Distinguishing Inflammatory from Noninflammatory Arthritis, Enthesitis, and Dactylitis in Psoriatic Arthritis: A Report from the GRAPPA 2010 Annual Meeting

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ABSTRACT. The most widely applied criteria for classifying psoriatic arthritis (PsA) are the CASPAR (ClASsification of Psoriatic ARthritis) criteria. A patient who fulfills the CASPAR criteria must have evidence of inflammatory arthritis, enthesitis, or spondylitis, and may have an inflammatory musculoskeletal component, dactylitis. Although the criteria were developed by rheumatologists, not all patients with PsA are seen by rheumatologists. Thus, it is important for clinicians such as dermatologists, primary care providers, physiatrists, and orthopedists, and patients themselves, to be able to recognize the presence of inflammatory musculoskeletal disease and distinguish it from degenerative or traumatic musculoskeletal disease. At their 2010 annual meeting, members of the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) discussed the steps they are taking to define the key variables that must be present to distinguish inflammatory arthritis, enthesitis, and dactylitis from degenerative, traumatic, mechanical, or infectious forms of these conditions. (J Rheumatol 2012;39:415–7; doi:10.3899/jrheum.111237)

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The CASPAR (ClASsification of Psoriatic ARthritis) criteria (Table 1), the current most widely applied criteria for classifying psoriatic arthritis (PsA), require the patient to have evidence of inflammatory arthritis, enthesitis, or spondylitis before determining if enough additional elements are present to fulfill the criteria[1]. One of the additional elements is an inflammatory musculoskeletal component, dactylitis. The CASPAR criteria were developed by rheumatologists, who can understand and accurately distinguish between inflammatory and noninflammatory musculoskeletal disease through observation of patient history, physical examination, and laboratory and imaging characteristics. Complete confidence in the diagnosis would require biopsy of inflamed tissue, but this step is invasive and impractical in the clinic. However, not all patients with PsA are seen by rheumatologists. Thus, it is important for dermatologists, primary care providers, physiatrists, orthopedists, and the patients themselves to be able to recognize the presence of inflammatory musculoskeletal disease and distinguish it from degenerative or traumatic musculoskeletal disease. Such recognition would lead to referral to rheumatologists and to prompt institution of appropriate therapy to prevent longterm musculoskeletal damage and the morbidity and mortality from comorbidities associated with inadequately treated inflammatory disease.

Members of the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) recognize the need to define for nonrheumatologists the key signs and symptoms that distinguish inflammatory arthritis, enthesitis, and dactylitis from degenerative, traumatic, mechanical, or infectious forms of these conditions. This article explores the steps in the process of identifying inflammatory arthritis, enthesitis, and dactylitis. In a companion report in this issue Gladman explores the process in relation to inflammatory spine disease[2].

The first step in distinguishing inflammatory from noninflammatory musculoskeletal disease is to ascertain from expert clinicians and patients the key identifiers of a clinical condition. Symptoms of inflammatory arthritis, particularly rheumatoid arthritis (RA), may include joint swelling, metacarpophalangeal involvement, bilaterally symmetric joint involvement, prolonged morning stiffness, elevated C-reactive protein (CRP), and periarticular osteopenia on radiograph. By contrast, features of osteoarthritis (OA) could include bony crepitus, distal interphalangeal (DIP) joint involvement, minimal morning stiffness, normal acute-phase reactants, and periarticular osteophytes. PsA, another inflammatory arthritis, represents a conundrum because DIP involvement is also common, and thus it overlaps with OA in this aspect of joint distribution. Patient history and physical

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Table 1. Diagnostic criteria for psoriatic arthritis (CASPAR)*.

