



Case report and literature review:

LANGERHANS CELL HISTIOCYTOSIS OF THE PETROUS APEX WITH INNER EAR INVOLVEMENT

Palabras clave: Histiocitosis de células de Langerhans, Hueso temporal, Neoplasias del oído.

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ABSTRACT

Temporal bone involvement in Langerhans Cell Histiocytosis (LCH) is the second most common site of involvement in the head and neck area, with the mastoid and squamous portion of the bone as the most frequent site where LCH manifests. Since there are not many cases reported in the literature, it is possible to state that primary manifestation of histiocytosis affecting the inner ear structures is uncommon. This article reports the case of a patient with involvement of the petrous apex of the temporal bone that was referred to the Fundación Hospital de la Misericordia, and carries out a literature review in order to discuss the manifestation, treatment and outcome of this disease.

INTRODUCTION

Langerhans Cell Histiocytosis (LCH), known as histiocytosis X until 1985, was first described in 1893 as part of a multisystemic disease that mainly affects population under the age of 16 **(1)**. It is a monoclonal proliferation of dendritic cells with typical Langerhans cells features **(2)**.

LCH is a rare condition with a reported incidence that ranges from 4 to 9 cases per million and its etiology has not yet been established; however, several theories in this regard have been proposed, including those stating LCH has a neoplastic or an immune reaction origin **(2)**. Clinically, LCH may manifest by affecting a single system or organ, being the skeletal system the most frequently compromised, or involving more than two organs **(3)**.

Head and neck areas involvement by LCH ranges from 53% to 70%. In these areas, the cranial vault ranks first in terms of involve-

ment by this disease, while the temporal bone comes in second or third place **(1-4)**. On the other hand, the mastoid part of the temporal bone is one of the areas where greater LCH involvement can be observed. Damage of inner ear structures as primary manifestation site is atypical, since there are few cases describing this situation reported in the literature.

CLINICAL CASE

Two years old female referred by a second level health institution due to a four days clinical course of disequilibrium episodes triggered by changes in the patient's position with no other symptoms associated. A prior episode of acute otitis media (AOM), with its laterality not specified by her caregivers and treated with antibiotics and analgesia until complete resolution of symptoms, was reported.

Through physical examination it was determined that the patient was in a good general condition, hydrated and afebrile. Left ear otoscopy showed that the patient had detritus in the ear canal and an opaque non-convex tympanic membrane. There was not nystagmus in the vestibular examination, but instability, indifferent lateropulsion and 15 seconds long increase of the support polygon when changing the body position to sitting or standing were observed. Facial symmetry was observed, while no neurological deficit was found. The remaining of the physical examination was within normal limits.

The referring institution sent very poor quality images where a lesion in the left jugular foramen was seen, thus a contrast-enhanced computed tomography (CT) of the patient's ears was requested. The CT scan showed the following findings: an osteolytic lesion with complete destruction of the pe-

trous apex, involvement of the internal auditory canal in its entirety, involvement of the basal turn of the cochlea and the posterior semicircular canal, and bone limits variation in both the carotid and jugular canals, which in turn did not allow limits differentiation. Soft tissue occupying the mastoid without bone

remodeling or osteolytic lesions were also observed (Figure 1). The cranial nerves magnetic resonance imaging (MRI) showed an isointense lesion on T1 and T2 with a slight signal increase with the FLAIR sequence. There was not any evidence of vascular involvement by the mass (Figure 1).

