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CASE REPORT

Systemic Langerhans Cell Histiocytosis with Bilateral Temporal Bone Involvement in an Adult

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Langerhance Cell Histiocytosis is a granulomatous disorder, with a variable clinical expression, usually diagnosed in children. Its systemic form carries a poor prognosis.

We present a 45 years old male with vertigo and otorrhea lasting three months, with history revealing former resection of eosinophilic granuloma from the right tibia and diabetes insipidus. The patient underwent biopsy from the left mastoid and the histopathological examination was consistent with Langerhance Cell Histiocytosis. Due to evidence of lung involvement the patient was treated with several chemotherapy and steroids. There were two incidences of recurrence; both treated with radiation and additional ARA C protocols. Since then all his vestibular and neuropathic symptoms resolved and his lung lesions subsided.

Conclusion: Langerhance Cell Histiocytosis is a rare cause of temporal bone disease in an adult especially in the systemic form. Suspicion is warranted in cases of unresponsive ear disease. Histopathological diagnosis is essential to ensure prompt local treatment and for early recognition of potential multifocal and systemic involvement.

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Introduction

Langerhance Cell Histiocytosis (LCH) is a group of rare disorders with unknown etiology and pathogenesis, characterized by a monoclonal proliferation of cytological benign hisitocytes[1]. The hallmark of LCH is the proliferation and accumulation of a specific histiocyte – the Langerhance cell. The disease may be focal or systemic and most commonly involves bones, lungs, CNS, liver, skin and lymph nodes. LCH may involve any bone, but most commonly involves the calvaria and the temporal bone[2]. The estimated annual incidence of LCH is one in 5.4 per million [3].

LCH may present in several different forms: 1.Eosinophilic Granuloma (EG), 2.Hand-Schuller – Christian disease and 3.Letterer- Siwe disease. In contrast to this traditional classification, it is more useful to define LCH as either a unifocal, multifocal or systemic.

LCH is generally a granulomatic disorder that occurs mainly in children and young adults, with a male predominance. We present an unusual case of an adult with extensive bilateral temporal bone involvement, which was a part of systemic LHC.

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Case Report

A 45-year-old male was referred to our otology outpatient clinic due to otorrhea, hearing loss, vertigo and unsteadiness, lasting for three months. The patient was initially treated with nasal decongestants and antibiotic otic drops for presumed otitis media with effusion and external otitis. Past medical history revealed resection of an eosinophilic granuloma (EG) from his left tibia, a year previously. Ever since, the patient has suffered from diabetes insipidus.

Otomicroscopy revealed narrowing of the bony external auditory canal with granulation tissue. Tympanic membranes were both opaque. The facial nerve, as well as all other cranial nerves well normal. Neurotologic exam revealed a bilateral positive head thrust (Halmagyi) test, a wide gait, and a positive oscillopsia test, consistent with bilateral peripheral vestibular loss. The rest of the head and neck and complete physical examination were normal.

The audiogram demonstrated bilateral moderate to severe, mixed hearing loss, worse on the left, with discrimination score of 72% on the left and 92% on the right (Figure 1).

A high resolution CT scan of the temporal bone demonstrated soft tissue occupying the mastoid cavity, the middle ear and the medial ear canal, bilaterally (Figure 2). Also noted was the destruction of cortical and labyrinthine bone, with invasion into the vestibule and semicircular canals (Figure 2). Cranial CT demonstrated a preserved sela turcica. MR study of the head demonstrated a calvarial midline lesion, infiltrating the dura (Figure 3). Gadolinum enhanced T1 sequence demonstrated an enhancing heterogeneous mass, filling the temporal bone (Figure 4). The chest X- ray was normal.

A month later, a cortical mastoidectomy was performed on the left side. A reddish- yellow lobulated mass filled the mastoid cavity. Biopsies were taken from this mass, and the calvarial lesion was excised. Ventilation tubes were inserted into the tympanic membrane, bilaterally.

