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Title: Langerhans-Cell Histiocytosis: a clinic case report

Título: La histiocitosis de células de Langerhans: propósito de un caso clínico

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ABSTRACT

Langerhans cell histiocytosis is a rare pathology, characterized by the proliferation of histiocytic cells, its etiology is not clear. The clinical case of a 10-year-old male patient was presented, admitted to the Pediatric Hospital of Holguin with the diagnosis of moderate Odontogenic Facial Cellulitis. He was attended at the Maxillofacial Surgery Service, and due to the torpid evolution it was decided to interconsult with Oncology and perform complementary studies. By means of Computerized Axial Tomography of the Facial Mass, an extensive lesion was detected, involving the entire right hemiarch, solid, with heterogeneous internal structure and great bone destruction of the jaw. Incisional biopsy detected extensive areas of granulomas, eosinophils, affecting bone, skin and

oral mucosa, redirecting the diagnosis to Langerhans cell histiocytosis. The patient underwent polychemotherapy and is currently under clinical and radiological monitoring. The grouping of its main manifestations may enrich pediatric scientific research efforts.

Key Words: Histiocytosis; Oral Surgery; Biopsy; Drug Therapy

RESUMEN

La histiocitosis de células de Langerhans es una patología infrecuente, caracterizada por la proliferación de células histiocitarias, su etiología no está clara. Se presentó el caso clínico de un paciente masculino de 10 años de edad, ingresa en el Hospital Pediátrico de Holguín bajo el diagnóstico de Celulitis Facial Odontógena moderada. Es atendido en el Servicio de Cirugía Maxilofacial, ante la tórpida evolución se decide interconsultar con Oncología y realizar estudios complementarios. Mediante Tomografía Axial Computarizada del Macizo Facial se detectó lesión extensa, que compromete la totalidad de la hemiarcada derecha, sólida, de estructura interna heterogénea y gran destrucción ósea de la rama mandibular. La biopsia incisional detectó áreas extensas de granulomas, eosinófilos, que afectaba hueso, piel y mucosa oral, lo que redirige el diagnóstico a Histiocitosis de células de Langerhans. El paciente fue sometido a poliquimioterapia y se encuentra bajo control clínico y radiológico actualmente. La agrupación de sus principales manifestaciones puede enriquecer los esfuerzos de investigación científica pediátrica.

Palabras clave: Histiocitosis; Cirugía Bucal; Biopsia; Quimioterapia

INTRODUCTION

Langerhans cell histiocytosis (LCH) is a rare, uncommon pathology characterized by the proliferation of histiocyte cells in one or more organs.[1] The cause of histiocytosis is unclear. It is thought to be a neoplastic process, but sometimes there are spontaneous regressions; it is also thought that the histiocytosis arose in response to an antigen leading to an uncontrolled reaction of histiocyte cells, with the appearance of macrophages, eosinophils, T lymphocytes in the area, resulting in a very pronounced immune response.[1, 2]

Both the classification and nomenclature of this disease have been modified over time.[2] In 1987 the Histiocyte Society first classified histiocytic disorders into three groups: the LCH group, another group for non-Langerhans histiocytoses, and a third for malignant histiocytoses. In turn, LCHs were grouped into four entities according to their clinical

manifestations: eosinophilic granuloma, Hashimoto-Pritzker, Hand-Schüller-Christian disease and Letterer-Siwe disease. [2]

LCH is present at any age, from the neonatal stage to adulthood, but it is more frequent in children under 18 years of age (67% of cases). There is a slight male predominance, with a male to female ratio of 1.5:1.7. There is a predominance of Caucasian race.[2]

The annual incidence varies from four to nine cases per million children under 15 years of age, with an age range at diagnosis between three and six years. In Mexico, the incidence is estimated at 4.3 cases per million children under 18 years of age, and approximately 100 new cases are reported each year.[2] In our country, this disease is considered very rare.

