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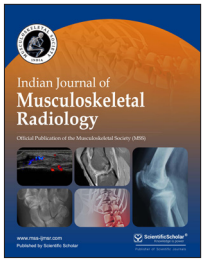

Pictorial Review

Peripheral Seronegative Spondyloarthritis – Updates on Critical Criteria

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ABSTRACT

In the past decade, new clinical and imaging criteria have vastly improved the diagnosis and outcome of patients with seronegative spondyloarthritis (SpA). It is estimated that up to 30% of patients with SpA may exhibit predominant (or only) peripheral manifestations of SpA. Lack of awareness can lead to a diagnostic delay of up to 8–9 years which can lead to significant patient morbidity. It is, therefore, essential to diagnose and treat SpA as early as possible. The aim of this pictorial review is to emphasize the important aspects of current peripheral SpA classification system and demonstrates the imaging findings related to peripheral SpA. Patients referred for imaging of peripheral joints can be from a wide referral source. Recognizing and reporting imaging features suggestive of peripheral SpA will allow appropriate and timely specialist referral with the aim of avoiding treatment delay.

Keywords: Seronegative, Peripheral spondyloarthritis, Non-axial, Criteria, Enthesitis

INTRODUCTION

In the past decade, new clinical and imaging criteria have vastly improved the diagnosis and outcome of patients with seronegative spondyloarthritis (SpA). Both axial and peripheral SpA have an approximate global prevalence of 1%. It is estimated that up to 30% of patients with SpA may exhibit predominant (or only) peripheral manifestations of SpA. Furthermore, in several documented cases, a diagnostic delay of up to 8–9 years has occurred and it is, therefore, essential to diagnose and treat SpA as early as possible.[1] SpA affects both males and females equally and usually within their second decade of life. In those diagnosed with SpA, there is a strong association with human leukocyte antigen-B27, which can be present in more than 90% of patients.[2] The clinical manifestation of peripheral SpA includes most of the features common to the other forms of SpA. Patients are often referred for isolated large joint imaging by various specialties such as orthopedics who may be unaware of symptoms and criteria related to SpA, as they may be focused on orthopedic specific pathology [Figure 1]. Thus, it is important that the radiologist raises the suspicion of SpA and specialist review in these cases to avoid potential delay in diagnosis and early intervention.[3] Enthesitis on its own does not equate to SpA as enthesitis can be inflammatory, mechanical, or metabolic in nature. SpA can only be diagnosed in the appropriate clinical context which is why it is important to suggest specialist review in radiology report. The most commonly affected entheseal sites in SpA are shown in [Figure 2].

