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The "birth of death": MRI step-by-step reveals the early appearance of a bone marrow infarct

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Abstract

The magnetic resonance imaging (MRI) appearance of an "established" bone marrow infarct is well-known, consisting of an area of preserved bone marrow signal surrounded by a serpiginous line. We report the uncommon observation of the very early phases of appearance of a bone marrow infarct, showing its progressive de novo appearance on MR images paralleling clinical symptoms and high-dose systemic steroid administration in a young female patient, presenting with acute knee pain. The initial knee MR examination performed one week after pain onset showed no abnormality. One week later, a second examination showed subtle ill-defined dotted signal abnormalities of the bone marrow of uncertain significance, of high signal on PDFS sequences. A third MR study obtained again one week later showed more evident findings with confluence of the high signal "dots" into a serpiginous line with a geographical appearance of the lesion, corresponding to the typical MRI presentation of bone marrow infarcts. Follow-up MRI at seven weeks showed definitive stability of this bone marrow infarct. A whole-body MRI performed for whole skeleton screening revealed multiple bone marrow infarcts typical for systemic avascular necrosis. This case represents a novel observation of the "birth" of a bone marrow infarct, from early intriguing changes to its typical ring-shaped appearance on MR images. It also reminds of the key role of MRI for early diagnosis of bone marrow infarcts and illustrates the emerging role of whole-body MRI for the detection of multifocal, asymptomatic skeletal involvement by ischemic lesions in systemic osteonecrosis.

Keywords

Bone marrow, infarcts, magnetic resonance imaging, MRI, knee, corticosteroids

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Introduction

Osteonecrosis (ON) results from loss or reduction in the blood supply to the bone. The femoral head, femoral and tibial metaphysis or diaphysis, the distal femur and proximal tibia, and the talus and scaphoid are all common sites of ON. In medical practice, the term "avascular necrosis" is applied when the subchondral bone of an epiphysis is affected, presenting a risk of subsequent collapse, and "bone infarct" is used for diaphyseal or metaphyseal involvement (1). Although ON may be "idiopathic," it is usually associated with known causative or predisposing conditions, such as trauma, corticosteroid intake, and alcohol abuse. Magnetic resonance imaging (MRI) is the most sensitive and specific imaging modality for identification of ON, outperforming radiographs and computed tomography (CT), and allowing early diagnosis and treatment (2–6).

The MRI appearance of bone marrow infarcts has been described for more than three decades (7). It typically consists in areas of preserved marrow signal surrounded by a ring-shaped, serpentine, or serpiginous

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border of low signal intensity on T1-weighted (T1W) MR images, and variable signal intensity (sometimes a double line appearance) on T2-weighted (T2W) images (8). These features are characteristic of "established" bone marrow infarcts. Previous or early phases of the lesions are poorly known.

This case report illustrates the step-by-step early appearance of a bone marrow infarct at MRI and its evolution to the known typical appearance.

Case report

A 25-year-old woman, with a three-year history of high-dose systemic corticosteroid therapy for connective tissue disease, was referred by the rheumatologist for the work-up of acute severe left knee pain. Her medical history included Raynaud's disease, perionyxis, myositis, pulmonary hypertension, two episodes of pericarditis, and positive anti-nuclear antibodies: anti-RNP (anti-Ribonucleoprotein). Recently, the steroid dose had been increased because of exacerbated arthralgias and myalgias, and for the last six months, the patient was on up to 32 mg of oral methylprednisolone per day with one intravenous dose of 1 g of Solu-Medrol per month. Her physical exam was normal, especially demonstrating normal joint mobility and no joint effusion.

In this clinical context, corticosteroid-induced disorders (avascular necrosis, stress fracture, etc.) were suspected and a left knee MRI exam was requested (Fig. 1).

This initial MRI examination performed one week after pain onset showed no abnormality (Fig. 1a).

