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Case Report

Diffuse periostitis as the primary presenting radiological finding in an AML patient with disease relapse

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ABSTRACT

Acute myelogenous leukemia is a hematologic malignancy defined by the presence of myeloid blasts causing bone marrow infiltration. Evaluation and workup of acute myelogenous leukemia is based on comprehensive medical history, physical examination, laboratory evaluation, and bone marrow sampling. Magnetic resonance (MR) imaging is the study of choice in the evaluation of this disease including the initial evaluation, treatment follow-up, and complications. Herein, we report a case of relapse of the acute myelogenic leukemia in an adult patient who presented with diffuse periostitis in his lower extremities diagnosed on MR imaging and confirmed on Technetium bone scan, which also showed periostitis along the bilateral humeri. To our knowledge, this was not previously reported in the English literature.

Introduction

Acute myelogenous leukemia (AML) is a heterogeneous hematologic malignancy defined by the presence of myeloid blasts in the peripheral blood, bone marrow, or other tissues [1]. It is the most frequent leukemia in adults with an incidence of 3.7 per 100,000 persons. AML is a fatal disease with patients ultimate dying of bone marrow failure–related complications [2]. Clinical presentation of AML reflects the underlying process of leukemic bone marrow infiltration resulting in neutropenia, anemia, and thrombocytopenia. Children typically present with fever, fatigue, pallor, infections, and bleeding [3]. Adult patients may present with anemia and fatigue, decreased energy level lasting several weeks, dyspnea on exertion, and dizziness. Older patients with coronary artery disease may present with anginal chest pain and the myocardial infarction may be their first presenting symptom [4,5]. Evaluation and workup is based on comprehensive medical history, physical examination, laboratory evaluation, and bone marrow analysis [1].

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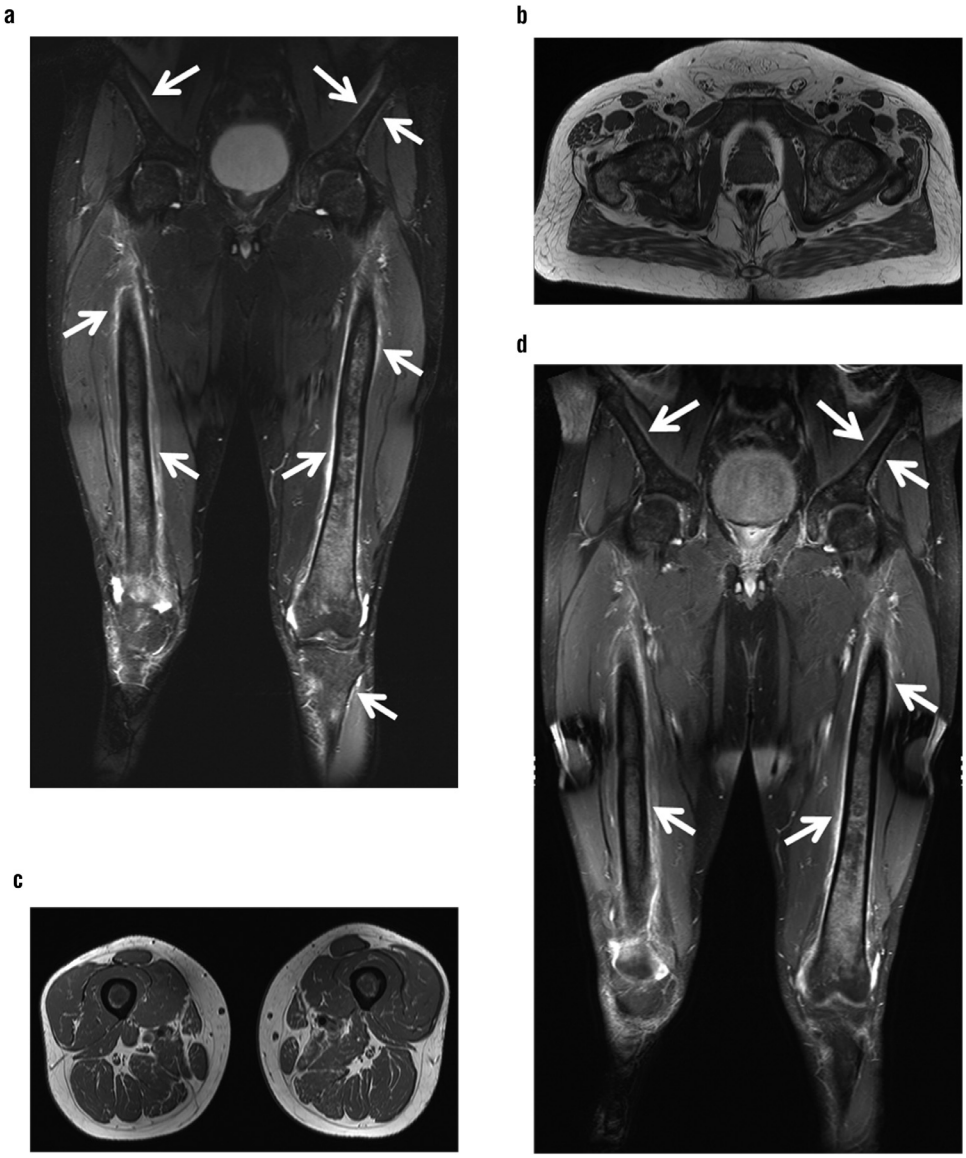