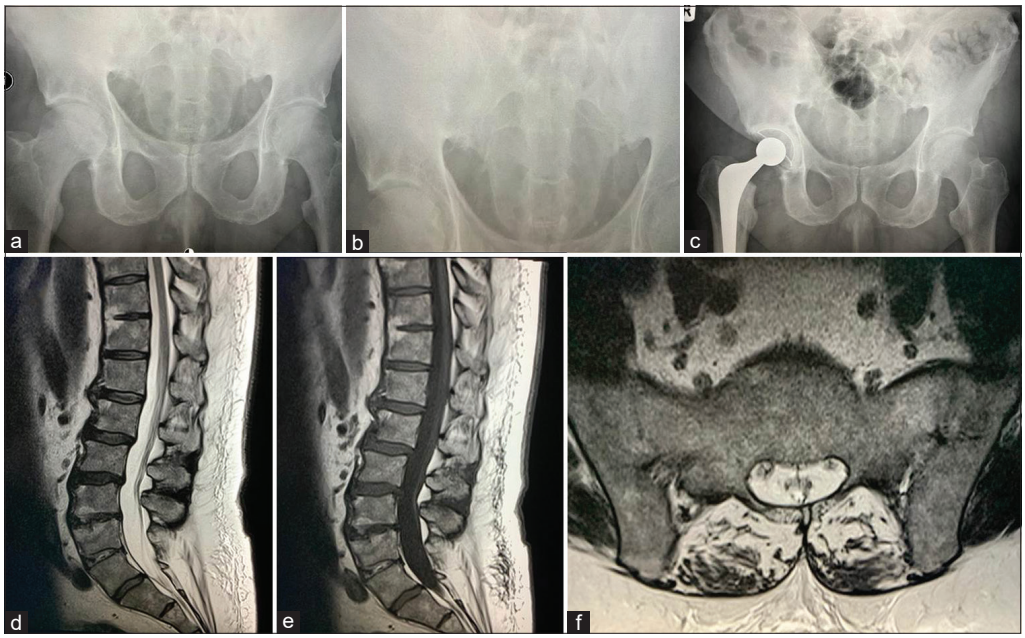

Figure 1: Patient presented with persistent right hip pain to the hip surgeon. An initial plain radiograph (a) was performed for the right hip pain which showed no significant degenerative change. The patient represented to orthopedics 1 year later with persistent pain and a subsequent pelvic radiograph (b) again demonstrated no degenerative change in the right hip. A right hip replacement was subsequently performed, though indications were not clear (c). Note that on all three radiographs, (a-c) bilateral sacroiliac joint (SIJ) sclerosis is present but was not reported, and therefore, patient was not referred for a rheumatological opinion. (d,e) The patient's hip pain continued post-hip replacement and (f) subsequent referral to spine surgeons was made for sciatica. Imaging of the spine with the last magnetic resonance imaging slice through the SIJs demonstrates ankylosis of the SIJ, corner fat lesions, and syndesmophtyes in the spine.

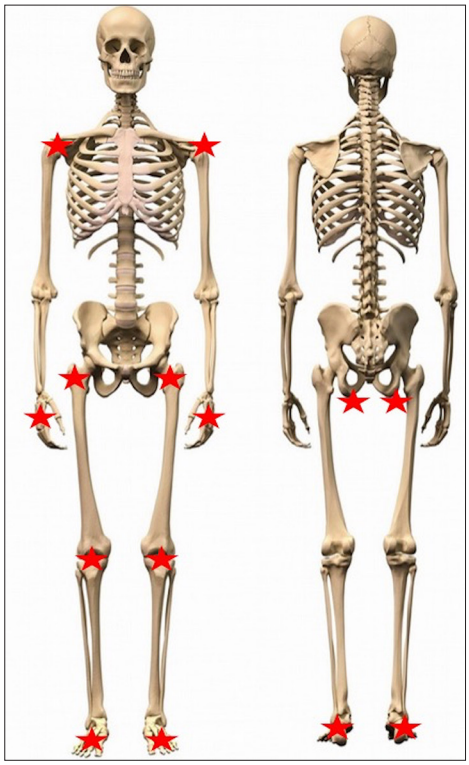

Figure 2: Pictorial representation of the most common entheseal sites affected in the appendicular skeleton shown by the red stars.

DISCUSSION

Pathophysiology

The characteristic of peripheral SpA is inflammation of the enthesis (a thin fibrous or fibrocartilaginous region joining the tendon or ligament to bone).[4,5] SpA is associated not only with synovitis but also with spondylitis (spinal inflammation), dactylitis (sausage digit), and enthesitis (inflammation of the ligament, tendon, or capsule-bone insertion). Synovitis is characterized by inflammation of the synovial membrane which differs from enthesitis, where only specific inflammation of the fibrocartilage entheseal complex occurs. The distribution of enthesitis is usually periarticular but can also occur at sites distant from the joints. Entheseal inflammation is triggered by an innate immune response. Immune cell migration and deposition of inflammatory infiltrate at the entheses usually facilitate vasodilatation and hyperemia, which are the earliest signs revealed on magnetic resonance imaging (MRI) and ultrasound (US). Bone marrow edema at the enthesis is also seen. In the late stage, the proposed inflammatory pathophysiology involves a local release of pro-inflammatory cytokines and growth factors from the enthesis causing a secondary synovitis. Chronic synovitis in SpA results in both bone and cartilage erosion analogous to rheumatoid arthritis. A well-described enthesis

is the Achilles tendon and it can commonly be involved in SpA [Figure 3]. Microanatomical changes occurring at entheseal fibrocartilage are linked to specific imaging findings as follows: (1) Bone marrow inflammation – periarticular osteopenia, (2) enlarged transcortical vessels – cortical bone irregularities and erosions at insertion sites, and (3) osteoblast differentiation and mesenchymal proliferation – calcification and new bone formation.[4,5] The lower extremity entheses are more often involved in SpA compared to those of the upper extremities.[6,7] Heel enthesitis is the most common followed by enthesitis of the patella and the tibial tubercle.

