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Peritendinous inflammation in anti-CCP positive at risk individuals

Kulveer Mankia[1,2], Maria Antonietta D'Agostino[1,3], Jorge Murillo-Gonzalez[5], Andrew Grainger[2,4], Paul Emery[1,2]

1. Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Chapel Allerton Hospital, Leeds, UK

2. NIHR Leeds Biomedical Research Centre, Leeds Teaching Hospitals NHS Trust, Leeds, UK

3. Department of Rheumatology, APHP, Hopital Ambroise Paré, Boulogne-Billancourt, Paris, France. INSERM U1173, Laboratoire d'Excellence INFLAMEX, UFR Simone Veil, Versailles-Saint-Quentin University, 78180 Saint-Quentin en Yvelines, France.

4. Department of Radiology, Leeds Teaching Hospitals NHS Trust, Leeds, UK

5. Department of Anatomy and Embryology, School of Medicine, Complutense University of Madrid, Madrid, Spain.

Corresponding author:

Dr Kulveer Mankia, Leeds Institute of Rheumatic and Musculoskeletal Medicine, Chapel Allerton Hospital, Chapeltown Road, Leeds, LS7 4SA, UK.

k.s.mankia@leeds.ac.uk

We thank Deng et al for their interest in our study (1), in which we identified MRI interosseous tendon inflammation (ITI) in anti-cyclic citrullinated peptide positive at risk individuals (CCP+ at-risk) without clinical synovitis (2). Given the MRI appearances and absence of a tendon sheath on histological examination, we suggested ITI is a peritendonitis rather than a tenosynovitis. ITI was originally described as a tenosynovitis by Rowbotham et al (3). However, in the discussion it was acknowledged that this may not be the correct terminology as the MRI features were not typical of tenosynovitis and the microstructure of the tendons had not been well described (3). Indeed, it was conceded that ITI may be better described as peritendinous inflammation or 'paratenonitis' rather than a true tenosynovitis. The lack of a tendon sheath demonstrated in the current study certainly supports this assertion.

We were interested in the view that ITI represents a fasciitis which may be considered an extra-articular manifestation of RA, similar to rheumatoid lung or rheumatoid vasculitis (1). We agree that ITI, like these other features, may be viewed as an extra-articular consequence of RA autoimmunity. However, other extra-articular manifestations in RA are not peri-articular and have different associations, generally seen in the setting of longstanding joint disease with increased prevalence in males and smokers (4). They are also very unusual to find in at risk individuals prior to the development of arthritis. Instead ITI appears to frequently precede arthritis and occurs adjacent to the metacarpophalangeal (MCP) joints, raising important questions about its role in the development of RA.

Although, to the best of our knowledge, the current study is the largest MRI study in CCP+ at-risk individuals, we agree larger studies should be done to confirm our findings. We also agree that ITI may not be specific to RA, and may be associated with mechanical factors or other conditions; we could not assess these factors in our study and acknowledged this in the discussion of the manuscript. Deng and colleagues questioned whether the results could be gender-biased as our subjects were predominantly female (1). However, RA is more frequent in females, with a sex ratio

of around 3:1. As such we aimed to describe ITI and its associations in a population representative of the condition of interest rather than the general population. Similarly, the mean age of the RA patients included in our study was between 50 and 60 years, which is representative of the RA demographic (5). Whether ITI is as prevalent in different age groups is an interesting question which could be addressed in future work.

In describing histological findings, we followed the Histological Terminology of the Federative International Committee on Anatomical Terminology (2008) (6). We regret that some of the abbreviations were accidentally omitted from the figure legend (EPM, epimysium; MF, muscle fascicles and EM, endomysium).

Finally, we agree that it would be interesting to know if peritendinous inflammation or fasciitis is a generalised phenomenon found at other sites in symptomatic at-risk individuals. For example, CCP+ at-risk individuals often present with foot pain without synovitis (7) and it is possible that extra-capsular inflammation may be responsible. Further imaging studies would certainly be useful in this regard.

References

1. Deng ZL, H; Lu, W. Interosseous tendon inflammation of rheumatoid arthritis: what's the real meaning? Annals of the rheumatic diseases. 2019.
2. Mankia K, D'Agostino MA, Rowbotham E, Hensor EM, Hunt L, Moller I, et al. MRI inflammation of the hand interosseous tendons occurs in anti-CCP-positive at-risk individuals and may precede the development of clinical synovitis. Annals of the rheumatic diseases. 2019.
3. Rowbotham EL, Freeston JE, Emery P, Grainger AJ. The prevalence of tenosynovitis of the interosseous tendons of the hand in patients with rheumatoid arthritis. Eur Radiol. 2016;26(2):444-50.
4. Young A, Koduri G. Extra-articular manifestations and complications of rheumatoid arthritis. Best practice & research Clinical rheumatology. 2007;21(5):907-27.
5. Innala L, Berglin E, Moller B, Ljung L, Smedby T, Sodergren A, et al. Age at onset determines severity and choice of treatment in early rheumatoid arthritis: a prospective study. Arthritis research & therapy. 2014;16(2):R94.
6. Terminologia Histologica: International Terms for Human Cytology and Histology by the Federative International Committee on Anatomical Terminology (FICAT). Philadelphia: Wolters Kluwer/Lippincott Williams & Wilkins
7. Nam JL, Hunt L, Hensor EM, Emery P. Enriching case selection for imminent RA: the use of anti-CCP antibodies in individuals with new non-specific musculoskeletal symptoms - a cohort study. Annals of the rheumatic diseases. 2016;75(8):1452-6.