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Langerhans cell histiocytosis of the spine in children: Long-term follow-up

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LANGERHANS CELL HISTIOCYTOSIS OF THE SPINE IN CHILDREN

LONG-TERM FOLLOW-UP

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Background: Langerhans cell histiocytosis causes destructive lesions in a child's spine. Few large, long-term studies have evaluated the clinical and radiographic presentation, natural history, outcomes of modern treatment approaches, and maintenance of normal spinal growth and stability after the diagnosis of this disease in children.

Methods: Twenty-six children with biopsy-proven Langerhans cell histiocytosis involving the spine were treated at our institution between 1970 and 2003. They had a total of forty-four involved vertebrae (twenty cervical, fourteen thoracic, and ten lumbar). Vertebral body collapse was measured on radiographs and classified as grade I (0% to 50% collapse) or grade II (51% to 100% collapse) and subclassified as A (symmetric collapse) or B (asymmetric collapse). Lesions of the posterior elements of the spine were classified as grade III. Twenty-three children were followed for two years or more (mean, 9.4 years), and the analyses of treatment and long-term outcomes were performed in that group of patients.

Results: There was a predominance of lesions in the cervical spine (p ≤ 0.02). Sixteen (62%) of the twenty-six children were found to have multifocal skeletal disease. Cervical and lumbar lesions were more commonly associated with multilevel spinal disease. The extent of the initial collapse seen radiographically was grade IA for twenty vertebrae, IB for three, IIA for ten, IIB for nine, and III for two. Grade-I lesions were more likely to be associated with symmetric collapse than were grade-II lesions. Spinal deformity developed in four children, and two later required spinal fusion. No relationship was observed between the grade of the initial collapse and the subsequent development of spinal deformity. Despite heterogeneous treatment, all patients were alive and well with resolution of all presenting signs and symptoms and no evidence of active disease at the time of the most recent follow-up.

Conclusions: We found a particularly high prevalence of lesions in the cervical spine and a high prevalence of multiple skeletal lesions. In contrast to the classic finding of vertebra plana, we found that more severe lesions often led to asymmetric collapse; yet, asymmetric collapse was not found to be associated with the development of subsequent spinal deformity. The natural history of these lesions in the spine in the absence of systemic disease or spinal deformity is such that aggressive surgical management is usually not indicated; only follow-up is necessary to monitor recovery and spinal balance.

Level of Evidence: Therapeutic study, Level IV (case series [no, or historical, control group]). See Instructions to Authors for a complete description of levels of evidence.

The three described clinical entities of Langerhans cell histiocytosis (formerly known as histiocytosis X) are Letterer-Siwe disease, Hand-Schüller-Christian disease, and eosinophilic granuloma. Once thought to be three separate entities, these disorders are now recognized as different manifestations of the same disease process—a clonal proliferation of Langerhans cells[1,2]. Langerhans histiocytes are dendritic cells whose main role is in presenting antigens. They are commonly found in isolation in the epidermis; however, they are also normally present in small numbers throughout the body. Letterer-Siwe disease, the most malignant form, leads to widely disseminated clusters of Langerhans cells throughout the body. Hand-Schüller-Christian disease classically presents with a triad of a skull lesion, exophthalmos, and diabetes insipidus. Eosinophilic granuloma is a benign proliferation of Langerhans histiocytes occurring in a unifocal or multifocal manner that commonly affects the skeletal system[3].

In a large series of 314 patients with Langerhans cell histiocytosis seen at the Mayo Clinic, 188 (60%) had at least one skeletal lesion[4]. The most frequent sites of these skeletal lesions were, in descending order, the skull, femur, mandible, pelvis, and spine. Despite heterogeneous treatment, the vast majority of the patients did well, and there was no evidence suggesting that any treatment was more advantageous than another[5].

A recent study by Ghanem et al. also indicated that children with only skeletal lesions have excellent outcomes, whereas those with systemic involvement have a widely variable potential for healing[6].

Combining the data from the large series of children with skeletal Langerhans cell histiocytosis seen at the Mayo Clinic with the data from two other large series (forty and fifty-three children) showed that forty-six (17%) of 265 children with skeletal lesions had spinal involvement[1,5,7]. These series suggest that lesions in the spine are a unique feature of the pediatric population with Langerhans cell histiocytosis, in contrast with the adult population with the disorder. As a result of the low frequency with which vertebral lesions are encountered in clinical practice, there are very few studies in the literature focusing on the spine. We found several series of ten or fewer patients[8-12], but only four that included more than ten patients[13-16].

We analyzed the distribution and presentation of spinal Langerhans cell histiocytosis in twenty-six children diagnosed at our institution between 1970 and 2003. Data on treatment and long-term outcomes are presented for twenty-three children in this group who were followed for at least two years. To the best of our knowledge, this is the largest series of spinal lesions reported to date. The objective of this study was to evaluate the distribution and extent of disease at presentation as well as to determine the long-term prognosis of the disease in terms of both disease recurrence and progressive spinal deformity or instability. We hypothesized that spinal deformity is more likely to develop in patients who present with asymmetric vertebral collapse than it is in patients who present with symmetric collapse.