The essentials of peripheral SpA classification

Broad division of SpA is based on the involvement of the spine and axial skeleton and split, respectively, into axial SpA and peripheral/non-axial SpA. The Assessment of SpA International Society (ASAS) has developed the classification criteria for SpA, with emphasis on the role of presenting symptoms and imaging findings. The classification of peripheral SpA requires two steps in the algorithm to make the diagnosis [Figure 4].[8]

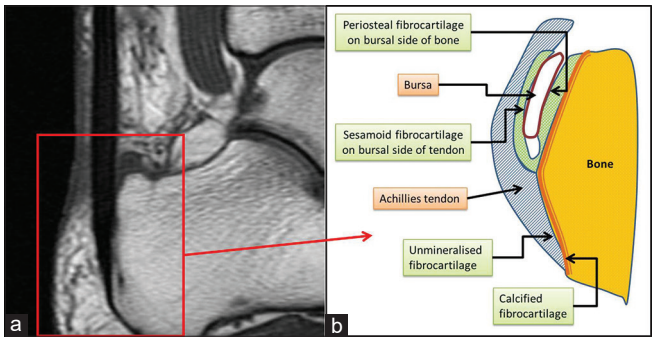

Figure 3: Demonstration of the different entheseal fibrocartilage at the Achilles tendon. (a) T1-weighted sagittal image of the attachment of the Achilles tendon on the calcaneum. (b) Diagrammatic representation of different fibrocartilage at the insertion of the Achilles tendon. Entheseal fibrocartilage is not only noted at the tendon-bone junction but also at the sesamoid and periosteal fibrocartilage (which form the boundaries of the bursa). All these areas are prone to entheseal inflammation.

Until recently, imaging diagnosis relied on conventional radiography. Radiographic changes of sacroiliitis in SpA usually develop at least 5 years after symptom onset, with poor interobserver reliability, which lead to delayed diagnosis and treatment. MRI is now part of the ASAS classification criteria, in early detection, disease monitoring, and the diagnosis of complications of peripheral SpA manifestations. The assessment criteria, role of imaging, and findings in the sacroiliac joint in seronegative arthritis are well established, whereas non-axial findings on MRI are still being recognized. The understanding of the appropriate terminology applied in the rheumatological classification systems in combination with the divisions of SpA allows a clinical centered reporting strategy for the radiologist.[9,10] This will allow radiologists to suggest appropriate referral to a specialist and considers further imaging of the axial skeleton with appropriate clinical and immunological assessments to expedite diagnosis.

Imaging findings

Both US and MR imaging are highly specific in detecting inflammatory and chronic enthesis-centered abnormalities.[11] Clinically, enthesitis is often underdiagnosed due to low sensitivity and specificity of clinical tests. Therefore, imaging plays a key role. US features of enthesitis can show decreased echogenicity with thickening, calcification, and increased Doppler vascularity [Figure 5a,b]. Osseous surface irregularity may represent erosions or enthesophytes which may also clinch the diagnosis. Power Doppler imaging can often demonstrate increased signal suggesting synovial and fat pad inflammation.

MRI is sensitive in detecting enthesitis and can evaluate both soft tissue changes and intraosseous abnormalities of

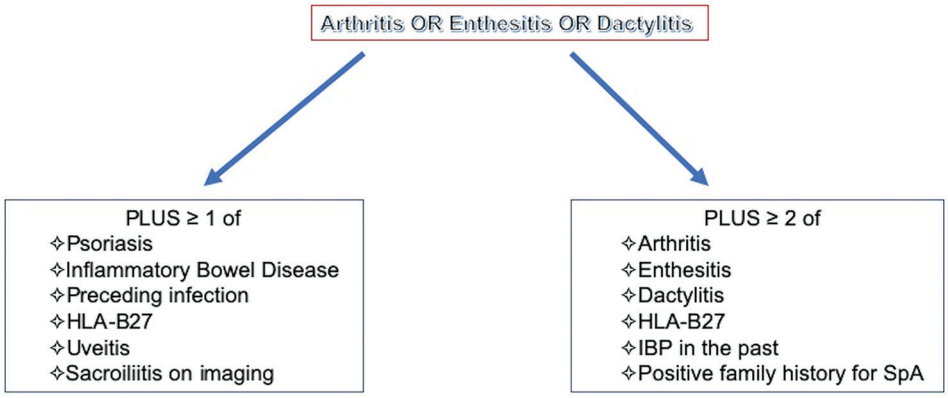

Figure 4: The Assessment of Spondyloarthritis (SpA) International Society two-step algorithm for the diagnosis of peripheral SpA.