Fig. 1 – Marrow infiltrative process and diffuse periostitis on MR imaging. (A) Coronal STIR MR image of the pelvis and bilateral femora shows diffusely heterogeneous appearance of the bone marrow with patchy increased signal intensity, which is most pronounced in the bilateral femora. Note diffuse high signal intensity periostitis about the pelvis and bilateral femora (white arrows). Axial T1-weighted MR images of the hips (B) and bilateral femora (C) demonstrate patchy areas of low-signal intensity consistent with bone marrow replacement in keeping with marrow infiltrative process. (D) Coronal gadolinium-enhanced T1-weighted fat-saturated MR image of the pelvis and bilateral femora demonstrates extensive periosteal enhancement (white arrows) consistent with periostitis.

Role of imaging in AML workup and follow-up is limited. As per National Comprehensive Cancer Network, imaging is recommended in presence of focal symptoms such as neurologic deficits requiring head computed tomography (CT) or brain MR imaging. Nuclear imaging in the form of PET/CT can be utilized in cases with suspected extramedullary disease [1]. Whole-body MR imaging has also been studied in children with AML for assessment of extramedullary disease, particularly chloromas [6]. Additionally, MRI is performed for suspected various coexisting and/or unrelated posttraumatic, inflammatory or infectious conditions, if clinically indicated.

Imaging, particularly MR imaging, can be helpful in patients undergoing therapy in differentiating the treatment changes and disease complications. We present a case of diffuse periostitis as the primary presenting radiological finding in an AML patient with disease relapse.

Case report

A 45-year-old male was diagnosed with AML with initial flow cytometry showing 45% myeloid blasts with inversion of

chromosome 16 and deletion of chromosome 5q. The bone marrow biopsy showed significant fibrosis. The patient was subsequently treated with 7+3 induction chemotherapy, but did not undergo consolidation due to social issues. At 3-month follow-up, repeat bone marrow biopsy showed extensive fibrosis (3+ on a scale from 0 to 3) but without definitive evidence of residual AML.

Approximately 8 months after induction chemotherapy, the patient presented to the emergency department with bilateral, right greater than left, hip and knee pain. He described the pain as achy and chronic in nature with acute worsening prior to presentation. Patient denied fevers, chills, trauma, falls, or recent changes in his activity. On physical examination, the patient was found to have tenderness over his bilateral hips without focal neurologic findings. Laboratory evaluation revealed elevated inflammatory markers.

Patient subsequently underwent emergent right hip MR imaging, which included pelvis, bilateral femora, and knees. MR imaging revealed diffuse heterogeneous appearance of the bone marrow throughout the pelvis, bilateral femora, and proximal tibiae and fibulae with heterogonous decreased signal intensity on T1-weighted sequences and increased signal on STIR and T2 weighted with fat saturation sequences. There was diffuse high signal intensity periostitis on the fluid sensitive sequences along the pelvis and imaged bilateral lower extremities, which showed enhancement on the post intravenous Gadolinium-based contrast T1-wighted sequences with fat saturation (Fig. 1). There were no additional abnormal findings on the MR imaging study. Further workup was performed with radiographs of the pelvis and long bones of bilateral lower extremities, which showed no evidence of acute process including periostitis. Follow-up whole-body Technetium bone scan 3 days later showed mildly increased activity within the bilateral femora and humeri, related to periostitis, with questionable diffuse soft tissue uptake (Fig. 2).

