

Letters to the Editor

High-resolution magnetic resonance imaging of knee inflammatory arthritis in mice

Sirs,

We report MRI changes related to joint inflammation and degradation in mice with collagen-induced arthritis (CIA), a reliable model of rheumatoid arthritis (1). Sophisticated approaches have been developed to evaluate joint disease and advances have been made recently in the radiographic imaging of small animals. Magnetic resonance imaging (MRI), in particular, has shown promise for monitoring arthritic disease in animal models, as it noninvasively generates three-dimensional images that can be obtained repeatedly over time to visualize and quantify changes in soft tissue and in bone. Studies in various experimental models (2, 3) have determined the appearance of normal hyaline cartilage and of cartilage lesions produced by osteoarthritis in these animals (4). In arthritic rat knee, MRI has been used to investigate changes produced by inflammation (5) and to evaluate the effect of the treatment (6).

We performed MRI of the knee in four DBA/1 anaesthetized mice with CIA (1) and in seven normal controls mice. We use a Bruker DRX300 spectrometer (vertical bore, 7 tesla) equipped with a mini-imaging accessory.

On T1-weighted sagittal images (TR/TE 500/10) of the normal knee (Fig 1A), the cortical bone and ligaments generated low signal, the periarticular tissue intermediate signal, and the subcutaneous and fatty tissue high signal. Midline sagittal images showed the patellar ligament connecting the patella to the tibia in a straight line. Hoffa's ligament was seen as an anterior triangular fatty zone generating a high signal just behind the patellar ligament. In arthritic mice, the fatty zone was absent or smaller and heterogeneous on T1-weighted images (Fig. 1B). On T2-weighted sagittal images (TR/TE 2000/50), an area of high signal was seen anteriorly behind the ligaments, around the distal femur and posteriorly, denoting joint capsule distension and accumulation of synovial fluid (Fig. 1D). These areas of high signal on T2-weighted images were absent in the normal mice (Fig. 1C). To visualize synovial proliferation, we acquired images after an injection of gadoterate meglumine (Gd-DOTA). In normal mice, the injection was followed by moderate signal enhancement (Figs. 1E and 1F) corresponding to the normal synovial membrane. In the arthritic mice figure, Gd-DOTA injection produced marked enhancement of the synovial membrane (Figs. 1H and 1I) but also in the suprapatellar bursa and posteriorly in comparison with non-injected arthritic mice (Fig. 1G). Images acquired early (10 min) (Fig. 1H) and late