Materials and Methods

Twenty-six children with a biopsy-proven diagnosis of Langerhans cell histiocytosis and at least one lesion in the spinal column were treated in our department between 1970 and 2003. The group included fourteen boys and twelve girls with a total of forty-four involved vertebrae. The mean age at the time of the diagnosis was 8.2 years (range, 0.2 to 16.4 years). A biopsy of a spinal lesion established the diagnosis in sixteen patients, whereas a biopsy of a more easily accessible location in the skeleton established the diagnosis in the remaining ten patients.

The clinical presentation, radiographic presentation, operative records, treatment, findings at the follow-up evaluations, and follow-up radiographs were reviewed. Twenty-three patients were followed clinically for two years or more (Table I). Two others had been diagnosed less than two years before the time of the review, and one had been lost to follow-up. The mean duration of follow-up for the twenty-three patients was 9.4 years (range, two to 22.7 years). All twenty-six patients are described in the sections on clinical and radiographic presentation, but only the twenty-three patients who had been followed for at least two years are included in the sections on treatment and long-term outcomes.

Investigators at our institution reviewed the diagnostic radiographs of twenty-four of the twenty-six patients. The radiographs of the other two patients were not available, and therefore the radiology reports were used to define the extent of the vertebral collapse. Two of the authors of this study (S.G. and J.P.D.) performed the radiographic grading, and they agreed on all classifications. To test our hypothesis, a new classification system for vertebral collapse based on both morphology and the extent of maximal collapse was created. Vertebral body collapse was classified as grade I (0% to 50% collapse) or grade II (51% to 100% collapse) and was subclassified as either A (symmetric collapse) or B (asymmetric collapse, such as lateral, anterior, or posterior wedging). Lesions of the posterior elements of the spine (transverse process, spinous process, facet joints, pedicle, and/or lamina) were classified as grade III (Fig. 1). The classic finding of vertebra plana would be assigned a grade of IIA with this system. The extent of maximal collapse was assessed by measuring the vertebral height and comparing it with the mean of the heights of the vertebrae immediately cephalad and caudad to the affected vertebra.

Statistical analysis was done with use of JMP IN statistical software (version 4.04; SAS Institute, Cary, North Carolina, 2001). Probability testing for the distribution of the lesions was done with use of the null hypothesis that there is a 7 of 24 probability of a lesion being found in the cervical spine, a 12 of 24 probability of a lesion being found in the thoracic spine, and a 5 of 24 probability of a lesion being found in the lumbar spine. The Pearson chi-square test was used to determine significance in all frequency testing.

Results

Distribution

The forty-four vertebral lesions found in our twenty-six patients were distributed throughout the spinal column. Twenty lesions (45%) were found in the cervical spine; fourteen (32%), in the thoracic spine; and ten (23%), in the lumbar spine. The twenty cervical lesions were found in a total of eleven patients (six male and five female); the fourteen thoracic lesions, in ten patients (six male and four female); and the ten lumbar lesions, in ten patients (six male and four female). Two (5%) of the forty-four lesions were located in the posterior elements of the vertebra, whereas the other forty-two lesions occurred in the vertebral body. Both of the posterior lesions were in the cervical spine. This distribution revealed a predilection for the cervical spine (p ≤ 0.02), and there were fewer lesions in the thoracic spine than had been expected given its large number of segments relative to the entire spinal column (p ≤ 0.006). With the numbers available, neither gender nor age at the time of the diagnosis had a significant relationship with the distribution of lesions (p > 0.5 for both).

Of the twenty-six patients, fifteen had involvement of a single vertebra and eleven had involvement of multiple vertebrae. Multiple vertebral involvement was found in seven of the eleven children with cervical lesions and five of the ten children with lumbar lesions. Both cervical disease (p ≤ 0.03) and lumbar disease (p ≤ 0.04) were associated with multilevel involvement.

Eleven of the twenty-six patients had evidence of disease in the skeletal system outside the vertebral column. There were

TABLE I Clinical and Radiographic Data on Twenty-three Patients with Spinal Langerhans Cell Histiocytosis					➤
Case	Gender	Age at Diagnosis (yr)	Site of Spine Lesions	Other Skeletal Lesions	Visceral Disease
1	F	11.8	T3, L2	+	+
2	M	0.2	T8, T12	+	+
3	M	9	T5	–	–
4	F	2.5	L4	+	–
5	F	4.7	L2	+	–
6	F	4.7	T8, T9	+	–
7	M	5	C3, C6, T5, T11, T12, L4	+	–
8	F	3.4	C1, C2, C4, C5, C7	+	–
9	F	13.3	L2	–	–
10	M	2.7	L1	+	–
11	F	5.5	T11	+	–
12	M	10.9	C4	+	–
13	M	3.6	L4	–	–
14	F	7.5	C5	–	–
15	F	9.2	C1, C2	–	–
16	M	12.1	C4, C5	–	–
17	F	6.1	C3, L4	–	–
18	M	6.9	C6, L1	–	–
19	M	15.5	T6, L5	–	–
20	M	12.7	C5	–	–
21	M	6.4	C6	–	–
22	F	3.9	C4, C6	+	–
23	M	16.4	T6	–	–
Mean		7.6			

