Childhood Leukemia Presenting as Sternal Osteomyelitis

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Musculoskeletal manifestations are the presenting complaint in up to 20% of patients with pediatric leukemia.[1] Therefore, orthopedic surgeons often become involved before a formal diagnosis of leukemia has been made. Because of similarities in presentation, many of these patients are initially diagnosed with osteomyelitis, transient synovitis, or arthritis, resulting in a delay in appropriate treatment.

We present a case of a sternal lesion initially diagnosed and treated as osteomyelitis. We hope this case report raises awareness of this important and potentially lethal entity.

Case Report

A 3-year-old boy initially presented several times to an outside emergency department (ED) for abdominal pain and fevers to 101°F (38.3°C). A workup that included complete blood cell (CBC) count with differential, electrolytes, urinalysis and culture, abdominal ultrasound, and kidney-urinary-bladder x-ray (KUB) was negative. After symptoms persisted for 3 weeks, the boy was brought to the ED at a large tertiary-care pediatric referral center for further evaluation.

On presentation, the boy was afebrile and appeared well. Clinical and abdominal examinations were benign. The only abnormal laboratory finding was an elevated sedimentation rate (ESR): 126 mm/h. KUB and abdominal computed tomography (CT) scan were negative. The patient was discharged after intravenous hydration and was given a follow-up appointment in gastroenterology.

He returned to the ED 2 weeks later with persistent abdominal pain and fevers. He had been seen by a gastroenterologist and was started on lansoprazole, but his symptoms did not improve. Again, he was afebrile and had a benign abdominal examination. However, the patient now localized pain to the upper abdomen and intermittently cried with pain. Laboratory studies were again remarkable for an elevated ESR (94 mm/h) with normal white blood cell (WBC) count and hematocrit. Repeat KUB was negative.

Because of the persistence of symptoms and elevated ESR, the patient was admitted to the general pediatric service for further workup. A full rheumatologic workup was performed, but all laboratory results were normal, including a purified protein derivative (PPD) test. On further blood tests, a decreasing hematocrit was noted. The hematology/oncology department was consulted, and, after review of a normal-appearing peripheral smear, a diagnosis was made of anemia of chronic disease with low likelihood of malignancy. Soon after admission, the patient's examination began to localize to the sternum, and x-rays of the area revealed a periosteal reaction (Figure 1). A bone scan demonstrated intense tracer uptake in the mid to low sternum (Figure 2). Subsequent CT and magnetic resonance imaging (MRI) of the chest demonstrated diffuse demineralization and edema of the bone marrow and surrounding soft-tissues—all consistent with osteomyelitis of the sternum. The orthopedic service was consulted, and a CT-guided biopsy was performed to obtain material for culture and pathology. Cultures remained negative, but the tissue was of insufficient quantity for permanent pathology. The general surgery department, consulted for consideration of open biopsy for pathology, recommended a trial of antibiotic therapy to assess response.

A peripherally inserted central catheter line was placed, and the patient was discharged home on high-dose antibiotic therapy with cefazolin for treatment of presumed sternal osteomyelitis.

He returned to the ED 1 week later with daily fevers to 103°F (39.4°C) and was readmitted, with normal laboratory tests except for an ESR of 100 mm/h. C-reactive protein on admission was normal (0.56) but rose to 31.6 during admission. Repeat MRI showed increased soft-tissue and bone marrow edema consistent with worsening of the presumed osteomyelitis. Because of concerns about inadequate antibiotic coverage, an open biopsy of the sternum was scheduled. Preoperative blood tests now demonstrated leukopenia, thrombocytopenia, and anemia. Hematology/oncology, consulted again, performed a bone marrow biopsy, which confirmed pre–B-cell acute lymphoblastic leukemia (ALL).

The patient was subsequently transferred to the oncology service for induction of chemotherapy.

Literature Review

Childhood leukemia is a myeloproliferative neoplasm, accounting for almost 30% of all cancers in children younger

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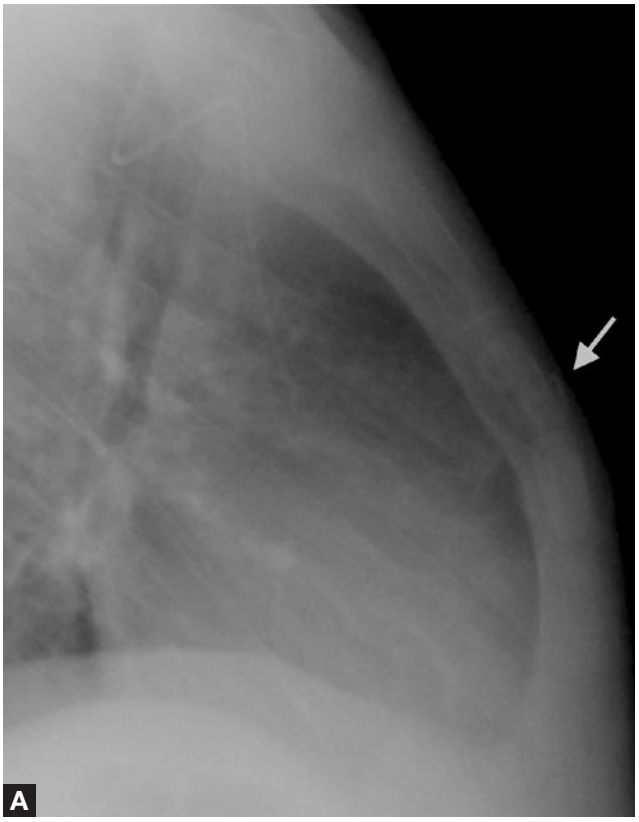

Figure 1. Lateral x-ray of sternum shows periosteal reaction (arrow).

