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ARTICLE

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Magnetic resonance imaging in coccidioidal arthritis

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Abstract *Objective.* The authors assessed the MRI findings of appendicular coccidioidal arthritis.
Design. T1- and T2-weighted MR images of affected joints, both with and without intravenous gadopentetate dimeglumine, were performed in nine adult patients (ten studies) and evaluated by three masted readers, using a four-point certainty scale for: synovial abnormality, articular cartilage loss, subarticular bone loss, abnormal marrow signal, enhancement of osseous and articular structures, and assessment of disease activity. Findings were correlated with biopsy results or clinical course.
Results. Eight patients had active and one had inactive arthritis, involving the knee (five patients), ankle (two patients), and elbow (one patient). Synovial complex was the most common finding in active arthritis ($P<0.025$). Cartilage and subarticular bone loss were seen 56% and 89% of patients with active disease, respectively. Abnormal marrow signal was uncommon (two patients). All cases showed synovial and/or osseus enhancement.
Conclusions. MRI findings in coccidiodal arthritis are described. Enhancement of thickened synovium and erosions was seen after intravenous gadopentetate.

Key words Coccidioidomycosis · Arthritis · MRI

Introduction

Coccidioidomycosis (CM) is a systemic fungal infection caused by coccidicides immitis endemic to the southwestern United States and other parts of the western hemisphere. The high rate of infectivity and increasing travel to endemic areas have brought CM to non-endemic regions. CM is primarily a pulmonary disease and extrapulmonary manifestations occur in less than 1% of infections [1]. When dissemination occurs, bone and joint involvement is common, ranging from 10% to 50% in previous studies [2–5]. Early diagnosis is important as disseminated infections are associated with high morbidity, and intervention may be life-saving. Previous imaging literature has described the radiographic findings of CM arthritis [4, 6, 7]. MRI with intravenous gadopentetate dimeglumine (Gd) has been described in rheumatoid synovitis [8], but to our knowledge this technique has not been applied to the evaluation of coccidioidal arthritis.

The purposes of this study were to evaluate the MR appearance and describe the patterns of Gd enhancement in coccidioidal arthritis.

Subjects and methods

Ten MR studies of peripheral joints were performed in nine nonconsecutive patients (eight men, one woman), ranging in age from 26 to 82 years (mean 45 years), referred from the infectious disease service between January 1990 and December 1993 at the University Medical Center and Veterans Administration Medical Center, Tucson, Arizona. Eight patients had symptoms of joint pain or swelling and one patient was asymptomatic. All patients had a known history of coccidioidal arthritis. The study was approved by the Institutional Review Board. Six patients were Caucasian and four were non-Caucasian (two African-American, one Hispanic, one Native American). White blood cell count (WBC), Westergren erythrocyte sedimentation rate (ESR) and complement fixation (CF) titers were obtained. Definitive diagnosis of active coccidioidal arthritis had been established by isolating the fungus or identifying spherules from the aspirate or biopsy of the affected

joint. In seven patients, positive aspirate cultures (n=3) or surgical specimens (n=4) of the symptomatic joints were confirmed between 3 months prior to and 10 months after MRI. One patient was presumed to have active disease based on clinical findings and positive aspirate from another joint. One patient who had active arthritis in the past and became symptom free and had normal WBC, ESR and decreasing CF titers was considered to have inactive disease.

MR studies were performed with 0.5-T or 1.5-T (GE Signa, Milwaukee, Wis.), 0.5-T (Toshiba, Japan) or 1.0-T (Picker Vista, Highland Heights, Ohio) machines. T1- and T2-weighted MR images (T1WI/T2WI) of the symptomatic peripheral joint in at least two planes were obtained in all patients. Ten intravenous Gd-enhanced sequences (0.1 mmol of Gd per kilogram of body weight) were obtained. Pre-contrast imaging sequences included five T1WI with fat presaturation, three T1WI without fat presaturation, and two gradient echo sequences (flip angle 15°–30°) with fat presaturation. Imaging planes for the post-Gd sequences were chosen after reviewing the standard MR and most recent radiographs for the location of osseous, synovial, or soft tissue abnormalities. The images were obtained using 4 mm slice thickness, 256×192 matrix, and 18–20 cm fields of view. One patients had a follow-up study performed 11 months after the initial MRI.

Each study was read by three radiologists experienced in musculoskeletal MRI and blinded to the disease activity. A four-point certainty scale (1=definitely not present, 4=definitely present) was assigned to: synovial abnormality (effusion, mass or thickening) articular cartilage loss, subchondral bone loss, bone marrow abnormality, enhancement of synovial and osseous structures, and overall impression of presence or absence of active coccidioidal arthritis. Log-odds ratio and linear regression were employed to compare findings.