Histopathological examination (Figure 5) revealed large histiocytes with grooves in the nucleus, and a large amount of eosinophils, plasma cells and granulocytes. Histiocytes were immunohistochemically positive for S- 100 protein

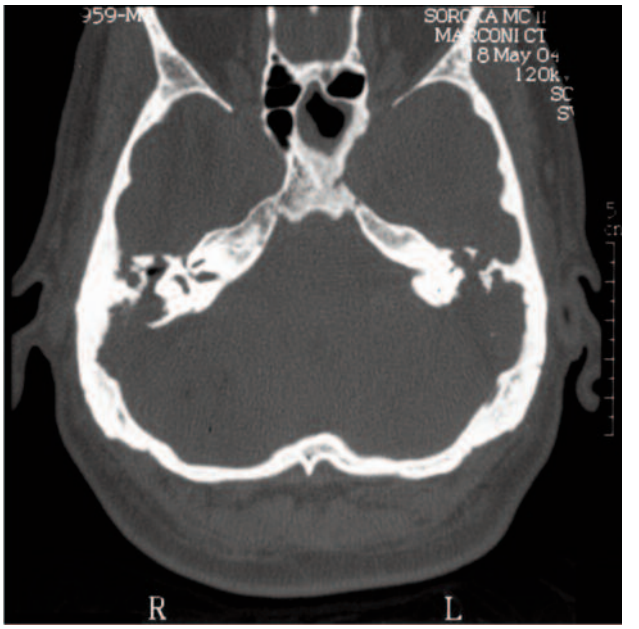

Figure 2. High resolution CT scan of the temporal bone in the axial plain demonstrate bilateral lytic lesions shown

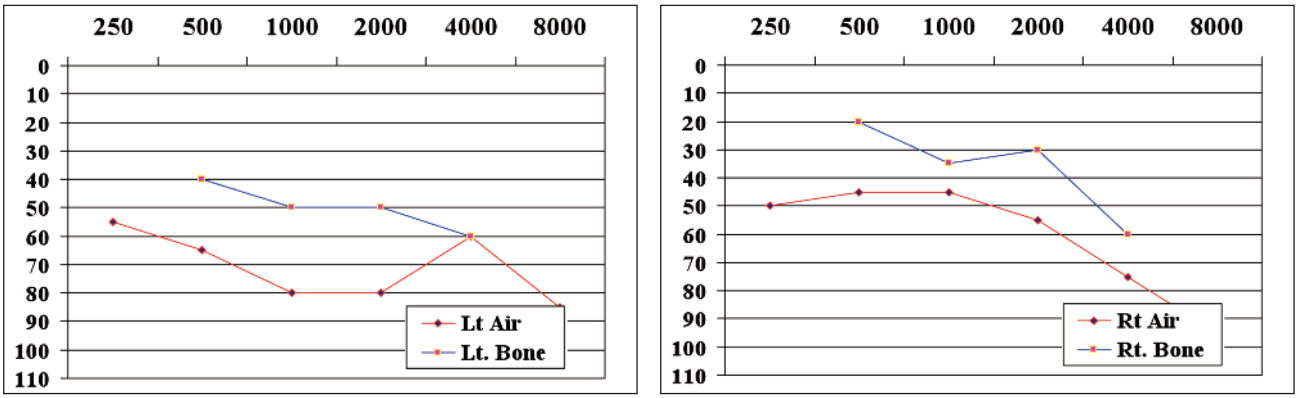

Figure 1. Pure tone audiogram demonstrates bilateral moderate to severe, mixed hearing loss, worse on the left, with discrimination score of 72% on the left and 92% on the right

