

CASE REPORT

Case Report of the Langerhans Cells Histiocytosis: A Rare Disease With Many Questions And Little Answers

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Introduction

Langerhans cells histiocytosis (LCH) is a rare disease in which there is pathologic proliferation of immature hystiocytes associated with excessive production of cytokines. Inflammation and damage occur in tissues affected by the deposition of these cells. For clinical purposes, LCH is divided in three different groups: Eosinophilic granuloma, Hand-Schüler-Christian disease, and Letterer-Siwe disease. This herogeneity implicates in the course of LCH, which can present as an indolent condition, with spontaneous resolution or it could develop into a more severe progression, which may lead to serious sequelae and even death. Patients with single system disease that means, restricted to one organ have a better prognosis in comparison with disseminated disease which is characterized by multiple organ involvement. [1, 2, 3]

The disease affects specially toddlers with slight predominance in males. [6] Because it's such a rare disease with 1 to 2 cases in a million in adults and 3 to 5 cases in a million in children [4] and children are the most affected by the disease, most studies and therapies are focused on the second group. [5]

The cause of the disease is still uncertain, but some hypotheses suggest it occurs due to an immunological imbalance leading to an abnormal interaction between Langerhans cells and T lymphocytes leading to uncontrolled inflammation [7]. Still, its clonal aspect among several mutations reinforces a neoplastic origin [8, 9, and 10].

Case Report

This patient is 48 years old female was admitted to hospital care with complains of backache at the level of T10 to L1, diffuse feeling of pain all over the body, 33pound weight loss. She reported progressive asthenia and hoarseness that began 6 months ago. She denied fever episodes. Two years ago, she had aseizure and started using 200mg of Carbamazepine 3 times a day.

On examination patient was hypocorated (2+/4+), afebrile, tired, hydrated, eupneic, lucid and oriented. She looked skinny and there was no sign of motor or sensitive deficit.

Physical exam attested palpable cervical adenomegalies, the greater one with 2 cm. There was also a hyperchromic plate under arpisto (figure 1).

The complete blood count attested Hb of 11.7 g/dl (N = 12 to 15.8 g/dl), Ht of 36.5% (N = 33 to 44.5%), white blood cells



Figure 1: Hyperchromic plate under bilateral armpits

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= 5100 (N = 3600 to 11000/ mm³), serum iron of 25 ug/dL (N = 35 to 150 ng/mL), ferritin of 708 ng/mL (N = 12 to 150 ng/mL), index of transferrin saturation of 18% (N = 20 to 55%), VHS of 103 mm/h (N < 20 mm/h).

The electrophoresis of serum urinary proteins and immunofixation of serum and urinary proteins were all normal. Upper and lower endoscopies attested no alteration. Mammography was normal. The X-Ray of the skull presented with little osteolytic lesions in the cranial calote. The skull base had anatomic embossing, as well as the Sella turcica which all had normal outlines and diameters. The X-Ray of the cervical with intervertebral spaces between C5 and C7 were reduced and it was associated with a narrowing and a sclerotic lesion of the bone. There was also bilateral uncarthrosis of bones among at the level of C5-C6. The thorax and lumbosacral X-Ray attested anatomic alignment among vertebral bodies. There were diffuse sclerotic bone lesions on the vertebral bodies.

The intervertebral space of the spine was preserved as well as the pedicles and the elements of the posterior arch. The vertebral canal had normal outlines and diameter and no abnormality was seen in the lumbosacral junction. The pelvic bone x-Ray attested preserved spaces in the hip and sacroiliac joint. Pubis symphysis had no abnormality. The multiple sclerotic lesions were seen along with osteophytes on the left iliac crest.

The tomography (CT) of the neck presented lymph node enlargement in the right II chain, measuring 2.4 x 1.2 cm. The adipose and muscular planes were preserved; the submandibular and parotid glands had no sign of injury. There was no tomographic change in the projection of the tongue and floor of the mouth. The parapharyngeal space was preserved; there was no sign of injury in the pterygopalatine fossa or infratemporal fossa. The presence of a hypodense nodule in the right lobe of the thyroid, measuring 5mm. The CT of the thorax presented diffuses multiple sclerotic lesions along the region of the thorax and abdomen (Figure 2).