The proliferation and accumulation of pathologic Langerhans cells can occur in any organ, which makes the manifestations of LCH very varied. The most frequently affected organs are bone (80% of cases), skin (30-50%) and pituitary (25%), followed by liver, spleen, lung and hematopoietic system. The kidneys and gonads are generally not affected.[2]

LCH involves the head and neck region quite frequently, particularly the cranial and maxillary bones. In Dentistry, it usually begins in the periapical region of the tooth in the posterior region of the mandible, causing erosion of the lamina dura and may lead to a decrease at the height of the mandibular ramus.[4]

There is gum pain and inflammation, finding on palpation a swelling corresponding to the accumulation of Langerhans cells, causing oral ulceration with the possibility of producing tooth loss. Bone destruction, dental loss and periodontal disease are the most suggestive signs of histiocytosis.[4]

The radiological images show the dental organs, the typical lesion being lytic in shape, with well delimited borders, surrounded by a radiolucent granulomatous material, especially in the initial stages of the disease, displacing the germs of the teeth in formation.[4]

There are different treatment modalities and all have demonstrated effectiveness and low recurrence rates. Treatment depends on the extent of the process, a single lesion tends to disappear with the use of chemotherapy or spontaneously. Also diagnostic biopsy with or without injection of a steroid can initiate cure. Patients with multisystem

disease may benefit from steroid and cytostatic treatment or even stem cell transplant.[3, 4]

The appearance of this pathology in the facial region is uncommon in our country, 10 years ago no case was reported in the Pediatric Teaching Hospital Octavio de la Concepción y de la Pedraja, this is a reason for its dissemination within the scientific community and can enrich the pediatric research efforts.

CASE REPORT PRESENTATION

Reason for admission: Increased volume in the right hemiface.

History of the present illness: A 10-year-old male patient, white, from a rural area, with a previous health history; who was diagnosed with Moderate Odontogenic Facial Cellulitis in Primary Care, was referred to the Maxillofacial Surgery Service of the Pediatric Hospital of Holguín due to a persistent increase of volume in the right hemiface, which began one month before the consultation, accompanied by moderate pain that was aggravated occasionally. It was decided to admit him for further study and treatment.

Anamnesis: The patient complains of continuous and throbbing pain in the affected region. The patient's mother reports previous antimicrobial treatment with Ciprofloxacin, Metronidazole and amoxicillin; with no apparent improvement.

Positive findings on physical examination

General physical examination: Patient without physical, functional, sensory and motor alterations.

Regional physical examination of the head: (Picture 1)

Inspection

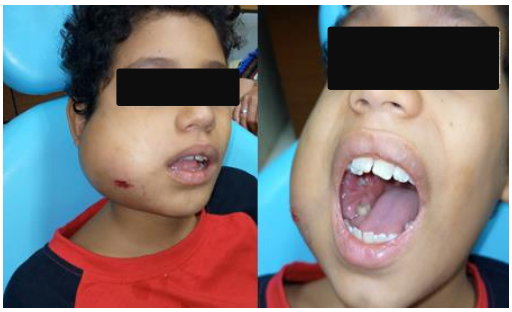
Large increase in volume (gross edema in the right cheek) covering the aponeurotic spaces: parotid, masseteric and submandibular, with no apparent change in color. Presence of moderate trismus.

Mouth: Late mixed dentition. Angle's Class II, Subclass 1 dental malocclusion. The edema covers intrabuccally the occlusal surfaces of the molars of the lower right hemiarch. The gingiva is hypercolored, smooth, shiny and enlarged associated with the remaining root of tooth 85^{th}, hypertonic mucosa located in the right retromolar space.

On palpation: The mass had a woody consistency; on clinical examination it was normothermic, with no mobility and well-fixed to the deep tissue planes.

Immediate treatment: The patient was quickly admitted to the Pediatric Hospital of Holguín, where he was given antimicrobial treatment with ceftriaxone (1 g/ 10 ml bulb) at a dose of 100 mg/kg per day, intravenous every 12 hours diluted in 10 cc of 0.9% sodium chloride; in combination with Metronidazole (250 mg tablet) at a dose of 250 mg every 12 hours orally. A horizontal incision was made below the masseteric space and a rubber drain was placed to allow drainage of the septic process. In addition, the patient was hydrated with 0.9% sodium chloride, analgesics, sedatives, heat therapy, adequate diet and oral hygiene, mouthwashes with plantain and warm honey. On the third day a new assessment was performed and as the patient was progressing successfully, it was decided to perform extraction of the remaining root of tooth 85th.