*No patient had evidence of active disease at the time of the most recent follow-up.

six lesions in the femur; five lesions in the humerus, ribs, and skull; four lesions in the pelvis; two lesions in the tibia, clavicle, and mandible; and one lesion each in the patella, scapula, and sternum. These lesions were discovered with diagnostic radiographic studies such as skeletal surveys and technetium bone scans. At least one of those studies was performed in twenty-four of the twenty-six patients. The two patients without secondary imaging studies may have had additional, nonsymptomatic lesions; however, this cannot be determined retrospectively in the absence of those studies. Of the eleven patients with extraspinal disease, five had involvement of only one vertebra whereas six had involvement of multiple vertebrae. Overall, sixteen (62%) of the twenty-six patients had more than one skeletal lesion. Only two (8%) of the twenty-six patients were found to have extraskeletal disease. The extraskeletal lesions were located in the lungs and bone marrow in one patient and in the lungs and liver in the other. Both of those patients also had involvement of multiple vertebrae and of skeletal sites outside the spinal column.

Clinical and Radiographic Presentation
Back or neck pain was the presenting symptom in all twenty-six patients, and it was the only presenting symptom in seventeen. Four patients had the additional finding of torticollis, and three had abnormal gait. Only three patients presented with neurologic symptoms, and none had a neurologic deficit. The symptom in each case was pain radiating down the upper extremity as a result of a cervical lesion. The neurologic symptoms, the torticollis, and the gait abnormalities all resolved with treatment of the underlying disease.

Thirty of the forty-four involved vertebrae had symmetric collapse, and twelve had asymmetric collapse. The radio-

		Radiation	Duration of	
Biopsy Site	Chemotherapy	Therapy	Follow-up (yr)	Notes*
L2	+	+	21	
Bone marrow	+	–	12.3	
T5	–	–	11	28° scoliosis
Femur	–	–	22.7	15° scoliosis
Skull	+	–	7.5	
Fibula, patella	+	–	16.7	
Ischium	+	+	11	
Skull, acetabulum	–	+	8.5	
L2	–	+	6.5	
Ilium	+	–	8	
T11	–	–	13.5	
Sternum	+	–	2	Posterior spine disease
L4	–	–	5.2	
C5	+	–	6.9	
C1	–	–	3.1	Halo applied after biopsy
C4, C5	–	–	6	Hemilaminectomy
C3	+	–	9	Posterior spine disease, C3 spinous process removed at biopsy
C6	+	–	13	C6 corpectomy and bone graft done 3 mo after biopsy because of kyphosis
L5	–	–	6.1	
C5	–	–	5.3	
C6	–	–	10.9	
Femur	–	–	2	
T6	–	–	7	T3-T8 fusion done 7 yr after diagnosis because of kyphoscoliosis
			9.4	

TABLE I (continued)

graphic classification was grade IA for twenty vertebrae, IB for three, IIA for ten, IIB for nine, and III for two. Grade-I lesions were significantly associated with symmetric collapse (p ≤ 0.03), whereas grade-II lesions were not associated with either symmetric or asymmetric collapse.

Treatment

Treatment of the twenty-three children who had been followed for two years or more consisted of chemotherapy (combinations of oral methotrexate, oral prednisone, or intravenous vinblastine) in ten patients and radiation therapy in four patients. Two patients had both chemotherapy and radiation therapy. All four patients who received radiation therapy were treated prior to 1991. Six of the ten patients treated with chemotherapy had multiple vertebral lesions and seven of the ten had extraspinal lesions. All but one of the patients who received radiation ther-

apy had both involvement of multiple vertebrae and extraspinal lesions. Of the two patients with extraskeletal disease, both received chemotherapy and one also received radiation therapy. All other patients were treated symptomatically and followed clinically and radiographically. A spinal orthosis was used only for comfort for a few weeks following the biopsy.

