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The ultrasound phenotype of palindromic rheumatism

Dear Editor

We thank Sanmarti et al (ref) for their interest in our recent paper in which we describe the distinct imaging phenotype of palindromic rheumatism (PR) (1). As the authors point out, we identified a high prevalence of ultrasound (US) extra-capsular inflammation (ECI) in flares of PR, often without co-existent US synovitis. This US pattern was specific for PR and may be useful in distinguishing PR from early persistent arthritis.

In an earlier US study of a Spanish PR cohort, Sanmarti and colleagues performed US assessment in 10 patients during flares of PR (2) and reported US power Doppler synovitis in seven, with five of these fulfilling criteria for US defined synovitis. The authors did not identify US peri-articular changes and none of these patients had peri-articular inflammation clinically. This imaging pattern is different to that identified in our cohort but, as the authors surmise, this could be explained by key differences in the respective PR cohorts. Our cohort consisted of PR patients relatively early in their disease course (median 2.5 years), 90% of whom were naïve for disease-modifying anti-rheumatic drugs (DMARDs). In contrast, PR patients in the Spanish cohort had longstanding disease (median 11.6 years) and the majority were on treatment; 85% of patients had received DMARD therapy, with 61% established on at least one DMARD at the time of imaging. As such, it is possible that the imaging phenotype described in our study better reflects true *de novo* untreated PR and with more prolonged disease duration and/or therapy, this disease pattern may change. For example, it is possible that extra-capsular inflammation is an early phenomenon which may be suppressed by DMARD treatment. Indeed, US extra-capsular abnormalities (including tenosynovitis and/or peri-articular soft tissue inflammation) without synovitis have also been described in a Chinese PR cohort, 62% of whom were DMARD-naïve (the remaining 38% having received hydroxychloroquine) (3).

The complete absence of clinical peri-articular inflammation during PR flares in the Spanish study is interesting and certainly differs from our experience. Indeed, peri-articular inflammation was described as an important clinical hallmark both in the original description of PR (4) and subsequently (5). The absence of this characteristic feature,

perhaps due to the effect of therapy, is consistent with the imaging pattern observed by Sanmarti and colleagues.

We thank Sanmarti et al for identifying the error in units for median CRP levels; this should be mg/L rather than mg/dL as suggested. While we compared the imaging pattern in PR with that seen in new-onset rheumatoid arthritis (NORA) and anti-CCP positive individuals with musculoskeletal symptoms (CCP+ at-risk), we did not specifically address whether the flare imaging pattern is predictive of progression from PR to RA. This would require a larger longitudinal study and would certainly be an important area for future investigation. Interestingly although Sanmarti and colleagues report only two of their six patients with US synovitis during flare developed RA, Chen et al reported a significantly higher progression to RA in patients with US synovitis during flare compared to those without US synovitis (37.7% vs 3.7%, OR 15.05) (3). Intra-synovial power Doppler signal is also highly predictive of progression to clinical arthritis in CCP+ at-risk, both at joint and patient level (6).

Despite the recent studies on PR, there are many unanswered questions and the research agenda remains broad. The unique phenotype of this condition raises important questions about the pathogenesis and the optimal approach to treatment. Identifying biomarkers for accurate clinical risk prediction is also an important ambition. Well phenotyped, treatment-naïve inception cohorts will be crucial to furthering our understanding of this fascinating disease.

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