LANGERHANS CELLS HISTIOCYTOSIS IN THE DORSAL SPINE IN A PEDIATRIC PATIENT

Histiocitosis de células de Langerhans en columna vertebral dorsal en paciente pediátrico

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ABSTRACT

Introduction: Langerhans cell histiocytosis (LCH) is a rare histiocytic disorder and its incidence is not exactly known. It occurs in all age groups but is more common in the pediatric population. It is characterized by single or multiple osteolytic-type lesions caused by clonal proliferation of cells histologically like Langerhans cells; its clinical presentation is heterogeneous.
Clinical case: An 11-year-old man with a 6-month history of back pain and walking limitation. Magnetic Resonance Imaging (MRI) showed a lesion of the dorsal spine in D8, D9, and D10 and flat vertebra D9 that caused spinal compression. The diagnosis was made based on the histopathological study of the vertebral body with the finding of eosinophilic granuloma, being treated with outpatient chemotherapy, external fixation with a plaster corset, and physical therapy. The clinical evolution was favorable, achieving improvement in muscle strength and walking with support at discharge.
Conclusion: Langerhans cell histiocytosis with vertebral involvement is a highly relevant pathology, despite being rare. Timely diagnosis and adequate treatment are essential since it allows to prevent or limit the spinal cord involvement caused by this pathology.

Keywords: *Histiocytosis, Langerhans-Cell, Spine, Back Pain, Eosinophilic Granuloma (Source: MeSH NLM)*

RESUMEN

Introducción: La histiocitosis de células de Langerhans (HCL) es un trastorno histiocítico raro y su incidencia no se conoce con exactitud. Se presenta en todos los grupos de edad, pero es más común en la población pediátrica. Se caracteriza por lesiones únicas o múltiples de tipo osteolítico causadas por proliferación clonal de células histológicamente similares a las células de Langerhans; su presentación clínica es heterogénea.
Caso clínico: Varón de 11 años, con cuadro clínico de dolor dorsal y limitación para la marcha de 6 meses de evolución. La Resonancia Magnética (RMN) mostró lesión de la columna dorsal en D8, D9 y D10 y vértebra plana D9 que causaba compresión medular. El diagnóstico se hizo en base al estudio histopatológico de cuerpo vertebral con hallazgo de granuloma eosinófilo siendo tratado con quimioterapia ambulatoria, fijación externa con corsé de yeso y terapia física. La evolución clínica fue favorable logrando mejoría de la fuerza muscular y deambulando con apoyo al momento del alta.
Conclusión: La Histiocitosis de células de Langerhans con compromiso vertebral es una patología de gran relevancia, a pesar de ser poco frecuente. El diagnóstico oportuno y un tratamiento adecuado es fundamental puesto que permite prevenir o limitar el compromiso medular causado por esta patología.

Palabras Clave*: Histiocitosis de Células de Langerhans, Columna Vertebral, Dolor Dorsal, Granuloma Eosinófilo. (Fuente: DeCS Bireme)*

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Langerhans cell histiocytosis (LCH) is a disease characterized by single or multiple osteolytic-like lesions secondary to clonal proliferation of cells histologically similar to Langerhans cells in one or more organs. In children, histiocytosis is classified as class I or histiocytosis X; class II or hemophagocytic syndrome (associated with infection or family); and class III or malignant histiocytosis, associated with acute monocytic leukemia and true histiocytic lymphoma. LCH is a rare histiocytic disorder and its exact incidence remains unknown. It has been diagnosed in all age groups, but it is more common in the pediatric population, especially in the first 10 years of life. The reported incidence is estimated between 3 and 5 cases per million children and 1 to 2 cases per million adults. The clinical presentation is heterogeneous and varies according

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to the site of the lesion and the age of presentation, one of the most common being lytic lesions in bone. [1]

In the pediatric population, the most frequent site of presentation is the skull (40% of cases); in adults it occurs predominantly in the jaw (30%) and extremities (17%). Few cases of LCH have been reported in the literature with involvement of vertebral bodies in the pediatric population. In these lesions, interleukin 1 (IL-1) is produced, which is involved in bone destruction; This cytokine also contributes to bone resorption, fibrosis, and necrosis. [2]

The following describes the case of a patient who was diagnosed with LCH with involvement of the vertebral and adjacent soft tissues.

