

## Langerhans' Cell Histiocytosis of the Spine: Report of a Case Follow-up for 15 years with symptomatic recurrence and Review of the Literature

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**Abstract:** Langerhans' cell histiocytosis (LCH) is a benign bone lesion, it is now recognized as a pathologic entity distinguished by a clonal proliferation and accumulation of a specific histiocyte: the Langerhans' cell. LCH can involve any bone in the body, Spinal involvement accounts for 6.5% to 25% of all skeletal LCH cases. LCH is rare in clinical practice, and a single case follow-up for 15 years has not been reported before. We report a 17-year-old man complained of persistent thoracic pain for 2 months. He was diagnosed of LCH of thoracic spine. 15 years later the lumbar spine was involved. Pre-operative CT scans demonstrated a lesion in the first lumbar vertebral body. After 3 months observation, the pain deteriorated with instability. A gross resection with internal fixation was applied and complete pain relief without any complication was experienced.

**Keywords:** Langerhans' cell histiocytosis; cervical spine; lumbar spine; surgical treatment.

### INTRODUCTION

Langerhans' cell histiocytosis (LCH) is a rare condition (1:1,500,000 per year), which includes Eosinophilic Granuloma, the systemic Hand-Schuller-Christian disease, and Letterer-Siwe disease [1]. These 3 entities are very different in presentation and outcome.

They are now recognized as one pathologic entity distinguished by a clonal proliferation and accumulation of a specific histiocyte: the Langerhans' cell [2]. In skeletal LCH, known as Eosinophilic Granuloma (EG), the most frequent site of the skeletal lesions is the skull, followed by the femur, mandible, pelvis, and spine [3]. The thoracic vertebrae are involved most often, followed by the lumbar and cervical vertebrae. 79% of all LCH bone lesions are solitary EGs, in 7% of cases multiple EGs are found, and 14% belong to other forms of LCH [4]. Many studies on patients with LCH of the spine are well documented in the literature, but most of these studies focus on management of the disease. No report emphasizing on long time follow-up of LCH patients has been published. In the present study, we aimed to report a LCH case with 15 years of follow-up to help understanding the long time prognosis of LCH.

### CASE REPORT

#### History

A 32-year-old man with history of moderate back pain and limited motion that had persisted for 1 months admitted in our hospital. The pain started when he was carrying some heavy goods. The pain localized to the upper thoracic spine area without radiation and neurological deficits. The pain could be aggravated by motion, especially standing, walking, forward bending movement and could be relieved by bed rest. His pain

was initially 3/10 in severity but worsened to 6/10 3 months later. There was no history of trauma recently. Laboratory examinations consisted of complete blood count, electrolytes, liver, renal function tests, and urinalysis. They were all normal, except remarkable evaluation of C-reaction protein level. Before admission, he was treated with analgesics. However, the pain persisted.

When he was 17, he had a similar back pain located at the thoracic region. It was a dull pain without significant motional aggravation. He was treated with rest and analgesics/anti-inflammatory drugs. A few months later, he developed a local kyphosis. X-ray examination showed a vertebra plana deformity, and the pain disappeared. He was diagnosed of Eosinophilic Granuloma. Since the lesion was focal, he was close follow-up. He had a history of cardiac surgery to repair atrial septal defect when he was 6 years' old.

#### Examinations

At neurologic examination, spinal movements were painful and restricted. Physical examination revealed normal motor and sensory function of both sides. The manual muscle strength test demonstrated 5/5 strength on the left and 5/5 on the right. Increase of deep tendon reflex was not noted. Babinski sign was negative bilaterally. Muscle tonus of all extremities was

not increased. X-ray findings indicated a typical vertebra plana and local kyphosis deformity at the T6 level. At the same time, a compressive change and density increase of vertebral body was noticed at the L1 level. (Fig. 1) Because of the multiple skeletal lesions, technetium Tc-99m bone scan was conducted. However, there was no positive finding, except T6 and L1 lesions. At the T6 level, Computed tomography (CT) revealed a density increase of the “plana”. At the L1 level, there was some lytic lesions with bone formation. The transverse processes and laminae of both sites were intact. (Fig. 2) Magnetic resonance imaging (MRI) confirmed the presence of lesions at the T6 and L1 levels. The lesion had a low signal on T1-weighted images and intermediate signal on T2-weighted images. Intravenous infusion of gadolinium increased the intensity of the signal of the lesion non-harmoniously. There were remarkable para-spinal soft-tissue mass at both T6 and L1 levels, and a soft-tissue mass compressing the L1 spinal cord. (Fig.3)