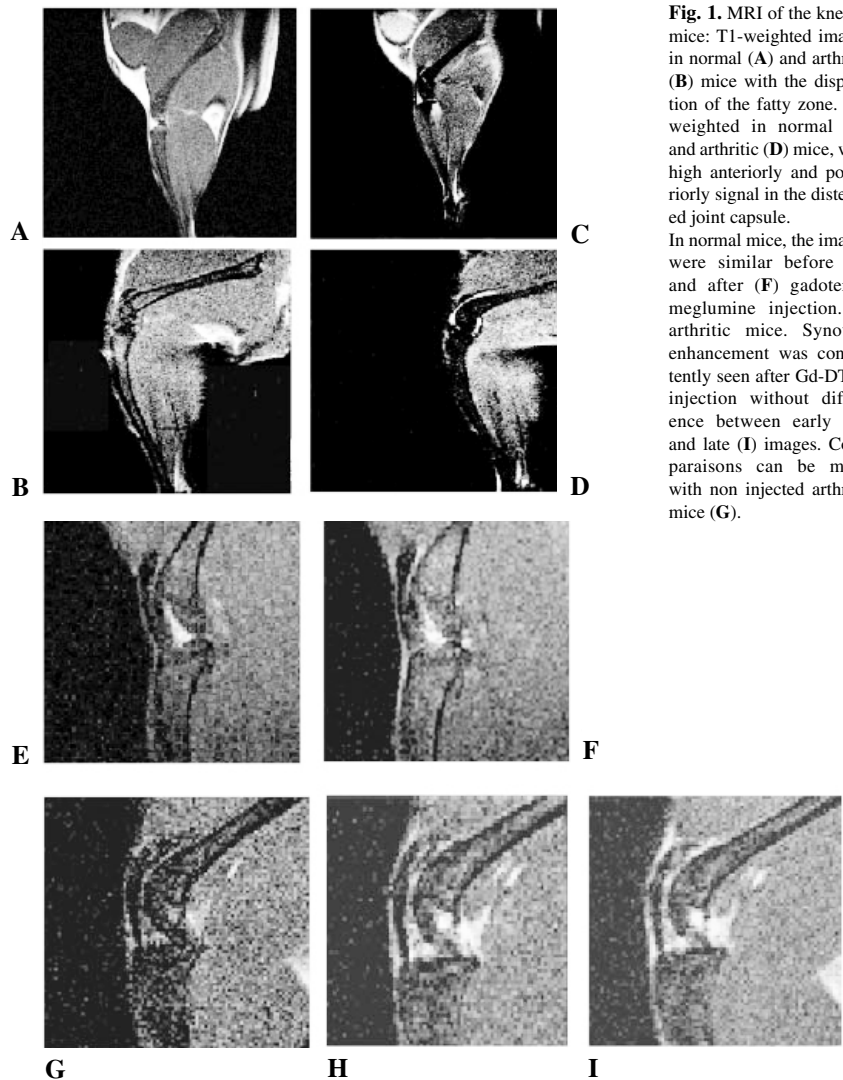


Fig. 1. MRI of the knee in mice: T1-weighted images in normal (A) and arthritic (B) mice with the disparition of the fatty zone. T2-weighted in normal (C) and arthritic (D) mice, with high anteriorly and posteriorly signal in the distended joint capsule. In normal mice, the images were similar before (E) and after (F) gadoterate meglumine injection. In arthritic mice. Synovial enhancement was consistently seen after Gd-DTPA injection without difference between early (H) and late (I) images. Comparisons can be made with non injected arthritic mice (G).

(45 min) (Fig. 1 I) after the Gd-DOTA injection were similar, so that we could not distinguish between synovial proliferation and synovial fluid.

The images presented in this report illustrate this ability of MRI to supply an accurate evaluation of changes in soft tissue and bone in arthritic joints of mice studied *in vivo*. In the only previously reported study of MRI in arthritic mice, ultrasmall supermagnetic iron particles were used to obtain quantitative information on joint inflammation (7). In arthritic rat knees (10 times greater in size than mouse knees), MRI was effective in detecting and grading the severity of chronic synovitis and progressive joints destruction (8). Bone destruction and cartilage damage have never been studied in arthritic mice. In STR/ORT mice, a model of osteoarthritis, MRI was effective in evaluating focal cartilage erosion and subchondral sclerosis (9) with more information than did radiography (10). In our study, MRI failed to provide good images of cartilage damage (not shown). The MRI system had mid-range field strength and

limited capabilities, which required the use of suboptimal protocols and provided images with limited temporal and spatial resolution.

MRI has emerged as a valuable non-invasive research tool that provides detailed information on soft tissue and bone changes in arthritic joints. However, further work is needed to improve image resolution.

N. SAIDENBERG-KERMANAC'H, MD¹
F. LECLERCQ, PhD²
J. HERSCOVICI, PhD³
D. SCHERMAN, PhD³
M.C. BOISSIER, MD, PhD¹

¹INSERM ERI 18 and Department of Rheumatology, Avicenne Hospital (AP-HP) and University of Paris 13, Bobigny, France; ²UMR 7001 CNRS/ENSCP/Aventis, Paris, France; ³U640 INSERM UMR 8151 CNRS-Université Paris 5-ENSCP Paris, France.

Correspondence and reprint requests to: M.C. Boissier, Service de Rhumatologie, Hôpital Avicenne, 125 route de Stalingrad, 93009 Bobigny Cedex, France.
E-mail: marie-christophe.boissier@avc.ap-hop-paris.fr

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Priapism related to an antiphospholipid syndrome in a patient with systemic lupus erythematosus

Sirs,

Priapism is persistent penile erection not associated with sexual stimuli. Its pathophysiology remains unclear but is partially related to venous outflow occlusion, unregulated overflow into the penis and autonomic dysregulation (1). Antiphospholipid syndrome (APS) is defined as the association of a thrombotic event and the presence of an antiphospholipid antibody. Priapism has never been reported as a clinical manifestation of APS. The case we reported occurred after the withdrawal of antivitamin K treatment from a patient with a history of

APS secondary to systemic lupus erythematosus (SLE).

