DETECTION OF JOINT PATHOLOGY BY MAGNETIC RESONANCE IMAGING IN PATIENTS WITH EARLY RHEUMATOID ARTHRITIS

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SUMMARY

Magnetic resonance imaging (MRI) permits the visualization of anatomical structures not appreciated by conventional radiographic imaging, and may assess inflammatory disease and its progression with greater sensitivity than conventional radiography. In this study of 30 patients with early rheumatoid arthritis (RA), which could be considered as a pilot study because of the relatively small number of patients, we compare MRI of the knee and the fifth metatarsophalangeal joint with clinical and radiographic findings. A parallel study of 10 healthy individuals served as a reference group. In all but one of the 30 patients, MRI revealed some kind of joint abnormality, whereas conventional radiography was normal in 14 patients. The present study thus suggests that MRI may detect inflammatory and/or destructive joint changes in patients with early RA, and that these changes may occur in the absence of clinical symptoms or signs and/or radiographic signs in the examined joint. If these data prove to be confirmed in further controlled studies, MRI may be of importance both for the assessment of prognosis and for the decision to treat in the early critical stages of RA.

KEY WORDS: Rheumatoid arthritis, MRI, Synovitis, Knee, Foot.

RHEUMATOID arthritis (RA) is a disease of unknown aetiology characterized by an inflammatory synovitis and a potential to destroy bone and cartilage, leading to functional impairment and poor outcome. Recent data indicate that about half of the patients with RA seen in a clinical setting will run an unfavourable course [1]. Early institution of potent anti-inflammatory drugs in such patients might improve outcome [2, 3]. Bone erosions on plain radiographs of hands and feet are today the core criteria of a destructive disease course. At the time erosions are first seen, however, the disease is often quite established [2]. Thus, reliable indicators of outcome are needed earlier in the disease process. Magnetic resonance imaging (MRI) may be one such indicator since it is more sensitive than conventional radiographs in demonstrating joint effusion and pathology in synovial tissue, cartilage and bone [4–6]. After i.v. injection of gadolinium contrast medium, which enhances the synovial tissue, MRI can visualize and delineate this tissue from the surrounding tissues, and from joint effusion [7–11]. Against this background, we found it germane to investigate the potential of MRI for the detection of joint effusion, synovitis, and cartilage and bone destruction in patients with early RA. We report here some results of MRI in 30 patients with RA of recent onset. The patients are included in an ongoing, prospective, long-term, multicentre, observational study of early RA: ‘BARFOT’ [12].

PATIENTS

Thirty consecutive patients with RA according to the ACR criteria [13] having a disease duration of <1 yr were examined with MRI of the knee and the fifth metatarsophalangeal joint (MTP) on the dominant side, irrespective of any clinical symptoms or signs in these joints. In all 30 patients this was the right side. Disease onset was defined as the time of earliest joint symptoms or signs according to history at the initial visit. The patient material consists of 23 women and seven men with a mean age of 59 yr (range 24–80). The mean disease duration at the time of MRI was 8 months (range 2–14). The patients underwent a clinical evaluation including general physical examination and detailed musculoskeletal examination by an experienced rheumatologist.

METHODS

MRI was performed with 1.0 T MR equipment (Siemens Magnetom Impact) using a quadrature surface coil for extremities. The subjects were examined in a supine position. The knee joint was examined with the following pulse sequences: (a) sagittal T2-weighted (double echo) turbo spin echo (TR/TE 4200/15, 105 ms, echo train length 7, 252 × 256 matrix, 145 mm field of view, 3.0 mm slice thickness with 0.3 mm interslice gap); (b) coronal T2-weighted (double echo) turbo spin echo [identical parameters with sequence (a)]; (c) sagittal three-dimensional (3D) T2-weighted gradient echo DESS (Dual Echo Steady State) (TR/TE 30/9, 45 ms, flip angle 40°, 256 × 256 matrix, 160 mm field of view, 1.6 mm effective slice thickness); (d) sagittal T1-weighted spin echo (TR/TE 630/15 ms, 256 h × 256 matrix, 145 mm field of view, 3.0 mm slice thickness with 0.6 mm interslice gap); (e) transverse 2D FLASH (TR/TE 110/4 ms, flip angle 70°, 256 × 256 matrix, 250 mm field of view, 5.0 mm slice thickness with 4 mm interslice gap); (f) the contrast medium