One week later, because of persisting symptoms, a second MRI examination was obtained, showing subtle ill-defined "intriguing" dotted high signal abnormalities of the bone marrow of uncertain significance on proton density fat-saturated (PDFS) images, on the proximal tibial meta-diaphysis. Almost nothing was seen on the T1 images (Fig. 1b). One week later, although the patient's symptoms had almost completely resolved spontaneously, a third MRI was performed as a follow-up, as the prior imaging result was non-specific and did not bring a definitive diagnosis. It showed a more evident lesion with confluence of the high PDFS signal

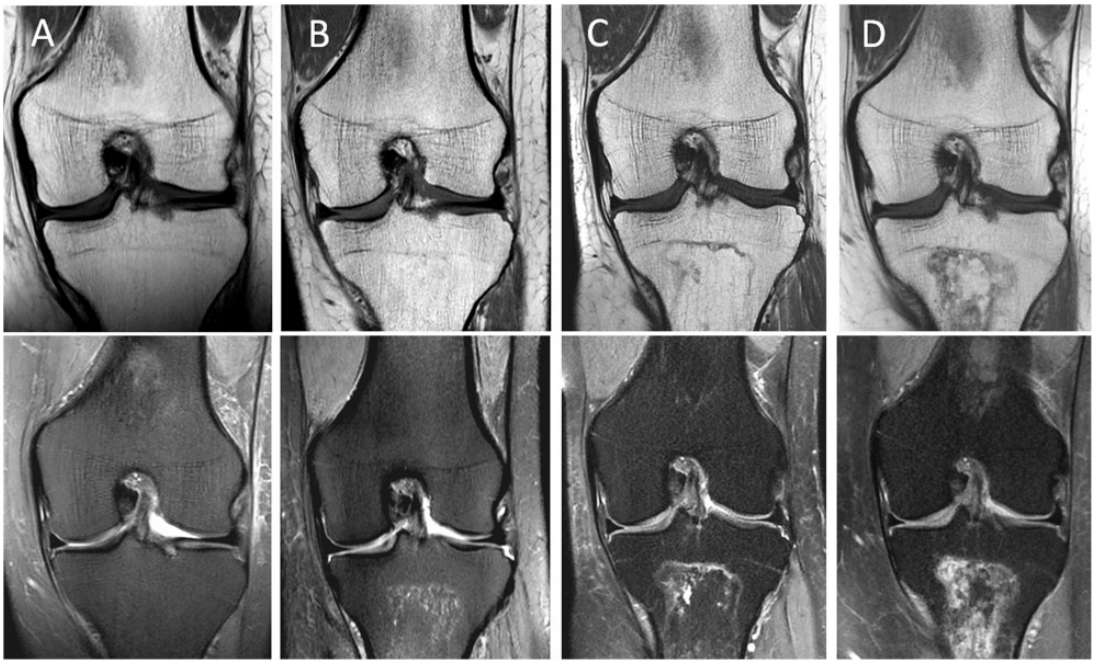

Fig. 1. The different figures parts first illustrate consecutive MRI studies of the left knee obtained at one week (a), two weeks (b), three weeks (c), and seven weeks (d) after onset of severe knee pain in a 25-year-old woman, on chronic systemic corticosteroid therapy for connective tissue disease, referred for acute severe knee pain. (a) T1W (top) and PDFS-weighted (bottom) MR images of the left knee show no abnormality. (b) Corresponding T1W (top) and PDFS-weighted (bottom) MR images obtained one week later show subtle ill-defined dotted high signal abnormalities of the bone marrow of uncertain significance on PDFS on the proximal tibial meta-diaphysis. Almost nothing was seen on the T1. (c) Corresponding T1W (top) and PDFS-weighted (bottom) MR images obtained two weeks later show confluence of the high PDFS signal "dots" into a serpiginous line, giving a geographical appearance to the lesion, also becoming evident on the T1 image as a low signal line. (d) Corresponding T1W (top) and PDFS-weighted (bottom) MR images obtained seven weeks later show confluence and thickening of the peripheral T1 and PDFS signal abnormalities. Note that the abnormal signal areas seen in the distal femurs on all T1 and the PDFS sequence in D are all partial volume artifacts.