Results

Eight patients had active disease on the basis of synovial biopsy or arthrocentesis, and one asymptomatic patient with normal CF titers and clinical evaluation was presumed to have inactive arthritis. WBC counts were normal in all patients. CF titers were abnormally elevated in six of the eight patients who had active disease. Of the two patients with normal serology, one had human immunodeficiency virus and one had been on fluconazole for 3 years prior to the MR study. Prior coccidioidal pneumonia had been diagnosed radiographically in four patients and cutaneous CM nodules were found in two. The primary site of infection was not identified in four (44%). The knee was the most common joint involved (67%). One patient had involvement of two joints.

Synovial abnormality was the most common finding, and was present in all cases with active disease (Fig. 1). The only patient without a synovial abnormality had inactive disease clinically at the time of study but had had a positive knee aspirate culture for coccidioidal synovitis 2 years previously. This patient also had a minimally enhancing mixed signal synovial mass without cartilaginous or osseous abnormality. Articular cartilage loss was seen in five (56%) patients and subchondral bone loss or erosion in eight (89%) patients with active disease. Diffuse or regional abnormal marrow signal (non-subarticular) was seen in only two patients. Eight patients (one with inactive disease) showed synovial enhancement and two patients with active disease showed subarticular osseous enhancement. Non-subarticular marrow enhancement was not observed. In the patient who had an 11-month follow-up MRI, no significant differences in MRI findings or assessment of disease activity were seen.

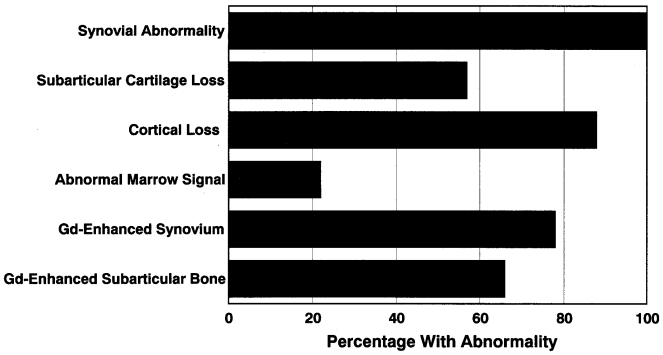

Fig. 1 MR abnormalities in active coccidioidal arthritis

Discussion

At least three risk factors have been identified for disseminated CM: (1) race (Filipinos, African-Americans, Native Americans, Hispanics>European descendants) [6], (2) gender (men>women), and (3) immunosuppression, particularly T-cell deficiencies, acquired immunodeficiency syndrome (AIDS), and organ transplant [9]. In our series, four of nine patients were African-American, Hispanic or Native American. Also, the mean age (45 years), male/female ratio (8:1) and immunosuppression prevalence in our study correlate with previous literature [10]. Similar to previous studies, four (44%) patients had clinical or radiographic evidence of primary coccidioidal pneumonia [9, 11].

Coccidioidal arthritis has a predilection for large weight-bearing joints. The knee is most commonly affected in other reports and involved 66% in our series [6]. A hypersensitivity syndrome consisting of polyserositis, and sterile, often migratory benign polyarthritis termed ‘‘desert rheumatism’’ has been reported, but was not encountered in this series [10]. The more chronic progressive joint involvement is almost always the result of hematogenous spread from an initial pulmonary infection. Bone and joint dissemination are frequent, second only to skin involvement [12]. Two sites of involvement were seen in only one of nine patients, whereas previous studies have reported multiple skeletal lesions in 45–64% of cases [10, 12]. Less frequent involvement of multiple sites may relate to increased awareness, earlier diagnosis and treatment, or the limited number of immunosuppressed patients in our series.

