondylitis and sacroiliitis?

Therefore, there may be different ways to define psoriatic spondylitis:

- alone or in combination with peripheral manifestations
- based on inflammatory spinal symptoms
- based on radiographic sacroiliitis
- based on other radiographic signs of spondylitis
- based on MRI
- using combinations of features such as the New York criteria[2] and European Spondylarthropathy Study Group criteria[3]

Dafna Gladman, of Toronto, Canada, presented results from the University of Toronto Psoriatic Arthritis Clinic Database looking at how different definitions of spinal disease function. She presented 2 studies. The first looked at progression of spinal disease over time, and was an update of a study published in 1988, when it was shown that there was progression of syndesmophytes and sacroiliac score over an average of 57 months of followup, although there was no significant difference in the signs and symptoms of these patients. The followup study included 244 patients with manifestations of inflammatory neck or back pain, clinical sacroiliitis, radiographic evidence of spondylitis sacroiliitis grade $\geq$ 2, and/or syndesmophytes (cervical, thoracic, or lumbar), who were followed for at least 5 years. Over the followup period there was a decrease in inflammatory neck pain but not in inflammatory back pain. There was a significant reduction in neck mobility, forward spinal flexion, and lateral spinal flexion. Grade 2 sacroiliitis was detected among 35% of the patients who did not have it at baseline, and 36% of the patients with sacroiliitis at baseline showed progression to a higher grade. New syndesmophytes were detected in 15% of the patients. Thus over time

Personal non-commercial use only. The Journal of Rheumatology Copyright © 2009. All rights reserved.

Downloaded on April 17, 2024 from www.jrheum.org

patients with psoriatic spondylitis have reduced neck pain but deterioration of metrologic assessment and progression of radiological features.

The second study looked at different definitions of spinal involvement in PsA used in the prediction of developing psoriatic spondylitis over followup. Included in this study were patients who did not have evidence of spondylitis at entry into the clinic but who developed evidence of spondylitis according to the following definitions: (1) Bilateral sacroiliitis grade ≥ 2, or unilateral sacroiliitis ≥ 3 (NY radiographic criteria); (2) At least unilateral sacroiliitis grade ≥ 2 and inflammatory neck and/or back pain (IBP); (3) NY radiographic criteria and IBP; (4) NY radiographic criteria and IBP and limited spinal mobility; (5) NY radiographic criteria and IBP or limited spinal mobility (NY criteria for AS); (6) At least unilateral sacroiliitis grade ≥ 1 and IBP or limited spinal mobility. The prevalence of psoriatic spondylitis defined radiographically is slightly higher than that associated with the classic definition of AS.

This likely reflects the fact that patients with PsA are less symptomatic than patients with AS. The risk factors detected by both definitions are very similar and include number of radiographically damaged joints, a high erythrocyte sedimentation rate, and enthesitis. This study suggests that the radiographic definition may suffice for defining psoriatic spondylitis.

José Luis Fernández-Sueiro, of La Coruña, Spain, presented the Spanish experience in comparing patients with PsA to those with AS, as well as comparing patients with PsA with and without spondylitis. The definition of psoriatic spondylitis was based on the presence of clinical features and at least unilateral grade 2 sacroiliitis. Among the 100 patients with PsA, 46 had spondylitis; in 4 it was isolated and in 42 it was associated with peripheral arthritis. Among 103 patients with AS, 30 (29%) had evidence of peripheral arthritis. Patients with AS were younger at diagnosis, had less peripheral arthritis, and had worse spinal radiological changes than patients with psoriatic spondylitis. PsA patients with axial disease tended to be men, with longer disease duration than those with peripheral arthritis only. Modified Schober test, lumbar side flexion, and cervical rotation discriminated between patients with and without axial involvement and are therefore good measures to evaluate spinal disease in PsA. Bath AS Disease Activity Index[4] and Bath AS Functional Index[5] were also found to be good measures in psoriatic spondylitis. Fernández-Sueiro recommended that radiographs of the sacroiliac joint should be done routinely in patients with PsA, and if at least unilateral grade 2 sacroiliitis is present along with spinal symptoms, patients should be evaluated in clinics as having spinal disease irrespective of peripheral joint involvement.

