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Case Report

Tibialis Posterior Tenosynovitis as a First Presenting Feature of Pre-clinical Rheumatoid Arthritis: A Case Report and Literature Review

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ABSTRACT
Tenosynovitis in Preclinical Rheumatoid Arthritis (RA) has been reported. The Tibialis posterior (TP) tendon is the second most commonly affected tendon in the foot and ankle in established RA, but in preclinical RA has not been reported.
In this case report, we present a 27 years old lady from Dhading, Nepal, with Preclinical RA with first presentation with Tibialis posterior Tenosynovitis. She was anti-cyclic citrullinated Peptide (CCP) positive but had no arthralgia or morning stiffness. Initial treatment with Non-Steroidal anti-inflammatory drugs failed to alleviate her symptoms. Methotrexate helped improve her symptoms.
Keywords: Methotrexate; Rheumatoid Arthritis; Tenosynovitis; Tibialis Posterior Dysfunction

INTRODUCTION
Preclinical Rheumatoid Arthritis (RA) is characterized by abnormalities of autoantibodies and other biomarkers in the absence of clinically apparent inflammatory arthritis that describes RA [1], and up to 80% of cases have been reported to be having tenosynovitis at this stage of the disease.[2] Tenosynovitis at two or more anatomical sites was associated with the later development of RA.[1] TP tendon is the second most common tendon affected in the foot and ankle in established RA with a prevalence between 13-64%, [3,4] but in preclinical RA has not been reported. Diagnosing the case in the preclinical phase provides a window of opportunity to treat and prevent further damage incurred due to the disease.
In this case report, we present a 27 years old lady from Dhading, Nepal, with Preclinical RA with her first presentation with TP tenosynovitis.

CASE REPORT
Twenty-seven years old lady from Dhading, Nepal, presented to the Out Patient Department (OPD) of the National Trauma Center, a Tertiary hospital in Kathmandu. She was employed and treated at a nearby medical center but did not improve, so she landed at the Hospital. She had developed pain and swelling over her left ankle, more on the medial side, for two months, which was gradually progressive. At the time of the presentation, due to pain, she had difficulty standing for a long time or walking and could not wear her shoes, which had already started taking a toll on her job. She was a non-smoker and did not involve in any sports activity. She had no fever and had no other known illness. She had no arthralgia or morning stiffness.

On examination of the left ankle, gross swelling around the medial malleolus extending proximally nearly 10 cm above and below with normal-looking skin color. The medial arch was present, and the ankle was in slight valgus as it was on the contralateral side. The local swelling temperature was not raised, and tenderness could be elicited just posterior to the medial malleolus. She could perform single heel raise bilaterally.

Weight-bearing Antero-posterior and lateral views of the ankle on plain radiography (Figure 1) showed no bony pathology and suggested soft tissue swelling. Blood investigation revealed an Erythrocyte sedimentation rate (ESR) of 40 mm/hr, C-reactive protein (CRP) positive with a value of 8.3 IU/ml. Her total leucocyte count was 9500/mm3 with a neutrophil of 62%.

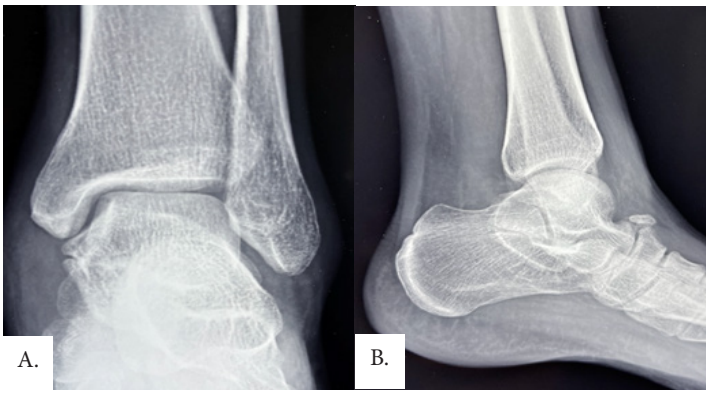

Figure 1: Weight-bearing Plain radiography of left ankle Anteroposterior (A) and Lateral (B) views

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The patient denied undergoing Magnetic Resonance Imaging (MRI), citing financial issues, so Ultrasonography (US) was ordered, which was performed by Radiologist on a Samsung Ultrasound machine with a linear probe with 15 MHz frequency, and it was reported as having features suggestive of Tenosynovitis of TP tendon. The tendon was thickened by 4.9 mm compared to the normal side of 2.8 mm (Figure 2) and had thickened synovial sheath of 9 mm (Figure 3). The minimal fluid collection was noted around the tendon sheath, and Color Doppler showed increased peripheral vascularity suggesting active inflammation. She was diagnosed with a case of TP tenosynovitis with tendon dysfunction of stage I.