The abdominal-pelvic CT presented with multiple sclerotic lesions scattered in the abdomen. There was a solid, oval nodular lesion measuring 2.6 x 1.0 cm, coupled to the left lateral fascia. Small oval lesions scattered in the subcutaneous abdomin-pelvic tissue with the largest one measuring 1, 2 cm, in the pre-pubic region on the right. Small intussusceptions of the small intestine in the mesogastrium, with no signs of obstruction (Figure 3). There was also a small net distension of ileal loops, downstream of intussusceptions.

The magnetic resonance (MRI) of the brain revealed thickening of the pituitary gland, alteration of the deep white and gray matter signal (notably in the region of the hypothalamus, brainstem and cerebellum), as well as lytic lesions in the cranial cap with gadolinium impregnation. There were areas of leukocortical gliosis/encephalomalacia in the upper frontal gyrus's, notably on the right (Figure 4).

The cervical MRI attested the presence of smooth homogeneous contours lymphadenopathy at the IB levels on the right

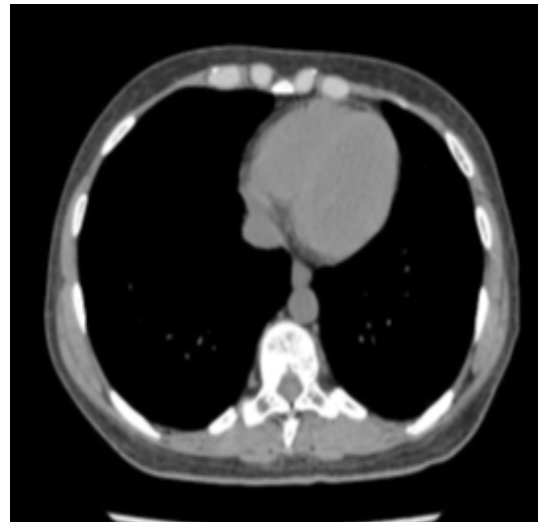


Figure 2: Sclerotic lesions in the thorax.

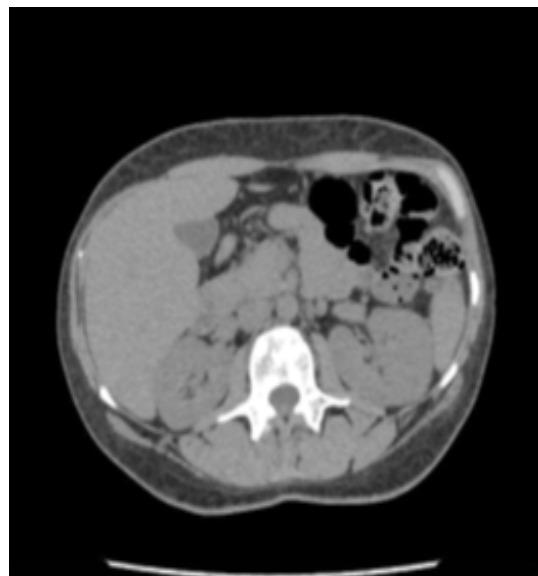


Figure 3: Sclerotic lesions in the abdomen.

(measuring 2.3 x 1.3 cm), II on the right (measuring 2.5 x 1.4 cm) and III on the left (measuring 1.4 to 0.8 cm). Lymph nodes at the IB and IV levels on the left were prominent but didn't establish as lymph node enlargement. There was thickening, edema, and increased diffuse enhancement of the glottic and supraglottic larynx. The adipose and muscular planes were preserved.

The bone marrow of the vertebral bodies had a diffusely heterogenous signal, with multiple nodular lesions. Multiple small hyperintense lesions with T2 signal were also noticed in the cerebellar peduncles, mesencephalon and adjacent to mammillary bodies measuring between 0.2 and 1.2 cm. There were degenerative changes in the cervical spine predominating in C5-C6, leading to stenosis of the vertebral canal at this level, where there was also central disc protrusion, causing compression on the Dural sac and spinal cord.