Clinical Follow-up

Of the twenty-six patients, twenty-three with a total of forty-one involved vertebrae were followed clinically for at least two years (mean, 9.4 years; range, two to 22.7 years). None of the twenty-three patients with adequate clinical follow-up had evidence of persistent or active disease at their last clinical encounter. All presenting signs and symptoms of the disease had resolved. None of the patients who had received radiation therapy had a secondary malignant lesion at the
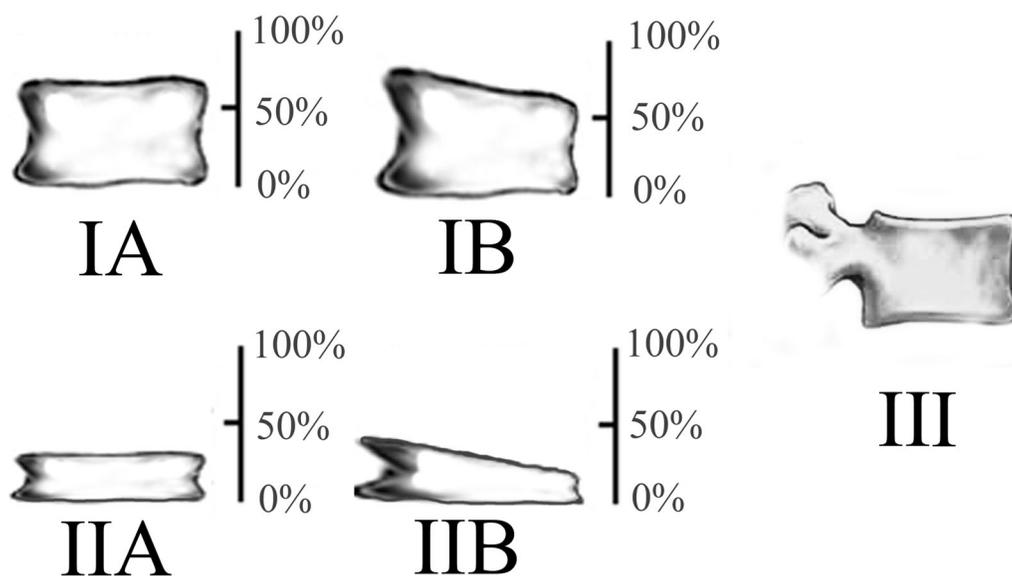
Fig. 1

System for radiographic classification of maximal vertebral collapse. Grade-I lesions have 0% to 50% collapse, and grade-II lesions have 51% to 100% collapse. The lesion is also graded as either A (symmetric) or B (asymmetric), on the basis of the morphology of the vertebral collapse. Grade-III lesions involve the posterior elements of the vertebra and are not subclassified as A or B.

time of the most recent follow-up.

Some degree of spinal deformity developed in four patients with long-term follow-up (Table II). Spinal deformity was defined as scoliosis of >10° or a sagittal plane deformity that was >10° greater than the normal range of cervical lordosis, thoracic kyphosis, or lumbar lordosis. Two of these patients had a grade-IIA lesion, and two had a grade-IIB lesion. On the basis of these results, the hypothesis that asymmetric collapse predisposes patients to the development of spinal deformity was rejected. In our series, both major and minor deformities developed both early and late after diagnosis. There was no relationship between the development of deformity and the initial grade of the vertebral collapse.

Discussion

Clinical and Radiographic Presentation

Children with Langerhans cell histiocytosis of the spine most often present with dull back pain as their only symptom[8-15,17]. This was true for our series, with all patients complaining of back or neck pain at the time of presentation. Neurologic symptoms were very uncommon, occurring in only three patients. The three patients all had shooting pain in the upper extremity that resolved promptly following the biopsy. Two of the three patients had chemotherapy with oral prednisone and methotrexate. Our findings support prior descriptions of prompt resolution of neurologic symptoms following treatment of spinal lesions in earlier case reports[8,18-20].

Interestingly, the classic radiographic presentation of spinal lesions as vertebra plana was the exception rather than the rule. In fact, although severe (grade-II) lesions were equally divided between patients with symmetric and asymmetric collapse, less severe (grade-I) lesions were significantly associated with symmetric collapse (p ≤ 0.03).