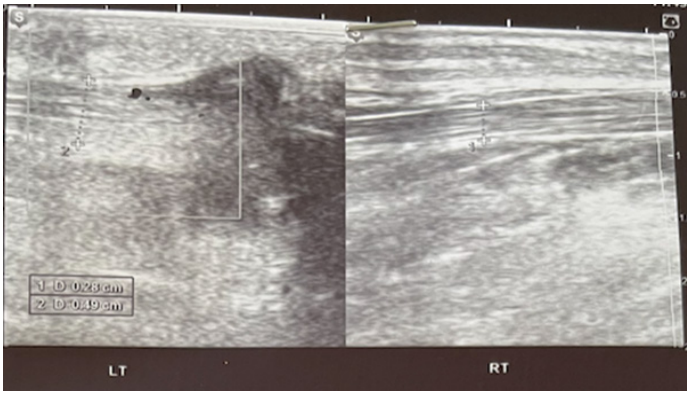

Figure 2: Ultrasonographic views of the tibialis posterior tendon of both sides, comparing the transverse diameter (Left 4.9mm, Right 2.8mm)

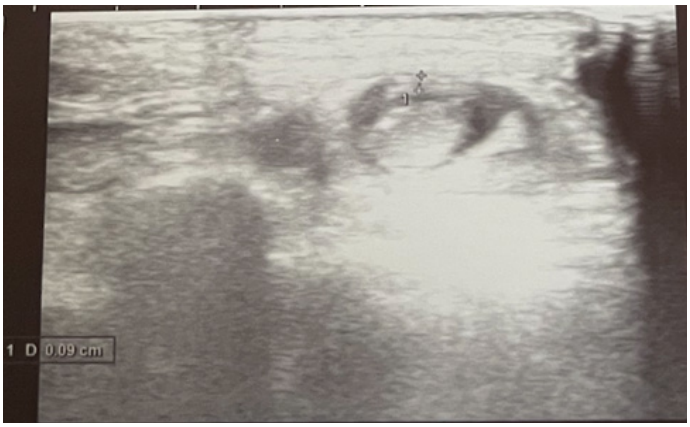

Figure 3: Ultrasonographic views of left tibialis posterior tendon showing thickened sheath and fluid around.

She was started on NSAIDs, a boot cast, and advised rest as the standard early treatment for tenosynovitis so that it allows healing of the tendon. She followed up after one week with increased pain, so the cast was removed, and increased swelling was evident. A medial arch was present. On retrospective inquiry, all three sisters were diagnosed with RA and were on regular treatment. So, for further confirmation, anti-CCP and Rheumatoid Factor (RF) were sent; both came out positive and had significantly raised the anti-CCP value of 192 IU/ ml. She was diagnosed with pre-clinical RA and was started on oral Prednisolone 10mg once a day for one week and 15 mg of Methotrexate once a week for four weeks, with coverage of folinic acid. Pain and swelling decreased significantly on follow-up after one week. The boot cast was reapplied for the rest of the tendon, and the next visit was scheduled after one week, but the patient didn't show up. After one and a half months, she followed up, and on the patient's request cast was removed; swelling had decreased, but occasional pain persisted. She resumed going to the office. She was compliant with medications, and her pain and swelling dramatically subsided, and she could put on her shoes quickly. But she could not perform single heel raise on her left ankle, so her tendon dysfunction increased. She was advised to continue Methotrexate but denied ankle foot orthosis or cast. On follow-up after six weeks, she had improved symptoms and is continuing with her job. She has no arthralgia or morning stiffness. Eccentric strengthening exercises for the posterior Tibialis were started, and Methotrexate continued. She is suggested for regular follow-ups, and the possible natural history of the disease has been explained to the patient.

