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Bone marrow lesions on magnetic resonance imaging in hand osteoarthritis are associated with pain and interact with synovitis

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SUMMARY

Objective: To determine the association between bone marrow lesions (BMLs) and (teno)synovitis as assessed on magnetic resonance (MR) imaging in patients with pain in hand osteoarthritis (OA).
Methods: In 105 consecutive primary hand OA patients (83% women, mean age 59 years), who were diagnosed by rheumatologists and included in the HOSTAS (Hand OSTeoArthritis in Secondary care) cohort, contrast enhanced MR imaging of right distal and proximal interphalangeal joints were obtained. In 92 patients joint site specific pain upon palpation was assessed within 3 weeks of magnetic resonance imaging (MRI) examination.
MR features were scored (0–3) following the Oslo hand OA score: BMLs, synovitis, cysts, flexor tenosynovitis (FTS). Additionally, extensor tendon inflammation (ETI) (0–3) was scored. Odds ratios (OR, 95% confidence interval (CI)) were calculated using generalized estimating equations for MR features with joint pain, adjusted for putative confounders. Stratified analyses were performed to investigate interaction.
Results: BMLs, synovitis, cysts, FTS and ETI were demonstrated in 56%, 90%, 22%, 16% and 30% of patients, respectively. BMLs (grade 2/3 vs 0: 3.5 (1.6–7.7)) and synovitis (3 vs 0: OR 3.6 (95% CI 1.9–6.6)) were severity-dependent associated with joint pain, but FTS and ETI were not. Stratified analyses showed that BMLs did not associate with pain in the absence of synovitis, whereas synovitis was associated with pain in the absence of BMLs. Interaction was seen between BMLs and synovitis grade 2 or 3.
Conclusion: In hand OA patients severe synovitis is associated with joint pain, which is worsened when BMLs co-occur, suggesting synovitis as primary target of treatment.

Introduction

Hand osteoarthritis (OA) can result in a high clinical burden. Especially hand pain can lead to a decreased quality of life[1]. Knowledge of the underlying pain mechanisms in hand OA enables optimal treatment of hand pain. Many ultrasonography studies in hand OA patients demonstrated that synovial inflammation is present in hand OA and plays a role in the presence of hand pain. Tenosynovitis of the flexor tendon is also present in hand OA and associated with hand pain[2,3], but the involvement of the extensor tendon is unknown.

Magnetic resonance (MR) studies have indicated that in the subchondral bone of osteoarthritic joints ill-defined areas of high signal intensity can be visualized on fat-suppressed T2 weighted or short tau inversion recovery (STIR) sequences, so-called bone marrow lesions (BMLs)[4]. Histologically BMLs represent mainly areas of fibrosis, necrosis and trabecular bone abnormalities[5]. In knee OA these BMLs have been widely investigated and play a role in knee pain[6]. BMLs in hand OA have been rarely studied. In two studies of late stage hand OA patients the presence of BMLs has been demonstrated[2,3]. Haugen *et al.* showed an association between BMLs and hand pain, both cross-sectionally and longitudinally[2,3,7].

Since no data of BMLs in patients in earlier stages of hand OA are available, we set-up a study to determine their prevalence in patients presenting themselves to our Rheumatology outpatient clinic. It is unclear how BMLs relate to synovitis in osteoarthritic hand joints and therefore we do not know whether synovitis or

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BMLs are crucial in hand pain. Hence we investigated their co-occurrence and interaction with respect to pain, to be able to determine which target is most promising to alleviate pain. This is also important, since imaging synovitis is difficult due to the need for contrast enhanced MR imaging, which adds cost, complexity and risk to the MR imaging protocol. We also investigated whether extensor tendon inflammation plays a role in hand OA.

Methods

Study design

Cross-sectional data were used of the HOSTAS (Hand OSTeoArthritis in Secondary care) study, an ongoing cohort. This cohort enrolled consecutively diagnosed patients with hand OA since 2009 to investigate determinants of outcome in hand OA. Patients were included when they consulted a rheumatologist at the outpatient clinic of the Leiden University Medical Center (LUMC) for hand complaints and these hand complaints were diagnosed as primary hand OA.

Exclusion criteria include any other pathological condition that could explain existing symptoms, secondary OA and routine magnetic resonance imaging (MRI)-contraindications.

For the present analysis, only patients were included who received a contrast enhanced MRI (CE-MRI).

Written informed consent was obtained from all participants. The study was approved by the LUMC medical ethical committee.

Demographics and clinical characteristics

Standardized questionnaires were used to collect demographics and clinical characteristics. Participants underwent standardized physical examination of their hands by a trained research nurse. All distal interphalangeal (DIP), proximal interphalangeal (PIP) joints, metacarpal phalangeal (MCP) joints, first interphalangeal (IP) joints and first carpometacarpal (CMC) joints were evaluated for site specific pain upon palpation (0–30, additive scale)[8].