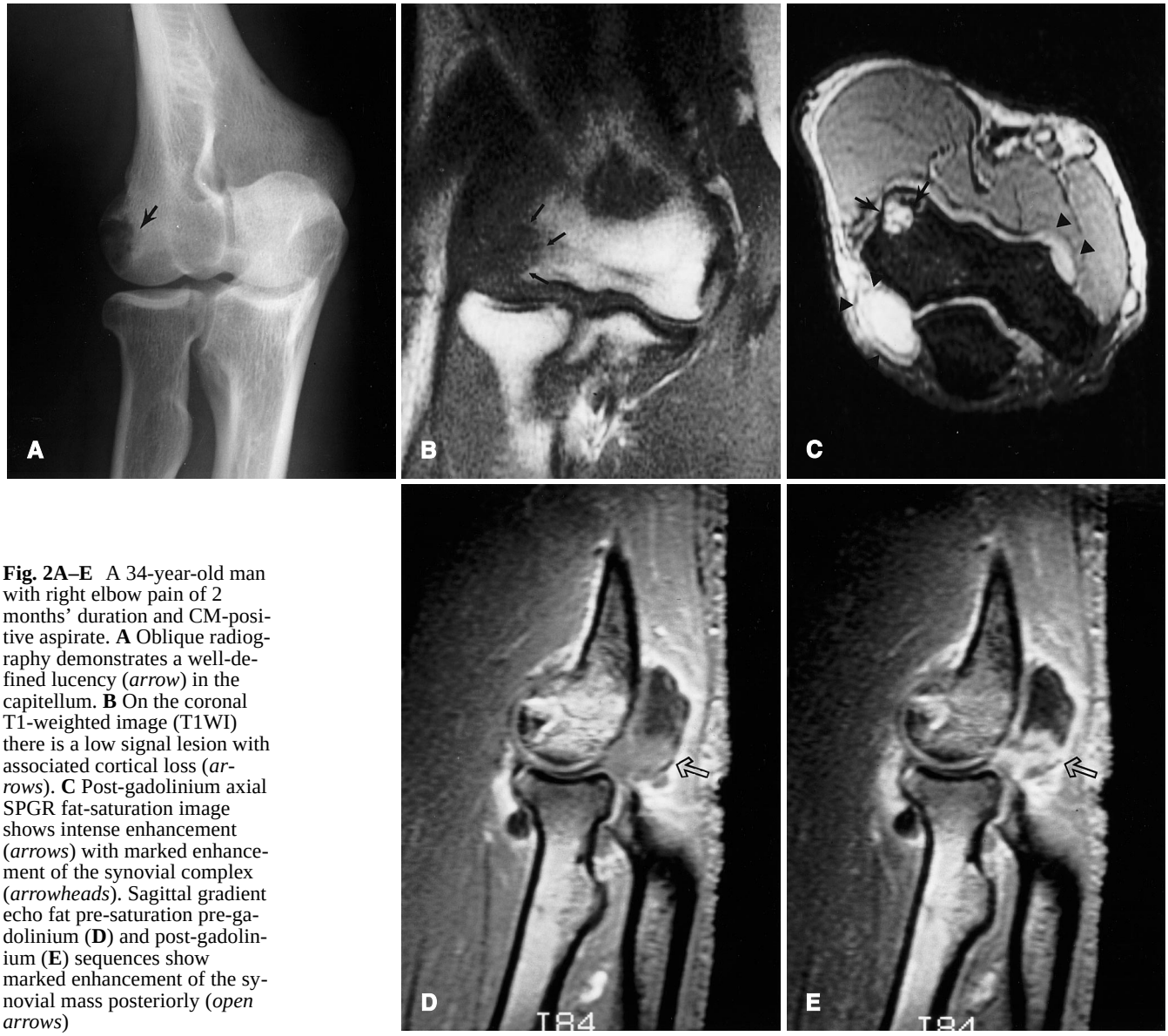

Fig. 2A–E A 34-year-old man with right elbow pain of 2 months' duration and CM-positive aspirate. **A** Oblique radiography demonstrates a well-defined lucency (*arrow*) in the capitellum. **B** On the coronal T1-weighted image (T1WI) there is a low signal lesion with associated cortical loss (*arrows*). **C** Post-gadolinium axial SPGR fat-saturation image shows intense enhancement (*arrows*) with marked enhancement of the synovial complex (*arrowheads*). Sagittal gradient echo fat pre-saturation pre-gadolinium (**D**) and post-gadolinium (**E**) sequences show marked enhancement of the synovial mass posteriorly (*open arrows*)

In keeping with proposed mechanisms of articular disease progression in granulomatous infections, bony involvement adjacent to involved joints showed a marginal predilection, although in more advanced disease subchondral bone was also destroyed (Fig. 2). Imaging findings in coccidioidal arthritis are nonspecific and may be purely synovial or synovial with subarticular destruction and osseous extension. Histologically, villonodular granulomatous synovitis is typical, and probably corresponds to the enhancing articular abnormalities (Fig. 3). Tuberculosis, chronic bacterial infection and other fungal infection may produce similar patterns of involvement. Noninfectious inflammatory arthropathies such as rheumatoid arthritis and seronegative spondyloarthropathies could produce similar findings, although we found that erosions and synovial abnormalities are typically larger and more focal in coccidioidal arthritis. Dialysis-related amyloid arthropathy and pigmented villonodular synovitis (PVNS) may produce focal, large erosions and synovial masses, but can sometimes be distinguished by the characteristic signal patterns of synovial abnormalities in these entities [13, 14].