Diagnosis

Some authors have recommended not performing a vertebral

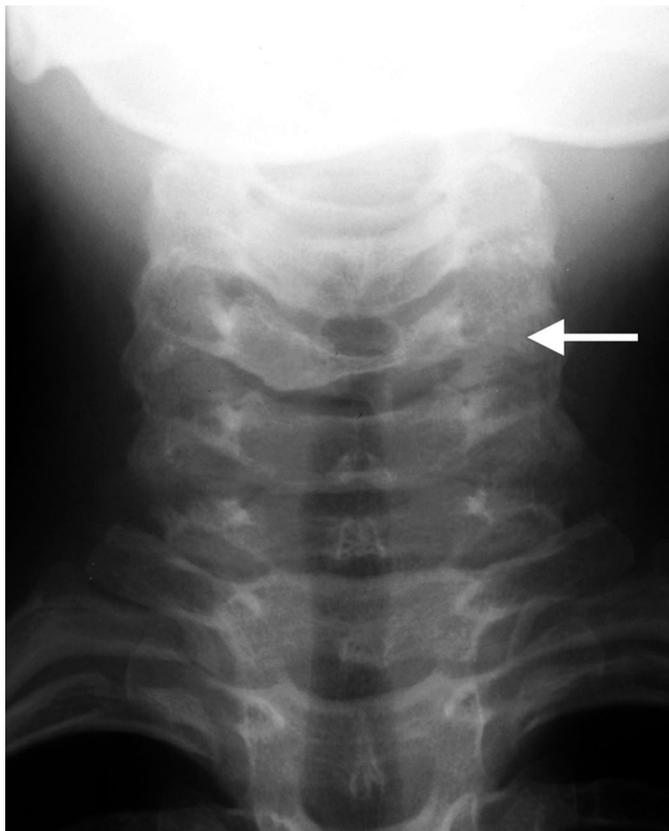|	Grade of			
Case	Lesion	Deformity	Indication for Surgery	Surgical Treatment
3	IIB	28° scoliosis	None	None
4	IIB	15° scoliosis	None	None
17	IIA	Cervical kyphosis	Progressive cervical kyphosis	Anterior vertebrectomy and reconstruction of C6
23	IIA	21° scoliosis with 50° kyphosis	Progressive spinal deformity with neurologic symptoms from nerve-root compression	T3-T8 posterior spinal fusion with instrumentation

TABLE II Description and Treatment of Spinal Deformity in Patients with Spinal Langerhans Cell Histiocytosis

Fig. 2-A

Fig. 2-B

Figs. 2-A, 2-B, and 2-C Case 14. Radiographic images demonstrating a grade-IIB lesion of C5 in a seven-year-old girl with Langerhans cell histiocytosis. **Fig. 2-A** Anteroposterior radiograph of the cervical spine showing the C5 lesion (arrow). This view demonstrates asymmetric collapse of the C5 vertebral body with >50% loss of height. Note also the preservation of the disc spaces cephalad and caudad to C5, a common finding in patients with Langerhans cell histiocytosis. **Fig. 2-B** Lateral radiograph demonstrating the C5 lesion (arrow). The full extent of the vertebral body collapse is difficult to appreciate on this lateral view because of the asymmetric nature of the collapse. Note the lack of extraspinal spread.

Fig. 2-C Sagittal T2-weighted magnetic resonance image of the cervical spine, demonstrating the C5 lesion (arrow). Note the small soft-tissue mass in the epidural space. This atypical feature prompted a biopsy in order to make a definitive diagnosis. This image also demonstrates complete preservation of the intervertebral discs both cephalad and caudad to the affected vertebra.

Fig. 2-C

biopsy if the lesion has the classic radiographic characteristics of Langerhans cell histiocytosis and can be followed closely[16,21]. The classic radiographic findings include vertebral collapse, maintenance of disc spaces, lack of extraspinal spread, and lack of a soft-tissue mass. Magnetic resonance imaging is performed to rule out a soft-tissue mass, which would suggest a more aggressive cause of vertebral collapse. The advantages of this approach are avoidance of an unnecessary biopsy in typical cases and avoidance of the very low risk of inadvertently damaging the vertebral growth plates during biopsy[7,21]. On the basis of the findings in this study and the excellent long-term natural history observed in this study, this strategy for deciding when to perform a biopsy seems prudent.

We believe that a tissue diagnosis is essential in suspected cases of spinal Langerhans cell histiocytosis only if there are any atypical features such as a soft-tissue mass, disc space involvement, or neurologic symptoms (Figs. 2-A, 2-B, and 2-C). Children with typical radiographic findings of spinal Langerhans histiocytosis should be followed closely clinically and radiographically to ensure that the lesion is benign and resolving. Children presenting with vertebra plana can potentially have a variety of different malignant tumors, including Ewing sarcoma, osteosarcoma, leukemia, and lymphoma, which underscores the need for an appropriate and thorough work-up (including biopsy when appropriate) and good follow-up[22-25]. If multiple skeletal sites are involved, only the most accessible site needs to be biopsied to confirm the diagnosis of Langerhans cell histiocytosis[14,15].