CLINICAL CASE

History and examination: An 11-year-old male patient, with no medical history, who attended the Almenara Hospital emergency room in August 2019 with a 6-month history of disease characterized by progressive back pain that did not resolve with analgesics, associated with limitation to the March. The examination found a patient in a wheelchair, awake, oriented, with pain on palpation at the lower dorsal level, without palpation of mass, with decreased muscle strength in lower limbs (LL) 4/5, without sensitive compromise , with preserved reflexes, gait limited by pain and decreased strength.

Laboratory tests: Hemogram, inflammatory markers, coagulation profile, liver and kidney function, urinalysis, blood culture, urine culture, TORCH profile, serologies for hepatitis B and C, HIV and syphilis did not show alterations. The vertebral tomography showed an asymmetric decrease in the height of the D9 dorsal vertebral body and an adjacent soft tissue injury. Magnetic resonance imaging (MRI) of the dorsal spine showed vertebral collapse D9 "flat vertebra" with bone spinal edema and a break in continuity at the level of both vertebral endplates, anterior and posterior wall, with slight posterior retropulsion that compressed the ventral surface of the dural sac and it invaded 50% of the medullary canal. Furthermore, hyperintensity was observed in T2 at the level of the bodies and pedicles of D8, D9 and D10; as well as a lesion suggestive of an anterior prevertebral hematoma (*Figure 1*).

Treatment: The patient was scheduled for a vertebral biopsy, which was performed using a percutaneous needle at the level of vertebra D9. The histopathological study was reported as: Langerhans cell histiocytosis, predominantly bone, when the finding of eosinophilic granuloma was confirmed (*Figure 2*). He was evaluated by pediatric oncology who indicated outpatient chemotherapy (based on prednisone and vinblastine) once a week. For chemotherapy treatment, a port catheter was placed.