After the extraction, the patient's progress was poor, so it was decided to perform some additional tests and to interconsult the case with the Oncology Department.

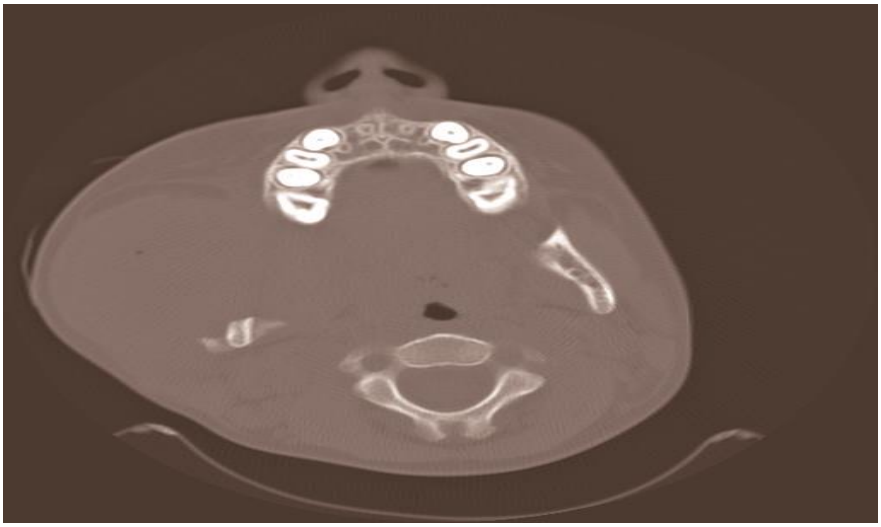


Picture 1.

Tests:

Hemochemistry: without changes

CT scan of simple Facial Mass: it is performed with a slice thickness of 3 mm, showing a space-occupying lesion, extensive, involving the entire right hemiarch, solid with heterogeneous internal structure, with an average density of 41 HU. In axial section it measures 70x48 mm and in sagittal reconstruction 60 mm with calcification in its interior compressing and displacing the ipsilateral masseter, visualizing great bone destruction of the jaw.



Picture 2.

Simple skull CT scan: performed with a slice thickness of 5 mm, without abnormalities.

Simple computed axial tomography of the chest and abdomen: performed with a slice thickness of 5 mm, without abnormalities.

Elevated tumor markers (alpha-fetoprotein and β-human chorionic gonadotropin)

In order to establish a definitive diagnosis of the lesion based on its histological features, an incisional biopsy of the lesion was performed in the Maxillofacial Surgery Department through the following procedure: under general orotracheal anesthesia, an incisional sample was collected through a flap surgery in the affected area, and a sample of affected tissue such as bone, dental and soft tissue was collected.

Upon analysis, extensive areas of granulomas and eosinophils were observed in the right mandibular region affecting bone, skin and oral mucosa.

Diagnosis:

Considering the positive findings on questioning, physical examination and the additional test results, it is concluded that this patient presents: Langerhans cell histiocytosis. It was decided to carry out chemotherapy treatment in the Oncology Service.

Treatment plan:

In the Oncology Department he underwent polychemotherapy treatment with vinblastine (bulb 10 mg/10 ml) at a dose of 6 mg/m2/day intravenously, etoposide (bulb 100 mg/5 ml) 150 mg/m2/day, diluted in 300 ml of dextrose 5% for 2 hours and prednisone (tablet 20 mg) at a dose of 40 mg/m2/day. He was also administered zofran (ampules 8 mg/ 4

ml) dose of 0.15 mg/ kg, diluted in 10 ml of dextrose 5% and alusil (gel) dose of 10 ml after breakfast, lunch and lunch, omeprazole (bulb 40 mg/ 10 ml) dose 1 mg / kg/ day and allopurinol (tablet 100 mg) dose 8 mg/ kg/ day. He was hydrated and kept under adequate diuresis monitoring.

Possible surgical resection of the bone lesion is evaluated.