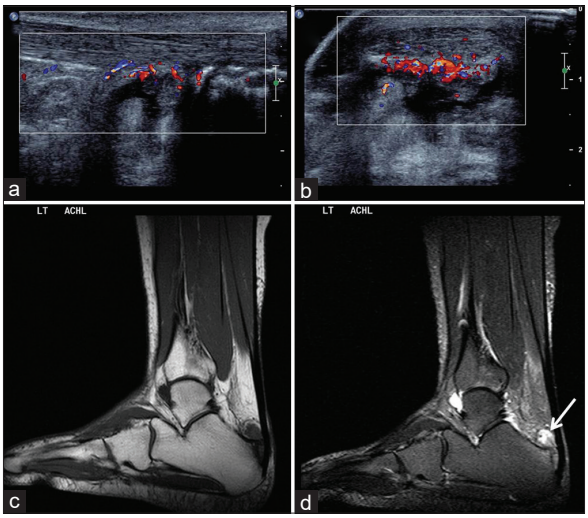

Figure 5: Magnetic resonance imaging (MRI) and ultrasound (US) findings of Achilles enthesopathy in a patient confirmed to have axial spondyloarthritis. Longitudinal (a) and transverse (b) US section through the Achilles tendon demonstrating abnormal vascularization of the cortical bone insertion on power Doppler imaging. The corresponding MRI [T1W sagittal (c) and short tau inversion recovery (d) sequences] demonstrates fluid in the bursa (white arrow) and surrounding edema and inflammation. Note the inflammation in the different fibrocartilage areas as previously discussed in Figure 1. Cortical irregularity, erosions, and bilaterally are also other pertinent findings to help differentiate from isolated Achilles tendinitis and consider spondyloarthritis as an underlying cause.

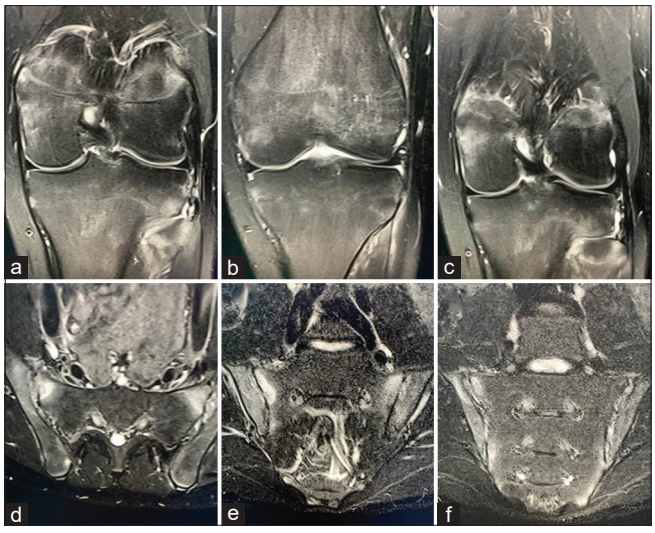

Figure 6: An 18 years old with knee pain and no trauma. Short tau inversion time recovery (STIR) coronal of the left knee (a-c) and STIR oblique axial of the sacroiliac joints (SIJs) (d-f). There is enthesitis at nearly every ligament in the knee – particularly the iliotibial band syndrome, both collateral, semimembranosus, and proximal tibiofibular joint. There is reactive synovitis with capsular enthesopathy. The corresponding SIJs demonstrate erosions, capsulitis, and fat metaplasia which are pathognomonic for SpA.

active enthesitis. In SpA, edema and inflammatory changes are diffuse and not confined only to the enthesis. Hallmark of enthesitis is bone marrow edema [Figures 6,7] as well edema and inflammatory foci within the perienthesis soft tissues [Figures 5c-d and 8-12]. More chronic enthesopathic changes manifest as erosions and enthesophytes, which are extensions of marrow contents isointense to the medullary bone. To evaluate enthesitis, one must assess a number of structures on MRI, as shown in Table 1. Typically, inflammatory MR findings manifest as areas of high signal on fluid-sensitive sequences and regions of low SI on T1-weighted (W) imaging. Structural lesions such as erosions or enthesophytes are best seen on T1W sequences. Other features of inflammation such as tenosynovitis should prompt the reporting radiologist to consider SpA. One must ensure that sequences are sensitive enough to detect marrow edema which can be affected by low-field strengths and field inhomogeneity when using inversion recovery sequences. Dixon algorithm-based sequences may be a solution to produce uniform fat suppression.[12]

