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Ultrasound detected inflammation is associated with the development of new bone erosions in hand osteoarthritis: a longitudinal study over 3.9 years

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SUMMARY

Objective: To evaluate the association between ultrasound (US) detected inflammation at baseline and the subsequent development of new bone erosions at follow-up in patients with hand osteoarthritis (HOA).

Method: 32 of the 35 (10 controls, 12 patients with non erosive HOA (non-EHOA), 13 with EHOA subjects originally studied were re-evaluated 3.9 years after the initial study, by means of standard radiography and US examination. Kellgren–Lawrence (K-L) and Kallman scores were utilized to evaluate 576 interphalangeal (IP) joints. US detected synovial inflammation features were scored as present/absent. US detected bone erosions were also investigated. The association between synovial inflammation features at baseline and the development of new bone erosions was evaluated using the generalized linear mixed model (GLMM) after adjustment for patient effect, age, gender, body mass index.

Results: In HOA patients, radiographic scores worsened and bone erosions progressed. In HOA patients similar percentages of joints with Power Doppler Signal (PDS) and gray scale (GS) synovitis were found comparing baseline and follow-up examinations, whilst a significant increase was found in the joints with effusions. Only a minority of joints were positive on both occasions (between 2 and 6 %), the majority fluctuated between positive and negative and vice versa. PDS positivity was associated with new radiographic central erosions and US-detected bone erosions, whereas GS synovitis and effusion were not.

Conclusions: Radiographic scores and bone erosions increased over a period of about 4 years. Synovial inflammation as detected by PDS was associated with the appearance of new bone erosions.

Introduction

The hand is one of the most common sites of osteoarthritis. The clinical form has a prevalence of about 20% in people aged 65 years and over[1] and a higher prevalence (80% in the elderly population) can be seen if radiographic definition alone is taken into account[2]. Hand osteoarthritis (HOA) is a leading cause of disability of the hands: this disability is more pronounced if severe involvement of the first carpo-metacarpal joint (CMC1) is present or if severe radiographic changes, called central erosions, are detected in the distal and proximal interphalangeal joints (DIP/PIP)[3–6]. The latter form of HOA is called erosive or inflammatory, since it is characterized by episodes of swelling and tenderness (sometimes associated with redness) and acute pain in one or more IP joints[7,8]. Central erosions are areas of subchondral bone collapse in the central zone of the joint, without clear evidence of central bone breaks.

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A considerable number of people with HOA will develop the erosive disease, which can appear at variable time intervals from the diagnosis of HOA[5,9–11]. The association of bone erosions and the presence of inflammation, both clinically and at US examination, has led to the suggestion that bone damage may be induced by synovitis, as seen in Rheumatoid Arthritis (RA). Indeed, the erosive disease does not appear to be a distinct entity from the non erosive form, since the joint topography of the structural damage[12,13] and the presence of systemic complications (hypertension, dyslipidemia, autoimmune thyroiditis) are similar in both forms[14,15], though this remains a matter of debate.

We, and others, have demonstrated that US-detected synovitis (GS synovitis), effusion and PDS are frequently observed in erosive HOA (EHOA), particularly, but not exclusively, in joints with central erosions[16–20].

To date, the majority of studies carried out on US-detected synovitis and structural damage in HOA have been cross sectional[16–20], therefore unable to evaluate the association between synovitis and the progression of damage, along the lines of what has already been soundly demonstrated in patients with RA, both at patient and joint levels[21]. Not long ago, two longitudinal studies carried out by the same group assessed the role of synovial inflammation in the appearance of new structural damage and pain in HOA patients[22,23] Hence, we performed a longitudinal prospective study evaluating the US inflammatory (synovitis) features and radiographic US-detected bone erosions in a series of subjects, including cases with either no clinical or X-ray HOA or with non erosive and erosive forms of HOA.

The primary evaluation of this series of subjects has already been reported[17]. The same subjects were then re-evaluated after an average of 4 years, when we considered the relationship between the US features of synovial inflammation at baseline and new bone erosions detected after this 4-year period (follow-up).

