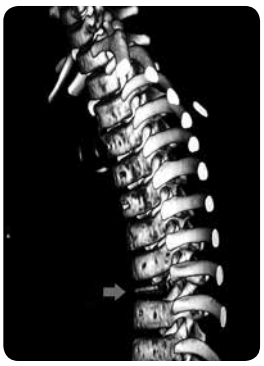

Langerhans Cell Histocytosis: Case Report and Literature Review

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Key words (MeSH)

Histiocytosis, Langerhans-cel
Granuloma
Tomography, X-ray computed

Summary

Langerhans cell histiocytosis is a rare disease that involves bone structure, soft tissues and even specific injuries to organs such as lung. This paper presents a literature review of Langerhans cell histiocytosis and it reports the case of a previously healthy 7-year-old female patient, without pre-, peri-, and postnatal history, who after an own height fall presents neurological alterations in her lower limbs affecting her muscle strength and the response to the osteotendinous reflexes. Imaging studies showing typical bone lesions of histiocytosis were performed.

Palabras clave (DeCS)

Histiocitosis, células de Langerhans
Granuloma
Tomografía computarizada por rayos X

Resumen

La histiocitosis de células de Langerhans (HCL) es una entidad rara que compromete estructuras óseas, tejidos blandos e incluso lesiones específicas de órganos como el pulmón. Se presenta la revisión de la literatura de la histiocitosis de las células de Langerhans y el caso de una paciente de 7 años de edad, sin antecedentes pre, peri o posnatales, previamente sana; quien, posterior a caída desde su propia altura, manifiesta alteraciones neurológicas de sus miembros inferiores que afectan su fuerza y la respuesta a los reflejos osteotendinosos. Se practicaron estudios imagenológicos que mostraron lesiones típicas óseas de la histiocitosis.

1. Introduction

The term Langerhans cell histiocytosis (LCH) was first coined in 1868 by Paul Langerhans, but the pathology was described earlier, in 1865, by Thomas Smith, and even from Hippocrates painful non-fatal lesions affecting the skull were described (1).

LCH involves a set of disorders characterized by lesions that include a common primary event, that is, the accumulation and infiltration of monocytes, macrophages, and dendritic cells into affected tissues (2).

Its broad clinical spectrum is reflected in the many synonyms used to name this disease, including eosinophilic granuloma (focal chronic), Hand-Shuller-Christian disease (disseminated chronic), and Letterer-Siwe's disease (disseminated acute). The risk organs of this entity are skin, bone, liver, spleen and bone marrow (3).

Since the first reports of the pathology, bone lesions of the skull and central nervous system have been reported, involving the hypothalamus-pituitary axis, with diabetes insipidus as a fundamental manifestation. Less frequently, granulomatous lesions have been documented in meninges, choroidal plexus, pineal gland or cerebral parenchyma (4).

2. Epidemiology

It is a rare disorder, with an incidence of 4 to 5 cases per million inhabitants per year, whose age groups vary according to the presentation; the multisystemic form is generally found before the age of 3 years, and the unifocal form in late childhood. It occurs less frequently in adulthood, with an average age of 35 years. Men are more affected than women in a 2:1 ratio, however, the multi-organic form is more evident in women (5,6).

It occurs occasionally in children previously treated for acute T-cell lymphocytic leukemia (7). Permanent consequences have been reported in children, including diabetes insipidus, orthopedic abnormali-

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ties, hearing loss and neurological problems. The incidence in adults is almost unknown, so the disease can be underdiagnosed, but has been estimated to affect 1 to 2 in 1 million people (2).

In Colombia, according to Ariza et al., a 10-year case series study reports that the age range varies from 4 months to 47 years. Multi-systemic involvement was documented in 47% of patients, with papular rash as the most common dermatological lesion in 23.5% of individuals. In addition, during the monitoring period, there was a 20.5 % mortality rate (8).

On the other hand, in Medellín, Colombia, 10 cases of the disease were registered, in which no differences were found by sex, the mean age was 33 months and different manifestations were observed, such as in the multisystemic-multifocal, unisystemicunifocal, unisystema-multifocal and eosinophilic granuloma forms (9).

3. Etiology

Unknown (2-10); however, genetic predisposition related to increased family incidence, increased appearance of identical twins and their relationship to human leukocyte antigen, such as HLA-DRB1*03, CW7 and DR4, has been suggested. The lesions seen in LCH are usually polymorphisms that vary from person to person, and the same applies to the site where it occurs (2).