A 39 year-old man was admitted on the first of February 2004 for priapism. Since 1991, he had suffered SLE, diagnosed in the presence of auto-immune hemolytic anemia associated with auto-immune thrombocytopenia. In 1996, he developed a right kidney infarction related to a lupus anticoagulant and antivitamin K treatment was started. In 2003, the patient presented with a nephrotic syndrome related to an extramembranous glomerulonephritis. Treatment with azathioprin (100mg/dj) and prednisolone 1mg/kg was associated with his previous treatment (hydroxychloroquine, candesartan-cilexetil, acenocoumarol). The treatment stabilized proteinuria at between 2 and 3g/day, albuminemia at around 22 g/L, creatininemia at between 75 and 95 µmol/L.

On the first of February 2004 at noon, the patient presented with priapism in the Urology department. INR was 1. The medical treatment (intracorporal injection of 5mg of Ephedrin, renewed) was ineffective and the patient therefore underwent surgery at 2 pm. These surgical procedures were also ineffective and detumescence was finally obtained by bilateral cavernous spongiosal shunting. Ten hours after, penile erection reoccured. Arterial blood was extracted manually but detumescence was not achieved. The patient was discharged on day 8 with a persistent painless semi-penile erection treated with cyproterone acetate and prolonged antivitamin K therapy (INR > 3). One month later, recovery was complete, detumescence persisted and fibrosis of corpora cavernosa was developed, INR was 2.54. In September 2005, lupus was still quiet, hemoglobinemia was 12.7 g/dl, platelet count 283000/ml and creatininemia 92 µmol/l. Proteinuria varied between 1 and 1.25 g/24 hours, and the INR was 2.7.

This is the first case report of priapism related to an antiphospholipid syndrome in a SLE patient. There are many possible causes of priapism (1). The most common are medications. Other common causes are pelvic tumors (including prostate adenoma), spinal cord damages, pelvic arterial-venous shunt, hematological disorders for example polyglobulia, thrombocytopenia or venous thromboembolism. Some causes are less common : toxic causes (marijuana, cocaine, alcohol), amyloid, intravenous hyperlipidic nutrition and Fabry disease. The occurrence of priapism in systemic diseases is exceptional, but has nevertheless been reported during Behçet disease (2), Henoch-Schönlein purpura (3), Crohn's disease and ulcerative colitis (4) and Kawasaki disease (5). The only case reported in a SLE patient was described during a nephrotic syndrome associated with SLE in a 29 year-old patient (6). During nephrotic

syndrome, the risk of developing venous thrombosis is elevated and inversely related to the antithrombin III level (antithrombin III is excessively cleared by the kidney) (7). In our case, the nephrotic syndrome was moderate when the priapism started (proteinuria 2.64 g/24 hours and albuminemia 25 g/l), and there was an evident relationship between the withdrawal of antivitamin K treatment 2 days before, the normalisation of INR and the occurrence of a priapism related to a thrombosis of cavernous spongiosal. APS usually requires an INR above 3 to avoid recurrences (8) and some authors (9) proposed to target INR between 2.5 and 3 in APS patients without other risk factors for thrombosis.

In conclusion, our observation adds a new clinical manifestation to APS, and suggests that cases of unexplained priapism should be tested for APS.

H. GIL¹,
N. MAGY¹,
F. KLEINCLAUSS²,
N. MEAUX-RUAULT¹,
H. BITTARD²,
J.L. DUPOND¹

¹Department of Internal Medicine,

²Department of Urology, Jean Minjot Hospital, Besançon, France.

Please address correspondence and reprint requests to: Helder Gil, MD, Service de Médecine interne, niveau +1, CHU Jean Minjot, 25030, Besançon, France.
E-mail : hgil@chu-besancon.fr

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