Distribution of Disease

Only two (8%) of the twenty-six patients in our study had extraskeletal disease. This finding is consistent with those of four large previous studies, in which a total of six (10%) of sixty-two patients with Langerhans cell histiocytosis involving the
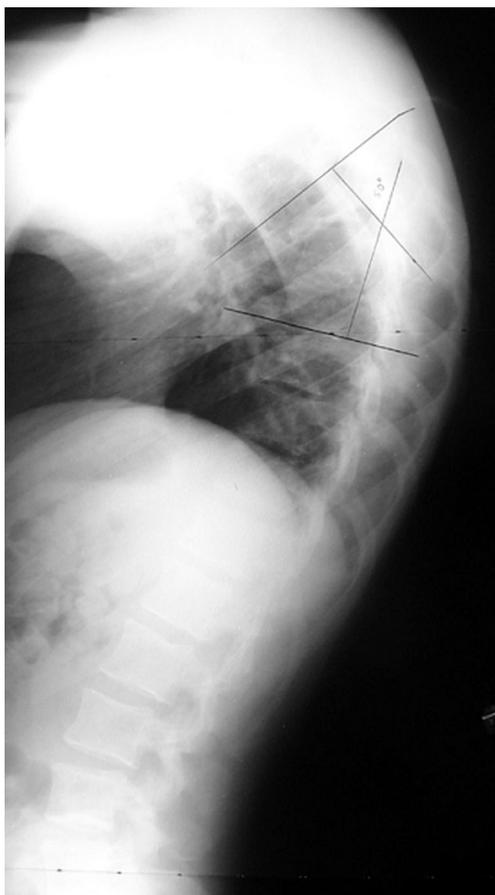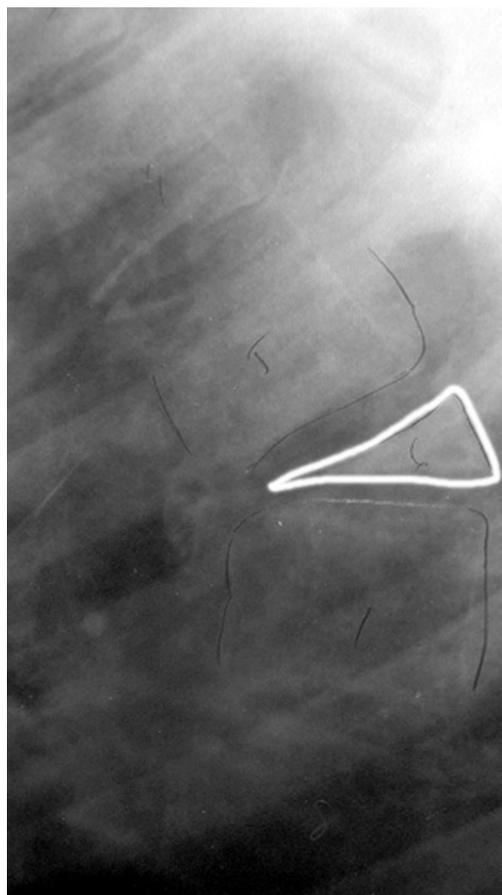

Fig. 3-A

Fig. 3-B

Figs. 3-A, 3-B, and 3-C Case 23. Radiographic images demonstrating a sharp thoracic kyphosis in a twenty-one-year-old man with Langerhans cell histiocytosis. He was initially seen at an outside institution at the age of sixteen with a classic vertebra plana lesion (grade IIA) but was not followed clinically. A spinal deformity slowly developed; it was progressive, and it ultimately led to neurologic symptoms from nerve-root compression and the need for surgery at our institution. **Fig. 3-A** Lateral radiograph of the spine showing a sharp short-segment 50° deformity that developed five years after the initial diagnosis. **Fig. 3-B** Close-up of Fig. 3-A, showing persistent wedge-shaped deformation of T6 (outlined), which led to the sharp kyphosis.

TABLE III Distribution of Langerhans Cell Histiocytosis Lesions by Spinal Segment			
Study	Cervical	Thoracic	Lumbar
Yeom et al.[16] (1999)	8/38 (21%)	21/38 (55%)	9/38 (24%)
Raab et al.[15] (1998)	2/16 (13%)	7/16 (44%)	7/16 (44%)
Floman et al.[14] (1997)	9/24 (38%)	7/24 (29%)	8/24 (33%)
Nesbit et al.[13] (1969)	3/35 (9%)	20/35 (57%)	12/35 (34%)
Combined	22/113 (19%)	55/113 (49%)	36/113 (32%)
Current study	20/44 (45%)	14/44 (32%)	10/44 (23%)
Normal spine segments	7/24 (29%)	12/24 (50%)	5/24 (21%)

spine also had extraskeletal disease[13-16]. The predominance of isolated skeletal disease may reflect an actual trend in patients with lesions involving the spine, but it may also be due to referral bias at our institution. It is worth noting that, in the large study of 314 patients seen at the Mayo Clinic[4], spanning nearly fifty years, fewer spinal lesions were identified than were seen in the current study. Moreover, since our cases were collected with use of our institution's comprehensive musculoskeletal tumor database, we believe that our series included

Fig. 3-C
Sagittal T2-weighted magnetic resonance image of the spine, which better demonstrates the sharp kyphosis centered at T6.

all children with spinal lesions seen at our institution.

