Isolated Langerhans Cell Histiocytosis of the T12 Vertebra in an Adolescent

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Langerhans cell histiocytosis (LCH) represents a group of rare, benign, histologically similar disorders of relatively unknown etiology and pathogenesis.[1] Research suggests that the etiology is multifactorial, possibly involving the patient's environment, infection (human herpes virus 6), immune response, and/or genetics.[2] While some controversy exists over which disease subtypes should be classified within this grouping, disorders such as solitary eosinophilic granuloma, Hand-Schüller-Christian disease, and Letterer-Siwe disease are typically included,[3] representing unifocal, multifocal, and disseminated variants, respectively.[2] Although it was once believed that these 3 diseases were separate entities, it is now recognized that they are different manifestations of the same disease process, involving a clonal proliferation of Langerhans cells.[4]

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LCH is a disease of childhood, with a peak incidence between 5 and 10 years of age,[5] although recent studies have shown a shift in the trend toward even younger children, predominantly aged 1 to 4 years.[2] Nearly 85% to 90% of cases of LCH primarily affect bone, although other organ involvement has been reported.[5] Despite LCH's high percentage of bone involvement, the incidence of vertebral involvement ranges from only 7.8% to 25%.[6] As the incidence of LCH is approximately 5.4 million children per year,[2] or 1:2,000,000 per year,[6] the number of cases involving the vertebra is likely less than 1 million per year.

We report the case and follow-up of a 15-year-old boy with isolated LCH of the T12 vertebra.

Case Representation

A 15-year-old active male with a past medical history of insulin-dependent diabetes mellitus presented with a 1-month history of worsening lower back pain that had begun spontaneously without injury and did not respond to anti-inflammatory medicines. The pain was well localized to the thoracolumbar region. The patient rated the pain 7 out of 10, which initially he experienced at night, but over the course of a few weeks it progressed to a state of constancy. The pain was aggravated by activity, particularly heavy lifting. The patient reported that the day prior to presentation, he experienced severe pain in the low back and difficulty walking after picking up a 30-pound package; this pain did not radiate to the lower extremities. Eventually, the patient went to the local emergency room to be evaluated; there, he was prescribed propoxyphene, which offered him some moderate relief.

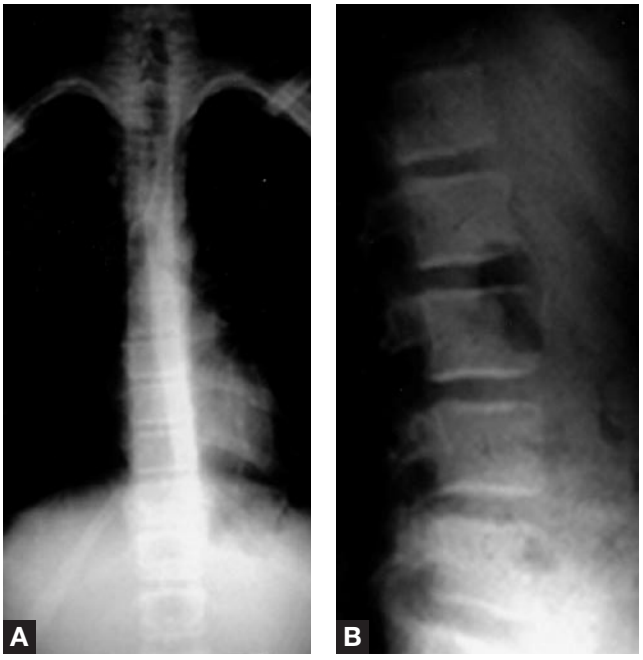

Figure 1. Anteroposterior and lateral radiographs of the spine reveal no evidence of definable lesions involving the clinically localized zone of back pain.

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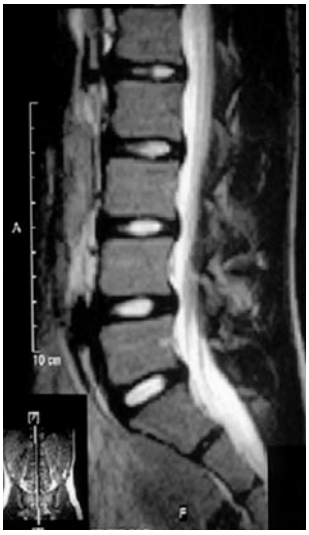

Figure 2. Sagittal T_2-weighted magnetic resonance imaging shows evidence of a mild focus of increased intensity in the T12 vertebral body.

