Enthesitis and Synovitis on Magnetic Resonance Imaging are Frequently Found in Psoriatic Patients without Arthritic Symptoms: Clinical Considerations of this Finding

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Abstract

Patients with skin psoriasis often perceive complaints such as fatigue and vague aches and pains in the joints, often diagnosed as fibromyalgia or psychogenic. We showed in psoriasis patients, without complaints or signs of arthritis on knee magnetic resonance imaging, evidence of subclinical inflammation at the attachments of tendons (enthesitis) and of the joints. These findings indicate that enthesitis may be an early sign (perhaps the earliest) of subclinical psoriatic arthritis and may, for example, explain a lot of problems these psoriatic patients perceive. We discussed our findings in the light of recent literature regarding enthesitis as an early sign in spondyloarthropathies like psoriatic arthritis and also in early osteoarthritis and the possible clinical implications. Our findings may change the paradigm regarding arthritis complicating this skin disease and lead to a different treatment approach of these patients.

Keywords: Knees magnetic resonance imaging clinical considerations, psoriasis, subclinical enthesitis and synovitis

Introduction

Patients with psoriasis often have problems such as fatigue, vague aches and pains in the joints, which may be diagnosed as fibromyalgia or psychogenic. These complaints often were thought to be psychogenic. We proved that the causes of these problems are probably due to subclinical inflammation around the attachments of tendons and also of the joints themselves. I first review the studies we performed to arrive at this finding.

How to Diagnose Patients with Early Arthritis?

For a clinician, it is often difficult to make a correct diagnosis in a patient with arthritis, especially in the beginning of the disease, when often only a few joints are swollen and painful.

We studied magnetic resonance imaging (MRI) imaging of the knee joint among patients with arthritis of unknown cause or diagnosis.[1] We compared enhanced MRI findings of the knee joints in three groups of patients: undifferentiated arthritis (UA) \( n = 25 \), established rheumatoid arthritis (RA) \( n = 15 \) and spondyloarthropathies (SpA) \( n = 15 \). We found that enthesitis was a common finding on MRI in the SpA group, but was totally absent in the group of patients with RA and was observed in three patients in the UA group. We concluded that enthesitis as found on MRI could help to classify patients presenting with UA of the knee joint.[1] These data suggested that MRI can separate subsets of early synovitis patients on the basis of two principal imaging patterns: one in which the inflammatory changes are located primarily in the synovium and another in which the periarticular entheses are inflamed in association with intense oedema of the adjacent bone.

These two patterns are proposed to broadly classify patients with early synovitis into an ‘RA’ phenotype where synovitis is the primary process and a ‘spondyloarthropathy’ phenotype where enthesitis is the primary process and synovitis occurs on a secondary basis.[2] Hence, we confirmed that showing inflammation at the so-called ‘entheses’ may help to make...
We found enthesitis in the knees of 56 patients.

To avoid misinterpretation due to the ‘magic angle’ effect, we relied on long TE pulse sequence for the assessment of tendon or ligament fibres. In case of disagreement, the findings were discussed according to the previous standards until agreement was reached. Among 48 patients (96 knees), a total of 90 entheseal lesions were detected, with no enthesitis in only 2 cases (6.3%). Signs of continuing inflammation bilaterally were frequently found: STE (n = 52), BME (n = 20), perientheseal BME (n = 3), cartilaginous erosions (n = 42) and bone erosions (n = 27).

In controls, two (10%) patients had BME and another five (25%) showed cartilaginous erosions, and none showed evidence of enthesitis. Significant correlations were observed between the number of entheseal lesions of both knees versus STE (present vs. absent; r = 0.314, P = 0.030) and STE (number of lesions; r = 0.351, P = 0.014). Enthesitis (unilateral vs. bilateral) was significantly and positively correlated with STE (r = 0.304, P = 0.036), cartilaginous erosions (r = 0.304, P = 0.036) and villous projections (r = 0.347, P = 0.016).

On MRI, the knee joints of patients with skin psoriasis without clinical arthritis showed evidence of subclinical synovitis and enthesitis. Enthesitis was positively and significantly correlated with other important MRI signs, such as villous projections, STE and cartilaginous erosions that were indicative of continuing of a silent subclinical synovitis. These findings indicate that enthesitis may be an early sign (perhaps the earliest) of subclinical PsA.