In our series, twenty (45%) of the forty-four lesions were found in the cervical spine, a much higher percentage than described in the four largest previous case series[13-16], in which a total of twenty-two (19%) of 113 lesions were in the cervical spine. This difference may be a reflection of the interest of the senior author (J.P.D.) in the pediatric cervical spine; however, to our knowledge, all patients who presented to our institution with spinal lesions were seen in our department. In contrast, there were relatively fewer lesions in the thoracic spine than we had expected, given the large size of this segment as compared with the cervical and lumbar segments. Only fourteen (32%) of the forty-four lesions were in the thoracic region, as opposed to fifty-five (49%) of 113 lesions in the four largest previous case series. The skewed frequency distribution in our series was strongly significant for the cervical spine predilection ($p \leq 0.02$) and for the relative infrequency of thoracic lesions given the large size of the thoracic spine ($p \leq 0.006$). Moreover, cervical and lumbar lesions were found to be significantly associated with multilevel disease ($p \leq 0.03$ and $p \leq 0.04$, respectively). Neither of these novel findings was identified in the previous large studies of spinal lesions[13-16].

Because of the high frequency of multiple skeletal lesions in patients who are found to have a spinal lesion, we recommend that a technetium bone scan or a skeletal survey be performed early in the evaluation of every child with a suspected spinal lesion. Although all of the initial spinal lesions in the children in our series were diagnosed primarily after the patient complained of back pain, all additional lesions were found on secondary imaging. The finding of multiple sites of disease allows the physician to have increased confidence in the diagnosis since other entities that may present with vertebral collapse do not occur at multiple sites. Furthermore, this information can help to determine whether chemotherapy is needed. Finally, it is important to monitor all sites of disease for progression and pathologic fracture.

The decision whether to perform a technetium bone scan or skeletal survey in the initial phases of the diagnosis continues to be debated in the literature[26-28], and there is no conclusive evidence showing the superiority of one study over the other. The fact that the total radiation dose is less in a tech-
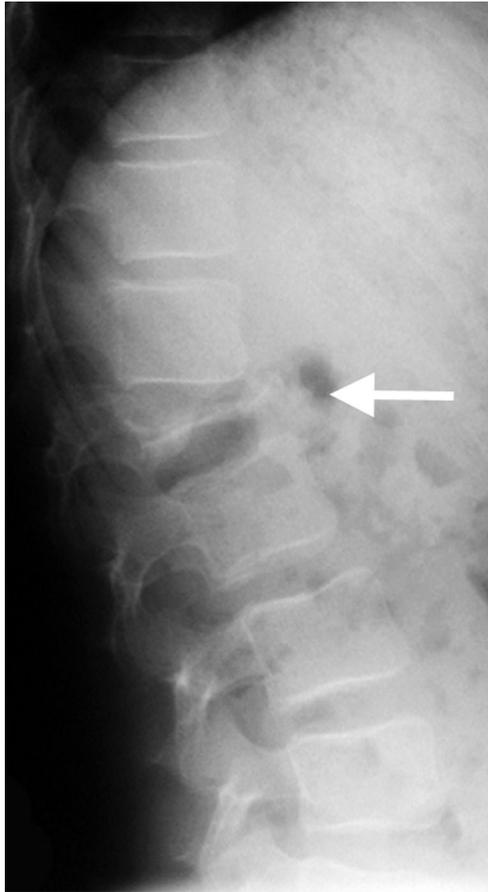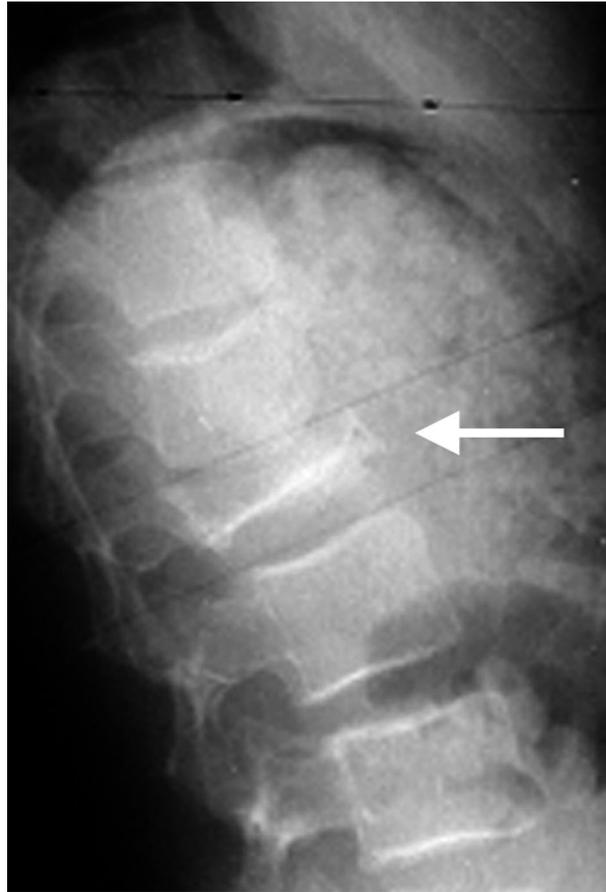
Fig. 4-A

Fig. 4-B

Figs. 4-A, 4-B, and 4-C Case 9. Serial radiographs demonstrating reconstitution of vertebral height in a girl diagnosed, at the age of thirteen, with Langerhans cell histiocytosis at L2. **Fig. 4-A** Lateral radiograph of the lumbar spine made at presentation, showing nearly complete collapse of the L2 vertebral body (arrow). **Fig. 4-B** Lateral radiograph made when the girl was fifteen years old, two years following the diagnosis, showing some interval reconstitution of the height of the L2 vertebral body (arrow).

netium bone scan than it is in a skeletal survey led us to prefer the first method[28,29]. A large, multicenter, prospective study is needed to identify the best screening tool.