Patients and methods

Patients

We performed an X-ray and US re-evaluation of the 35 cases from the original study (Baseline, 10 controls without joint disease, 12 patients with non erosive HOA and 13 with EHOA). Consecutive patients affected by HOA according to the ACR classification criteria[24] were recruited in our rheumatology outpatient clinic. Patients with erosive disease were identified by conventional radiology (i.e., by the presence of the classic central erosion patterns – gull-wing or saw-tooth appearance-in at least two joints). Control subjects were randomly selected from people attending our outpatient clinic for minor, non-specific complaints: these subjects had no finger joint pain and/or tenderness and no finger nodes; therefore they were classified as clinically normal controls (NC). Exclusion criteria were: trauma to or operation on the hands during the 6 months, or an intra-articular injection during the 3 months prior to inclusion, the assumption of oral corticosteroids 1 month prior to inclusion. People with positive rheumatoid factor or psoriasis or a history of psoriasis in first degree relatives were excluded. In addition, subjects with signs or symptoms suggestive of connective tissue disease, other inflammatory arthritides or inflammatory bowel diseases were also excluded from the study. Finally, a history or imaging suggestive for gout and chondrocalcinosis (calcium pyrophosphate deposition disease) were also considered as exclusion criteria. All patients and NC gave written informed consent and approval from the ethics committee of our institution was obtained. The second imaging study was performed after 3.9 years (Mean ± SD: NC = 3.88 ± 0.38; non-EHOA patients = 3.96 ± 0.29; EHOA patients = 3.95 ± 0.33). Three subjects (1 normal control, 2 non erosive HOA patients) were lost to follow up: one refused to be re-evaluated and two moved away. None of the studied cases received corticosteroid treatment (oral, parenteral or intrarticular) for any reason during the follow-up period.

Radiographs

Posterior-anterior radiographs of both hands of the 32 subjects were obtained within a maximum of 3 weeks from the US examination and the radiological involvement of the single joints was graded according to the K&L and Kallman scoring systems[25–27]. We evaluated the 18 interphalangeal (IP) joints of each patient. Results of K&L and Kallman scores are given either per joint or per patient: the evaluated items in Kallman score were osteophytes (0–3), joint space narrowing (0–3), subchondral cysts (0–1), subchondral sclerosis (0–1), lateral bony deviation ($\geq 15^{\circ}$; 0–1), and cortical collapse (0–1). Score range: per joint K&L 0–4, Kallman 0–10. We evaluated the presence of bone erosions: central bone erosions (CE) characterized by the classic gull-wing and saw-tooth patterns and marginal bone erosions with cortical bone breaks localized between the edge of the articular cartilage and the joint capsule.

All the images were blinded for identifying data and time sequence; the radiological scoring was performed in random order by a rheumatologist (O.A.) with experience in hand radiological scoring. She evaluated all the X-ray films and DVDs, unaware of the US findings. The intra-reader variability was obtained on the re-examination of 15 randomly selected radiographs. The ICC values for intra-reader reliability for single joint K&L and Kallman scores were excellent: 0.99 (0.99–0.99) for K-L, and 0.91 (0.850–0.96) for the Kallman score.

Ultrasound (US) procedure

US joint examination was performed using light pressure and a large quantity of visible scanning gel between the transducer and the skin. Patients were in a comfortable position with their hands completely relaxed in order to avoid movement artifacts and with the finger joints in a neutral position, but extended and flexed as required for the visualization of pathology. We used the same model (Acuson Antares Siemens apparatus) and machine setting (11.4 MHz, 30 dB/DR60, MapE/VEOff, RS3/SCOff) for all patients and controls. Longitudinal and transverse US examination was performed on both hands on the volar and dorsal sides using a multifrequency linear transducer (VFX 13e5 MHz, 18 fps; TIS 1.2/TIB 1.2). Measurements were conducted to the depth of 20 mm. Power Doppler settings were standardized with a lower pulse repetition frequency (305 MHz) and a Doppler frequency of 8 MHz; wall filters were set at the lowest value (F1). Colour priority was maximized to evaluate vessels that were not visible on GS. We set the colour gain by turning up the Doppler gain until random noise was encountered and then it was lowered until the noise disappeared (3–4 dB). A total of 576 joints were examined: proximal interphalangeal (PIP) 1–5 and distal interphalangeal (DIP) 2–5 joints. Indicators of synovial inflammation were: 1) PDS, defined as a signal within a region of GS synovitis, was assessed as present/absent (since only a small minority of PDS positive joints score 2 plus and none 3 plus)[28] 2) synovial thickening - GS synovitis (present/absent), 3) joint effusion (present/absent) [using the Outcome Measures in Rheumatoid Arthritis Clinical Trials (OMERACT) definitions developed for RA][28]. Structural pathology was investigated by evaluating the presence of erosions (an intra-articular discontinuity of the bone surface that is visible in two perpendicular planes on imaging)[28]. Joints with ankylosis were excluded from US evaluation. US