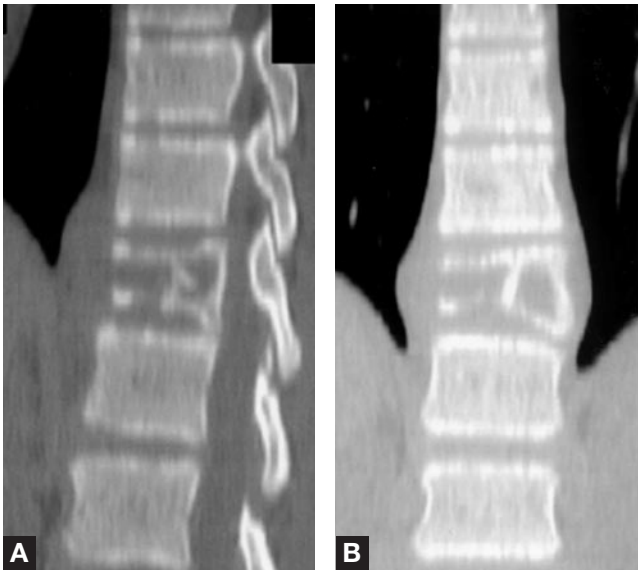

Figure 3. Sagittal and coronal computed tomography images reveal a lytic permeative lesion involving T12 vertebra with mild paraspinal soft-tissue changes.

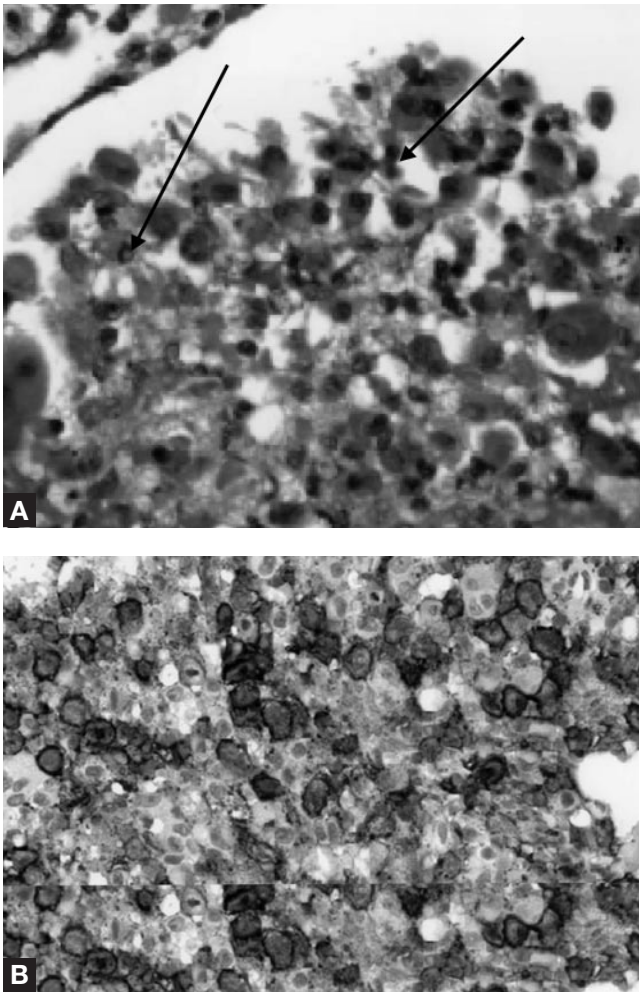

Figure 4. **(A)** There is a chronic inflammatory infiltrate consisting of multinucleated cells, histiocytes, eosinophils, and lymphocytes. Arrows point to Langerhans-type histiocytes characterized by ample cytoplasm and vesicular, frequently clefted, or kidney-shaped nuclei (hematoxylin-eosin, original magnification ×100). **(B)** Immunohistochemical stain using antibody to CD1a produces a characteristic membranous staining pattern with a paranuclear dotlike positivity in the Langerhans cells.

He had no prior history of back pain, and denied fevers, chills, night sweats, and recent weight loss. He also denied numbness and paresthesias in the lower extremities as well as bowel and bladder symptoms.

On examination, the patient appeared to be otherwise healthy. He could heel- and toe-walk without difficulty, except for pain in the lower lumbar spine. The patient was markedly tender over the left paraspinal musculature of the lumbar spine. He also had some scoliotic deformity. He had 5/5 motor strength in all extremities bilaterally, intact sensation throughout, symmetric reflexes, and bilaterally symmetric pulsations.