Dactylitis

Diffuse soft tissue swelling within a digit, with uniform thickness and the non-recognition of a joint swelling is

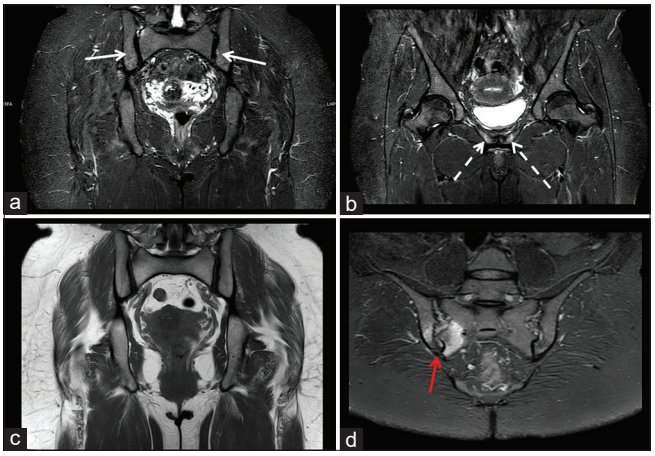

Figure 7: Magnetic resonance imaging (MRI) was performed on a young female patient who presented with heavy menstrual bleeding with lower pelvic and back pain. Initial MRI imaging of the pelvis was performed (coronal short inversion time inversion-recovery [a-b] and [c] T1-weighted sequences) which demonstrated no abnormality in both sacroiliac joints (SIJs) (solid white arrow). Periarticular bone marrow edema in both pubic symphyses (dashed white arrow) was noted in keeping with a diagnosis osteitis pubis. No gynecological cause for the pain was identified. It was noted that the patient's pain occurred in flares and related to catamenial inflammation. A subsequent MRI of the SIJs (d) performed 6 months later and demonstrated the manifestations of axial SpA (red arrow) and the patient was later fully diagnosed with psoriatic arthropathy.

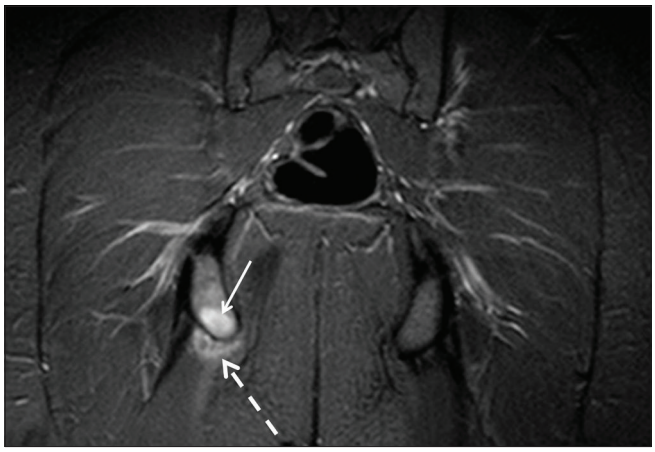

Figure 8: Coronal short tau inversion recovery magnetic resonance imaging image of a female patient demonstrating thickening and high T2 signal intensity edema/inflammation of the hamstring tendon and bursa, at its insertion on the right ischial tuberosity (dashed white arrow). Associated osteitis and bone marrow edema are noted in the right ischial tuberosity (white arrow). The patient presented with and was investigated for the left hip pain. These imaging findings should prompt the radiologist to suggest undiagnosed SpA. The patient was diagnosed with psoriatic arthropathy.