Established inflammatory musculoskeletal disease (joint, spine, or entheseal), with 3 or more of the following:	
1. Psoriasis	
(a) Current†	Psoriatic skin or scalp disease present today as judged by a qualified health professional
(b) History	A history of psoriasis that may be obtained from patient or qualified health professional
(c) Family history	A history of psoriasis in a first- or second-degree relative according to patient report
2. Nail changes	Typical psoriatic nail dystrophy including onycholysis, pitting, and hyperkeratosis observed on current physical examination
3. A negative test for rheumatoid factor	By any method except latex but preferably by ELISA or nephelometry, according to the local laboratory reference range
4. Dactylitis	
(a) Current	Swelling of an entire digit
(b) History	A history of dactylitis recorded by a qualified health professional
5. Radiological evidence of juxtaarticular new bone formation	Ill-defined ossification near joint margins (but excluding osteophyte formation) on plain radiographs of hand and foot

* Specificity 98.7% and sensitivity 91.4%. † Current psoriasis assigned a score of 2; all other features are assigned a score of 1. CASPAR: CIASsification of Psoriatic Arthritis; ELISA: enzyme-linked immunosorbent assay.

examination results are practical and feasible for initial screening purposes; laboratory and imaging results will increase specificity. A method of harmonizing these inputs is necessary because patients and clinicians may identify clinical features in different ways and with different weighting of importance.

The next step in the process is to study a group of patients with inflammatory musculoskeletal disease compared with control groups of patients with other diseases (e.g., OA, traumatic or degenerative tendonitis), apply the list of features to them, and identify which features are most discriminative and practical to use in a simple screening algorithm. Validation steps can then be performed in larger sets of prospectively evaluated patients in clinics where patients with inflammatory arthritis are seen.

A good example of this type of exercise was conducted by the Assessments in SpondyloArthritis (ASAS) international society to determine a practical definition of inflammatory back pain (IBP)[3]. Utilizing a list of features deemed characteristic of IBP, 13 expert clinicians examined 20 patients with chronic back pain and suspected axial spondyloarthritis (SpA). Of this list, the highest sensitivity and specificity for the presence of IBP was met in the presence of 4 out of 5 variables: (1) age at onset < 40 years, (2) insidious onset, (3) improvement with exercise, (4) no improvement with rest, and (5) pain at night (with improvement upon getting up; sensitivity 77.0%, specificity 91.7%). A validation step was also conducted, in which this definition of IBP was employed in a study of 686 patients with chronic low back pain who were evaluated in an ASAS multicenter exercise to establish criteria for axial SpA. In this study, presence of 4 out of 5 variables yielded a sensitivity of 79.6% and specificity of 72.4%[3].

Inflammatory Arthritis

Of the variables that could be considered for the definition of inflammatory synovitis, some features can distinguish the overall set of inflammatory arthritides from noninflammatory ones, and others can help distinguish between the inflammatory arthritides, e.g., RA versus PsA. Features that are common to all inflammatory arthritides, including RA, PsA, and SpA when inflammation involves the synovial joint, include the presence of joint-line tenderness, swelling, and potential elevation of inflammation markers such as erythrocyte sedimentation rate and CRP. Laboratory biomarkers may be present for specific diseases, such as rheumatoid factor and cyclic citrullinated peptide antibody in RA and the genetic marker HLA-B27 in SpA. RA may be polyarticular and symmetric in distribution, whereas PsA is often asymmetric and may be polyarticular, oligoarticular (< 5 involved joints), or even monoarticular. In axial SpA, peripheral synovitis is not as common. In RA, involvement of DIP joints is uncommon, whereas in PsA and OA it is very common, often with associated psoriatic nail disease in PsA. In RA and PsA, involvement of the metacarpophalangeal, proximal interphalangeal (PIP), wrist, elbow, shoulder, sternoclavicular, hip, knee, ankle, and metatarsophalangeal joints is common, whereas in OA, involvement of the DIP, PIP, carpometacarpal, hip, knee, and first metatarsophalangeal joints is common. Stiffness is a classic feature of inflammatory arthritis, often lasting hours in the morning or after prolonged periods of stillness, whereas stiffness tends to be minimal with OA. Crystalline arthritis typically presents in a monoarticular or oligoarticular manner, not unlike PsA; but unlike PsA, it is typically more intense and transient.