"dots" into a more continuous serpiginous line, giving a geographical appearance to the lesion, also becoming evident on the T1W MR image as a low signal line, corresponding to the typical MRI presentation of "established" bone marrow infarcts (Fig. 1c). A seven-week follow-up MR examination was performed to document the evolution of the disease and showed the stability in size of this bone marrow infarct, but more evident confluence and thickening of the peripheral T1 and PDFS signal abnormalities (Fig. 1d).

Knowing the multifocal skeletal presentation of "systemic" ON, a whole-body MRI examination was performed for all skeleton screening. This examination revealed multiple bone marrow infarcts in femoral and tibial diaphyses and metaphyses, in line with systemic avascular necrosis; no epiphyseal involvement was observed (Fig. 2).

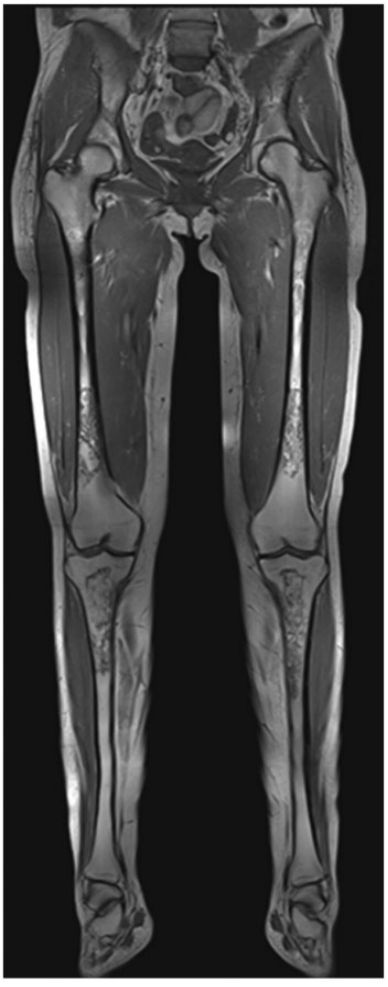

Fig. 2. Whole-body coronal T1W MR image obtained five weeks after symptoms onset shows multiple low T1 serpentine low signal intensity infarcts within the femoral and tibial diaphyses and metaphyses consistent with bone marrow infarcts.

Discussion

ON is a known condition induced by insufficient blood supply to the bone. When ON is subchondral epiphyseal, ON can lead to devastating consequences for the joint whereas metaphyseal or diaphyseal locations have usually no severe consequences (1). ON can be focal, mainly in post-traumatic conditions affecting the femoral neck or scaphoid for example, or multifocal when associated to systemic conditions such as connective tissue diseases, hematologic disorders, corticosteroid therapy, or alcohol abuse (9).

In traumatic ON, disruption of the vascular supply is at the origin of bone necrosis. For non-traumatic ON, many hypothetical theories exist to explain the underlying pathophysiology. Among these, vascular occlusion, altered fat metabolism or fat emboli, intravascular coagulation, and mechanical stress have been proposed (9).

Regarding clinical history, patients usually present with non-specific symptoms such as pain and limited range of motion. Hence, imaging becomes mandatory for an early and reliable diagnosis (1).

It's well-known that plain radiographs are insensitive to detect the early stages of ON; radiographic changes such as peripheral sclerosis and central lucency appear at late stages of bone structure alteration. CT is of great value when assessing articular collapse location and extent (10,11) but lacks sensitivity for an early detection of ON (11,12). MRI is considered the most sensitive and specific imaging modality for identification of ON (2–6) with positive imaging findings appearing within one week of the vascular insult (13).

Single-photon-emission computed tomography (SPECT) appears promising in detecting ON and has been shown able to detect cold epiphyseal areas before MRI became positive in one study on renal transplant patients (14).

The typical MRI appearance of ON is a focal area of yellow marrow presenting a normal signal intensity surrounded by a low signal intensity rim of reactive sclerosis at the lesion borders. This rim is usually serpentine, ring-like, crescent-like, or band like (1). The infarcted bone marrow presents preserved signal because the devitalized fatty marrow maintains its T1 and T2 signal on non-advanced stages (mummified fat). Whereas the peripheral line presents low signal intensity on T1W MR images, a "double rim sign" can be seen on T2 images where low and high signal intensity rims are supposed to represent a sclerotic rim and a more hydrated reparative granulation tissue at the normal/infarct bone interface (1). However, this double line sign most importantly results from a chemical shift artifact (8). In the advanced stages, especially when epiphyseal collapse appears, the lesion signal

becomes less homogenous within the infarcted area, presenting mostly low intensity on T1W images and variable signal on T2W images (15).