Ennio Lubrano, of Italy, presented data on the assessment of the severity of spinal disease in PsA using the Bath AS Radiological Index[6] (BASRI) and modified Stoke Ankylosing Spondylitis Spine Score (mSASSS). This was a multicenter Italian study. Axial involvement at the cervical and lumbar spine without sacroiliac involvement was observed in 7/71 patients by BASRI (9.8%). Twenty-two patients had fusion of the zygo-apophyseal joints. They developed a PsA spinal radiological index (PASRI), which used a combination of features from the BASRI and mSASSS and which also included assessment of the cervical facet joints. The PASRI functioned well against the BASRI and modified Stoke AS Spine Score, and demonstrated some advantages over them. This instrument now requires confirmation in other cohorts and use in longitudinal studies.

Jurgen Braun, of Herne, Germany, discussed the relationship between psoriatic spondylitis and AS. He highlighted the question of whether psoriatic spondylitis is a separate disease or AS associated with psoriasis. There is currently an effort to develop new classification/diagnostic criteria for AS through the ASsessments in Ankylosing Spondylitis (ASAS) working group, and further studies are necessary to define psoriatic spondylitis.

Philip Mease, of Seattle, USA, discussed the SPondyloarthritis: Assessment of CuRrent Epidemiology, Management and Knowledge (SPARK) initiative. Currently, there is a paucity of information about epidemiologic and diagnostic characteristics of the SpA patient population and its management in rheumatology practices. For example, it is unclear how many patients have a clearcut form of SpA such as AS, PsA, spondyloarthritis of inflammatory bowel disease, or reactive arthritis versus patients with a less well characterized form of spondyloarthritis (SpA), generally referred to as "undifferentiated SpA," or how these subtypes are being managed in routine clinical practice. Recent clinical trial evidence has shown efficacy of anti-tumor necrosis factor agents in patients with undifferentiated SpA, yet these therapies may not be accessible in practice because of lack of formal regulatory approval. It is unknown whether earlier effective therapy will make a difference in longterm outcomes, since this is less well studied than in rheumatoid arthritis.

The goal of the SPARK survey is to recruit approximately 500 physicians and 3900 patients in 9 countries (Belgium, Canada, France, Germany, Italy, The Netherlands, Spain, UK, and the US). Recruitment has already been completed in Europe, and is under way in multiple sites in the US. The survey is planned to characterize the nature of SpA and its management in rheumatology practices in parts of Europe and North America.

Following the plenary presentations, the group was divided into 4 breakout groups that were asked to address the following:

- What are the most important elements for diagnostic criteria for psoriatic spondylitis?
- What is the best way to go about this?
- Is it important to distinguish between different phenotypes of spondylitis associated with psoriasis?

Summary of breakout group discussions. Group 1 was co-

Personal non-commercial use only. The Journal of Rheumatology Copyright © 2009. All rights reserved.

Downloaded on April 17, 2024 from www.jrheum.org

chaired by Dafna Gladman and José Luis Fernández-Sueiro. The group identified the following as the most important elements for diagnostic criteria for psoriatic spondylitis:

- Inflammatory back pain (defined?) and/or
- Limitation of mobility and/or
- Radiographic changes/MRI/computed tomography (CT) and/or HLA-B*27

It was suggested that the best way to address the definition was through a research agenda. It was important to identify the different phenotypes of spondylitis associated with arthritis including those that fulfil criteria for AS, those that have IBP but do not demonstrate radiographic sacroiliitis or syndesmophytes and those that have radiographic changes without symptoms. The group identified the following research areas:

- Definition of inflammatory back pain in PsA
  Look at ASAS dataset of patients with psoriasis
  New proposed ASAS criteria in existing databases
  Biomarker study to look at PsA prospectively — could potentially build-in MRI
- Compare radiographic changes of PsSpA and controls — role of CT

Group 2 was co-chaired by Philip Mease and Gerd Marie Alenius. The group suggested that for diagnosis, radiographs and MRI were important. It was important to monitor those items that change over time. In clinical trials the items used for the assessment of AS should be included. The group recommended that GRAPPA discuss the ASAS radiographic tool.