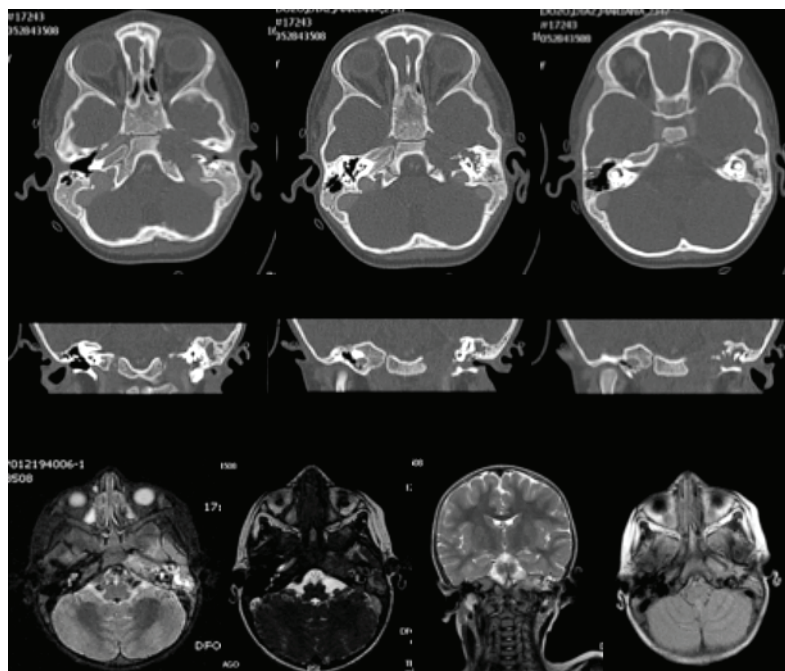


Fig 1. CT scan and MRI where it is possible to see an osteolytic lesion compromising the petrous part of the temporal bone with erosion towards the jugular foramen and structures of the inner ear.

Source: Images obtained from the data collected in the study.

Pure-tone audiometry reported a hearing response at 30 dB in open field and specific frequency auditory evoked potentials and absence of V wave in the left ear and preservation of auditory sensitivity in the right ear.

Based on these findings, a diagnostic impression of LCH vs. temporary rhabdomyosarcoma was made. Given the difficult transmastoid access for conducting a biopsy, a middle cranial fossa approach was performed with the cooperation the neurosurgery staff.

At an intra-surgical level, a soft tissue mass with similar color of the surrounding healthy bone in the petrous apex of the temporal bone that extended to the internal auditory canal (IAC) was found. Through frozen section biopsy rhabdomyosarcoma diagnosis was temporarily discarded. During surgery, the patient went through pulseless electrical activity while handling the mass, which was easily reverted by the anesthesiology staff.

In the immediate postoperative period the patient developed adrenal insufficiency of critical patients and neurogenic bladder. These conditions were treated medically. A grade V/VI House-Brackman left peripheral facial paralysis with absence of lacrimation while weeping was reported in the fourth postoperative day.

The official pathology report showed a granulomatous lesion with abundant eosinophils positive for CD-1^a and S100 in immunohistochemistry. The pediatric hematology/oncology staff confirmed the diagnosis of LCH in its polyostotic monosystemic form af-

fecting the temporal and the sphenoid bones and started a six weeks chemotherapy treatment with vinblastine 6 mg/m² and prednisone 40 mg/m².

After completing an irregular chemotherapy treatment, control images were obtained. These images showed a significant decrease of the lytic lesion with osteoneogenesis at the affected sites, as well as postsurgical changes (Figure 2). During the final physical examination performed by otolaryngology service, resolution of the instability and persistence of the peripheral facial paralysis were observed.

