New Insights in Occult Psoriatic Arthritis

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ABSTRACT. Since the 1970s, asymptomatic involvement of several musculoskeletal structures was described in patients with psoriatic arthritis (PsA). We recently designated this clinical condition as occult PsA. This concept addresses an “underground” inflammatory process that can eventually cause structural damage. The percentage of PsA cases occurring in an occult manner remains to be determined but it does not seem small. From a teaching perspective, we suggest differentiating occult PsA into 3 subsets: real occult PsA, characterized by a continuous asymptomatic course; temporary occult PsA, in which the clinical course remains asymptomatic for a period; and limited occult PsA, which occurs asymptomatically in some areas of the body but is clinically evident in others. Some serum biomarkers could identify patients to be studied with imaging techniques to discover real occult PsA. Since an asymptomatic course was also reported for other spondyloarthropathies, the concept of occult arthritis could be expanded to the whole field of such conditions. (J Rheumatol Suppl. 2012 Jun;89:22–23; doi:10.3899/jrheum.120236)

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We have outlined in a recent editorial that psoriatic arthritis (PsA) can occur in an asymptomatic manner in the spine, the sacroiliac joints, the peripheral joints and entheses, and the tenosynovial sheaths. We suggested the designation of occult PsA for this clinical condition1. In that editorial we reviewed all studies on patients having occult PsA who were identified by means of different imaging techniques including radiography, ultrasound (US), magnetic resonance imaging (MRI), and scintigraphy. The concept of occult PsA represents an expansion in the definition of arthritis, which is usually based on the presence of pain and joint swelling. In addition, this concept focuses the attention of rheumatologists on an “underground” inflammatory process that can eventually lead to structural damage. At present, the evolution of occult PsA without symptoms and detectable signs has no certain explanation, but it is probable that the inflammation level is below the symptomatic threshold. The percentage of PsA cases occurring in an occult manner remains to be determined but it does not seem small by the analysis of the reviewed literature1. In addition, an unknown percentage of patients with occult PsA showing lesions on US, MRI, and scintigraphy will never develop structural bone damage on radiographs.

For educational purposes, occult PsA can be differentiated into 3 subsets: (1) real occult PsA characterized by a continuous asymptomatic course; (2) temporary occult PsA in which the clinical course remains asymptomatic for a period; and (3) limited occult PsA that occurs asymptomatically in some parts of the body but is clinically evident in others. Real occult PsA. Patients with real occult PsA are always asymptomatic. Cases are identified by chance on musculoskeletal imaging examinations performed for other reasons. The early phases of real occult PsA can be disclosed only by MRI, US (restricted to the peripheral manifestations), and scintigraphy (limited by a low specificity). In the late phases, radiographs can detect the erosive damage and the new bone formation typical of PsA. Interestingly, in some patients severe structural damage can also develop without symptoms in both peripheral joints (i.e., finger shortening) and axial skeleton (i.e., spinal stiffness)2.

Today, the routine examination of subclinical lesions is not possible in every patient with psoriasis because of the huge target population, and therefore should be restricted to research settings. Recent studies suggest the possible usefulness of serum biomarkers to distinguish patients with psoriasis who also have arthritis from those who do not. In the study by Alenius, et al, serum interleukin 6 (IL-6) levels were significantly higher in subjects with psoriasis and inflammatory joint disease compared with those having skin lesions alone3. A Canadian study found that increased levels of highly sensitive C-reactive protein, osteoprotegerin, matrix metalloprotease 3, and C-propeptide of type II collagen/collagen fragment neoepitopes Col2-3/4 long mono are biomarkers of PsA in patients with psoriasis4. In the study by Dalbeth, et al, patients with PsA had higher circulating
concentrations of Dickkopf-1 and macrophage-colony stimulating factor compared with those with psoriasis and healthy controls. Bowes, *et al* recently genotyped 2 single-nucleotide polymorphisms (SNP), rs20541 and rs1800925, mapping to the IL-13 gene in 1057 patients with PsA and 778 patients with type I psoriasis vulgaris. Genotype frequencies were compared to those of 5575 healthy controls. Both SNP were found to be highly associated with susceptibility to PsA but neither SNP was significantly associated with susceptibility to psoriasis vulgaris.

These biomarkers and other future ones could identify patients to be studied with imaging techniques to discover real occult PsA. However, currently it is not certain that serum biomarkers could also be useful in identifying the occult forms of PsA because the inflammatory process might be different from that of symptomatic PsA.

**Temporary occult PsA.** Temporary occult PsA can be identified when the preclinical course of the disease is sufficiently long to give erosive changes or new bone formation. In this case, the discrepancy between the short duration of symptoms and the presence of radiographic findings due to longstanding disease allows us to make a diagnosis of temporary occult PsA.

**Limited occult PsA.** In limited occult PsA, musculoskeletal involvement is more extensive than clinically detectable involvement. MRI and US are useful tools to assess all the inflamed sites of limited occult PsA. The number of involved joints is one of the measures used to define the extent of PsA, with the aim of planning an adequate therapeutic program. In the presence of limited occult PsA, this number is underestimated. Swollen joint count is one of the 2 useful measures recently identified as predictors of response to anti-tumor necrosis factor agents in PsA. Therefore, future studies should investigate whether the number of inflamed sites detected by imaging techniques can have a similar role.

**OCCULT ARTHRITIS: AN EXPANDING CONCEPT?**

Although most of the studies concerning occult involvement are about PsA, several studies describing other asymptomatic spondyloarthopathies (SpA) have been published. In 1978, Hochberg, *et al* described 5 cases of ankylosing spondylitis (AS) with painless axial disease in a group of 45 patients. In 1996, the Bath group outlined the asymptomatic occurrence of spondylodiscitis in patients with AS. In 2005, Erdem, *et al* studied foot involvement by MRI in 23 patients with AS. They found MRI abnormalities in 21 subjects (91%), while pain and swelling were present in only 3 (13%).

In 1978 a Dutch group reported sacroiliac without clinical features in 2% and 18% of their patients with IBD, respectively.

In a recent study, enthesal involvement was evaluated by US in 60 patients with SpA (18 AS, 18 PsA, 15 undifferentiated SpA, 8 reactive arthritis, 1 IBD-associated SpA). The clinical examination of 600 entheses revealed enthesitis in 56 (9.3%) sites, while US detected 331 active sites out of the 544 asymptomatic ones (60.8%).

The concept of occult arthritis could be expanded to the whole field of the SpA.

**REFERENCES**