Radiographs of the lumbar spine performed the day prior to presentation (Figure 1) showed no evidence of any obvious lesions. Magnetic resonance imaging (MRI) of the lumbar spine (Figure 2) revealed a mild focus of increased intensity in the T12 vertebral body. The patient also had a computed tomography (CT) scan performed (Figure 3) that revealed a lytic permeative lesion involving T12 vertebra with associated expansion and paraspinal soft-tissue changes. Technetium-99m methylene diphosphonate radioisotope bone scans revealed increased uptake of T12 at the left pedicle and superior endplate without any other areas of focal involvement.

The differential diagnosis included histiocytosis, trauma, bone cysts, Ewing sarcoma, neuroblastoma, lymphoma, leukemia, and hemangiomatosis, with histiocytosis being the most concerning given the appearance of the lesions. CT-guided biopsy confirmed a diagnosis of LCH (Figure 4).

The patient was given a protective brace to be worn full-time and a walker to help with ambulation. One month later on follow-up, radiographs revealed findings of vertebral wedging (Figure 5). The patient reported that his pain had improved to 1 or 2 out of 10. He was able to ambulate around the house independently. There were no neurologic findings. He was encouraged to continue wearing

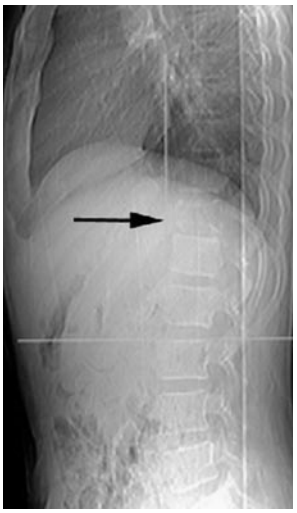

Figure 5. Lateral radiograph of the spine at 1-month follow-up demonstrates early wedging of the vertebra due to Langerhans cell histiocytosis involvement, as well as radiolucency at the T12 vertebral body.

the brace full-time for the next couple of months and then weaned off its use gradually as tolerated. He continued to improve further and at 3-month follow-up no longer had any back pain and remained neurologically asymptomatic. Radiographs revealed a characteristic vertebra plana (Figure 6). The patient was encouraged to participate in swimming-type activities and begin a formal physical therapy program to improve paraspinous and abdominal muscle strength and restore proper body mechanics and posture.

Discussion

LCH involvement of the vertebrae is known to occur in 10% to 15% of pediatric spine tumor cases.[7,8] Spinal lesions commonly affect the thoracic vertebrae, specifically the vertebral body[9]; very rarely are the posterior vertebral elements affected. Typically, they appear as solitary, well-defined osteolytic lesions with scalloped borders on radiograph.[10] LCH may eventually cause a complete or incomplete collapse of the vertebral body resulting in the classic finding of "vertebra plana" on imaging. This process typically involves only 1 vertebra, spares the intervertebral discs, and shows increased radiodensity of the involved bone.[6] Vertebra plana, however, appears in only 15% of cases,[9] so it is not a sensitive marker for LCH. In the absence of this classic finding, a differential diagnosis should be considered, including osteomyelitis, Ewing sarcoma, leukemia, lymphoma, metastatic neuroblastoma, hemangioma, Gaucher disease, osteogenesis imperfecta, and aneurysmal bone cyst.[6,11]

"Many children who present with pain report that it subsides rapidly after bed rest.[6]"

Clinical presentation of LCH of the spine varies from extreme pain, acute or gradual in onset, to asymptomatic, in which case the lesion is detected as an incidental finding on imaging. These patients can present with back pain limited to the affected spinal segment and possibly associated with radiating or referred pain.[4] Painful scoliosis can also be a manifestation of these lesions, similar to osteoid osteoma lesions and some inflammatory spinal conditions.[4] In a study of 263 adult and pediatric patients, 62% complained of localized pain and 48% described soft-tissue swelling.[2] Many children who present with pain report that it subsides rapidly after bed rest.[6] In rare instances, patients present with neurologic compromise due to cord compression or displacement.[10,12]