Synovial abnormality was the most common finding in active disease (Fig. 1). Intravenous Gd has been useful in evaluating pannus formation in active rheumatoid arthritis in humans [8] and animal models [15, 16]. Synovial enhancement was present in eight cases with associated subadjacent osseous enhancement in two others.

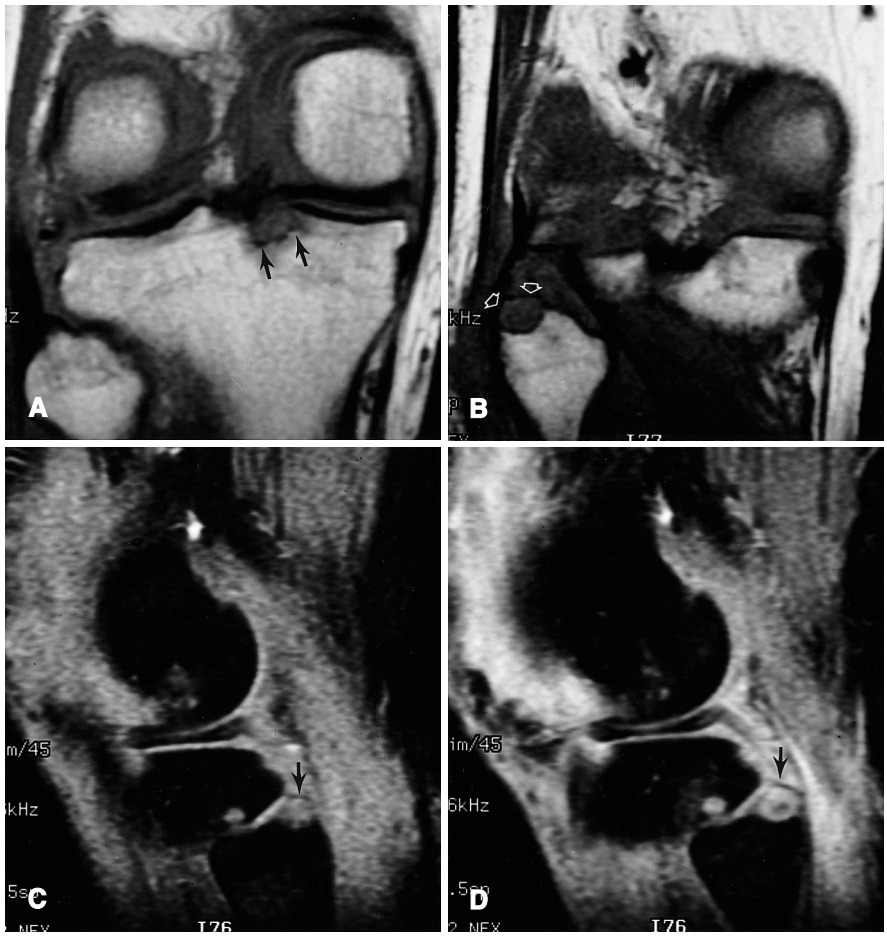

Fig. 3A, B A 35-year-old man with knee pain of 20 months' duration and CM-positive aspirate. **A, B** Coronal T1WI show intermediate signal intensity articular and periarticular erosions at the medial tibial eminence (*arrows*) and proximal fibula (*open arrows*). Pre-gadolinium (**C**) and post-gadolinium (**D**) sagittal gradient echo images show fibular and small tibial erosions which demonstrate enhancement (*arrows*). Also note the extensive synovial enhancement within the joint and suprapatellar recess

