Chapter 15
Case of a Young Child Who Refuses to Bear Weight and Has Back Pain due to Leukemia

David Gendelberg and Todd J. Blumberg

Brief Case Presentation

Chief Complaint

A 4-week history of progressive weakness, weight loss, back pain, and 4 days of refusal to bear weight after a fall at home.

History

A 4-year-old boy has had progressive lower extremity weakness over the last month, increasing back pain, and a 3 kg weight loss and now won't stand up or walk. He had been playing outside a few weeks ago when his parents report that he had an accidental fall. He seemed to recover, but was notably clumsier and unsteady on his feet and has fallen several times in the last week. Four days ago he really slowed down, stopped walking, and began scooting, and now he is refusing to walk at all. He complains of pain when his parents lift him under his arms or with attempts to make him stand. When he is resting or seated, he seems comfortable. There has been no change in his bowel or bladder function. He has had no fevers recently, but he did have an upper respiratory illness about 2 weeks ago. This has since resolved. Family

D. Gendelberg (✉)
Department of Orthopaedics and Sports Medicine, Harborview Medical Center, University of Washington, Seattle, WA, USA

T. J. Blumberg
Department of Orthopaedics and Sports Medicine, Seattle Children's Hospital, University of Washington, Seattle, WA, USA

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history is notable for multiple family members with autoimmune diseases on the maternal side. There has been no recent travel out of the country or sick contacts.

Physical Examination

His weight is 20.2 kg, height 114 cm, and temp 36.2. He is not ill-appearing. Development is normal. There is no lymphadenopathy, but has notable pallor. There are no petechiae or organomegaly. He has no pain at rest while supine; however, he is uncomfortable with strength testing of the extremities. Lumbar spine tenderness to palpation is noted. No scoliosis is noted. Neurological examination is challenging given the patient's age, but he was noted to be spontaneously moving his upper and lower extremities with spontaneous knee flexion and extension, plantar flexion, dorsiflexion, and movement of all the toes in flexion and extension. He responds appropriately to light touch and tickling of his feet. There is no clonus. Babinski is down going. Reflexes are symmetric and 2+. He is unable to ambulate for gait assessment.

Imaging and Radiographic Studies (Figs. 15.1 and 15.2)

Questions About the Case the Reader Should Consider

1. What are the red flags in this patient's history that raise your concern?
2. What may be the possible cause of this patient's vertebral compression fracture?

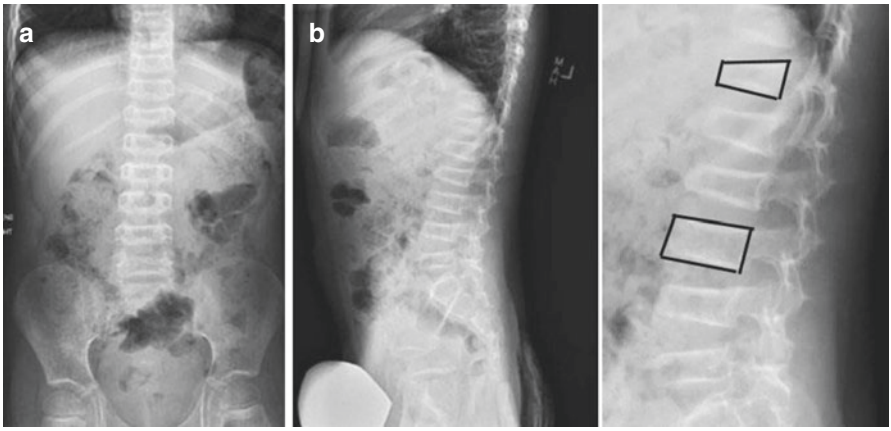

Fig. 15.1 (**a**) Full-length AP and lateral spine x-rays. (**b**). On closer inspection, there are multilevel compression fractures involving the thoracic and lumbar spine. The levels with most prominent height loss are T12, L4, and L5. Note the anterior wedging and height loss as compared to the adjacent normal vertebras. (Courtesy of Teresa Chapman, MD, Seattle Children's Hospital, Seattle, Washington)