Enthesial abnormalities were also found by ultrasonography (US) in clinically asymptomatic patients with psoriasis. In 162 patients with plaque psoriasis without musculoskeletal disease, Naredo et al. reported that patients with psoriasis had a significant prevalence of asymptomatic US synovitis and entheseopathy, which may indicate a subclinical musculoskeletal involvement. In addition, 49 (36%) patients

**Spondyloarthropathies and Enthesitis**

SpAs are a group of disorders affecting the back and joints often in young men and women. One of the typical symptoms is the so-called ‘enthesis’, this is the term used to describe inflammation at insertions (attachment at the bone) of tendons, ligaments or joint capsules. The term is included in the European Spondyloarthritis Study Group criteria for the classification of spondyloarthropathy.

The evaluation of entheseal-related changes at different joints by MRI became an important topic on the research agenda in patients with arthritis in whom the diagnosis was not sure yet. It appears that patients with early arthritis and such enthesitis on MRI could be differentiated from those without, making early diagnosis and appropriate treatment possible. One of the SpAs can be seen in patients with psoriasis, a skin disease of unknown cause that affects millions of people worldwide. McGonagle et al. described the characteristic MRI entheseal changes involving the knee joints in a cohort of ten patients with SpA (three of whom had psoriatic arthritis [PsA] with knee swelling of recent onset). They proposed that enthesitis may be the primary lesion in PsA and SpA.

Our group investigated enthesitis and enthesis-related changes shown on knee MRI among patients with several forms of SpA. We found enthesitis in the knees of 56 patients including 30 with PsA, five with ankylosing spondylitis, five with reactive arthritis, five with ulcerative colitis and five with Crohn’s disease.

An interesting finding was the presence of enthesitis of the knee joint among six patients with psoriasis without clinical synovitis, who were not receiving any disease-modifying anti-rheumatic drugs. In the psoriasis group (n = 6), one had bone marrow oedema (BME), enthesitis was detected in five patients at the patellar tendon insertion and in one case, in the medial patellofemoral ligament.

**Enthesitis and Synovitis in Psoriasis without Clinical Arthritis**

If enthesitis is the primary event and synovitis follows the presence of enthesitis, among patients with psoriasis with no evidence of clinical arthritis, this could be a predictor of PsA. With that in mind, we decided to look for enthesitis and entheseal-related changes in the knees among patients with only psoriasis without clinical evidence of peripheral or axial joint involvement and to analyse a possible relation between enthesitis and other variables (such as demographic data, disease characteristics, severity and extension of psoriatic lesions) with other MRI signs suggestive of continuing inflammation in the knee joints, such as soft-tissue oedema (STE), BME, perientheseal BME and cartilaginous and bone erosions.

In a case-controlled study, we evaluated enhanced MRI findings of knee joints in patients with psoriasis without clinically evident peripheral or axial joint involvement and correlated the MRI findings with skin disease indices and demographic variables. We evaluated a total of 48 psoriatic patients (96 knees) without clinical evidence of synovitis or enthesitis in any peripheral or axial joints. A random sample of twenty healthy controls without knee or other joint complaints and matched for age and sex served as controls. All patients and controls underwent enhanced MRI studies of both knee joints, and the MRI findings were compared. To avoid overreading or misinterpretation, potential entheseal sites were evaluated by T2-fat saturation and short-tau inversion recovery sequences for the assessment of the tendon fibres, together with proton-density fat saturation for the assessment of perientheseal STE and perientheseal BME with evident high signal intensity in case of enthesitis.

To avoid misinterpretation due to the ‘magic angle’ effect, we relied on long TE pulse sequence for the assessment of tendon or ligament fibres. In case of disagreement, the findings were discussed according to the previous standards until agreement was reached. Among 48 patients (96 knees), a total of 90 entheseal lesions were detected, with no enthesitis in only 2 cases (6.3%). Signs of continuing inflammation bilaterally were frequently found: STE (n = 52), BME (n = 20), perientheseal BME (n = 3), cartilaginous erosions (n = 42) and bone erosions (n = 27). In controls, two (10%) patients had BME and another five (25%) showed cartilaginous erosions, and none showed evidence of enthesitis. Significant correlations were observed between the number of entheseal lesions of both knees versus STE (present vs. absent; r = 0.314, P = 0.030) and STE (number of lesions; r = 0.351, P = 0.014). Enthesitis (unilateral vs. bilateral) was significantly and positively correlated with STE (r = 0.304, P = 0.036), cartilaginous erosions (r = 0.304, P = 0.036) and villous projections (r = 0.347, P = 0.016).