Self-reported pain

Pain intensity in the right hand was measured by a pain visual analogue scale (VAS). Furthermore, the Michigan Hand Outcomes Questionnaire (MHQ) pain subscale was filled in (5-point Likert scale and normalization to 0–100, higher scores = greater pain)[9]. Also the pain subscale of the Australian Canadian Hand OA Index (AUSCAN) in its Likert format was acquired[10]. Both MHQ and AUSCAN assess hand pain in both hands simultaneously.

Mental health

Subscales of the 36-item Short Form Health Survey (SF-36) were measured to calculate the mental health component score. This component score was standardized using data based on the norms from the Dutch population[11,12].

MR imaging

From March 2011 to October 2012, MR imaging was performed as part of the baseline examination of the patients included in HOSTAS, using an ONI-MSK-Extreme 1.5 Tesla (T) extremity MR imaging scanner (GE, Wisconsin, USA), with a dedicated 100 mm coil. The right hand PIP and DIP joints ($n = 8$) of each patient were examined, regardless of clinical features or dominance.

The following sequences were used: coronal T1-weighted (T1-w) fast spin echo (FSE) images (repetition time (TR)/echo time (TE) 575/11 milliseconds (ms), acquisition matrix (AM) 388 × 288, echo train length (ETL) 2, minimum TE), axial T1-w FSE images (TR/TE 500/10.2 ms, AM 340 × 288, ETL 2, minimum TE), coronal T2-w FSE images with frequency selective fat saturation (FSFS) (TR/TE 3000/61.8 ms, AM 300 × 224, ETL 7) and axial T2-w FSE images with FSFS (TR/TE 3000/57 ms, AM 336 × 192, ETL 7) before contrast injection, and coronal T1-w FSE images with FSFS (TR/TE 600/10.4 ms, AM 364 × 224, ETL 2, minimum TE) and axial T1-w FSE images with FSFS (TR/TE 650/7.7 ms, AM 320 × 192, ETL 2, minimum TE) after intravenous injection of Gadolinium-chelate (Gd) (gadoteric acid, Guerbet, standard dose 0.1 mmol/kg).

Coronal images had a field of view of 120 mm and 18 slices with a slice thickness of 2 mm and a slice gap of 0.2 mm. Axial images had a field of view of 100 mm and 24 slices with a slice thickness of 3 mm and a slice gap of 0.3 mm. Total acquisition time was 30 min.

MR imaging scoring was performed by one dedicated well-trained reader (RL) (supervised by radiologist MR with more than 20 years experience) using a modified version of the Oslo hand OA MR imaging scoring system[13] (Fig. 1). Scoring was performed blinded for demographic and clinical data.

Synovitis was defined as an area in the synovial membrane that showed post-Gd enhancement of a thickness greater than the width of normal synovium (>1 mm)[13] on T1-w images and seen on at least two consecutive slices. Scoring was based using thirds of the maximum potential volume of enhanced synovial tissue (0 = normal, 1 = mild, 2 = moderate and 3 = severe).

Flexor tenosynovitis (FTS) was defined as an area in the flexor tendon sheath that showed post-Gd enhancement of a thickness greater than the normal width of the tendon sheath (as shown in the Oslo atlas) on T1-w images, visible on at least two consecutive slices and involving the entire tendon sheath by being circumferential. Scoring occurred as follows: 0 = normal, 1 = <0.5 tendon thickness, 2 = ≥0.5 and <1 tendon thickness, 3 = ≥1 tendon thickness.

Extensor tendon inflammation (ETI) was defined as an area in the extensor tendon that showed enhancement of a thickness greater than the normal width of the tendon, is visible on at least two consecutive slices and when opposite sides of the extensor were enhanced. Scoring was performed according to the same scoring method as the flexor tendon: 0 = normal, 1 = <0.5 tendon thickness, 2 = ≥0.5 and <1 tendon thickness, 3 = ≥1 tendon thickness.

BMLs at distal and proximal joint site were defined as lesions within the trabecular bone with signal characteristics consistent with increased water content and ill-defined margins on T2. The distal and proximal part of the joint was scored separately for the proportion of bone with BML: 0 = no BML, 1 = 1–33 % of bone with BML, 2 = 34–66% of bone with BML, 3 = 67–100% of bone with BML. The highest score was taken as the BML score for the whole joint.

Cysts (0–1; absent or present) at distal and proximal joint site were defined as sharply marginated bone lesions with typical signal characteristics (Low signal intensity on T1 pre-gadolinium and high signal intensity on T2), which is visible in two planes without a cortical break.

One of the authors (RL) re-scored 11 randomly selected MR scans after at least 3 weeks, and the intra-reader reliability for synovitis, FTS, BML and cyst was high (intraclass correlation coefficient (ICC) ≥0.97), while the ICC for ETI was intermediate (ICC 0.76).

Radiographs

Conventional radiographs of the hands (dorso-volar) were obtained. The DIP joints, PIP joints, first IP joints, MCP joints and first CMC joints were scored by one of the authors (WD). The Kellgren–Lawrence (KL) grading scale (0–4, maximum score 120) was used for the scoring of structural osteoarthritic damage and the Verbruggen–Veys anatomical phase scoring was used for erosion (N-