Treatment

The current study covers a period of thirty-three years, and a variety of treatment modalities were used. Almost all of the patients in our series who were treated during the 1970s and 1980s were given chemotherapy or radiation therapy, or both. Oral chemotherapy with prednisone or methotrexate, or both, continues to be commonly used for multifocal skeletal and systemic Langerhans cell histiocytosis[4,30-32]. Patients who did not receive chemotherapy or radiation therapy were followed clinically and with radiographs. Spinal orthoses were not used for treatment of the spinal lesions; rather, they were worn, for comfort, for only a few weeks following the biopsy.

In the past, low-dose radiation therapy has been advocated for spinal lesions that continue to cause pain following biopsy[1,33-35]. It should be noted, however, that secondary malignant lesions following radiation therapy for systemic Langer-

hans cell histiocytosis were reported in four (4%) of eighty-nine patients[36]. Of these four patients, two who were two and eighteen years of age died of leukemia five and seventeen years, respectively, following the radiation therapy. The other two patients, who were two months and three years of age, died of thyroid cancer at twenty-eight and fifteen years after treatment[36]. Radiation therapy also poses a risk to the vertebral end plates, which are usually left unaffected by the disease process itself. Although we are not aware of any reported cases of growth arrest or secondary sarcoma following radiation therapy for spinal lesions, we believe that the risk associated with radiation therapy is unacceptable given the overwhelmingly positive natural history of this disorder. Radiation therapy is no longer used for this indication at our institution. This view is in agreement with those set forth in other recent large case series[7,14,37].

Except for open biopsy of the affected vertebra, surgery is rarely indicated for the spinal lesions in these patients. Normally, the only indications for spinal surgery are stabilization of an unstable segment of the spine that cannot be stabilized with an orthosis or neurologic symptoms due to compression of the

Fig. 4-C

Lateral radiograph of the patient at the age of sixteen, three years after presentation, demonstrating further reconstitution of the L2 vertebral body (arrow).

spinal cord by the collapsed vertebra. There have been sporadic case reports of spinal lesions requiring surgical stabilization[7,9,38]. In most patients, any spinal instability present following biopsy and curettage of the lesion can be supported in an orthosis until sufficient reconstitution has occurred to restore stability.

Long-Term Follow-up
Spinal Deformity
Initially, we hypothesized that a tilted vertebral body would be more likely to lead to scoliosis or kyphosis than would a flat vertebral body. We believed that the distorted shape had implications with regard to spinal balance, particularly in the growing spine. Our results failed to support this hypothesis. Both children who required surgery for spinal deformity had a grade-IIA lesion, and the other two children with spinal deformity had a grade-IIB lesion (Table III). Significant deformity occurred both early (Case 17) and late (Case 23) after the diagnosis (Figs. 3-A, 3-B, and 3-C). Although our initial hypothesis was rejected, since deformity occurred following both symmetric and asymmetric collapses, the results in this series underscore the need for close follow-up, through skele-

tal maturity, of all children with spinal lesions. We recommend radiographs every three months for the first year after the diagnosis to confirm the benign nature of the disease and annual radiographs thereafter, through skeletal maturity, to monitor spinal growth and balance. Any child with multifocal disease should be referred to an oncologist so that a decision can be made regarding the need for chemotherapy.

Natural History of the Disease
Our patients had excellent long-term results, a finding that is consistent with those in smaller previous studies of spinal lesions[8-16]. Despite differences in the types of treatment, which included chemotherapy, radiation therapy, both chemotherapy and radiation therapy, and no treatment, none of the twenty-three patients who were followed clinically for at least two years had any clinical evidence of disease. Use of a spinal orthosis does not appear to be necessary given the excellent results in this study without uniform use of orthoses. Aside from the two patients who had spinal fusion, the remaining patients are fully active children and young adults with no limitations of their activity or range of motion of the spine. The results had no relationship to the type of therapy that was used, a finding that adds to the body of evidence indicating that the natural history of these spinal lesions is that they resolve on their own.

There have been only a few studies with sufficient radiographic evidence to quantify the extent of reconstitution, and all showed excellent results, particularly in younger children[13,15]. Many of our patients had excellent reconstitution of vertebral height following diagnosis and treatment (Figs. 4-A, 4-B, and 4-C). Unfortunately, we did not have enough radiographic data to draw any substantial conclusions regarding long-term reconstitution of vertebral height. ∎

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