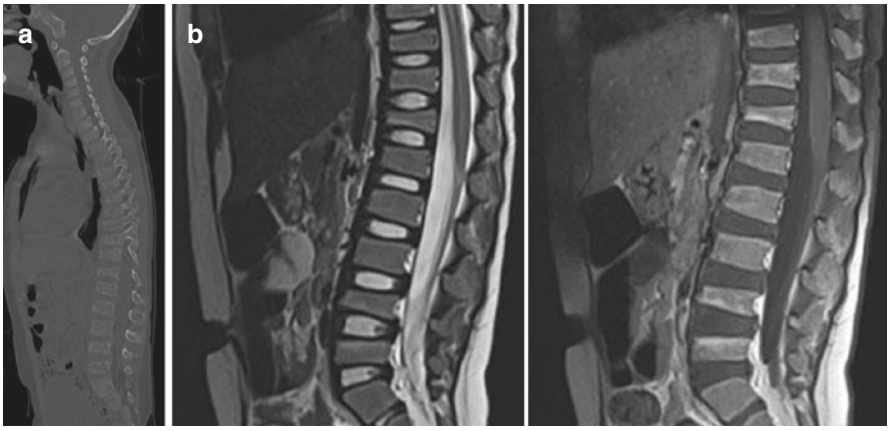

Fig. 15.2 (**a**) An CT ordered by the oncologist demonstrated diffuse osteopenia throughout the visualized axial skeleton with associated multilevel vertebral body height loss involving the thoracic and lumbar spine, in particular involving T12, L4, and L5 with at least 50% vertebral body height loss. These findings suggest a systemic underlying cause of demineralization and suspicion for pathologic vertebral body fractures. In this age group, leukemia is a primary consideration, although an underlying metabolic bone abnormality is also possible. (**b**) T2 sagittal and T1 contrast-enhanced sagittal images showing multilevel compression fractures and marrow enhancement of T12, L4, and L5. The oncologist or pediatric orthopedist will always obtain a contrast-enhanced MRI when evaluating for a tumor, inflammatory, or infectious process. (Courtesy of Teresa Chapman, MD, Seattle Children's Hospital, Seattle, Washington)

3. What tests should be ordered next?
4. What physical exam findings are often found with this diagnosis?
5. What is the appropriate referral?
6. What are the treatment options for this case?

Discussion

Leukemia can mimic several orthopedic pathologies in children at presentation. Therefore, it is important to obtain a thorough history and exam [1]. Many details in this patient's history should raise concern. Back pain in a 4-year-old is a red flag. Moreover, persistent back pain that wakes the child up at night and is debilitating to the point that the patient has difficulty ambulating requires an immediate and thorough evaluation [2–4]. As the child grows, gradual weight gain is expected. Therefore, unintended weight loss, especially over a short period of time, should raise concern. Increasing clumsiness or an unsteady gait is also very concerning. When encountering these symptoms, one should consider a differential diagnosis that includes tumor, infection, or systemic inflammatory arthritis [4].

The causes of bone demineralization during the course of leukemia are multifactorial, and it can be caused by the underlying infiltrative disease process, inactivity,

chemotherapeutic agents, and abnormalities in bone mineral homeostasis. This in turn leads to decreased bone density, to weakening of the bony architecture of the vertebral body, and ultimately to the development of compression fractures, even without trauma. Following treatment, patients often experience some degree of remodeling and improvement of bone mineral density [5–9].

When approaching a pediatric patient with back pain, weight loss, and refusal to bear weight, it is important to establish a differential diagnosis to guide further diagnostic evaluation. Many conditions may present similar to the patient described above necessitating further testing. The most urgent diagnoses are malignancy and infection. Leukemia is a malignancy affecting the white blood cells, often leading to an infiltrative process of the bone marrow and ultimately changes in the patient's peripheral blood composition. Infection, especially when severe, may also present with abnormal findings in routine laboratory blood tests. Therefore, initial diagnostic tests for suspected malignancy or infection should consist of a complete blood count (CBC) with differential and a peripheral blood smear. In addition to a CBC, erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP) should also be obtained, as inflammatory arthropathies and musculoskeletal infection may present similarly [10–13].

Leukemia can affect multiple organ systems throughout the body. Therefore, additional tests should be performed to evaluate the function of the additional viscera. This is achieved by ordering a basic metabolic panel (BMP), liver function tests, and coagulation studies.

Leukemia may present in multiple ways and mimics many self-limited diseases of childhood. Therefore, one needs to keep a certain index of suspicion and perform a thorough history and physical exam of the patient. A meta-analysis that included >3000 children from 33 studies found that more than half of the patients presented with at least one of the following exam findings: organomegaly, pallor, fever, or bruising. Organomegaly was found in over 60% of the cases and may manifest as weight loss, abdominal distension, or abdominal pain. Lymphadenopathy, which may be found in nearly half of the patients, typically presents as nontender, firm, and matted and does not respond to antibiotics. Lymphadenopathy in the posterior auricular, epitrochlear, or supraclavicular area should raise greater concern for malignancy. Fever is present in more than half of the patients with leukemia. Manifestation of hematologic abnormalities, such as bleeding (i.e., petechiae), pallor, and abnormal laboratory values are present in over 50% of patients. In addition, musculoskeletal pain has been found to be the presenting symptom in 43% of cases [14]. Less common findings include a mediastinal mass, headaches, or testicular enlargement. A mediastinal mass may cause swelling, dysphagia, or dyspnea secondary to compression of the superior vena cava or through direct compression [10].