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gadopentetate dimeglumine (Gd-DTPA) (Magnevist, Schering AG) was injected i.v. at a dose of 0.1 mmol/kg body weight and sequence (e) was repeated 10 times as a dynamic study with a total scan time of 10 min; (g) sequence (d) was repeated. Then the foot was examined (thus after contrast medium injection only) with the following pulse sequences: (a) sagittal 3D T2-weighted gradient echo DESS (TR/TE 30/9, 45 ms, flip angle 40°, 256 × 256 matrix, 160 mm field of view, 1.6 mm effective slice thickness without interslice gap); (b) transverse T2-weighted (double echo) turbo spin echo (TR/TE 4000/15, 105 ms, echo train length 7, 252 × 256 matrix, 160 mm field of view, 4.0 mm slice thickness with 6.0 mm interslice gap); (c) coronal T1-weighted spin echo (TR/TE 630/15 ms, 256 h × 256 matrix, 180 mm field of view, 3.0 mm slice thickness without interslice gap); (d) coronal T1-weighted spin echo with fat saturation (TR/TE 508/20 ms, 256 × 256 matrix, 140 mm field of view, 3.0 mm slice thickness without interslice gap). The transverse slices of the foot were oriented perpendicular to the metatarsal bones and the coronal slices were parallel with the metatarsal bones. Although the whole foot was imaged, the evaluation of the foot in this study included only the MTP 5 joint and the surrounding soft tissues.

Conventional radiographs (with FFD = 115 cm) of the knee in three different planes, weight bearing in the PA (posterior–anterior) projection, were obtained within 4 weeks from the MR examination, as were radiographs of the forefoot. All radiographs were read by one radiologist (one of the authors) and all MR examinations were evaluated by two radiologists (co-authors) who were blinded from all clinical information. The two radiologists reached a consensus for absence, presence, amount and localization of joint pathology. Joint pathology was graded using visual volume estimation of the effusion, synovitis, cartilage thinning and bone erosion according to a standardized protocol.

The extent of pathological change was graded as follows.

**MRI of the knee**

- **Effusion:** 0 = no or minimal amount of fluid; 1, 2, 3 = small, moderate, large amount of fluid.
- **Synovial thickening:** 0 = no or minimal volume of enhanced synovial tissue (less pronounced than the greatest amount observed in a reference group of 10 healthy individuals [14]); 1, 2, 3 = small, moderate, large volume of enhanced synovial tissue in the joint.
- **Cartilage thinning:** 0 = normal cartilage thickness; 1 = slight thinning (focal thinning <50%); 2 = moderate thinning (focal or general thinning ≥50%, but not total loss); 3 = pronounced thinning (general cartilage loss down to the bone). In each knee, this grading was made for five different portions (medial and lateral femoral surface, medial and lateral tibial surface, femoropatellar joint).
- **Bone erosion:** number and location of erosions.

**MRI of the forefoot**

- **Effusion and/or synovial thickening:** (not possible to separate as ~30 min have elapsed since contrast medium injection) 0 = no effusion or enhanced synovial tissue; 1, 2, 3 = small, moderate, large amount of effusion and/or synovial thickening.
- **Cartilage thinning:** 0 = cartilage was seen in joint space; 1 = no cartilage was seen.
- **Bone erosion:** number and location of erosions.

**Conventional radiography of the knee**

- **Cartilage thinning:** 0 = joint space ≥3 mm on weight-bearing film; 1, 2, 3 = slight, moderate, pronounced joint space reduction.
- **Bone erosion:** number and location of erosions.

**Conventional radiography of the forefoot**

- **Cartilage thinning:** 0 = normal joint space; 1 = all degrees of joint space reduction.
- **Bone erosion:** number and location of erosions.

**Clinical assessments**

The presence of clinical synovitis was based on patient history (symptoms) and clinical examination (signs), and defined as follows.

- **Knee joint symptoms:** experienced swelling and pain for ≥6 weeks. **Signs:** joint swelling and pain on motion and/or established inflammatory joint fluid.
- **MTP 5 joint symptoms:** experienced pain on load or tenderness and swelling for ≥6 weeks. **Signs:** swelling and pain on motion.

**RESULTS**

In all but one of the 30 patients, MRI revealed some kind of joint abnormality (Table 1).

- Synovial thickening grade 1–3 was detected in 20 knees. The extent of pathological changes was scored grade 1 in 10 (Fig. 1), grade 2 in eight (Fig. 2) and grade 3 in two patients (Fig. 3).
- Effusion was present in 14 knee joints. The effusion was scored as grade 1 in 11 and grade 2 in three patients. Baker cysts were noted in four cases. In the MTP 5, 10 patients had a synovial thickening and/or effusion grade 1 and seven had grade 2.
- Cartilage thinning of the knee was seen in 16 patients and in the MTP 5 in one patient. (For patients 1, 26, 27 and 30, the change is in the femoropatellar joint; Table 1.) Cartilage thinning was scored as grade 1 in six knees and grade 2 in 10 knees.
- Bone erosions were found in the knee in six patients (totally 18 erosions) and in the MTP 5 in 13 (totally 17 erosions). Marginal erosions were observed more often in the tibia than in the femur. The erosions in MTP 5 were all in the metatarsal bone.
- The menisci, cruciate and collateral ligaments were not evaluated.

