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Clinical Quiz

Regional Migratory Osteoporosis

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Case

A 42-year-old man presented with a 2-month history of persistent right hip pain, unresponsive to corticosteroid injections and non-steroidal anti-inflammatory drugs. He had no trauma history, was hemodynamically stable, and had no significant medical history. Clinical examination revealed localized pain in the right groin, anterior thigh, and greater trochanter, with impaired gait and decreased active and passive external rotation of the hip (20° deficit, compared to the contralateral side). Muscle strength was normal, and no neurovascular deficits were observed. Initial X-rays and laboratory examination did not show any abnormality [calcium=8.90mg/dL (nr=8.10-10.40), phosphate=4.8mg/dL (nr=2.5-5.0), 25-OH-D3 18.0 ng/dL (nr=7.6-75.0) and parathyroid hormone (PTH)=51.9 pg/ml (nr=18.5-88 pg/ml)], except for slightly elevated white blood cells (WBC)=11.1 K/μl (nr=4.0-10.0) and creatine reactive protein (CRP)=16.10 (nr <10.0). The magnetic resonance imaging (MRI) showed bone marrow edema in the femoral head, neck, and inter-trochanteric region, with joint effusion, sparing the medial femoral head (Figure 1A-C). Thus, the patient was diagnosed with transient osteoporosis (TO) of the right hip and was treated with bisphosphonates (risedronate sodium 35mg: x1/week), calcium (500mg: 1x2 for 2 months), 25-OH-D3 (1000IU: 2x1 for the 20 first days and consequently 1x1), and minimal weight-bearing.

Four months later, the patient's hip pain had resolved, but he developed right knee pain. MRI of the knee revealed bone marrow edema and a sub-chondral fracture in the medial part of the lateral femoral condyle, leading to the diagnosis of regional migratory osteoporosis (RMO) (Figure 2). Treatment continued with the same regimens.

Twenty months later and while the symptoms at his right hip and knee had fully resolved, the patient experienced similar symptoms located at the left hip joint. MRI confirmed the TO of the left hip (Figure 1 D-F). Treatment was adjusted to intravenous single-administration bisphosphonate therapy (zoledronic acid 5mg) and continued calcium and 25-OH-D3 supplementation. Furthermore, no weight bearing for 4 weeks and gradual partial weight bearing for another 4 weeks was suggested. The patient returned to normal activities within six months, with no recurrence over three years.

Commentary

Regional (transient) osteoporosis (RO) is a rare, self-limiting condition characterized by sudden joint pain, localized bone loss (osteopenia) within weeks, and spontaneous resolution1. It primarily affects the hip, with decreasing frequency in the knee, ankle, and foot. RO can occur as a single episode or recur in multiple joints, known as Regional Migratory Osteoporosis (RMO) in 10% to 41% of cases. RMO is often underdiagnosed and misclassified, typically affecting individuals in their fifth and sixth decades but occasionally younger and pediatric patients[1]. It predominantly affects men (3:1 ratio). The pathophysiology is unclear, possibly involving excessive bone remodeling from tissue damage, micro-fractures, neurological inputs, and ischemic episodes in