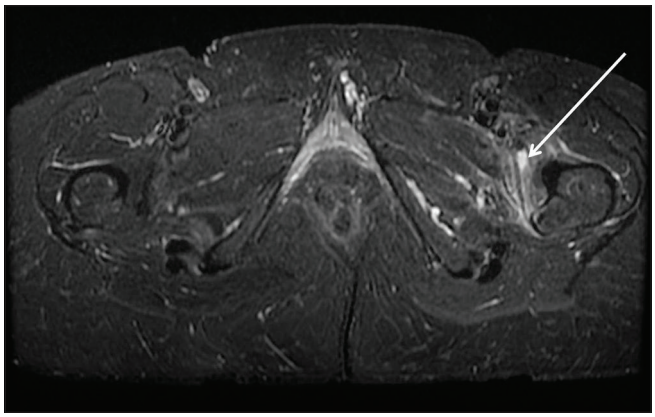

Figure 9: Axial short inversion time inversion-recovery magnetic resonance imaging image demonstrating inflammation and edema of the left iliopsoas myotendinous junction/bursa, at its attachment to the lesser trochanter (white arrow). Focal subtle bone marrow edema in the lesser trochanter enthesis with its surrounding increased adjacent soft tissue edema. Enthesitis and tendinopathy should warrant a raised index of suspicion for SpA.

characteristic of dactylitis. The disease process can involve the whole digit or a smaller proximal section. Dactylitis is frequently seen associated with psoriatic arthropathy where other features of psoriatic seronegative arthritis can be seen [Figure 13]. Within a dactylitic digit, both US and MRI play a crucial role in correctly delineating the specific tissue compartments involved. Flexor tendon tenosynovitis and joint synovitis are present nearly 90% of cases and can be

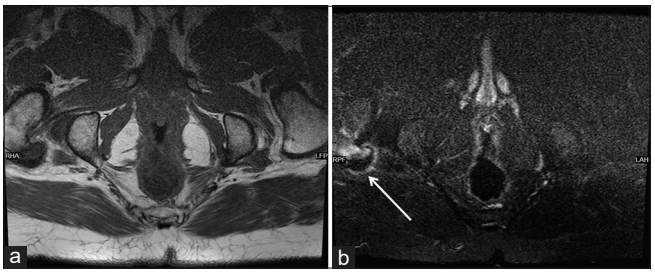

Figure 10: Patient presenting with right back pain and stiffness that had magnetic resonance imaging of the spine and sacroiliac joints (SIJs). Axial oblique T1 (a) and short tau inversion time inversion recovery (b) sequences demonstrate the right greater trochanter enthesitis (white arrow) at the gluteal medius insertion. This case highlights the importance of assessment of entheses at the edge of field in dedicated SIJ imaging. Confirmed MR stigmata of SpA were noted on the spinal and SIJ imaging.

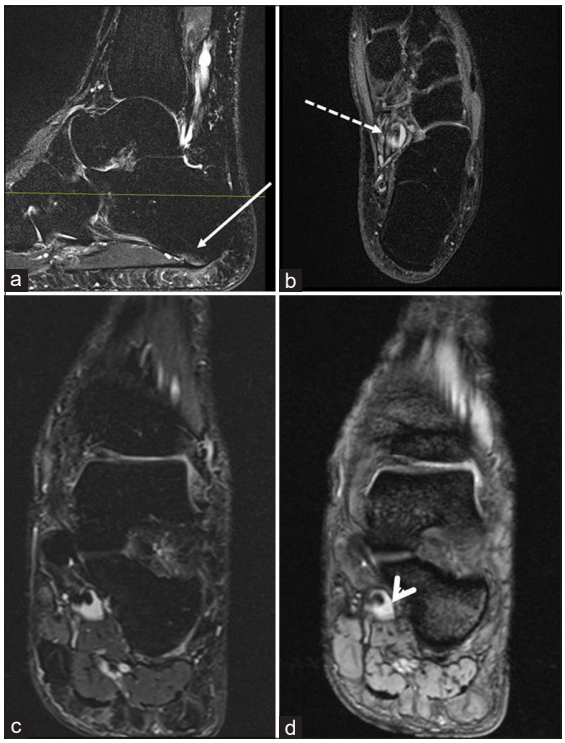

Figure 11: Patient presenting with recurrent left ankle pain. Magnetic resonance imaging of the ankle was performed demonstrating plantar fasciitis, calcaneal insertion enthesopathy, and flexor hallucis longus (FHL) tenosynovitis. The patient was later confirmed to have right sacroiliac joint inflammation and low back pain. Fluid-sensitive short tau inversion time inversion recovery (STIR) sagittal (a) and axial (b) sequences demonstrating focal high signal at the insertion of the plantar fascia on the calcaneum (solid white arrow) and tenosynovitis in the FHL tendon (dashed white arrow). Coronal STIR (c) and T2-weighted (d) sequences demonstrating fluid surrounding the FHL tendon (white arrow head). The remainder of the medial tendons is preserved. This case highlights the importance of high index of suspicion of SpA as a cause for the patients imaging findings and early referral.