The imaging findings were concerning for recurrence of patient's AML disease; therefore, repeat bone marrow core biopsy was performed, which showed increased cellularity with up to 25% immature blasts consistent with relapsed AML (Fig. 3). The blasts were positive for immature myeloid markers including CD34, CD117, and myeloperoxidase (MPO). The marrow fibrosis was still present (3+).

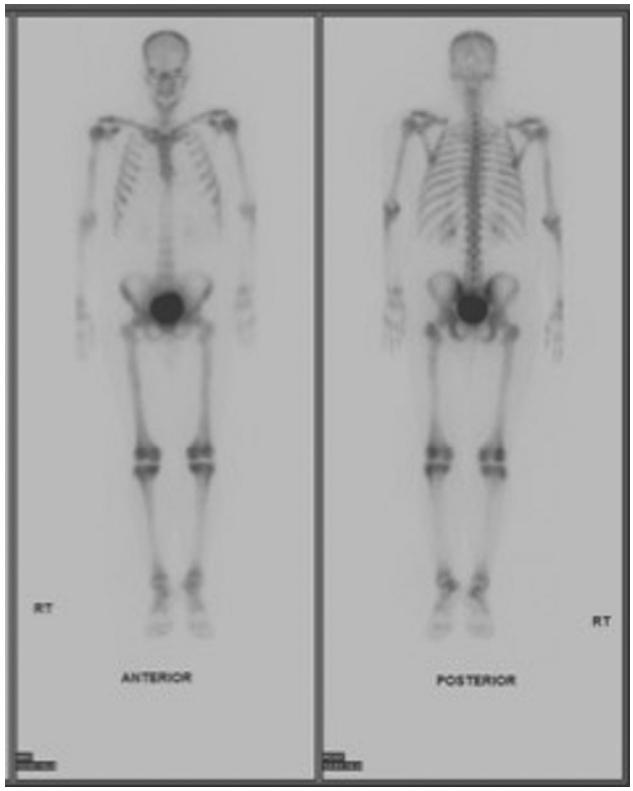

Fig. 2 – Periostitis on Technetium bone scan. Following administration of 21.9 mCi of Technetium-99m methylenediphosphonate intravenously, delayed imaging of the anterior and posterior whole body shows mildly increased periosteal radiotracer uptake in the bilateral legs and bilateral arms.

Discussion

Chemotherapy, radiation, or hematologic malignancies, among other causes, may result in bone marrow fibrosis. The usual course of bone marrow fibrosis is resolution after months in absence of the causative factor [7]. In our patient, the most likely reason for nonresolution of fibrosis is AML relapse.

A frequently reported cause of periostitis in immune deficient patients, particularly those with hematologic disorders, is use of voriconazole [8–11]. It is suspected that voriconazole-induced periostitis occurs secondary to accumulation of fluoride [9,11–13]. Typically, these patients are using voriconazole for 6 weeks to 53 months [11,12]. After thorough chart review and patient interview, it was determined that our patient had limited use of voriconazole for less than a week and at least 3 months prior to his presentation with periostitis. Given the short duration of use and long latency period prior to onset of symptoms, voriconazole-induced periostitis was not felt to be the primary culprit behind patient's presenting symptoms.

Other differential considerations of periostitis are provided in an exhaustive list including psoriatic arthritis, reactive arthritis, pachydermoperiostosis, hypervitaminosis A, prostaglandins, hypertrophic pulmonary osteoarthropathy, infection, malignancy, fracture, etc [14,15].

Osseous manifestations in AML have been described as diffuse osteoporosis, lucent metaphyseal bands, and areas of cortical luciences [16,17]. In pediatric population, diffuse periostitis has been described as a skeletal manifestation of AML [16,18,19]. However, diffuse periostitis as the primary skeletal manifestation in AML relapse in adult patient has not been reported in literature.

Extramedullary presentations are uncommon in AML patients [1]. In these instances, imaging can play an important role in evaluation of extramedullary AML relapse. Chloromas/granulocytic sarcomas have been described to have a high incidence of nearly 21% in patients with allogenic bone marrow transplantation. These present as soft-tissue nodules or masses in any part of the body, but favor breast, bone, and