Sansigiri et al. retrospectively reviewed MRI screening exams for children receiving chemotherapy protocols for acute lymphocytic leukemia or who had allogenic bone marrow transplantation (16). They observed in 21 patients subtle signal changes in the knees and hips that did precede the typical MRI appearance of ON. These changes were described as "thin indistinct single winding line of low T1 signal with a corresponding T2 STIR hyperintensity, marginating discrete area of normal marrow signal" (16). However, all the screening MRI exams were performed regardless of the presence or absence of any clinical symptoms after each reinduction chemotherapy (weeks 12–14 and 22–24 of treatment). The age range of the patients was 4–19 years; the second follow-up MRI exam that showed the progressed definitive MRI appearance of ON was performed after 1.6–18.5 months.

The current case illustrates the step-by-step appearance of a metadiaphyseal bone infarct at MRI in an adult non-oncologic patient. The first examination obtained one week after symptoms onset showed no MRI abnormality. The second exam obtained in the second week showed non-specific dotted signal abnormalities on PDFS MR images and almost no abnormality on T1W MR images, which suggests a very early observation, compared to the series of Sansgiri where T1W images appeared to show more evident abnormalities. The typical geographic appearance of an established infarct was seen on the MR examination obtained in the third week.

Our imaging series illustrates the "birth of death;" in other words, a clear and closely followed observation of the very early appearance of a bone marrow infarct. To the best of our knowledge, beside the series presented by Sansigiri et al., only one other study based on an experimental canine model reported on the early appearance of ON, showing marrow signal alteration on T1W MR images as early as one week after experimental devascularization (13). The "later" appearance of established bone marrow infarcts seen in avascular ON is well described in the literature, particularly in the knee, where it has to be distinguished from the mechanical condition known as "spontaneous" ON of the knee (17,18).

During the last two decades, whole-body MRI, with its extensive coverage of the skeleton and sensitivity to bone alteration, has emerged as a powerful tool for detecting and evaluating disorders that involves the musculoskeletal system in a multifocal fashion (19). Beside its oncologic applications, such as multiple myeloma, lymphoma, or bone metastases, whole-body MRI was proved useful in many non-oncologic disorders as rheumatologic diseases, chronic recurrent multifocal osteomyelitis (CRMO), and other multifocal disorders affecting the bone, including multifocal ON (19–22).

In our case, it is highly likely that the systemic ON was not uniquely due to the high-dose corticosteroid treatment, but also partly resulted from the patient's systemic disease. The early and follow-up MRI exams had a major role in reaching the definite diagnosis and monitoring disease progression. The corticosteroid treatment was gradually decreased and a whole-body MRI was performed to assess the disease extension and exclude articular lesion at risk of collapse.

In conclusion, this case illustrates the previously poorly known very early MRI appearance of a bone marrow infarct, showing its progressive delineation on consecutive examinations obtained at one-week intervals. These early findings may help support an early diagnosis of a suspected ON in the appropriate clinical setting. We also think that a close follow-up MRI is highly reasonable despite a first negative MRI exam, in acutely symptomatic patients with clinically suspected ON.

Declaration of conflicting interests

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References

1. Murphey MD, Foreman KL, Klassen-Fischer MK, et al. From the radiologic pathology archives imaging of osteonecrosis: radiologic-pathologic correlation. *Radiographics* 2014;34:1003–1028.
2. Resnick D, Niwayama G. Osteonecrosis and osteochondrosis. In: D Resnick, G Niwayama, editors. *Diagnosis of Bone and Joint Disorders*. 4th ed. Philadelphia, PA: Saunders, 1998: 3238–3288.
3. Glickstein MF, Burk DL Jr, Schiebler ML, et al. Avascular necrosis versus other diseases of the hip: sensitivity of MR imaging. *Radiology* 1988;169:213–215.
4. Piyakunmala K, Sangkomkamhang T, Chareonchonvanitch K. Is magnetic resonance imaging necessary for normal plain radiography evaluation of contralateral non-traumatic asymptomatic femoral head in high osteonecrosis risk patient. *J Med Assoc Thai* 2009;92:147–151.
5. Kamata N, Oshitani N, Sogawa M, et al. Usefulness of magnetic resonance imaging for detection of asymptomatic