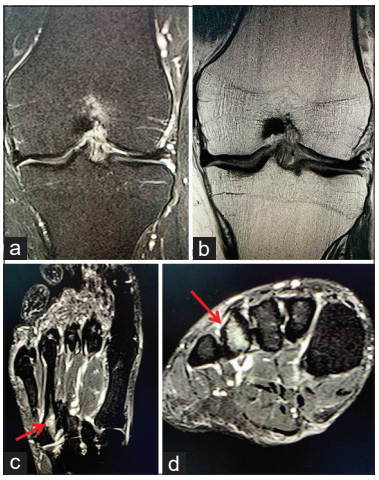

Figure 12: Psoriatic arthropathy presenting in the intercondylar notch. Coronal magnetic resonance imaging (MRI) T2FS (a) and intermediate weighted (b) images depicting erosions in the anterior cruciate ligament enthesis and focal osteitis with bone marrow edema. The same patient presented with enthesopathy of the intermetatarsal ligaments and the tarsometatarsal joint capsule of the fourth toe as seen on the MRI of the left foot coronal short tau inversion time inversion recovery (STIR) (c) and axial STIR (d) images and highlighted by the red arrows.

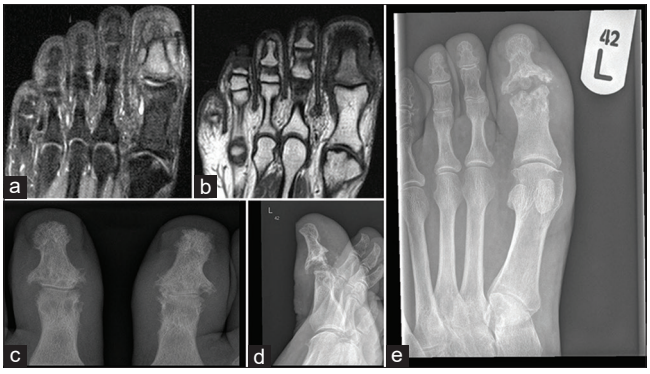

Figure 13: Psoriatic arthritis (PsA) Ivory phalanx. This commonly involves the hallux and is important when joint changes are not present. Features are "cloaking" of bone with new bone formation which is an uncommon but specific finding in PsA. Foot magnetic resonance imaging: Short tau inversion time inversion recovery (a) and proton-density (b) coronal images demonstrating signal changes of periosteal and endosteal bone formation in the big toe. An uncommon but specific finding in PsA. The corresponding plain radiographs of the big toes (c) and a separate case (d-e) demonstrating terminal phalangeal sclerosis with periosteal and endosteal bone formation. Note in (c) the increased radiodensity of the entire phalanx in a patient with psoriasis. This is termed the "Ivory Phalanx."

easily identified in both modalities. Furthermore, evident in up to 30% of cases is extensor tendon inflammation with or without extratendinous soft tissue thickening. On MRI, bone marrow edema can be present usually within a painful digit.

Table 1: A checklist for the structures one should evaluate during the assessment of enthesitis on MRI.

Evaluation of enthesitis on MRI
Thickness and signal intensity of tendons and ligaments
Perientheseal soft tissues for swelling or edema
Adjacent bone marrow to detect edema, best appreciated as high signal in fat-suppressed sequences
Adjacent bone for erosions
Adjacent bone for enthesophytes
Additional findings in adjacent structures (e.g., effusion, bursitis, and capsulitis)

MRI: Magnetic resonance imaging

CONCLUSION

Peripheral manifestations, especially enthesitis, dactylitis, and arthritis, are the hallmarks of SpA. Patients with joint pain can present to a number of medical specialties and may not come from rheumatology. Interpretation of imaging may be influenced by the referral specialty and imaging features of peripheral SpA can, therefore, often be misinterpreted. Unexplained ongoing pain in a peripheral joint containing fibrocartilage should prompt the radiologist to check for hallmarks related to SpA. It is important to be aware of the imaging features of peripheral SpA as the radiologist may be the first clinician to suggest a diagnosis of SpA.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms.

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Nil.

Conflicts of interest

There are no conflicts of interest.

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