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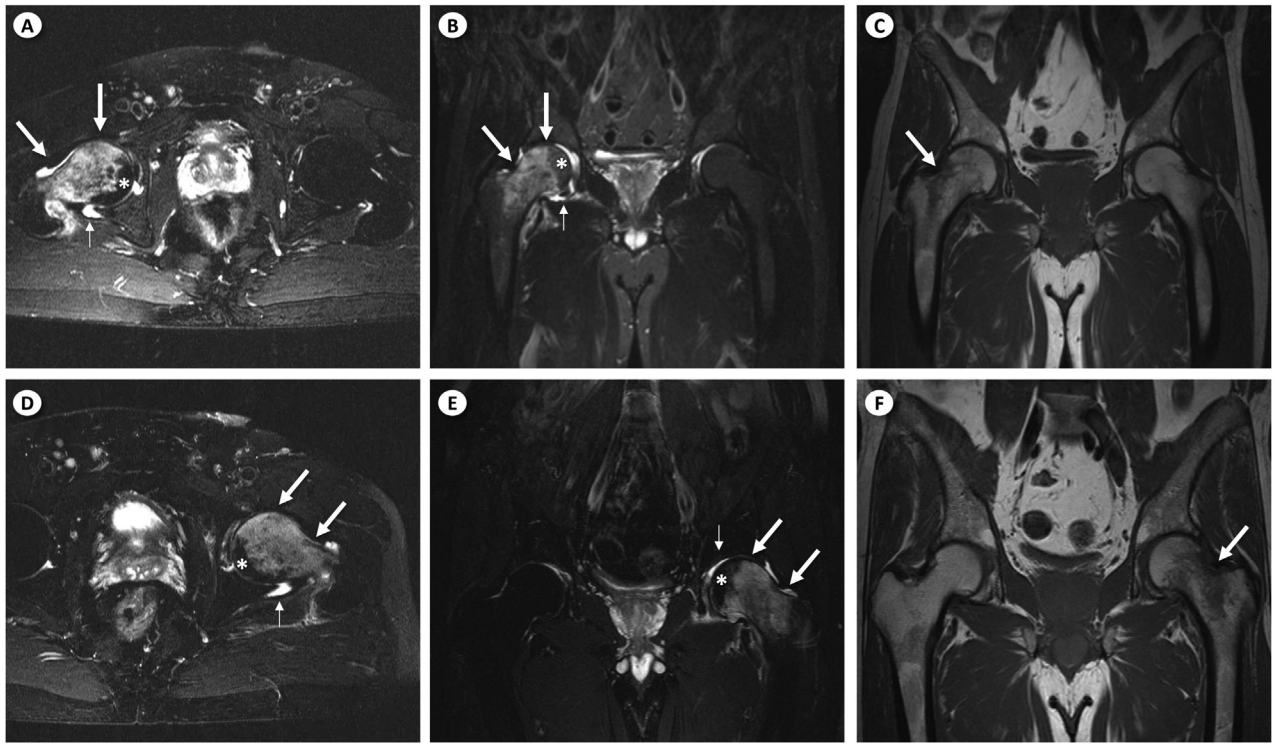

Figure 1. (A) Axial and (B) coronal T2-weighted fat-saturated magnetic resonance (MR) images of the hips demonstrate diffuse heterogeneous signal hyperintensity affecting the bone marrow of the right femoral head, neck, and part of the intertrochanteric region (thick arrows), indicating bone marrow edema. A mild joint effusion is also noted (thin arrows). (C) Coronal T1-weighted MR image of the hips displays areas with partial loss of the normal fatty marrow signal in corresponding bone marrow edema areas of the right hip (thick arrow), which is most evident when compared to the contralateral normal side. (D) Axial and (E) coronal T2-weighted fat-saturated magnetic resonance (MR) images of the hips from a different MR examination demonstrate diffuse heterogeneous signal hyperintensity affecting the bone marrow of the left femoral head, neck, and part of the intertrochanteric region (thick arrows), suggestive of bone marrow edema. A mild joint effusion is also noted (thin arrows). (F) Coronal T1-weighted MR image of the hips displays areas with partial loss of the normal fatty marrow signal in corresponding bone marrow edema areas of the left hip (thick arrow), likewise most evident when compared to the contralateral normal side. These findings are identical to those described for the right hip. Note that in both hips, the medial part of the femoral head is spared (asterisk), an imaging finding characteristic of transient osteoporosis of the hip (otherwise known as transient bone marrow edema syndrome of the hip).

small arteries[1]. RMO presents with gradually increasing joint pain, peaking in 2-3 months and worsening with movement[1,2]. Physical exams show tenderness, effusion, and swelling, with minor range of motion decreases. It can occur as single or recurrent episodes, affecting 2-7 joints over months to 2 years, sometimes simultaneously[2].