The patient has progressed positively, so at this moment he is discharged from the Oncology and Maxillofacial Surgery Service of the Pediatric Hospital of Holguin under periodic clinical and radiological check-ups.

DISCUSSION

This study reports a case with Langerhans cell histiocytosis, with most of the typical features described in the literature. These patients require multidisciplinary treatment, according to the presenting abnormalities.

The phagocytic mononuclear system has an important role in the body's immune defense mechanism, both non-specific and specific.[1] Langerhans cells are intraepidermal dendritic cells with dendritic processes extending between keratinocytes and into the dermal-epidermal junction.[2,4]

The intense, disordered and abnormal growth of a type of histiocytic cell with a phenotype very similar to Langerhans cells, giving rise to a pathology form known as Langerhans cell histiocytosis.[1]

Terms such as eosinophilic granuloma, Hashimoto-Pritzker, Hand-Schüller-Christian disease and Letterer-Siwe disease are replaced by a classification in which LCH are divided into three groups depending on the number of lesions and their location: high-risk multisystem involvement, low-risk multisystem involvement and single organ or system involvement.[2] In this case, the classification corresponds to the third group.

This classification provides guidance on the prognosis of the disease and allows to regulate the therapeutic conduct to be followed, so it is currently recommended.[2] Authors such as Morán Villaseñor, et. al.[1] and Cardeña Mamani, et. al.[5] have made reference to it in their research.

Most patients (between 70 and 92%) have limited involvement of a single organ or system, and only between 8 and 30% have multisystemic involvement, of which 43% will have damage to organs at risk.[4,6,7] In the case in question there was no multisystemic involvement, the lesion was limited to the stomatognathic system.

It is more common in children between three and ten years of age, although it can also appear at 15 years of age and is rare at older ages, because of its very low incidence in older patients it can be confused with lymphoma.[3,7] Medina et. al.[8] state that the most common sign is solitary painful bone lesions, although they can be disseminated and polyostotic, Cardeña Mamani et.al.[5] state that the skull is most frequently affected. However, in this case, involvement of the facial mass was observed.

The most common cutaneous features are brown papules, a purple, eczematous rash resembling that of a yeast infection. Other skin lesions include purple, petechial, vesicular or papulo-nodular pustules, which may occur in 60% of cases.[3, 8,9]

This group of idiopathic disorders characterized by the growth of Langerhans cells has numerous differential diagnosis, in the facial region Odontogenic Facial Cellulitis is one of them. According to Cardeña Mamani et. al. [5] and Medina Ruiz et. al. [6] some differential diagnosis to be considered are: central giant cell granuloma, squamous cell carcinoma, mandibular or maxillary tumor and ameloblastoma.

The final diagnosis in the adult patient was complex, due to the characteristics of the clinical features. The histological study by optical microscopy was essential because it guaranteed the correct interpretation of the morphological abnormalities present. The radiological study showed certain typicity in relation to that proposed by other authors such as Santana Garay. [10].

Recurrence is more frequent in multifocal and disseminated cases. Sequelae occur in about 64% of cases, at a three-year follow-up. According to the study by Barrios et al.[2], the prognosis for survival at 5, 10 and 20 years is 88% and 77% respectively, with an estimated average disease-free survival of 30% at 15 years.[9, 10] It is worth noting the good progress of this patient.

Treatment was carried out by interdisciplinary decision and according to established standards. There are different treatment modalities and all have demonstrated effectiveness and low recurrence rates. However, it should be noted that treatment depends on the extent of the process. Cardeña Mamani et. al [5], in their presentation recommend treatment with chemotherapy.

Langerhans cell histiocytosis is a disease with a wide spectrum of local and systemic features depending on the stage and involvement of the disease. It is characterized by a growth of Langerhans cells and its cause is unknown. It is rarely reported due to its low

incidence and prevalence. The findings obtained can be difficult to interpret, which is why the grouping of its main features increases the volume of data for the analysis of differential diagnosis to be considered by dentists, maxillofacial surgeons, oncologists and pediatricians, and can enrich scientific research efforts.