The first-line immune response against pathogens is made up of dendritic cells, which are located in the skin and mucous membranes. These, in turn, are divided into those found in the epidermis (Langerhans cells), and those found in mucous membranes and dermis (interstitial dendritic cells) (11).

4. Physiopathology

Studies of LCH as a malignant tumor have shown that this entity in non-pulmonary lesions corresponds to monoclonal cells or immature cells with cell cycle deregulation and telomere shortening. On the other hand, in support of LCH as a reactive process, they emphasize that monoclonal cell populations are common in the immune system and that phenotypically immature Langerhans cells often accumulate in areas of inflammation. The expression of cytokines, including IL-17, which is key in autoimmune processes, has also been reported (2).

The hypothesis of immune physiopathology is proposed as a reaction of hypersensitivity to an unknown antigen, together with stimulation of the macrophage-histiocyte system. Thus, tumor lymphocyte (T8) deficiency, altered immunoglobulins, autoantibodies, abnormal lymphocytic response to various mitogens, and structural changes in the thymus have been observed in advanced stages of the disease (12).

However, most studies seem to be more inclined towards a pathophysiological process of the neoplastic type, since recent findings suggest somatic type mutation that occurs in myeloid parents of the marrow and that involves a neoplastic process; although this somatic mutation that occurs in a more differentiated stage leads to a self-limited inflammatory process (13).

5. Clinical manifestations

LCH occurs with general manifestations including masses or inflammation, pain in the dorsal region or extremities, bone lesions in the skull and femur more frequently, and to a lesser extent at the level of the dorsal and lumbar vertebral discs, polyuria polydipsia and skin lesions. There may also be otorrhea, exophthalmos, lymphadenopathy, abdominal distention and torticollis (14,15).

Among the most common skin lesions is seborrheic eczema, mostly in children and neonates, characterized by the spread of red or brown papules with ulceration in the center. Erythema affects skin folds, such as the armpit, which can mimic candidiasis (16-17).

Another of the most affected organs is the lung, in which it appears with dyspnea, pleuritic pain or spontaneous pneumothorax. The diagnosis of this entity is difficult because the interval between the onset of symptoms and the diagnosis varies around 6 months (14,17).

Histiocytosis has three presentations: eosinophilic granuloma, Hand-Schüller-Christian disease and Abt-LettererSiwe disease. In the case of eosinophilic granuloma, it occurs in children between 5 and 10 years of age, as the most common form of histiocytosis. Hand-Schüller-Christian disease is characterized by a triad of lytic bone lesions, exophthalmos and diabetes insipidus. Finally, Abt-Letterer-Siwe disease is the most severe manifestation of LCH (16)

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6. Clinical case

A 7-year-old girl, who was admitted to hospital with a 5-day clinical picture of difficulty in walking, associated with multiple falls from her own height and progressive decrease in muscle strength in lower limbs, with no other symptoms. The mother said it was the first time she had had such a condition.

Among its antecedents: product of sixth gestation, vaginal home birth with poor prenatal controls. The physical examination found her alert, oriented, hydrated, afebrile, with vital signs within normal parameters. Head and neck unchanged, thorax normoexpandable, cardiopulmonary system unchanged, abdomen soft, depressible, painless. He didn't have edema in his extremities. The neurological examination found a patient with no deficit in cranial pairs, muscle strength 4/5 in lower limbs and 5/5 in upper limbs. Osteo-tendon reflexes with hyperreflexia: ++++/+++++ and positive bilateral Babinski's reflex.

She was evaluated by the Neuropediatrics department, who ruled out encephalitis and Guillain Barré by lumbar puncture; the electromyography of lower limbs was found to be normal. He had it done The CT scan of the spine showed flattening of the vertebral body T9, whose characteristics were suggestive of an infiltrative process (Figures 1 and 2), and an infectious process was considered in the differential diagnosis. Complementary evaluation was recommended by means of magnetic resonance imaging (MRI) with contrast dye, which showed infiltrative lesion in the vertebral body T9, with pathological crushing and epidural invasion, spinal cord compression and myopathy, which due to the age range, posed as a diagnostic possibility primary hematological compromise, such as histiocytosis of Largenhans-Granuloma eosinophilic (Calvé vertebrae) cells with T8 and T10 continuity compromise (Figure 3).