Group 3 was co-chaired by Proton Rahman and Neil McHugh. The group felt that it was important to define the phenotype for both clinical treatment and scientific investigation. In PsA there is more neck involvement. Therapies are based on definition of disease so it is important to define the entity. Molecular signatures may be important, including HLA-B*27, interleukin 23, and ARTS, and therefore the clinical phenotype is important to identify correct associations. An element important to consider is IBP, which needs to be identified correctly in a cohort that is older. Moreover, HLA-B*27 frequency is not as high in PsA as it is in AS. Natural history is important and requires study with biomarkers, genetics, imaging, and quality of life.

Group 4 was co-chaired by Philip Helliwell and Ennio Lubrano. The group felt that the elements necessary to define spondylitis include radiographic, both sacroiliac and spine, IBP (where there is currently no consensus but new ASAS criteria could be applied), and a host of other features including skin involvement, dactylitis, uveitis, enthesitis, family history, response to nonsteroidal antiinflammatory drugs, C-reactive protein, peripheral arthritis, and genetics. There was no point distinguishing the phenotypes since the aim is to identify axial involvement.

Summary and research agenda. Psoriatic spondylitis appears to be a unique form of spondylitis. The following problems may confound using AS criteria:

- AS criteria may not be fulfilled until late
- May be 2 diseases: PsA spondylitis and AS
- Spinal involvement may be asymptomatic
- May get spondylitis without sacroiliitis
- Spondylitis in PsA may be indistinguishable from DISH (diffuse idiopathic skeletal hyperostosis; prevalence 15% in those age 50+ years)

It seems that if patients with PsA have any radiological involvement, with or without symptoms, then they have spinal involvement. GRAPPA members agreed that proper definition for psoriatic spondylitis is necessary and that clinical and radiographic features are important in that definition. There is not complete agreement on the need to phenotype the individual features.

New criteria for AS are being developed by ASAS and may address some of these issues. These criteria may be tested in existing databases such as those from Leeds, Italy, Spain, Toronto, and the CORRONA database, although some may not have all the data available. Alternatively, a new cohort could be collected prospectively, consisting of 500 patients with PsA and physician-diagnosed spondylitis, and 500 patients with PsA without spondylitis, through GRAPPA membership. This could be done in conjunction with a biomarker study planned through Outcome Measures in Rheumatoid Arthritis Clinical Trials (OMERACT).

Further discussion regarding the feasibility of such a proposal will continue in the next few months and will be presented at the next GRAPPA meeting at the ACR convention (October 2008).

REFERENCES

1. Gladman DD. Axial disease in psoriatic arthritis. Curr Rheumatol Rep 2007;9:455-60.
2. Bennett PH, Burch TA. New York symposium on population studies in the rheumatic diseases: new diagnostic criteria. Bull Rheum Dis 1967;17:453-8.
3. Dougados M, van der Linden S, Juhlin R, et al. The European Spondylarthropathy Study Group preliminary criteria for the classification of spondyloarthropathy. Arthritis Rheum 1991;34:1218-27.
4. Garrett S, Jenkinson T, Kennedy LG et al. A new approach to defining disease status in ankylosing spondylitis: the Bath Ankylosing Spondylitis Disease Activity Index. J Rheumatol 1994;21:2286-91.
5. Calin A, Garrett S, Whitelock H et al. A new approach to defining functional ability in ankylosing spondylitis: the development of the Bath Ankylosing Spondylitis Functional Index. J Rheumatol 1994;21:2281-5.
6. Mackay K, Mack C, Brophy S, Calin A. The Bath Ankylosing Spondylitis Radiology Index (BASRI): a new, validated approach to disease assessment. Arthritis Rheum 1998; 41:2263-2270.

Personal non-commercial use only. The Journal of Rheumatology Copyright © 2009. All rights reserved.

Downloaded on April 17, 2024 from www.jrheum.org