Acute leukemia results from a clonal proliferation of myeloid or lymphoid cells originating in an altered multipotential stem cell. These neoplastic clones eventually replace normal hematopoietic cells of the bone marrow, leading to deficiencies in normal blood cells and leukemic cell infiltration of organs.1

A high index of suspicion for malignant disease should always be maintained by the treating podiatric physician when unusual presentations of infection persist. Infections accompanied by musculoskeletal pain, pallor, fatigue, local edema, or erythema should especially be monitored because leukemia can manifest as these types of problems.2, 3 Musculoskeletal pain may be present weeks to months before any indication of malignancy is discovered in the blood.4 Cytopenia is a typical finding on a complete blood cell count in patients with acute leukemia, with anemia and thrombocytopenia being the most common forms.5 Complete blood cell counts may show elevated (60%), decreased (35%), or normal (5%) leukocyte counts.2, 5

Case Report

An otherwise healthy 10-month-old boy was seen on an emergency basis for redness and drainage of his right fifth toe and a fever (temperature of 40° C). A hangnail was removed, and the infant was administered oral cephalexin for cellulitis. The following day, red streaking was noted from the fifth toe extending to the ankle. The infant was admitted to the local hospital with a diagnosis of cellulitis or osteomyelitis. A complete blood cell count (without differential) was ordered, and a white blood cell count of 21.7 × 10^3/μL was reported. Incision and drainage of the distal area of the fifth toe was performed, and appropriate cultures were taken, with ultimate growth of Staphylococcus aureus. The patient was administered intravenous nafcillin for 5 days, which was later changed to oral cephalexin. His white blood cell count decreased to 13.9 × 10^3/μL, with an erythrocyte sedimentation rate of 30 mm/h and a hematocrit level of 23.3%.

The patient’s erythrocyte sedimentation rate became elevated again 1 week later, to 35 mm/h. Radiographs showed only soft-tissue swelling, with no signs of osteomyelitis or foreign bodies. The swelling continued to increase, although there was no fever, pain, or red streaking. The erythrocyte sedimentation rate continued to increase, reaching 67 mm/h. An infectious disease consultation was never followed up on. Magnetic resonance imaging was recommended but was not available in the patient’s town. The infant was sent home with instructions for administration of oral ciprofloxacin for 3 days. The swelling decreased during the next week, but the erythrocyte sedimentation rate remained elevated at 68 mm/h. After 6 weeks with no improvement, the patient was referred to the University of California, San Francisco Children’s Hospital, with an admitting diagnosis of osteomyelitis.

The patient was admitted to the pediatric service with a temperature of 38.6°C and was given intravenous cefazolin to treat the previously diagnosed S aureus infection. His physical examination findings were normal except for mild lymphadenopathy in the neck and a red and swollen but nontender right fifth toe. Radiographs taken at the University of California, San Francisco, showed a smaller-than-normal
middle phalanx of the fifth toe that was also present on the left foot and thus was considered a normal variant. Ultrasound showed no evidence of focal fluid collection, joint effusion, or periosteal elevation.

An orthopedic consultation was requested, and the infant was seen by the author. Physical examination revealed a child with a pale complexion who was in no apparent distress. The right fifth toe was erythematous and swollen, with no streaking, effusions, or drainage and no pain evident on palpation. A complete blood cell count, with a differential blood cell count and a blood smear, was ordered. The results were as follows: white blood cell count, 18.4 × 10³/μL; hematocrit, 23.0%; neutrophils, 0.18 × 10³/μL (reference range, 1–8.5); lymphocytes, 5.15 × 10³/μL (reference range, 2–14); blast cells, 9.94% (within reference range); and atypical lymphocytes, 1.29% (reference range, 0–0.2). The values for mean corpuscular volume were not available.

The picture of leukocytosis, anemia, neutropenia, and atypical lymphocytes was cause for concern. The child was transferred to the pediatric oncology unit of the University of California, San Francisco Children’s Hospital, and underwent a bone marrow biopsy and lumbar puncture. Biopsy showed red blood cell schistocytes (fragments of red blood cells seen in hemolytic anemia), white blood cells with occasional blast cells (immature white blood cells), marked neutropenia, and thrombocytopenia. A preliminary diagnosis of acute myeloid leukemia was made. Chromosomal analysis showed an abnormal male karyotype that presented as 20 cells belonging to an abnormal clone characterized by a translocation between the long arms of the X chromosome and chromosome 11. The t(X;11) has been described in three cases of acute myeloid leukemia (acute nonlymphoblastic leukemia, M5 variant) in early childhood, as interpreted by the geneticist.