Due to neurological deterioration with reduced mobility and muscle strength, surgery was performed with the removal of the T8-T9 decom-

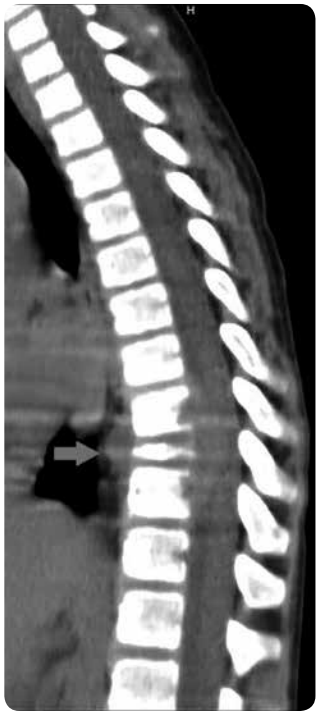

Figure 1. Sagittal section of CT in soft tissue window: note the flattening of the T9 vertebral body and the invasion of the soft tissue component into the extradural spinal canal (arrow).

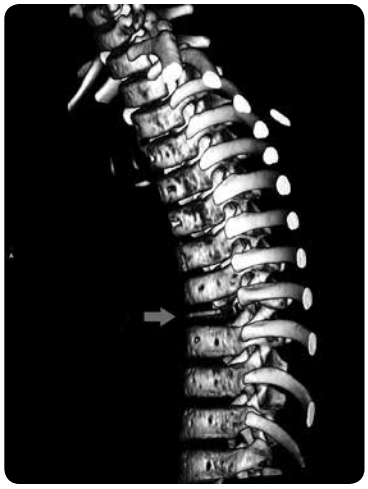

Figure 2. 3D reconstruction of thoracic-sagittal CT scan: flattening of the vertebral body T9 (arrow).

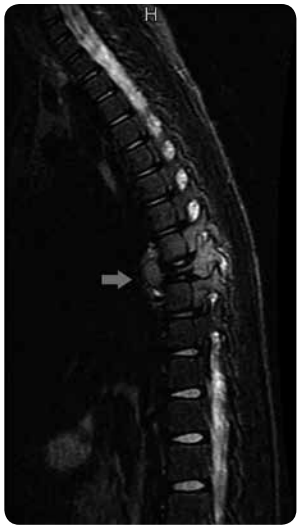

Figure 3. Thoracic-sagittal MRI sequence with T2 information: flattening of the vertebral body T9 with preservation of the signal from adjacent intervertebral discs. Note the high signal and increased volume of the prevertebral soft tissues (arrow).

pressive laminectomy T9 extradural spinal tumor and sent for an anatomopathological study. He was then admitted to the paediatric intensive care unit for invasive monitoring. The patient evolved satisfactorily.

Neurosurgery gave discharge with report of pathology "Langerhans cell histiocytosis versus lymphoma", and follow-up appointment with MRI post-surgical. He was referred to an institution with a Hematooncology service for confirmation of diagnosis and initiation of treatment. At hospital discharge, the patient persisted with muscle strength 5/5 in upper limbs and 4/5 in lower limbs, with a positive bilateral Babinski's reflex.

7. Discussion

Histiocytosis initially manifests itself with bone alterations in imaging studies such as X-rays, which are the most appropriate for the diagnosis of this entity; the flat bones of the skull are the most affected, followed by the jaw, ribs and spine (18).

In the spine, the region most affected is the vertebral bodies. Early lesions are lytic-type with flattening, as in this case. Comparing the MRI findings, a decrease in signal is observed in sequences with T1 information and an increase in intensity in sequences with T2 information with areas of enhancement. This finding is called the Calvé vertebra (18).

Among the differential diagnoses of this type of lesion are Ewing sarcoma, lymphoma, giant cell tumor, metastasis and spondylodiscitis (19). Sarcoma is a large soft tissue tumor, most common in long, flat bones. However, previous pathologies are common in older ages and less prevalent in children (19).

According to Huang et al., the most common radiographic features of vertebral LCH are lytic lesions, which lead to vertebral collapse, which is pathognomonic in children and adolescents, but requires confirmatory pathological studies (20).

In the literature review of this entity, the evident clinical manifestations are observed in advanced stages of the disease, therefore, imaging studies become a fundamental tool for the diagnostic suspicion of LCH. For this reason, X-rays should be observed in detail in patients with a family history of the disease, in order to look for bone abnormalities at critical ages of onset and, incidentally, to allow a glimpse of this pathology at earlier stages.

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