Early X-rays in the early stages of RMO are normal, but later show progressive demineralization, subchondral bone thinning, and preserved joint spaces[3]. In the hip, reduced femoral head density with an intact subchondral line and possible periosteal reaction on the femoral neck are seen. Remineralization can take up to 2 years post-symptoms. Bone scintigraphy detects increased radiotracer uptake in all phases shortly after symptom onset, before X-ray changes[1-3]. As symptoms improve, hyperemia decreases, but osteoblastic activity keeps radioisotope uptake high in the delayed bone phase for many months[2,3]. In MRI studies, bone marrow edema (depicted as areas of increased signal intensity on T2-weighted images, and decreased signal on T1-weighted images) is observed a few days after the onset of symptoms, along with joint effusion in 75% of patients[3]. In most cases, bone edema appears soon after symptoms onset and resolves in 4–11 months. Changes in the hip usually affect the femoral head, neck, and intertrochanteric region with increased intra-articular fluid, while in the knee, bone edema commonly occurs in the lateral femoral condyle[3]. In addition, the medial aspects of the femoral heads are typically spared from bone marrow edema in cases of transient osteoporosis of the hip, a finding that is very characteristic of this condition and has been described in up to 87.7% of patients[3]. This

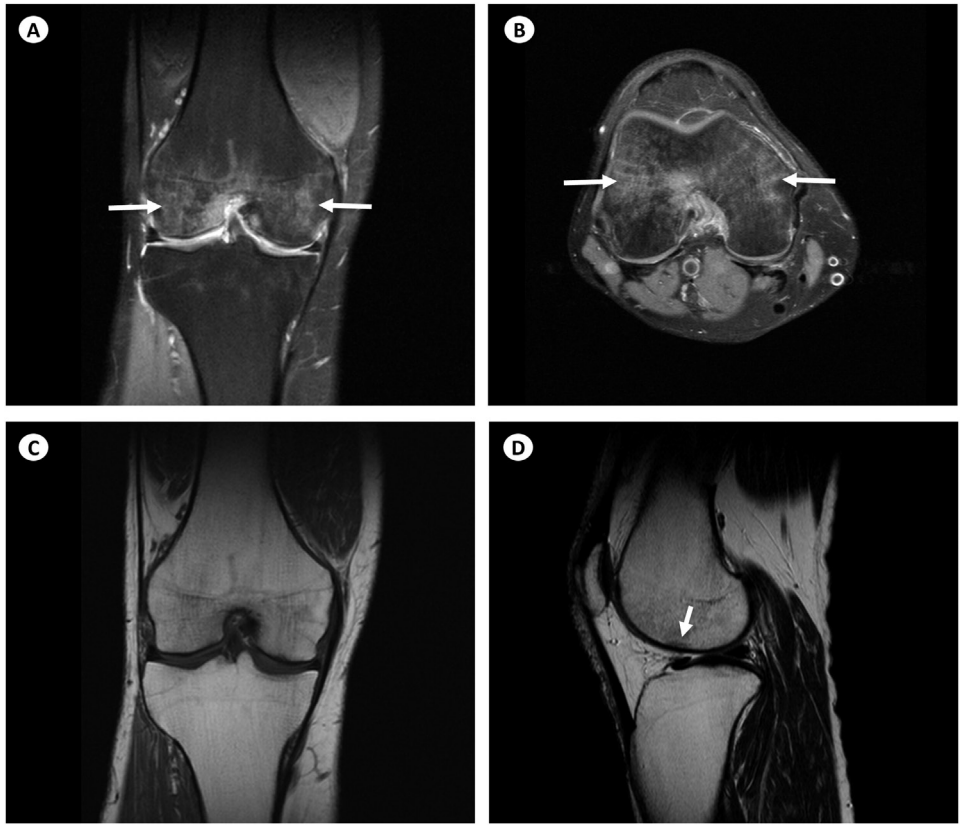

Figure 2. (A) Coronal and (B) axial proton density (PD) fat-saturated magnetic resonance (MR) images of the right knee demonstrate diffuse heterogeneous signal hyperintensity affecting the bone marrow of both femoral condyles (arrows), indicating bone marrow edema. (C) Coronal T1-weighted MR image of the right knee only displays mild areas with partial loss of the normal fatty marrow signal in the corresponding regions. (D) Sagittal T2-weighted, non-fat-saturated image at the level of the medial part of the lateral femoral condyle barely visualizes a thin subchondral fracture line of low signal intensity (arrow).

finding was unequivocally present in the MRI studies of both hips affected in the current case; thus, further supporting our diagnosis[3].