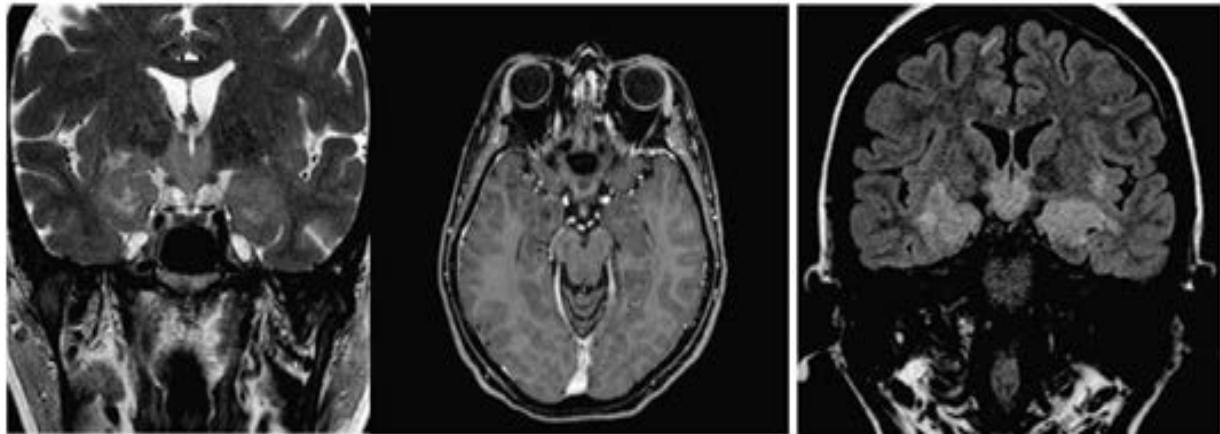


Figure 4: Lytic lesions in the cranial cap with gadolinium impregnation.

The bone scintigraphy attested multiple areas of anomalous hypercaptation of the radiopharmaceuticals that distribute diffusely by the axillary and appendicular skeleton.

The patient was submitted to a bone marrow biopsy in the region of the posterior iliac crest. The anatomopathological report found:

- A. Epithelioid granulomatous reaction in the spinal chambers with the following aspects: focal clusters of epithelioid histiocytes, mycobacteria screening by Fite-Faracco technique was negative, fungus screening by Grocott staining was also negative and there was no evidence of fibrosis from the Gomori staining analysis.
- B. Increased bone marrow cellularity for the patient’s age: 90% (N: 52%)
- C. Granulocyte/erythrocyte ratio: about 1/1
- D. Granulocytic series had increased cellularity, no maturation delay and no focal displacement of immature cells to the center of the intertrabecular space. Apparent eosinophilia.

The erythroid and megakaryocytic series presented increased cellularity associated with preserved morphological characteristics. The patient presented hypercellular bone marrow with hypercellularity of the granulocytic, erythrocytic, and megakaryocytic lines associated with a chronic granulomatous inflammatory process (Figure 5).

The immunohistochemical panel attested that the bone marrow fragment was normocellular for all three maturation hematopoietic lines. There were regions of large histiocytes concentration. These cells had convoluted nuclei, thin granular cytoplasm which formed blocks that expressed CD1a and S100 protein focally. The immunostaining for CD30 didn’t demonstrate atypical cells. Thus, the anatomopathological and immunohistochemical findings with presence of cells strongly marked with S100 suggest bone marrow infiltration by clonal histiocytes, according to the table below that describes

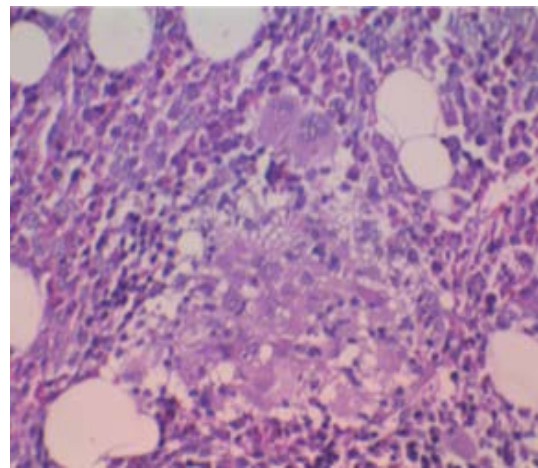


Figure 5: The patient presented hypercellular bone marrow with hypercellularity of the granulocytic, erythrocytic, and megakaryocytic lines associated with a chronic granulomatous inflammatory process.