Most MRI findings were not detected by physical examination or conventional radiographic imaging. Eighteen patients had experienced symptoms from the knee and 16 from the MTP 5; nine patients had had symptoms from both knee and MTP 5. On physical
TABLE 1
Pathological changes in MRI and conventional radiography compared with the symptoms and signs, as defined in Methods, from the knee and MTP 5 of 30 patients with early RA

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0, absence of pathology; +, pathology. 1, 2 and 3 represent the scoring of the volume of enhanced synovial tissue, where 3 denotes the largest volume.

examination of the joints under investigation, swelling of the knee joint was observed in seven patients and tenderness was noted in eight MTP 5s.

The conventional radiographs of the knees showed cartilage thinning in five cases, and two erosions were detected. Radiographs of the MTP 5 showed cartilage thinning in two cases and erosions in 13.

The dynamic MR images of the knee obtained during 10 min after contrast injection will be evaluated later and are not included here. The delineation of effusion from the enhanced synovial tissue was not more difficult on images obtained 10 min after contrast injection than on those obtained during the first minute after injection.

DISCUSSION

In this study of the knee and MTP 5 in 30 patients with early RA, which could be considered as a pilot study because of the relatively small number of patients, MRI appears to be more sensitive than clinical examination and conventional radiographic investigation in identifying joint abnormalities. Thus, clinical and radiographic examinations of our patients frequently failed to detect ongoing joint inflammation which could be demonstrated by MRI. Similar findings have previously been shown in two studies of knee arthritis, including RA [4, 9]—one concerning 17 patients with juvenile RA (JRA), RA, ankylosing spondylitis and monoarticular arthritis, and the other 24 patients with JRA. In the second study, contrast medium was added. Both studies showed that MRI was associated with clinically important abnormalities not detected by physical or conventional radiographic examinations, including proliferative synovitis, joint effusion, cartilage thinning and bone erosions. It is to be noted that all our patients had a disease duration shorter than 14 months, when MRI was performed, whereas the patients in previous studies on RA had longer disease duration.

Enhanced synovial tissue on MRI of the knee has been shown to represent synovitis in synovial biopsy obtained at arthrothomy [11, 15, 16]. Accordingly, we have found evidence of knee synovitis on MRI in 20 of our patients, although most of them only had subtle clinical symptoms. On the other hand, three patients lacking MRI changes complained of pain in the knee for >6 weeks. However, clinical examination did not verify this.
The striking difference in the ability to detect joint bone and cartilage destruction between MRI and conventional radiography in our study was most pronounced in the knee where only six patients had abnormalities on conventional radiography compared with 17 on MRI (Table I). Since cartilage thinning is an unspecific finding, it may be caused by osteoarthritis instead of RA in some of our patients who all had early RA. The bone erosions had, however, a typical appearance of RA lesions. The inability of conventional radiography to detect early knee joint lesions in RA may have created a partly false picture of the predilection sites for RA. In the MTP 5 joints, clinical evidence of synovitis and radiological signs of bone and/or cartilage destruction were more consistent with the MRI findings (Table I), possibly reflecting more advanced disease in these joints.

In several previous MRI studies [7, 10, 11, 16–18], a small number of apparently healthy subjects have undergone MRI of the knee after i.v. contrast injection. In these knees, no or minimal enhancement of the synovial tissue was seen after contrast injection. Our patients with synovial thickening grade 0 included a few patients with a minimal volume of enhanced tissue. They were scored as grade 0 because the changes were less pronounced than those observed in a contrast-enhanced MRI study of the knee of 10 healthy individuals [14]. It would have been preferable to
include healthy controls in the present study. However, the above-mentioned study of 10 healthy individuals [14] was performed parallel with the present study with all pulse sequence parameters identical for T1-weighted images before and after contrast injection, in order to make comparison possible. Images from the asymptomatic individuals in the study were used as reference images when the cases in the present study were evaluated. In addition to the data of others [7–11], this study demonstrates that also in early RA (Fig. 2) Gd-enhanced MRI allows differentiation between synovitis and effusion as well as between normal and inflamed synovial tissue. Hence, MRI seems to be a suitable method for the early detection of inflammation of the synovial membrane. This may turn out to be a proper instrument for treatment decisions and treatment evaluations.

Although the sagittal T1-weighted post-contrast images were obtained 10 min after contrast injection, we did not find it difficult to delineate the enhancing synovial tissue from the effusion. In one study [8], no change in signal intensity of the joint effusion was visually observed on images obtained 15 min after contrast injection compared with immediate post-injection images. Another study showed 1.46-fold enhancement of synovial fluid after 10 min due to diffusion of contrast medium into the joint space [19]. This is probably not enough to impair the evaluation of the synovitis.

In conclusion, the present study suggests that MRI may detect inflammatory and destructive joint changes in patients with early RA and that these changes may occur in the absence of clinical symptoms and/or radiographic signs in the examined joints. If these data prove to be confirmed in further controlled studies, MRI may provide information about joint inflammation and joint integrity in early RA of importance both for the assessment of prognosis and for the decision to treat in the early critical stages of the disease. This study is the first part of a prospective study with planned follow-up examinations after 1 and 3 yr. They will hopefully give some answers regarding the ability of this technique to detect changes in patients with progressive disease.

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