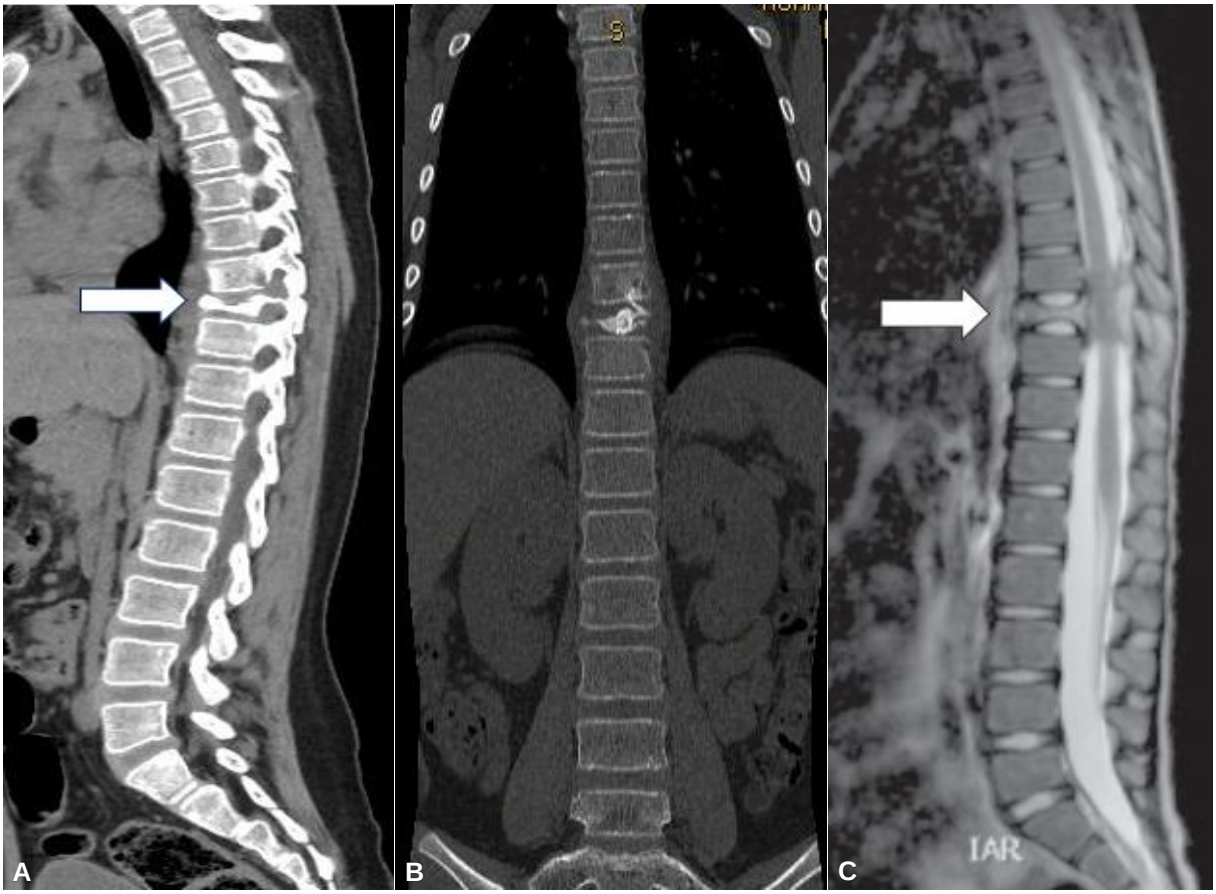

Fig 1. (A) Tomography (TEM) of the dorsolumbosacral spine (DLS) in sagittal section showing a decrease in the height of the D9 vertebral body. **(B)** TEM DLS column in coronal section showing asymmetric decrease in the height of the D9 vertebral body with extension to paravertebral soft tissues. **(C)** MRI in sagittal section and T2 sequence showing destruction of the D9 vertebral body, with a mass that invades 50% of the medullary canal and contacts the spinal cord in its anterior and posterior portion.

