Magnetic resonance imaging as a diagnostic modality in a child with acute lymphoblastic leukemia

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ABSTRACT

Acute lymphoblastic leukemia is the most common form of childhood cancer. It presents with nonspecific symptoms, such as bone pain, that can be easily misdiagnosed at initial presentation. We present a 2-year-old boy with bilateral foot pain that worsened over 6 months. X-rays of the feet showed no obvious abnormalities. Magnetic resonance imaging revealed abnormal bone marrow consistent with an infiltrative process. The patient was found to have precursor B-cell acute lymphoblastic leukemia. Cases such as these highlight the possible future use of magnetic resonance imaging in the early diagnostic workup for bone and muscle pain.

KEYWORDS Acute lymphoblastic leukemia; bone pain; limp; magnetic resonance imaging

Childhood leukemia has an incidence of 50 per million in the Western population, with 78% of these children having acute lymphoblastic leukemia (ALL).¹ Less than half of newly diagnosed children with leukemia are found to have bone pain or functional muscular impairment. Many times, this muscular pain is nonspecific at initial presentation and may be misdiagnosed as an inflammatory disorder, an infection, or an undetermined etiology if laboratory findings are normal. The pain associated with acute leukemia is refractory to nonsteroidal anti-inflammatory drugs.² Malignancy should be ruled out prior to the initiation of steroids for musculoskeletal pain. X-rays are the first radiographic modality of choice. Follow-up is recommended based on symptoms if the x-ray is normal. If symptoms reappear or do not improve, magnetic resonance imaging (MRI) is usually warranted. This report emphasizes the use of MRI in the initial diagnostic workup for patients presenting with bone pain without the classic laboratory findings or physical signs of leukemia.

CASE PRESENTATION

A previously healthy 2-year-old boy presented to his primary care physician with a 6-month history of bilateral foot pain progressing to a limp, followed by complete refusal to bear weight with regression to crawling only. He had an

abnormal gait and mild tenderness with range of motion testing of the hips but showed no joint swelling, hepatosplenomegaly, or lymphadenopathy. There was no history of prior traumas, fevers, changes in appetite, fatigue, weight loss, petechiae/bruising, changes in bladder/bowel habits, joint swelling, or recent illnesses. Plain radiographs of the hips and knees were normal. A bilateral hip ultrasound ordered by pediatric orthopedics was negative for any joint effusions, and the presumptive diagnosis was toxic synovitis. However, the patient's symptoms persisted, and he started experiencing daytime and nighttime enuresis with encopresis. A rheumatologic laboratory workup came back normal (*Table 1*). Subsequently, a podiatrist was concerned for possible structural deformities or pathologies and ordered an MRI of the bilateral feet without contrast.

This MRI showed diffusely abnormal bone marrow signal intensity (*Figures 1 and 2*), consistent with a marrow infiltrative process such as leukemia. Specifically, there were diffuse hypointense T1-weighted and hyperintense T2-weighted signals of the distal tibial diaphysis, metaphysis, and epiphysis. In the fibula, there was patchy decreased T1 signal and increased T2 signal in the distal diaphysis, metaphysis, and epiphysis. There was also an abnormal hypointense T1-weighted and abnormal hyperintense T2-weighted signal in all of the tarsal bones with relative sparing of the cuboid, as well as an abnormal signal at the metatarsal metaphyses.

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Given the diffuse and symmetric nature of signal intensity and normal blood count, radiology recommended an urgent oncology referral for possible leukemia. During his oncology consultation, the physical exam was benign with the exception of lower-extremity muscle atrophy and refusal to bear weight, the complete blood count was again normal, but the peripheral smear was concerning for possible lymphoblasts. A bone marrow biopsy with aspirate showed 66% blasts consistent with precursor B-cell ALL. The patient was admitted to the hospital later that day for central venous port placement and start of induction chemotherapy.

Table 1. Patient's laboratory results

	Value	Reference range
White blood cell count ($\times 10^9/L$)	5.9	4.8–13.5
Aspartate aminotransferase (IU/L)	42	10–55
Alanine aminotransferase (IU/L)	14	0–68
Albumin (g/dL)	4.4	3.8–5.4
Erythrocyte sedimentation rate (mmol/h)	14	0–15
C-reactive protein (mg/L)	3.0	0.0–3.2
Rheumatoid factor	Negative	Negative
Lactate dehydrogenase (IU/L)	297	120–450
Lyme antibody	Negative	Negative
Antistreptolysin O screen (IU/mL)	<100	<100

DISCUSSION

ALL is the most common form of childhood cancer. The peak incidence occurs between the ages of 2 and 5 and is more common among boys than girls. ALL typically presents with nonspecific symptoms and can therefore be difficult to distinguish from other pediatric pathologies. Some early signs and symptoms of ALL include hepatosplenomegaly, lymphadenopathy, musculoskeletal pain, mediastinal mass, and peripheral blood abnormalities.¹ Bone pain is a presenting symptom in 20% to 40% of cases of acute leukemia² but is also a common symptom in metastatic cancers and multiple other nonmalignant conditions. Blood work in ALL patients typically reveals anemia and/or thrombocytopenia with a normal to elevated white blood cell count, and a peripheral smear can contain lymphoblasts. The presence of atypical cells in peripheral blood, cytopenia in more than one cell line, and/or concerning symptoms such as hepatosplenomegaly, lymphadenopathy, or bone pain warrant a bone marrow examination.

The factors in this case presented an interesting challenge for diagnosis. The toddler's peripheral blood counts were normal without aberrations in any cell lines, and his multiple physical exams did not reveal obvious signs of malignancy. It was not until the MRI incidentally noted abnormal bone marrow signaling that malignancy came to the forefront of the differential diagnoses. The peripheral smear and bone marrow studies later confirmed the diagnosis. The absence of abnormal peripheral blood cell counts or smear can often delay the appropriate diagnosis of leukemia.

Based on the findings of Kato et al, MRI can potentially detect leukemia at an earlier phase than bone marrow aspiration and therefore could be useful in the initial

Figure 1. (a) T1 sagittal image of the abnormal marrow demonstrates widespread and nearly complete marrow replacement as evidenced by hypointense T1-weighted signal. Compare with (b) the normal patient, where there is a hyperintense marrow signal due to fatty yellow marrow.

Figure 2. (a) T2 fat-saturated sagittal image of the abnormal marrow demonstrates widespread and nearly complete marrow replacement, as evidenced by hyperintense signal. Compare with (b) the normal patient, where the signal from the normal fatty yellow marrow is hypointense because of the fat saturation application, which cancels out the fat signal and makes it dark.

diagnosis of ALL.³ MRI is not routinely performed as part of the diagnostic evaluation of acute leukemia. However, Lu et al also found that patients with leukemia may first present with musculoskeletal complaints and a normal peripheral blood cell count; they concluded that for such cases, MRI could be utilized as part of the early diagnostic workup.⁴ Therefore, in a patient presenting with bone pain without the classic laboratory findings or physical signs of leukemia, there is a potential role for MRI in attempts to avoid a delay in making the correct diagnosis.

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