#### Pathological findings and Pre-operative course

Since EG of the spine often improves spontaneously, achieving variable degrees of vertebral body height reconstitution. As a result, surgery is rarely required [5]. He was treated with analgesics, bed rest, bracing and close follow-up for 3 months. The thoracic back pain was relieved, however, the lumbar pain increased. The pain localized to the lumbar spine area without radiation and neurological deficits. The

pain could be aggravated by motion, especially standing, walking, forward bending movement and could be relieved by bed rest. His pain was initially 3/10 in severity but worsened to 6/10.

#### Surgical treatment

The differential diagnosis included aneurysmal bone cyst, osteoblastoma, giant cell tumor, fibrous dysplasia, and chronic infection. As the neoplasm of lumbar spine produced instability and clinical symptoms. Internal fixation of the lumbar spine and gross resection surgery were performed, at the same time kyphosis correction was performed at T6 level. Intra-operative frozen biopsy was obtained at both of the lesions. The frozen biopsy examination revealed aggregation of histiocytes and eosinophilic leukocytes, typical of EG. The patient recovered completely without complications. After an uncomplicated hospital course, he was discharged home 3 weeks later. After follow-up for 3 months, there was no recurrence of back pain, neurologic examination was normal, the VAS was 0. Now this patient is completely symptom free (Fig.4).

The design and performance of this study conformed to ethical standards of Helsinki Declaration and our national legislation. It was approved by Medical Ethical Committee of our institution. The patient was enquired whether or not willing to take part in a scientific research and informed consent forms were signed by himself.

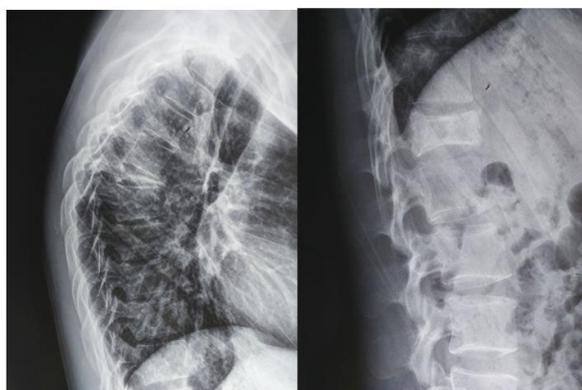
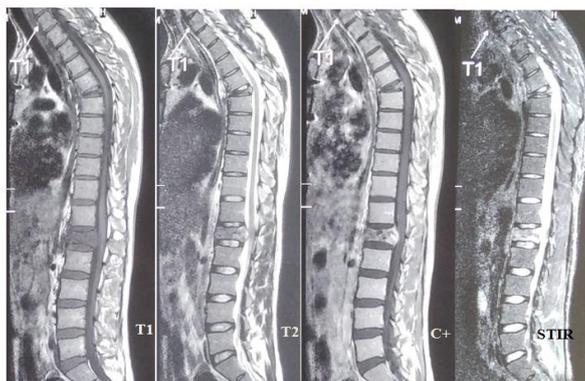