Upon suspicion of leukemia, the patient should be referred to a pediatric oncologist for further workup and diagnosis. The first step taken will be to obtain a bone marrow biopsy. Once the tissue is obtained, the pathologist will perform further tests to confirm the diagnosis and detect the subtype of leukemia present. Workup

of the bone marrow may include morphological assessment, cytochemical evaluation, or immunohistochemical analysis [10, 11]. When vertebral compression fractures or other fractures are present, the patient should be referred to a pediatric orthopedic surgeon for further evaluation and treatment. In these cases, CT or MRI may be ordered by the oncologist in collaboration with the pediatric orthopedist to better characterize the fractures and extent of disease.

Multidrug chemotherapy is the mainstay of treatment for leukemia. The exact regimen is dependent on the immunophenotype of the leukemia as well as the patient's risk category. Treatment is divided into multiple phases, and evaluation for central nervous system involvement with a lumbar puncture is necessary to determine if intrathecal chemotherapy is indicated (Fig. 15.3). Most treatment regimens take 2–3 years to complete. In addition, the patient should be treated whenever there is a suspected infection with broad-spectrum antibiotics, and any metabolic imbalances should be corrected. Back pain and joint pain will usually begin to improve a few weeks after the initiation of therapy. Typically, no active intervention is required. For multiple compression fractures, bracing may be helpful, but is sometimes not considered necessary unless there is the development of kyphosis on upright radiographs.

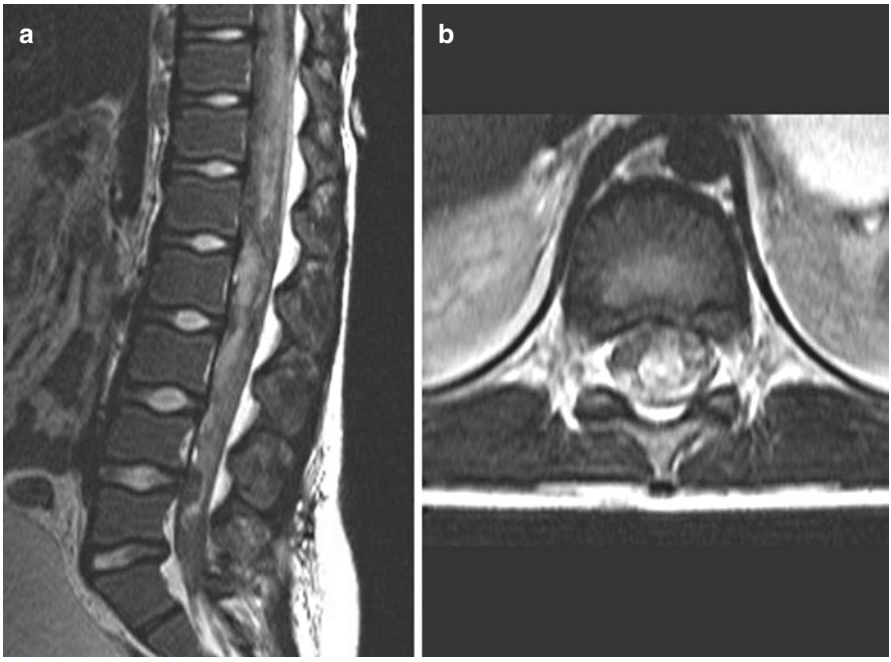

Fig. 15.3 T2-weighted sagittal and axial images displaying an example of central nervous system involvement with intradural enhancement in a patient with leukemia. (Courtesy of Teresa Chapman, MD, Seattle Children's Hospital, Seattle, Washington)

How to Approach the Case

Any young child who refuses to bear weight or is having unexplained weakness and clumsiness warrants further evaluation, with blood work and plain radiographs initially obtained to help narrow the differential diagnosis. Labs showed a normal white blood cell count of 6.1 K/mm^3, mild thrombocytopenia with a platelet count of 138 K/mm^3, and severe anemia, with a hematocrit 19.8%. CRP was mildly elevated at 1.8 mg/dL. ESR was markedly elevated at >140 mm/min.