DISCUSSION

It is evident by multiple studies that Rheumatoid Arthritis (RA) initially goes through a period when in the absence of clinically apparent inflammatory arthritis that characterizes RA, there are abnormalities of autoantibodies and other biomarkers; this period is termed pre-clinical RA.[2] In a mice study by Hayer et al. the expression of 3'-modified human TNF-α transgene, tenosynovitis, and the formation of osteoclasts precede the development of pannus-like lesions and chronic polyarthritis.[3] Among the autoantibodies for RA, commonly done ones are RF and antibodies to citrullinated protein antigens (ACPAs); commercially commonly available one is the anti-Cyclic Citrullinated Peptide (CCP) assay.[1] The European League Against Rheumatism (EULAR) summarizes phases that individuals may pass through before the development of RA phase B has laboratory abnormalities with no symptoms or signs of inflammatory arthritis, and the autoantibodies are present a median of 5 years before clinical RA. They also suggested the use of US/MRI to detect progression from Phase D (symptoms without arthritis) to Phase E (Undifferentiated Arthritis).[4]

It is evident that some of the patients with RA present with symptoms before the development of Clinical Arthritis. Recent qualitative research suggests pain, burning sensation, stiffness, fatigue, and weakness may be present before clinical arthritis.[4] In the case-control study done in 2003 by Rantapää-Dahlqvist and colleagues within the Northern Sweden Health and Disease Study and the Maternity cohorts of Northern Sweden, samples among blood donors that had been taken years before the onset of symptoms of RA were matched with control groups and Anti-CCP and RF were analyzed and found 33.7% prevalence for anti-CCP.[5] So, the presence of Anti CCP and RF predicted the development of RA. Similar findings were reported in a study by Nielen et al., who used stored serum samples from the Dutch Sanquin biobank of blood donation samples, including 79 patients with RA and controls.[6]

The individual risk increases threefold when individuals have first-degree relatives with RA. Genetic risk factors are

estimated at 50% in those with seropositive RA.[7] In our case, she had all her sisters tested positive for RA and were under treatment, so family history played a pivotal role in diagnosing the case. Our case is a non-smoker but belongs to low socioeconomic status, a risk factor for disease progression.[7]

TP tendon is the second most common tendon affected in the foot and ankle in established RA with a prevalence between 13-64%,[eight] but in preclinical RA has not been reported. In the study by Kleyer et al. tenosynovitis was present in 80% of ACPA-positive individuals with no arthritis. For the study, individuals were identified by randomly screening 1000 persons using a quick capillary blood test.[1] So, patients with tenosynovitis with positivity for autoantibodies for RA may represent pre-clinical RA, as is our case.

The use of US for the assessment of TP tendon in rheumatoid arthritis patients has been described in the study by Koraym et al. done in the Egyptian population, which included 20 (40 feet) RA patients.[9] Rogier et al. even argued that tenosynovitis at the level of the hand and feet joints is a feature that deserves to be added as the third classic trait of RA.[9] In our study also US diagnosed TP tenosynovitis. The US may have been underused in the diagnosis of such cases.

Screening only with autoantibodies is not recommended as they alone do not predict a high risk for progression to RA. In a Dutch cohort, the positivity of anti-CCP gave only 5% of the 5-year positive predictive value (PPV) for RA.[6]. Still, in the presence of genetic risk factors, autoantibodies increase the 5-year PPV for RA to 61% when positive.[10] New serum biomarkers like antibodies against carbamylated proteins (anti-CarP) have recently been described in RA patients, and exploration of its use for screening high-risk individuals is being undertaken.[11]

In pre-clinical RA, management is aimed to slow the progression of the disease to clinical RA by lifestyle modification, and the use of Disease Modifying Anti Rheumatic drugs (DMARDs) but its effectiveness in preventing or halting the progression of the disease is being studied.[7] Immunomodulatory treatments used for remission in early arthritis could also be effective in at-risk individuals as it is evident that immune dysregulation occurs in preclinical disease.[8] Larger multicenter randomized controlled trials for assessing the use of abatacept and rituximab in the pre-clinical phase of RA are underway.[7]

The further natural history and development of clinical RA in this patient are due for follow-ups.

CONCLUSION

Tibialis posterior tenosynovitis can be a presenting feature in Preclinical Rheumatoid Arthritis. Ultrasound is cheap and readily available for the diagnosis of Tenosynovitis. Early diagnosis and prompt treatment with DMARDs can improve the patient's symptoms in Preclinical RA and delay the progression.

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