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showed both synovitis and enthesopathy. As in our study, Naredo et al. observed using US, no significant differences between psoriatic patients with and those without joint synovitis in terms of demographic data and Psoriasis Area and Severity Index (PASI) scores.[7]

In our study, a total of 90 enthesal lesions had been identified by MRI in both right and left knees and in only three cases (6.3%), enthesitis was absent. This much higher percentage of enthesal lesions in our study may be explained by the sensitivity of MRI compared to US. Further, an important sign on MRI is BME, which can only be detected by MRI and not by US. In our study, 20 cases showed evidence of BME signs in both knees.

Other imaging studies have confirmed that enthesopathy is common in psoriatic patients without clinical arthritis.[8-10] It remains difficult to prove that enthesitis in human PsA is the primary lesion in all cases, although animal models with features of PsA or SpA can clearly be shown to start at the enthesis.[11]

**ENTHESIS IN OSTEOARTHRITIS AND PSORIATIC ARTHRITIS: NEW INSIGHTS**

Recently, it has been recognised that osteoarthritis (OA) is an inflammatory disease, with mostly the interaction between the synovium and articular cartilage being the driving process.[12,13] Patients with the so-called ‘inflammatory’ OA often have joint swelling and tend to be erosive on X-rays.[14] They also can have protracted morning stiffness, which can be reminiscent of inflammatory arthritis.[14]

Inflamed entheses are seen in most PsA joints as well as diffuse bone oedema on MRI; in advanced OA joints, typical degenerative entheses will be found often with osteophytes and cartilage loss and narrowed joint space. However, there is a subset of joints where there are overlapping features that can cause a diagnostic challenge, often with some degree of inflammation or degenerative changes that can be accepted as either OA or PsA.[11] Therefore, it is possible that some failures of anti-tumour necrosis factor therapy in PsA patients may be explained, at least in part, by the inability of clinicians to differentiate OA from PsA. This may also explain the findings of recent studies showing the inefficacy of methotrexate (MTX) in well-established PsA,[15] while other studies in patients with early PsA who had higher C-reactive protein showed good efficacy.[11,16]

We have to be aware of overlap of OA and PsA when advising biologics or MTX therapy in order to prevent apparent biologic therapy failure. While it may be easy to differentiate degeneration from inflammation at the two extremes, there may be a group of patients where differentiation is difficult or impossible.[11,16] These problems are especially relevant in patients with long-standing disease and less so in the early phase of the disease or in psoriatic patients who do not yet have clinical signs of arthritis as was the case in our study.

**CLINICAL CONSIDERATIONS OF THESE FINDINGS**

To the best of our knowledge, our articles[5,6] were the first to describe subclinical synovitis and enthesitis at different sites among patients with skin psoriasis without clinical evidence of arthritis, using MRI in the knee joints. These findings indicate that enthesitis may be an early sign (perhaps the earliest) of subclinical PsA. These novel findings may play important roles for early therapeutic decisions and open a new window of opportunities in this domain. This finding can for example explain a lot of problems these psoriatic patients perceive such as fatigue and vague aches and pains in the joints often diagnosed as psychogenic or as fibromyalgia. Our findings may change the paradigm regarding arthritis complicating this skin disease and lead to a different treatment approach of these patients. In the long run, these findings may positively affect the lives of millions of psoriasis patients globally.

**Acknowledgements**

We thank the patients and healthy controls for their willingness to participate in the study and the colleagues of the departments of rheumatology and rehabilitation, radiology, orthopaedics and dermatology of the Faculties of Medicine of Cairo and Al-Azhar Universities, Egypt, and of the Dr. Erfan and Bagedo General Hospital in Jeddah, Saudi Arabia, for their cooperation.

**Financial support and sponsorship**

Nil.

**Conflicts of interest**

There are no conflicts of interest.

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Psoriasis subclinical enthesitis and synovitis on MRI