Antibody	Clone	Results
CD15 – antigen of granylocytes and Reed-Sternberg cells	Carb-3 Negative	Negative
CD20 – antigen of B lymphocytes	L26	Negative
CD3 – T cell surface glycoprotein epsilon chain	SP7	Negative
CD30- antigen Ki-1	Ber-H2	Negative
Oncoprotein LMP-1 of Epstein-Barr virus	CS1-4	Negative
CD138 – plasma cell antigen	B-A38	Negative
Myeloperoxidase - cells of myelo granulocytic lineage	MPO-7	Negative
CD163 - hemoglobin haptoglobin complex	CD163	Positive
CD1a– langerhans cell antigen	O10	Positive
S100 protein	Polyclonal	Positive

Table1: Immunohistochemistry panel with polyclonal antibody was typical to Langerhans Histiocytosis.

the panel of polyclonal antibodies used in this analysis. All immunohistochemical analysis was performed with positive and negative controls, respecting the good practices of clinical analysis in the reference laboratory.

The clinical, laboratory, radiological and anatomopathological contexts suggested the diagnosis of Langerhans histiocytosis. Patient initiated the treatment for multisystemic Langerhans histiocytosis with a chemotherapy protocol with Prednisone (40 mg/m² for 4 weeks) associated with Vinblastine (6 mg/m² for 6 weeks). The patient presented excellent initial response to the selected protocol associated with the treatment of secondary endocrinopathies to neoplasia.

Discussion

LCH is a rare condition that consists in the formation of tumors of Langerhans cells that may affect different organs of the body and can manifest in the form of granulomas. Although it is more prevalent in children, adults can also develop LHC, specially smokers, which may present with the pulmonary form of the disease. [5]

The clinical picture of the disease is manifested by a broad range of signs and symptoms, which can affect only one organ, or may be manifested by diffuse involvement in more than one tissue, establishing the systemic form of the disease. [7] Bone lesions characterize one of the most common manifestations of the disease, which were quite prominent on radiological examinations of the patient from the observation of “perforated lesions”.

Because it is an atypical disease and can potentially affect different organs and systems, LCH can be initially confused with other disorder, such as Ewing sarcoma, leukemias, and lymphomas. Therefore, the clinical diagnosis should be aided by a combination of imagining tests and pathological reports, which all help support and confirm the diagnosis of this rare disease.

Particularly in the case described above, the age of the patient may cause diagnostic reasoning even harder, since LHC primarily affects children. Thus, most of the knowledge concerning causes, pathogenesis, and treatment is based upon the pediatric perspective.

Adults have been reported to present with lung involvement, which can be explained by the higher prevalence of the disease in smokers. Also, skeletal lesions are frequent in adults as well as involvement of the hypothalamus-pituitary region, important features which could aid in the diagnosis. [11]

In order to prevent misdiagnose, these clinical features seen specially in adults, must be identified. Besides, the imaging exams, histopathological and the immunohistochemical features of LHC help improve an assertive diagnosis in older patients. The therapeutic protocols involve alkylant agents and alkaloids of the vinca, and vinblastine is the chemoterapic reference. Generally, patients present a favorarel evolution at younger ages, but the course of the patient in adults is still uncertain, very likely by the rarity of presentation in patients

over 50 years.

This disease continues a rare type of the apresentation in the histiocytosis, disease with many questions and little answers.

Acknowledgement

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Consent of patients

Written informed consent was obtained from the patient’s next of kin for publication of this case report and any accompanying images. A copy of the written consent is available for review by the Editor-in-Chief of this journal.

Competing Interests

The authors declare that they have no competing interests. Authors’ Contributions Dr Bruna D. Diniz wrote the manuscript. All authors read and approved the final manuscript.

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