A 2-week course of chemotherapy was initiated. The infant was also given intravenous piperacillin-tazobactam, tobramycin, and amphotericin for fever and neutropenia. The redness and swelling of the toe improved markedly. The patient was discharged from the hospital after approximately 1 month and was recovering eventfully at 6-month follow-up.

**Discussion**

Acute leukemia can be classified into two main types: acute lymphocytic leukemia, representing 75% to 80% of the childhood cases of leukemia, and acute myelogenous leukemia, also known as acute nonlymphoblastic leukemia. Acute myelogenous leukemia represents most adult cases and composes approximately 15% to 20% of the leukemias in children. Some manifestations of leukemias as well as osteomyelitis, arthropathies, lymphomas, hemophilia, and sickle hemoglobinopathies may be clinical abnormalities in the musculoskeletal system. Malignant disease should always be suspected by the treating physician when unusual presentations of suspected infection persist, especially musculoskeletal pain. This pain occurs because of leukemic infiltration of the synovium, periosteal elevation of intraarticular and periarticular bone, hemorrhaging into the joint, and, rarely, crystal-induced inflammation.

In one study of six children, three had a positive antinuclear antibody test result that initially caused the leukemia to be overlooked.

Blood tests for hematogenous osteomyelitis may reveal an elevated white blood cell count in only 31% to 40% of the pediatric population and an elevated erythrocyte sedimentation rate in 91%. The latter is typically elevated with leukemia; therefore, the picture could mimic or be consistent with osteomyelitis or septic or rheumatologic arthritis, and blood test results for arthritic disease should be evaluated as well. The best test overall is a bone marrow biopsy to identify leukemic blast cells. Marrow cells can also be examined for the number and shape of chromosomes (cytogenetic examination) and immunophenotyping.

Blood tests should include a complete blood cell count with a differential blood cell count and a blood smear and should evaluate all cell lines. The erythrocyte sedimentation rate is not a marker for malignant disease and should not be used as such because it can be elevated in leukemia and osteomyelitis. It was followed closely throughout the case reported here because osteomyelitis was one of the diagnoses. If osteomyelitis had been present, a complete blood cell count and erythrocyte sedimentation rate would have been good monitors of this condition. The prevalence of chromosomal abnormalities in children and adults with acute myeloid leukemia may be as high as 80%.

A normocytic normochronic anemia with a decreased reticulocyte count is a common finding in patients with acute leukemia. The presence of blast cells (immature white blood cells) on a smear may be worrisome, although blast cells are usually found on a smear. Peripheral blast cells are seen in approximately 85% of patients with acute myeloid leukemia, with 80% having anemia and thrombocytopenia.

Radiographic abnormalities in leukemic patients may include osteopenia, sclerotic lesions, lytic lesions, metaphyseal bands, and periosteal new bone formation, resembling an osteomyelitic presentation. Subperiosteal calcification may occur as a reaction to the splenomegalia, hepatomegaly, and purpuric lesions that can develop with acute leukemia.
Abnormal bone scintigraphic findings resulting from leukemic infiltration of bone and marrow may lead to an early diagnosis of leukemia. Gallium citrate Ga 67 scintigraphy is an excellent diagnostic procedure for screening for chronic osteomyelitic conditions in patients with leukemia. This procedure is especially useful in patients who have unexplained fevers without any localizing symptoms, a situation that presents difficulty in detecting and differentiating patients with leukemia.

During the course of leukemias, lymphomas, and plasmacytomas, malignant cells may also be found in the dermal and subcutaneous tissues, forming ulcers, nodules, or plaques. In acute myeloid leukemia, young patients may develop nonulcerating, greenish lesions. Therefore, any newly developed cutaneous lesion with abnormal characteristics should arouse suspicion in the treating physician.

The cure rate for acute myeloid leukemia is approximately 40% to 50% and for acute lymphocytic leukemia is approximately 75% to 85%. First-line treatment for both includes chemotherapy, yielding complete remission in most patients with acute lymphocytic leukemia and approximately two-thirds of patients with acute myeloid leukemia. Bone marrow transplantations may be reserved for children experiencing a second remission of acute lymphocytic leukemia and after the first remission for patients with acute myeloid leukemia.

**Conclusion**

When treating any type of lower-extremity infection in the pediatric patient, the physician should always consider leukemias as a possible diagnosis. A blood cell count differential with smear should always be ordered as part of the complete blood cell count when evaluating these infections. The treating physician may then be able to identify a serious or life-threatening disease at the earliest possible stage.

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**References**