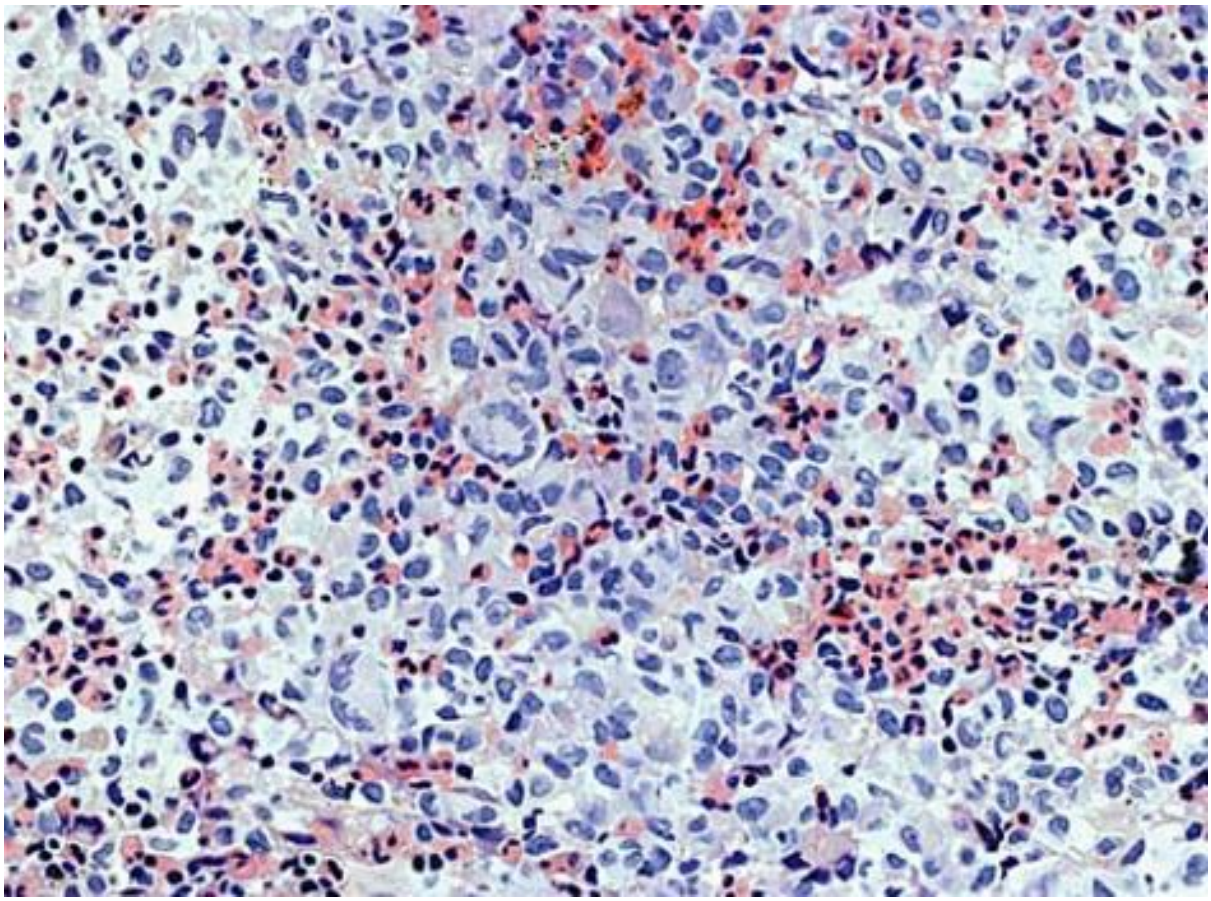

Fig 2. High power photomicrograph showing Langerhans histiocytes and numerous mixed eosinophils. Some of the histiocytes have fused to form multinucleated giant cells (hematoxylin and eosin stain, × 400)

Clinical evolution: In the postoperative period, the patient presented back pain that improved with analgesics and the use of a semi-rigid dorsolumbar corset, as well as decreased strength in LL (2/5) which improved in the following days with the help of physical therapy (to 4/5) getting to walk with walker support. He was discharged with an indication for the use of a corset, physical therapy, and an outpatient evaluation.

DISCUSSION

Langerhans cell histiocytosis (LCH), described by Liechtenstein in 1953, comprises a spectrum of different clinical expressions of a disease.[3] It is an immune regulation disorder rather than a fully developed neoplastic process. Langerhans cells are responsible for processing and presenting antigens to T lymphocytes of the cellular immune system.9 Langerhans cells can present local or systemic involvement, depending on their proliferation and type of infiltrated organ.10 It can present at any age, with a higher incidence between the first and fourth year of life. The prevalence in infants is 0.2 to 0.5 per million. The gender distribution is similar, with a male / female ratio of 2 / 1.6. Our case was an 11-year-old male patient who was not in the age group most affected.

The three clinical variants that occur in Langerhans cell histiocytosis include: A unique form of involvement with isolated lesions in bone or lung (eosinophilic granuloma, between 60-80% of cases) predominantly in older children, with a peak of incidence between 5 to 10 years of age; Another form, disseminated, rare, with very severe manifestations, is Letterer-Siwe disease; This form occurs in 10% of cases, being more common in children under three years of age and presenting mainly nodule and maculopapular skin manifestations. The third form of presentation is a chronic form known as Hand-Schuller-Christian disease, in 15 to 40% of cases, represented by the triad of head injury, diabetes insipidus and exophthalmos. In this disease, the organs that are commonly affected are: cortical bone, skin, CNS, bone marrow, oral mucosa, lymph nodes, liver, spleen, intestines, and the thymus. [12]

The unifocal manifestation in the bone tissue represents up to 80% of the cases in children under five years of age, the eosinophilic granuloma being its main manifestation, being able to compromise almost all the bone tissue with extension to soft tissues. Symptoms range from bone pain in 80 to 90% of cases, soft tissue inflammation, sensitivity, pathological fractures, among others. Between imaging studies, plain radiography, and computerized axial tomography (CT) allow the identification of lytic lesions and periosteal reaction, with extension of inflammatory changes to soft tissues. Positron emission CT and ultrasonography are useful for evaluating the activity of focal lesions in visceral organs, such as liver and lung, with ultrasonography presenting advantages in the identification of small lesions limited to soft tissues and adjacent to bone lesions, including lesions in skull. MRI is useful in delimiting the

lesion and establishing the local or systemic extension of the disease, as well as evaluating the degree of spinal cord involvement. [13]