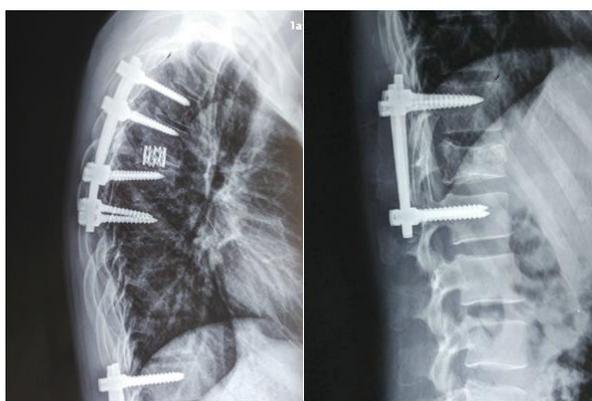
Fig-1: Pre-operative X-ray pictures



Fig-2: Pre-operative CT scans



**Fig-3: Pre-operative MR images**



**Fig-4: Post-operative X-ray pictures**

## DISCUSSION

Eosinophilic granulomas are focal bone lesions that are one of the three syndromic manifestations of LCH. Hand-Schuller-Christian disease (triad of skull lesions, diabetes insipidus, and exophthalmos) and Letterer-Siwe disease (disseminated lesions in visceral organs) are the other two forms of LCH, both of which have a poorer prognosis than EG [4]. Eosinophilic granuloma typically affects children and young adults, with a higher incidence in boys; adult cases have also been described. While typically presenting with pain and swelling, spinal EG can also cause radiculopathy [6]. Differential diagnosis is typically age-dependent and includes osteomyelitis, metastasis, Ewing sarcoma, osteosarcoma, neuroblastoma, aneurysmal bone cyst, chordoma, and leukemia or lymphoma [7]. Recurrence of Eosinophilic granuloma of the spine is a rare condition, with few cases reported in the literature. Recurrence is more likely in patients who are skeletally mature [8].

Patients with EG present with persistent back pain; restricted range of motion; deformity such as kyphosis, scoliosis, and/or torticollis; and, rarely, neurologic deficit. Bertram et al. [9] reported that LCH commonly occurs in the thoracic spine, followed by the lumbar and cervical spines.

The most common radiologic signs were a

lytic lesion of the vertebra which is not characteristic. The characteristics of a typical LCH vertebral lesion reported in the literature mainly consist of complete or incomplete collapse of the vertebral body (vertebra plana), preservation of the posterior element and the disc space [10]. The following radiologic features are typical of EG: 1. Only one vertebra is involved. 2. Adjacent discs of the involved vertebra are intact. 3. Disc space is about a third wider than the next space above and below. 4. Homogeneous density of the collapsed vertebral body is observed [11]. MRI and CT help confirm the diagnosis and can demonstrate associated soft-tissue mass. MRI images with the most common appearance being a lesion that is T1 hypointense, T2 hyperintense, and demonstrates contrast enhancement [12].

Technetium bone scintigraphy as a screening method for multiple EG lesions cannot be recommended because of poor sensitivity. Only 35% of all lesions showed increased uptake resulting from secondary reactions of bone remodeling after pathologic fractures. A complete skeletal survey may be necessary to exclude other lesions [13].

Solitary LCH is usually self-limited. Langerhans cell histiocytosis lesions might spontaneously heal over several weeks. A late biopsy might lead to a false-negative result. If the pathologic

result is negative without a tumor, we recommend that second biopsy and surgery are indicated if the symptom(s) persist longer than 4 weeks [14].

The treatments of spine LCH, including observation, immobilization, radiotherapy, chemotherapy, lesion injections (steroid, percutaneous vertebroplasty), targeted therapy. Orthoses are useful for pain and may help prevent kyphosis. Intra-lesional CT-guided steroid injection may be helpful for symptomatic solitary EGs of the spine. Low-dose radiation therapy has been used for cases with neurologic compromise; rarely, surgical curettage with stabilization may be needed if neurologic defects or spinal instability is observed. Yeom et al. [10] reported that the worst kyphosis is more often observed in patients who undergo surgery, particularly curettage and anterior fusion, which may damage the growth potential of the involved vertebra (e). Therefore, surgery should be strictly reserved for cases with severe instability, deformity, or progressive neurologic deficit. Chemotherapy may be used if EG is associated with systemic and/or multifocal disease; referral to an oncologist is appropriate for these individuals. It is reported that cytosine arabinoside is an effective and minimally toxic treatment for LCH bone lesions in adults. In contrast, vinblastine/prednisone results in poor overall responses and excessive toxicity [15].

Long-term prognosis is favourable, with extremely low rates of recurrence in skeletally immature patients. Recurrence is more likely in patients who are skeletally mature [6]. It is recommended that close clinical follow-up with spinal radiographs every 3 months for the first year after diagnosis to confirm the benign nature of the lesion, followed by annual radiographs through skeletal maturity to monitor spinal balance and growth. Given the self-healing tendency of spine LCH, typical lesions can be satisfactorily treated with conservative measures, namely, immobilization and observation [16].

## CONCLUSIONS

The most common clinical manifestations of LCH are neck or back pain, followed by restricted motion, neurologic symptoms, and deformity. Neurologic deficits were more frequent in adult patients. Vertebral plana is the typical imaging feature in children and adolescent patients but seldom in adults. Computed tomography is best for characterizing anatomy of the involved vertebra, and MRI is best for delineating marrow and soft tissue. The oversleeve-like or dumb-bell sign on MRI may be a feature of spinal LCH in children and adolescents. Rarely, surgical treatment is needed, especially in children. Long-term prognosis is favourable.

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