In this case, there were no clear localizing symptoms, and the onset was fairly insidious over several weeks. Infection would also be possible given his clinical presentation; however, without fever and only mildly elevated CRP, this is less likely. A blood culture may be ordered. A decrease in the production of platelets and red blood cells with multilevel pathologic compression fractures is concerning for a systemic process, and additional imaging is indicated to better evaluate whether an oncologic, infectious, or inflammatory process is occurring.

Red Flags for Back Pain
- Younger child
- Night pain
- Neurological findings
- Inability to bear weight
- Fevers
- Weight loss

Short Differential Diagnosis
- Infection – Always suspect infection when a tumor is suspected.
- Inflammatory arthritis – Juvenile idiopathic arthritis, reactive arthritis, inflammatory bowel disease-related arthritis.
- Other malignancies: Lymphoma, benign bone tumors, malignant bone tumors, tumors of the neural elements.
- Eating disorder or vitamin D deficiency.

Final Diagnosis

Leukemia in a 4-year-old boy.

Natural History and Treatment Considerations

Multilevel compression fractures in a young patient without kyphosis can be observed without bracing. Bracing, however, can be used to reduce pain in select cases. The compression fractures are pathologic fractures as the bone marrow has been replaced by rapidly dividing leukemic cells, in this case precursor B-cells. When this occurs, the energy needed to cause a compression fracture is markedly decreased, and even a simple fall in a young child may result in a fracture. Follow-up is needed with repeat upright radiographs to confirm that no kyphosis develops. Pain typically resolves with appropriate treatment of the underlying malignancy [6–9].

Referral – Emergency, Urgent, or Routine: And to Whom?

A young child presenting with back pain and refusal to bear weight should raise alarms and prompt immediate workup. Once there is suspicion for a malignant process, the patient should be *urgently* referred to a pediatric oncologist. In the event of a child with associated compression fractures, the patient should be referred to a pediatric orthopedic surgeon with expertise in spinal conditions for fracture management. In addition, the patient should be seen by a physician with experience in bone metabolism, such as an endocrinologist, for bone mineral density optimization. Many treatment regimens for leukemia include high-dose corticosteroids, which further weaken the bone density. Monitoring of bone mineral density should continue after remission as studies have found that bone metabolism and endocrine function continue to be affected into adulthood among pediatric cancer survivors [15].

Brief Summary

Refusal to bear weight in a young child is never normal and must be investigated until a cause is identified. While back pain is not uncommon in children, it is concerning if associated with refusal to bear weight, unintended weight loss, signs of motor weakness, and increased clumsiness or falls. In this case, the imaging helps to both explain the back pain and to identify a systemic cause for both the back pain and refusal to bear weight. Multiple compression fractures of the spine are not common in children without associated high-energy trauma. However, severe osteopenia and bone marrow infiltration predisposed this patient to them. The most common pediatric malignancy is leukemia, which accounts for nearly 30% of all pediatric cancers. Urgent referral to a pediatric oncologist and pediatric spine surgeon is indicated for appropriate staging and treatment for the malignancy and to assure no long-term sequelae from the compression fractures.

Key Features and Pearls

- Refusal to bear weight and persistent back pain in a young child should raise a red flag for a more involved process such as malignancy, infection, or inflammatory arthritis. These children should undergo a prompt workup and referral.
- Patients with leukemia that have involvement of the spine may sustain compression fractures secondary to local osteopenia. These fractures usually do not need surgical intervention and need follow-up as well bone mineral density optimization.
- Back pain will usually lessen a few weeks after treatment for the leukemia is initiated.

Editor Discussion

Leukemia is the most common cancer in childhood. Twenty percent of children with leukemia present with bone pain. Some children with leukemia will limp and some will stop walking. The most important aspect of this case is recognition! Keep leukemia high on your differential diagnosis in any child with back pain combined with fever, pallor, malaise, lymphadenopathy, hepatosplenomegaly, and easy bruising.

W.L. Hennrikus

Back pain in the child under 5 years of age is particularly concerning. Infection and tumor are both relatively rare in this age group, but a surprisingly common cause of back pain when an actual source is identified. So when you hear that a 3-year-old child has back pain, won't walk or walks very cautiously, and seems very stiff, think of inflammation in the spine. This could include discitis, a primary spinal cord tumor, or tumor affecting the spine such as leukemia. The hip joint in this age group is a more common reason a child might refuse to walk, either from transient synovitis or septic arthritis. So when the workup of the hip is negative, don't forget the spine!

R.M. Schwend

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