osteonecrosis of the femoral head in patients with inflammatory bowel disease on long-term corticosteroid treatment. *Scand J Gastroenterol* 2008;43:308–313.
6. Munk PL, Helms CA, Holt RG. Immature bone infarcts: findings on plain radiographs and MR scans. *Am J Roentgenol* 1989;152:547–549.
7. Gillespy T 3rd, Genant HK, Helms CA. Magnetic resonance imaging of osteonecrosis. *Radiol Clin North Am* 1986;24:193–208.
8. Duda SH, Laniado M, Schick F, et al. The double-line sign of osteonecrosis: evaluation on chemical shift MR images. *Eur J Radiol* 1993;16:233–238.
9. Assouline-Dayan Y, Chang C, Greenspan A, et al. Pathogenesis and natural history of osteonecsosis. *Semin Arthritis Rheum* 2002;32:94–124.
10. Yeh LR, Chen CK, Huang YL, et al. Diagnostic performance of MR imaging in the assessment of subchondral fractures in avascular necrosis of the femoral head. *Skeletal Radiol* 2009;38:559–564.
11. Stevens K, Tao C, Lee SU, et al. Subchondral fractures in osteonecrosis of the femoral head: comparison of radiography, CT, and MR imaging. *Am J Roentgenol* 2003;180:363–368.
12. Lee MJ, Corrigan J, Stack JP, et al. A comparison of modern imaging modalities in osteonecrosis of the femoral head. Clin Radiol 1990;42:427–432.
13. Brody AS, Strong M, Babikian G, et al. John Caffey Award paper. Avascular necrosis: early MR imaging and histologic findings in a canine model. *Am J Roentgenol* 1991;157:341–345.
14. Ryu JS, Kim JS, Moon DH, et al. Bone SPECT is more sensitive than MRI in the detection of early osteonecrosis of the femoral head after renal transplantation. *J Nucl Med* 2002;43:1006–1011.
15. Vande Berg BE, Malghem JJ, Labaisse MA, et al. MR imaging of avascular necrosis and transient marrow edema of the femoral head. *Radio Graphics* 1993;13:501–520.
16. Sansgiri RK, Neel MD, Soto-Fourier M, et al. Unique MRI findings as an early predictor of osteonecrosis in pediatric acute lymphoblastic leukemia. *Am J Roentgenol* 2012;198:432–439.
17. Lecouvet FE, Van de Berg BC, Maldague BE, et al. Early irreversible osteonecrosis versus transient lesions of the femoral condyles: prognostic value of subchondral bone and marrow changes on MR imaging. *Am J Roentgenol* 1998;170:71–77.
18. Hatanaka H, Yamamoto T, Motomura G, et al. Histopathologic findings of spontaneous osteonecrosis of the knee at an early stage: a case report. *Skeletal Radiol* 2016;45:713–716.
19. Lecouvet FE. Whole-body MR imaging: musculoskeletal applications. *Radiology* 2016;279:345–365.
20. Huang ZG, Yang MX, Chen XL, et al. Value of whole-body magnetic resonance imaging for screening multifocal osteonecrosis in patients with polymyositis/dermatomyositis. *Br J Radiol* 2017;90:20160780.
21. Albano D, Patti C, La Grutta L, et al. Osteonecrosis detected by whole body magnetic resonance in patients with Hodgkin lymphoma treated by BEACOPP. *Eur Radiol* 2017;27:2129–2136.
22. Lecouvet F, Michoux N, NzeusseuToukap A, et al. The increasing spectrum of indications of whole-body MRI beyond oncology: imaging answers to clinical needs. *Semin Musculoskelet Radiol* 2015;19:348–362.