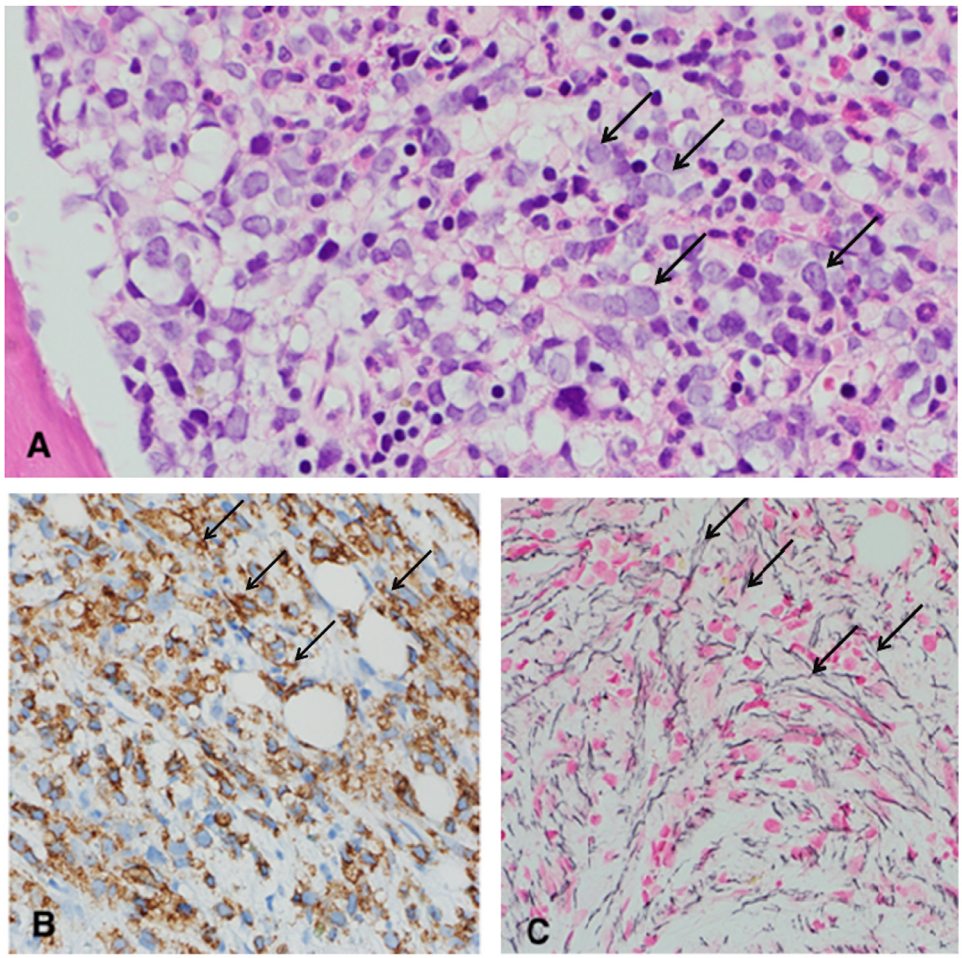

Fig. 3 – Bone marrow needle core biopsy showing AML relapse and bone marrow fibrosis. (A) Hematopoietic progenitors occupy the marrow space with many immature cells consistent with blasts (arrows). These have large nuclei, little cytoplasm, smooth chromatin, and prominent nucleoli. Hematoxylin & Eosin, original magnification × 400. (B) The cells stain positive for the cytoplasmic marker CD34 (arrows), as well as CD117 and MPO (not pictured), indicating they are myeloblasts. CD34, original magnification × 400. (C) The bone marrow is significantly fibrotic (3+ on a scale of 0-3+). Reticulin stain further demonstrates increase in reticulin fibers (arrows), original magnification × 400.

subcutaneous tissues [20]. Imaging features on ultrasound examination, CT, MR imaging, and PET/CT are similar to those of lymphoma. Biopsy is frequently performed under imaging guidance [20,21]. Chloromas are typically isointense to hypointense as compared to adjacent musculature on T1-weighted images and slightly hyperintense on T2-weighted images with avid enhancement on post contrast sequences [22]. Additional area of concern for extramedullary involvement, even though uncommon, is central nervous system. Choice of imaging modality in these instances is variable and should be appropriately selected based on patient's presenting symptoms [1].

Scattered areas of inhomogeneity may be present within the bone marrow as a result of preserved red marrow foci, which should not be mistaken for disease recurrence. Additionally, bone marrow fibrosis presents as hypointense signal on both T1- and T2-weighted sequences [23].

In conclusion, we present a case report of AML in an adult patient who presented with diffuse lower extremity periostitis associated with disease relapse. Thus, radiologist should be aware of periostitis as a possible imaging finding of AML relapse.

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