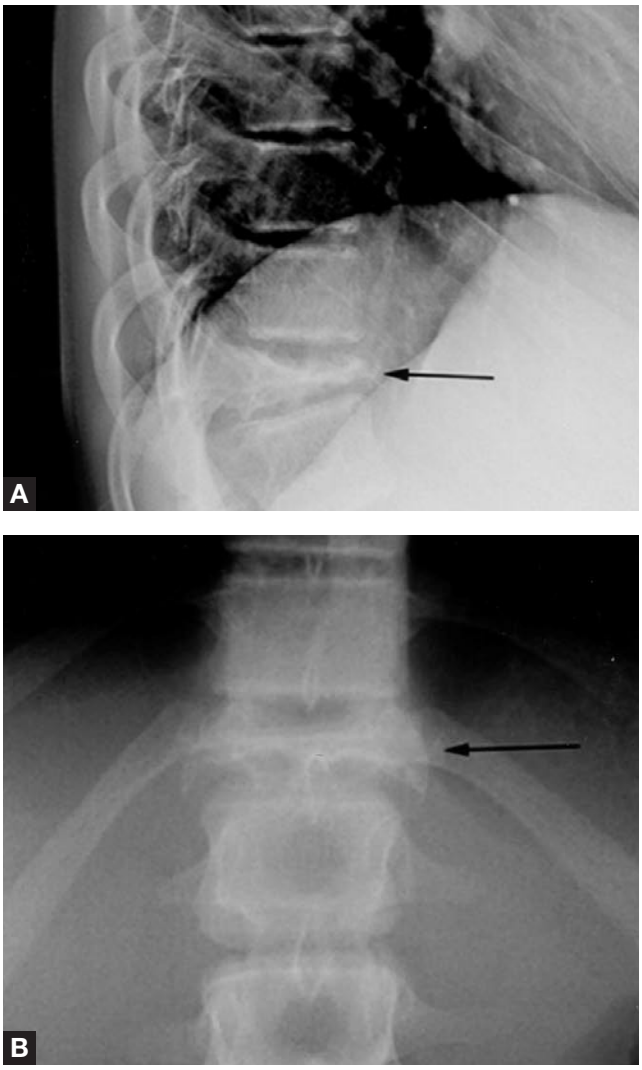

Figure 6. At 3-month follow-up, anteroposterior and lateral radiographs of the spine reveal "vertebra plana" lesion characteristic of Langerhans cell histiocytosis lesions in the spine.

Workup of these patients often involves an initial radiograph of the spine to search for signs of vertebra plana; MRI of the spine to rule out a soft-tissue mass, which would suggest a more aggressive cause of vertebral collapse; skeletal survey radiographs or technetium bone scan to search for multiple lesions; and, eventually, biopsy of the lesion to yield a diagnosis.[4] The decision to use a technetium bone scan versus a skeletal survey has been debated in the literature, but technetium bone scan is the

preferred method at our institution because of the lower total radiation dose.[4] Furthermore, it is equally important, given the differential diagnosis in the majority of cases that do not present in the classic manner, to also obtain a chest radiograph and blood chemistry with hematology, including peripheral blood smear.[6]

Currently, there is no consensus regarding the best therapeutic approach to treatment of patients with LCH. This is because of conflicting evidence as to whether LCH is a neoplastic, infectious, or immunodysregulatory disorder.[2] Bracing, radiation therapy, chemotherapy, and surgery have been used either alone or in combination, with similar success rates[10]; in fact, many cases have demonstrated a favorable outcome without any intervention, given that LCH is often self-limited and does not involve significant deformity or widespread organ dysfunction.[2] Therefore, current practice usually involves managing the patient conservatively with bracing and obtaining regular imaging studies to follow the lesion over time. More invasive or radical treatment options are generally reserved for refractory cases in which there is more extensive, multisystem involvement.[2] However, use of either radiation therapy or chemotherapy is not without complications, as research has demonstrated these patients to be at increased risk for developing a secondary malignancy. In the few studies that have obtained enough significant radiographic evidence to quantify the percentage reconstitution of the vertebrae over time, the results were excellent, particularly in younger children.[4] As research continues in this area, we hope to uncover a greater understanding of the etiology and pathogenesis of LCH to formulate a more definitive protocol in the management and treatment of these patients.

Conclusions

Back pain is a common complaint in pediatric patients, and it is important to be able to distinguish common musculoskeletal causes and injury from rarer conditions, such as LCH. Whereas mechanical back pain typically resolves with inactivity over the course of a few weeks, continuing or progressively worsening pain is a red flag. With high clinical suspicion that the pain is due to a pathologic process, it is important to image the spine with MRI and CT, even if the radiographs are negative; plain radiographs will often miss the lesion, as in this case. Furthermore, imaging studies should not be used to visualize solely the lumbar spine in cases of low back pain, since several types of lesions involving the spine, including LCH, commonly affect the thoracic region. If LCH is detected, a more complete workup should be performed to search for other sites of involvement to determine the prognosis and proper course of treatment.

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The authors report no actual or potential conflict of interest in relation to this article.

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