BIBLIOGRAPHIC REFERENCES

1. Morán Villaseñor E, Durán McKinster C, Orozco Covarrubias L, Palacio López C, Sáez de Ocáriz M, García Romero MT. Histiocitosis de células de Langerhans: nuevos conceptos moleculares y clínicos. DCMQ [Internet]. Marzo de 2018. [citado 27 de marzo de 2022]; 16(1): [Aprox 7 p.]. Disponible en: https://dcmq.com.mx/edici%C3%B3n-enero-marzo-2018-volumen-16-n%C3%BAmero-1/617-histiocitosis-de-c%C3%A9lulas-de-langerhans-nuevos-conceptos-moleculares-y-cl%C3%ADnicos#:~:text=La%20histiocitosis%20de%20c%C3%A9lulas%20de,formas%20localizadas%20hasta%20cuadros%20diseminados

2. Barrios K, Patiño O, Muñoz N, Moneriz C. Histiocitosis congénita de células de Langerhans. Biomed. [Internet]. 2020 Sep [citado 26 de marzo de 2022]; 40 (3): 464-471. Available from: http://www.scielo.org.co/scielo.php?script=sci_arttext&pid=S0120-41572020000300464&lng=en. Epub June 30, 2020. https://doi.org/10.7705/biomedica.5150.

3. Navarrete FG, Ramos GJA, González GM, et al. Histiocitosis sinusal cutánea. Estudio clínico-patológico de 33 pacientes en el Centro Dermatológico Pascua. Rev Cent Dermatol Pascua. 2021;30(2):61-67. doi:10.35366/101175.

4. Sosa GA, Dogliani P, Guidi AE, Marangoni MA, Lavarda M, Fainstein-Day P. Enfermedad de Erdheim-Chester: una rara Histiocitosis con excelente respuesta a cobimetinib. Rev Fac Cienc Med Univ Nac Córdoba. [Internet]. 2021 Dic [citado 27 de marzo de 2022];78(4): [Aprox 3 p.]. Disponible en: https://doi.org./10.31053/1853.0605.v78.n4.30852

5. Cardeña Mamani R, Arauco Nava P, Villena Pairazaman FF, Mejía Pelaez G, Flores Alvarez W. Histiocitosis de células de Langerhans: Serie de casos y revisión de la literatura. Rev. Cuerpo Med. HNAAA [Internet]. 2021 Abr [citado 26 de marzo de 2022]; 14 (2): 214-217. Disponible en: http://www.scielo.org.pe/scielo.php?script=sci_arttext&pid=S2227-47312021000200016&lng=es. http://dx.doi.org/10.35434/rcmhnaaa.2021.142.1067.

6. Medina Ruiz B, Arocho L, López Del-Valle LM, Molina Negrón D. Histiocitosis de células de Langerhans: seguimiento de 5 años del caso y revisión sistemática de literatura. Rev. Odontopediatr. Latinoam. [Internet]. 1 de julio de 2021 [citado 27 de marzo de 2022]; 11(2). Disponible en: https://www.revistaodontopediatria.org/index.php/alop/article/view/231

7. Da Fonseca R, López Del-Valle L, Arocho L, González D, González J, Perales de Anda E, Molina-Negrón D. Histiocitosis de Células de Langerhans. Rev. Odontopediatr. Latinoam. [Internet]. 21 de enero de 2021 [citado 27 de marzo de 2022];7(2). Disponible en: https://www.revistaodontopediatria.org/index.php/alop/article/view/141

8. Medina MA, Meyer W, Echeverri C, Builes N. Histiocitosis de células de Langerhans: reporte de caso y revisión de la literatura. Biomédica. 2021; 41:396-402. https://doi.org/10.7705.biomedica.5430

9. Ochoa Castillo MM. Diagnóstico precoz de la histiocitosis mediante las manifestaciones bucales. Revisión sistémica. [Guayaquil]: Universidad Católica de Santiago de Guayaquil; 2020. 27 p. Disponible en: http://repositorio.ucsg.edu.ec/handle/3317/16167

10. Santana Garay JC. Enfermedades óseas que afectan el complejo bucal. Histiocitosis. En: Santana Garay JC. Atlas de patología del complejo bucal. 2ª ed. La Habana: Ciencias Médicas; 2010. p. 155-177.