When history and physical or laboratory variables cannot adequately distinguish an inflammatory arthritis, imaging can aid the delineation. Plain radiography can detect characteristic features of RA, PsA, and OA when damage has occurred, such as joint space narrowing, erosions, or periarticular spurs, but is not sensitive to identifying inflammation prior to the occurrence of damage. Ultrasound, with gray mode and especially with the use of power Doppler, can sensitively assess for the presence of inflammatory synovitis. Ultrasound is increasingly being used in rheumatology clinics because it is an excellent

portable screening tool that can assess multiple joints at one sitting and is less expensive than magnetic resonance imaging (MRI). Its use is dependent on the skill and experience of the operator, requiring significant training. MRI is a highly sensitive tool to assess inflammation, but is somewhat limited in utility because of its expense and lack of availability.

Inflammatory Enthesitis

A unique feature of PsA and other spondyloarthritides is enthesitis, defined as inflammation at the attachment of tendons, ligaments, fascia, and joint capsule fibers into bone[4]. Clinically, enthesitis is reported to occur in 35%–50% of patients with PsA; however, the true prevalence of the condition may be underestimated, and a larger number of enthesial sites should be assessed, preferably using advanced imaging techniques such as ultrasound[5,6]. Common sites of enthesitis in PsA include the attachment of the plantar fascia and Achilles tendon, patellar tendons, as well as ligament insertion sites around the pelvis, ribs, and elbow. A good deal of enthesitis burden can occur in the spine at ligament insertion sites on the vertebra, as addressed by Gladman[2]. Patients may experience pain at enthesial sites, e.g., unusually persistent pain at the Achilles tendon insertion, often without a clear traumatic onset, but typically attributed to overuse. Often, the patient cannot distinguish the difference, e.g., patellar tendon pain from knee joint pain. Diffuse chest pain may not be recognized as inflammation arising from ligament insertion at the costochondral joints or ribs. The patient also may not recognize the presence of enthesitis until palpation elicits tenderness. Features that may indicate inflammatory enthesitis include lack of clear traumatic etiology, unusual persistence of pain, chronic enthesial site pain in the context of other features of SpA, and lack of response to measures such as physical therapy. Some features have not been studied, e.g., whether inflammatory enthesial pain more typically improves with nonsteroidal antiinflammatory therapy.

Dactylitis

Dactylitis is swelling with tenderness of a whole finger or toe, representing a combination of tenosynovitis, enthesitis, and synovitis of the whole digit. It is commonly seen in the spondyloarthritides, especially PsA, where it occurs in 30%–50% of patients[7]. Dactylitis can also be caused by a number of other diseases[8], such as infections (e.g., tuberculous, syphilitic) and other inflammatory diseases (e.g., sarcoid, gout). Dactylitis is one of the secondary elements that constitute the CASPAR criteria for PsA[9], and appears to be reliably assessed by rheumatologists but not by dermatologists[8]. Key variables that help distinguish dactylitis upon clinical examination include swelling of the whole digit that is discernibly different than adjacent digits (where asymmetry from the contralateral digit can be helpful), and tenderness along the shaft of the digit, between joints.

Next Steps Toward Defining Inflammatory Arthritis, Enthesitis, and Dactylitis

Several approaches may be undertaken to define, in an evidence-based manner, the key variables that must be present to distinguish inflammatory arthritis, enthesitis, and dactylitis from degenerative, traumatic, mechanical, or infectious forms of these conditions. At the 2010 annual meeting, GRAPPA members proposed sponsoring the following projects:

1. Convene a panel of experts to discuss and catalogue key variables that constitute these conditions
2. Conduct focus groups of patients to catalogue key variables from the patients' perspective
3. Conduct expert clinician and patient Delphi exercises to prioritize key variables, to reduce the variables to an acceptable number for further testing[9,10]
4. Apply top variables in an exercise similar to that conducted by the ASAS group described above[3], in which expert clinicians perform history and physical examination on patients to determine what combination of variables yield the most sensitive and specific set of variables
5. Validate this set in a larger trial of patients and control subjects.

It is hoped that development of simple and practical definitions for inflammatory arthritis, enthesitis, and dactylitis, as well as inflammatory spine disease, will help clinicians, especially nonrheumatologists, more accurately identify the presence of PsA and facilitate application of the CASPAR criteria.

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