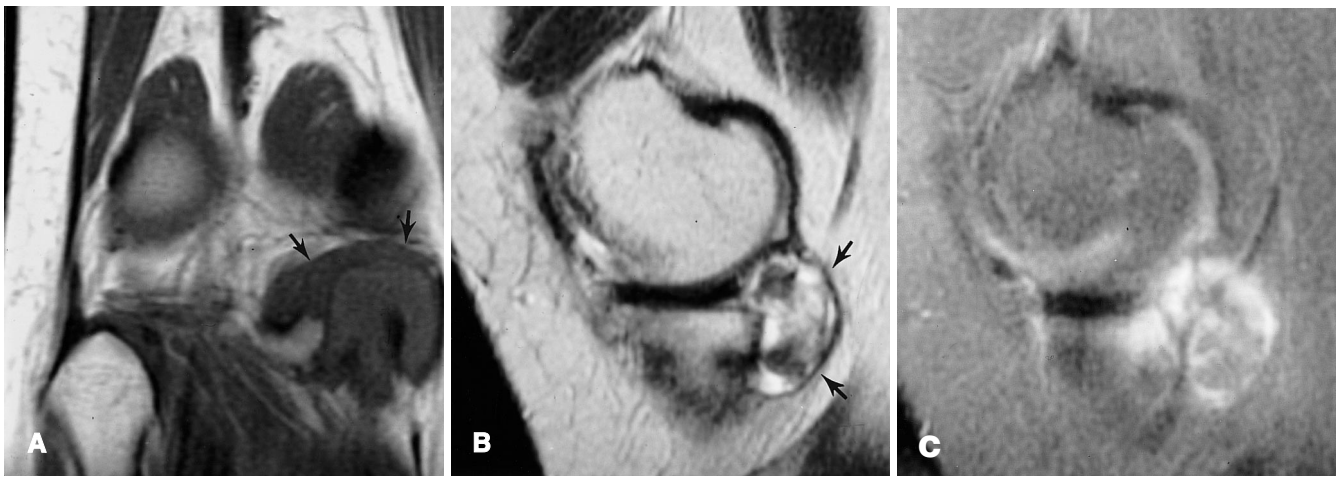

Fig. 4A–C A 26-year-old asymptomatic woman with treated coccidioidal arthritis. **A** Coronal T1WI shows an intermediate signal mass (*arrows*) in the medial posterior aspect of the knee. **B** The mass (*arrows*) has mixed signal on sagittal T2WI. **C** Enhanced sagittal T1WI with fat pre-saturation shows mild peripheral enhancement in this patient with clinically inactive disease

One patient, who had inactive disease clinically and no effusion, had a synovial-based mass with mild peripheral enhancement that may represent post-inflammatory fibrous tissue (Fig. 4). The location and pattern of synovial enhancement or the presence of an articular mass might be further investigated as a guide to synovial biopsy or synovectomy. Abnormal marrow signal seen in two patients with active disease was most probably secondary to hyperemia and edema rather than osteomyelitis. No focal periosteal collection or diffuse marrow enhancement was seen. The subarticular abnormalities probably denote osseous extension of the articular infection rather than hematogenous osteomyelitis. Hematogenous dissemination (primary) and articular extension of osteomyelitis (secondary) have been proposed as distinct mechanisms for articular involvement in coccidioidomycosis [6], although we did not find clinical or imaging patterns of disease to support the secondary hypothesis and believe that the arthritis in our series is most likely directly hematogenous in origin.

The limitations of the study include the small sample size, absence of a control population and only one patient with proven inactive disease. While Arizona is a highly endemic region for coccidioidomycosis, appendicular (nonspinal) arthritis remains relatively uncommon. Most patients are appropriately diagnosed and treated on the basis of clinical or arthrocentesis findings and are only referred for MRI when recurrent or recalcitrant disease is suspected. That we had only one patient with clinically inactive disease underscores this phenomenon and is in keeping with the typical course of the disease, which is at best mildly and slowly progressive with few exacerbations, and at worst rapidly progressive and destructive. The stability of MR findings over 11 months in a clinically active patient despite antifungal therapy further emphasizes the chronic nature of this infection. Most current treatment methods employ antifungal agents as primary treatment, reserving synovectomy for select, unresponsive cases. While no control population without symptoms of inflammatory arthritis was imaged, previous authors have described synovial enhancement patterns in normal volunteers [17].

Technical MRI variables (i.e., different field strengths and manufacturers) may have influenced our findings, although the majority of studies were performed on the 1.5-T system and equivalent parameters were used on the other systems. Sequence protocol differences among patients is a limitation although the low prevalence of disease necessitated a long study course. In all patients, sequences designed to optimize visualization of articular abnormalities and enhancement patterns (using fat saturation when available) while maintaining spatial resolution were employed.

Synovial, cartilaginous and osseous abnormalities in patients with coccidioidal arthrtis can be identified with MRI. Synovial abnormality was the most common finding in active disease. Synovial or osseous Gd enhancement was seen in all patients and intravenous Gd did not increase the specificity of the findings, although further studies addressing different enhancement patterns may yield more specific results. Prospective correlation of MR findings with specific biopsy sites is necessary to assess accurately the predictive value of individual findings.

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