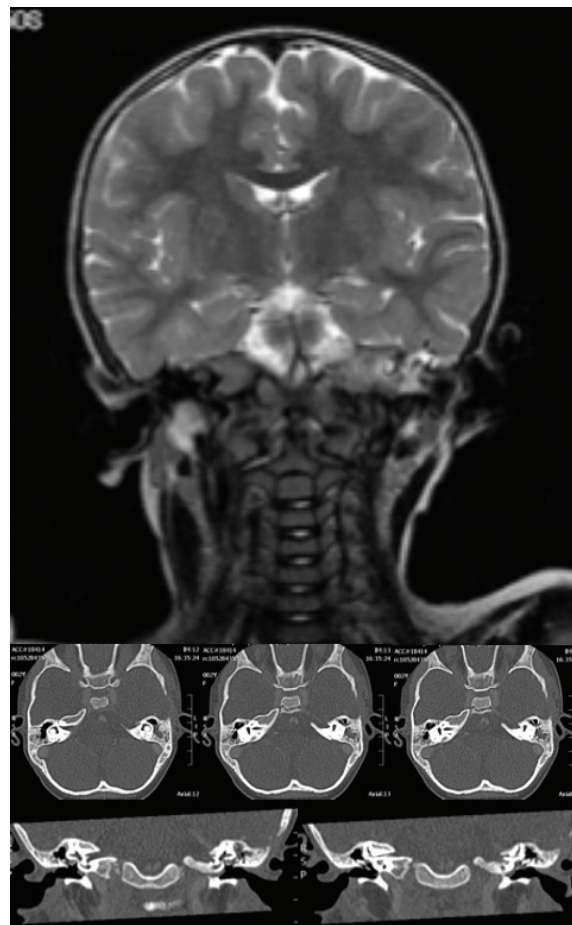


Fig 1. Six weeks CT scan after chemotherapy showing osteolytic mass resolution, osteoneogenesis and postoperative changes.

Source: Images obtained from the data collected in the study.

DISCUSSION

HCL is a rare disease that mainly affects patients under the age of 16, with subjects between 1 and 4 years old as the most prevalent age group to suffer this condition (5). It has a reported incidence of 4 to 9 cases per million and it can affect any organ or system of the body (2).

According to the current clinical classification proposed by the Histiocytosis Society of the European Society of Hematology and Oncology, HCL can be defined as a disease affecting a single organ or system (monosystemic) or more than one system (multisystemic) (3). In the case of bone involvement, HCL is regarded as monosystemic, even though several bones are affected by the disease (3).

Depending on the number and the systems affected, HCL can be classified under three different conditions with overlapping characteristics, namely:

- Eosinophilic granuloma: Single or multisystem involvement without altering the organ function. It usually occurs in people over 20 years old and it has an excellent prognosis.
- Litterer-Siwe disease: Skin, lymph nodes, lungs and liver involvement. It occurs in patients around three years old. It has a poor prognosis due to multiple organ.
- Hand-Schuller-Christian disease: Anterior pituitary involvement plus diabetes insipidus; exophthalmos and bone involvement. It affects patients between 2 and 3 years old (1).

LCH is a monoclonal proliferation of Langerhans type dendritic cells usually found in skin and lymphoid organs. Its etiology has not yet been elucidated, but two theories have been proposed: one referring to a neoplastic origin, while the other proposes an autoimmune

origin (2). In this regard, a family relationship up to 1% of the cases studied with a homozygote concordance of 92% has been found. Likewise, changes in the genome of the cells affected by chromosomal instability, telomere shortening and chromosomal loss of heterogeneity have been reported, which favors neoplastic over autoimmune theory (2).

Pathological diagnosis is made upon detection of cells with Langerhans cell phenotype where macrophages, eosinophils, multinucleated giant cells and T lymphocytes are observed. Diagnosis confirmation is reached when Birbeck granules, tennis racket like cytoplasmic organelles whose creation is induced by langerin, a Langerhans cells C-type lectin transmembrane receptor (6), are identified through electron microscopy. This technique has been recently replaced by CD1 and CD207 positive immunohistochemistry techniques as these markers are key testing elements for C-type lectin receptor (7). The use of such markers provided the confirmation of the pathological diagnosis in this case.

Skin and bone are the systems most affected by LCH, with an involvement of the head and neck areas between 50% and 70% of cases (1,4). In these areas, cranial structures are the most affected, being the cranial vault and the frontal bone the most frequent sites of LCH manifestation, followed by skin, where the condition usually manifests as a vesiculopapular rash that may affect any area of the face or the body (1).

In the United States of America, a study conducted in 22 patients with head and neck areas affected by LCH found a lower average age (five years) and a male preponderance (2:1). However, in this research there were not any statistically significant differences between multisystem or monosystem forms of the disease (7).

Regarding the temporal bone it is possible to say that it is affected in 19% to 25% of cases, with a higher prevalence in children younger than three years old, where the involvement is associated with a multisystem presentation of the disease. According to the literature, in a third of cases, LCH occurs bilaterally and the petrous part is the most affected **(5,6)**.