The differential diagnosis of RMO includes several other conditions with overlapping features and so it may often be delayed[2]. Differential diagnosis includes inflammatory arthropathies, malignancies, gout, tuberculosis, osteomyelitis, stress fractures, soft tissue diseases, myeloma and disorders of calcium metabolism[1,2]. In these cases, signs and symptoms, microbiological and laboratory examinations, as well as imaging findings allow for correct diagnosis. The underlying cause of RMO is not fully understood, but it is thought to involve a combination of vascular, mechanical, as well as inflammatory factors. Although, an elevated WBC and CRP are not typical findings in most RMO cases, these markers might be elevated due to localized inflammation associated bone turnover and resorption, contributing to the observed bone marrow edema and localized bone loss[1,5]. ROM must be differentially diagnosed from avascular necrosis (AVN) which is a progressive condition and could lead to joint destruction requiring surgical intervention[2]. Early-stage RMO and AVN share similar radiological findings, however, AVN is associated with specific risk factors, such as steroid use, alcohol abuse, chemotherapy, and renal disease, which are typically absent in RMO cases[1]. Radiologically, AVN is characterized by diffuse osteopenia, while early magnetic resonance imaging (MRI) shows an area of radiolucency surrounded by a region of sclerosis displaying the pathognomonic “crescent sign” on imaging, indicating subchondral fracture which can often progress to articular collapse.

Complex regional pain syndrome (CRPS) can present with similar symptoms but is usually related to trauma and affects the upper limbs more commonly, with additional vascular and skin changes absent in RMO. Chronic recurrent multifocal

osteomyelitis shares bone marrow edema on MRI but differs in radiographic findings, often involving the metaphysis and anterior chest wall[3].

The disease is self-limiting within 8-9 months[1,4,5]. Conservative measures can be used like rest, reduced weight-bearing and physical therapy[1]. Drug therapy for pain relief is managed with NSAIDs, and bisphosphonates (pamidronate) or iloprost can reduce bone marrow edema within weeks[1,4,5]. In patients with ROM, a single 5 mg intravenous dose of zoledronic acid has shown promising results providing rapid pain relief within 1-2 months and resolving bone marrow edema, with long-term remission and minimal side effects[4,5]. It significantly improves functional recovery and reduces the likelihood of disease recurrence[4,5]. In some cases, surgical core decompression may be considered with the risk of weakening the bone and inducing fractures[1,3-5].

Consent to publish

Written consent for publication was obtained from the patient.

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Questions

1. Which diagnostic imaging modality is most likely to show early changes in a patient suspected of having RMO?

A. Plain X-ray
B. MRI
C. CT scan
D. None of the above

Critique

MRI is the most sensitive imaging for detecting early changes in RMO. It can show bone marrow edema a few days after the onset of symptoms, with increased signal intensity on T2-weighted images and decreased signal intensity on T1-weighted images. Plain X-rays might not show any abnormalities in the early stages. CT scans are not sensitive for detecting bone marrow edema changes.
Correct Answer: B.

2. Which condition must be differentially diagnosed from RMO due to joint destruction if untreated?

A. Complex Regional Pain Syndrome (CRPS)
B. Avascular Necrosis (AVN)
C. Chronic Recurrent Multifocal Osteomyelitis (CRMO)
D. None of the above

Critique

AVN is a progressive condition that shares similar early-stage radiological findings with RMO but can lead to joint destruction requiring surgical intervention if not recognized and treated in time. It also has specific risk factors like steroid use and alcohol abuse, which are typically absent in RMO cases.
Correct Answer: B.

3. Which of the following clinical features is commonly associated with RMO?

A. Constant pain and joint swelling
B. Paroxysmal pain and transient joint swelling
C. Chronic pain with no periods of remission
D. None of the above

Critique

RMO typically presents with paroxysmal pain and transient joint swelling. Patients often experience periods of pain that can migrate from one region to another. Chronic pain without periods of remission and asymptomatic presentations are less characteristic of RMO.
Correct Answer: B.