Patients can be diagnosed with malignant tumors, lymphoma, or tuberculosis. On the other hand, flat vertebra with soft tissue mass can also be seen in a variety of spinal tumors, including Ewing's sarcoma, lymphoma, aneurysmal bone cyst, leukemia, malignant solid tumors, and tumors. metastatic. [14]

The gold standard is the histopathological study of the affected tissue. Spinal biopsy is necessary for a definitive diagnosis in atypical cases, although some authors insist that typical lesions on radiographs do not require biopsy and can be safely followed with serial imaging studies. [15]

There are different treatment modalities, and all have demonstrated effectiveness and low recurrence rates. Surgical curettage, radiotherapy and chemotherapy have been used alone or in combination with favorable results.[4] However, each treatment technique has a special indication, depending on the extent and severity of the disease, which is why it has been divided into two categories: Uni-systemic, subdivided into a single site (unifocal) (with good prognosis) or multiple (multifocal); and Multisystemic, which involves two or more organs at the time of diagnosis with or without dysfunction. There are organs at risk (liver, spleen, and hematopoietic system), which, when affected, have a poor prognosis and high mortality. [13]

For chronic focal forms that present surgical accessibility, thorough curettage is the treatment of choice, with the possibility of adding bone grafts in large lesions with the aim of preventing pathological fractures, as well as when curettage creates continuity defects. It can be performed using an anterior approach when: 1) Closed angle kyphosis 2) Invasion of the spinal canal by granulomatous tissue 3) Upper thoracic lesions. A posterior approach is indicated when there is only an isolated lesion of the posterior wall. [5] The use of radiation is indicated in those patients with inaccessible lesions or where surgical treatment could cause irreversible lesions. Children with multisystem involvement, paravertebral soft tissue involvement, as well as involvement of other extra-axial bone lesions require a more aggressive management associated with chemotherapy.

The prognosis of granuloma is favorable since most of the treatments are curative. The percentage of recurrences observed is 7.3%. Recurrence and the appearance of new lesions are often difficult to manage and require a combination of surgery and chemotherapy, and a longer follow-up.[6] Follow-up with imaging studies in the first year has been suggested to detect kyphosis or scoliosis.

Neurological involvement in patients with LCH of the spine is the main indication for surgical treatment, as it provides an opportunity for the rapid recovery of neurological function, especially if there is only involvement of one vertebral body, although in children both the indications and the type of surgical approach remains controversial. A single-stage posterior approach using pedicle screws is recommended, as it has fewer complications and allows the affected vertebral body to be preserved without representing any risk of recurrence according to some case reports.[7]

In our clinical case patient, a plaster brace was placed due to the risk of developing alterations in the physiological alignment of the spine (dorsal kyphosis), and the initiation of outpatient chemotherapy due to the contiguous infiltration of adjacent levels D8 to D10 , as well as extension to the paravertebral soft tissue of the lesions (D8-D9-D10). However, if neurological compromise occurs during follow-up after conservative management, this should be classified as failed and surgical decompression should be considered as a therapeutic option. Likewise, long-term follow-up is necessary to better understand the final result of patients with histopathological finding of eosinophilic granuloma, since there have been reports of patients with conservative management who, after years of follow-up, have had complete spontaneous healing with vertebral reconstruction. total.

CONCLUSION

Langerhans cell histiocytosis (LCH) with vertebral involvement represents a highly relevant pathology, despite being rare, because its prognosis changes if a timely diagnosis and adequate treatment is made, which can prevent or limit spinal cord involvement. At this moment, the best treatment scheme for Langerhans Cell Histiocytosis with spinal involvement is not fully defined, so it is recommended that it be individualized.

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Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Authors Contributions

Conception and design: All authors. *Drafting the article:* Murga. Critically revising the article: Basurco, Cari. *Reviewed submitted version of manuscript:* Murga. *Approved the final version of the manuscript on behalf of all authors:* Murga.

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