In a LCH temporal bone Case Report series conducted in Canada it was found that its most frequent manifestation consisted of a mass (70% of the cases), followed by external or otitis media difficult to treat. In 70% of cases unilateral involvement was observed and, in contrast with what it has been reported in the literature, the mastoid region was the site with the highest frequency of involvement, as seen in 70% of cases. Out of the ten patients of the study, eight had LCH multifocal involvement affecting the pituitary or the dura mater **(5)**.

In 2000, Italian researchers conducted a research in a total sample of 250 patients that had been diagnosed with LCH. Out of the 250, 34 had temporal bone involvement; besides, in all of them the disease occurred in its multisystem form. Patients' average age was 1.8 years; there was not gender preference. Otorrhea was the most common presenting symptom, while LCH diagnosis was only reached after performing several unsuccessful treatments for chronic otitis media (COM) and mastoiditis. In this study, researchers found that patients experiencing ear involvement were younger compared to those without it. In addition, they did not observe any difference in terms of organ dysfunction between both groups, but they noted there was temporal bone involvement with a worse prognosis regarding treatment response and a greater need for a second-line chemotherapy regime **(8)**.

Not a single case report described an inner ear structures primary involvement by LCH, which is probably due to the otic capsule higher resistance to the spreading of the disease. Up to 2008, only 13 cases describing IAC or otic capsule involvement and the resulting sensorineural hearing loss, vestibular symptoms and facial paralysis, which were found in 2.8% of these cases, had been reported **(5,9)**.

It has been stated that up to 10% of cases may present hearing loss, most of them being mixed hearing loss. In a literature review, 19 patients with involvement of the otic capsule or sensorineural hearing loss were found: two cases experiencing invasion of the IAC, a case with involvement of the vestibular aqueduct, nine cases with involvement of the semicircular canals and seven cases with involvement of other regions, all of them related to temporal mastoid injuries as the origin site of the disease **(9)**. Once chemotherapy was finished, researchers reported the following results: regardless of the site of injury, patients with profound hearing loss did not show any hearing improvement; those with severe hearing loss experienced improvement up to mild hearing loss; those with mild hearing loss went back to normal levels of hearing. Based on these results, a hearing loss final sequel in patients with HCL between 7% and 28% was calculated **(9)**.

The involvement of the temporal bone in LCH is not an atypical manifestation, but the involvement of the structures of the inner ear is uncommon.

The clinical picture of the patient, mainly obtained by symptoms of vestibular dysfunction, despite the fact she did not show recurrent AOM, COM or masses in the temporal region, and her age are enough reasons for the physician to carry out a deeper study of the

cause of vestibular symptoms, where temporal bone neoplastic lesions should be considered in the diagnostic possibilities. Diagnostic imaging, starting with a CT scan, is an ideal approach when a neoplasm in the temporal bone is suspected. Furthermore, audiological studies appropriate for the patient's age should be carried out in order to know the patient's baseline auditory profile prior to surgical or medical treatment and evaluate the hearing prognosis depending on the disease.

Pediatric otolaryngologists must have access to all the tools necessary to perform tissue sampling, whether this is done via a transmastoid approach or, as it happened in this case, through a middle fossa approach, since histopathologic diagnosis is fundamental to start an appropriate medical treatment.

The treatment of patients with LCH should always take place in an interdisciplinary context where the oncology staff has a main role in the implementation of the appropriate chemotherapy regime and the monitoring of the disease in conjunction with imaging and audiological control.

CONCLUSION

Otologic pathology in pediatric population is not limited to disorders related to Eustachian tube and different types of otitis media. The involvement of the temporal bone by neoplastic lesions should be considered in patients with AOM difficult to manage, including LCH.

However, rare presentations of the disease that come along with vestibular symptoms and sensorineural hearing disorders should be taken into account for a proper study and treatment of the disease, since these should raise suspicion of involvement of the structures of the inner ear. The patient reported in this case showed involvement of the inner ear with pro-

found hearing loss in the monosystem form of LCH, an unusual form of presentation that made necessary a different diagnostic approach.

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