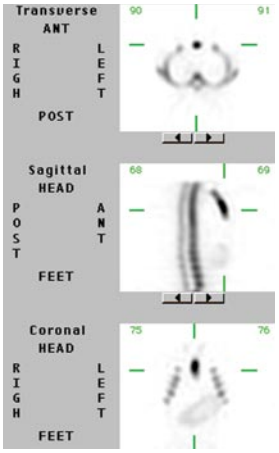

Figure 2. Bone scan shows intense tracer uptake in the mid sternum.

than 15 years and making it the most common childhood malignancy.[2,3] Approximately 3250 children are diagnosed with leukemia in the United States each year; the annual incidence is 15 to 33 per million in children younger than 15 years.[3] Approximately 75% of leukemia cases are classified as ALL, which can be further characterized by immunophenotyping, with the pre–B-cell subtype constituting approximately 25% of ALL.[4] Overall, males are affected slightly more often than females (1.2:1), and white children are affected more commonly than black children by a factor of 1.6 for leukemia in general and by a factor of 2 for ALL in particular.[3] Because of improvements in chemotherapy regimens, ALL survival rates are now approaching 80% in most age groups.[3]

Nonspecific complaints, such as lethargy, pallor, bruising, fevers, bleeding, are present in approximately 80% of pediatric leukemic patients on presentation.[1] Diffuse extremity aching, back pain, new-onset limping, bony tenderness, and joint pain and swelling are presenting complaints in approximately 20%.[1] Musculoskeletal manifestations of leukemia are the result of myeloproliferative changes occurring in the bone marrow and of infiltration of bone and soft tissues (eg, synovium) by malignant cells.[5] The hip and knee are the most commonly involved joints, but polyarthralgias are common findings.[6,7] Thorough history-taking and physical examination are essential. Chronic fatigue and fevers are common, and physical examination can reveal petechiae, bruising, pallor, joint pain, and swelling. Lymphadenopathy or hepatosplenomegaly is present in up to 60% of cases of pediatric leukemia.[8] Laboratory tests should include CBC count with differential and ESR. Increased production of abnormal cells often leads to thrombocytopenia and anemia, while the WBC count can be elevated, depressed, or normal.[1] Peripheral smears to detect blast cells are very helpful but are not routinely performed unless there is a high index of suspicion for malignancy. The typical constellation of leukopenia, anemia, thrombocytopenia, elevated ESR, and blasts on peripheral smear is believed to occur in up to 70% of cases of pediatric leukemia.[8] A bone marrow biopsy gives final confirmation of the disease and allows immunophenotyping for further subclassification before initiation of chemotherapy.

Radiographic examination of the affected limb can demonstrate osteopenia, lytic or sclerotic lesions, periosteal reactions, and metaphyseal bands (so-called leukemic lines) in 47% to 69% of children at time of presentation[9]; during the course of the disease, up to 90% of patients develop some of these features. Bone scans demonstrate scintigraphic changes with diffuse periarticular reactivity, most commonly around the knee, in up to 75% of cases.[10] However, the nonspecific nature of ALL on radiographic examination does little to distinguish ALL from other differential diagnoses, such as rheumatoid arthritis and osteomyelitis.

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Discussion

Musculoskeletal symptoms have been found to be the chief complaint in 14% to 20% of leukemia cases.[1,11] Not surprisingly, 11% to 17% of patients with ALL are initially referred to orthopedists[8] for workup of presumed juvenile rheumatoid arthritis,[12,13] septic arthritis,[14-16] or osteomyelitis.[17] Even

though many patients have radiographic abnormalities, these abnormalities tend to be nonspecific and can mimic other diseases, such as osteomyelitis. Furthermore, 25% to 60% of patients do not show any abnormalities on initial x-rays.[1,18]

The differential diagnosis is complicated by several factors, such as the much higher incidence of entities like osteomyelitis, transient synovitis, and rheumatoid disease, which present with similar clinical and laboratory findings, such as fevers and joint pains, changes in WBC count, and elevated ESR. Further compounding the issue is an apparent difference in laboratory parameters between cases with and without musculoskeletal symptoms at presentation. One study found significantly more normal hematologic parameters in the first group, resulting in increased time to diagnosis.[19]

It is unclear whether we can attribute all our patient's symptoms to leukemia, or if he indeed had osteomyelitis in the setting of ALL, which is a recognized but comparatively rare complication (<2% of cases).[20] However, this case demonstrates the importance of having a high index of suspicion when a seemingly common disease does not respond to adequate therapy.

Author's Disclosure Statement

The author reports no actual or potential conflict of interest in relation to this article.

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