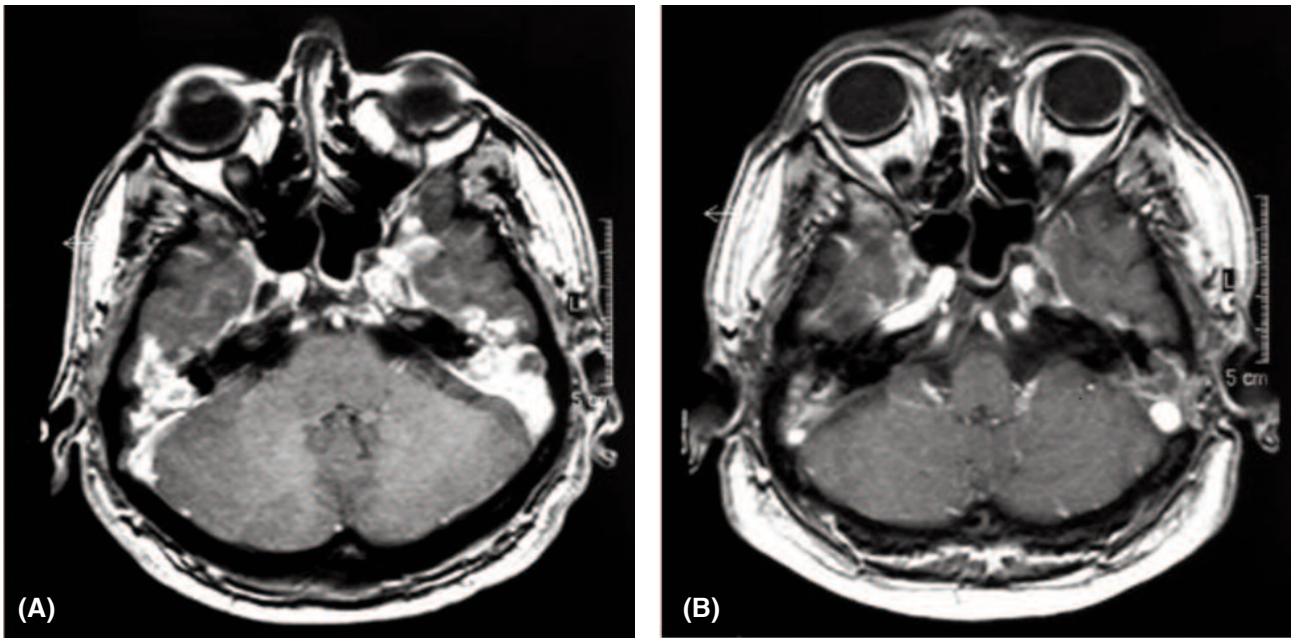

Figure 3. Axial MR imaging of the temporal bone. T1W sequence with Gadolinium. **(A)** Before biopsy of the mastoid and chemotherapy: An enhanced mass involving the temporal bone is demonstrated, bilaterally. **(B)** Five months later (following mastoid biopsy and chemotherapy) a decrease in volume and degree of enhancement is appreciated.

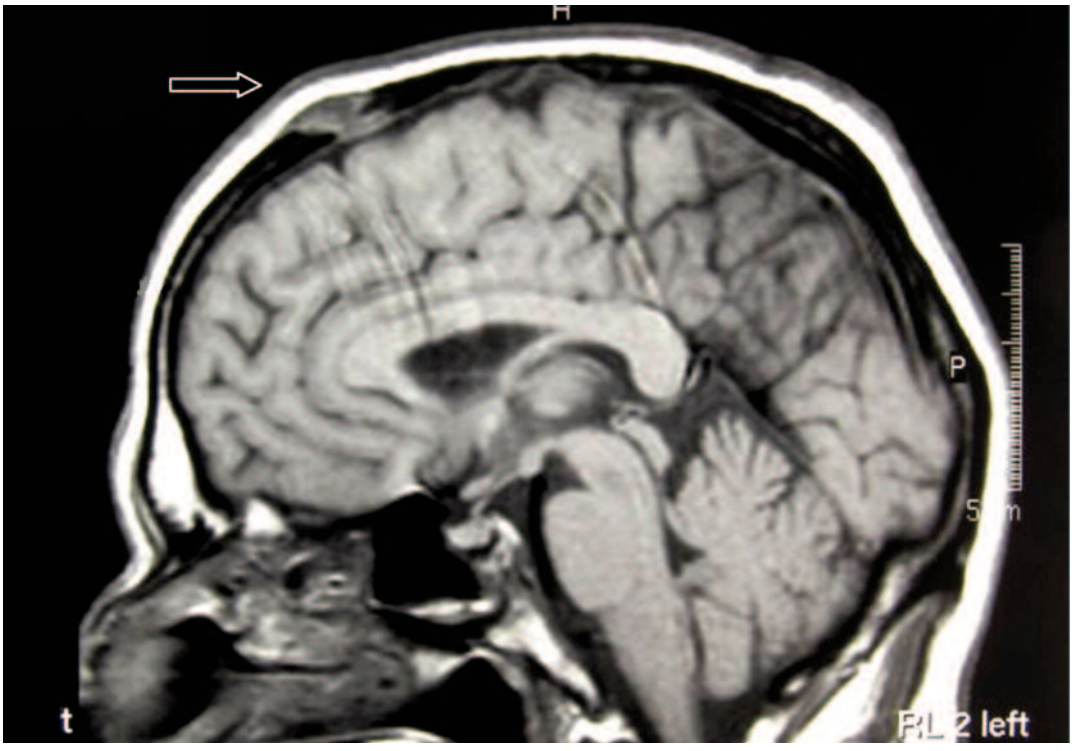

Figure 4. MR T1 Sagital reconstruction of brain. An enhanced lesion is seen to involve and slightly expand the calvaria, at the midline vertex. (Arrow)

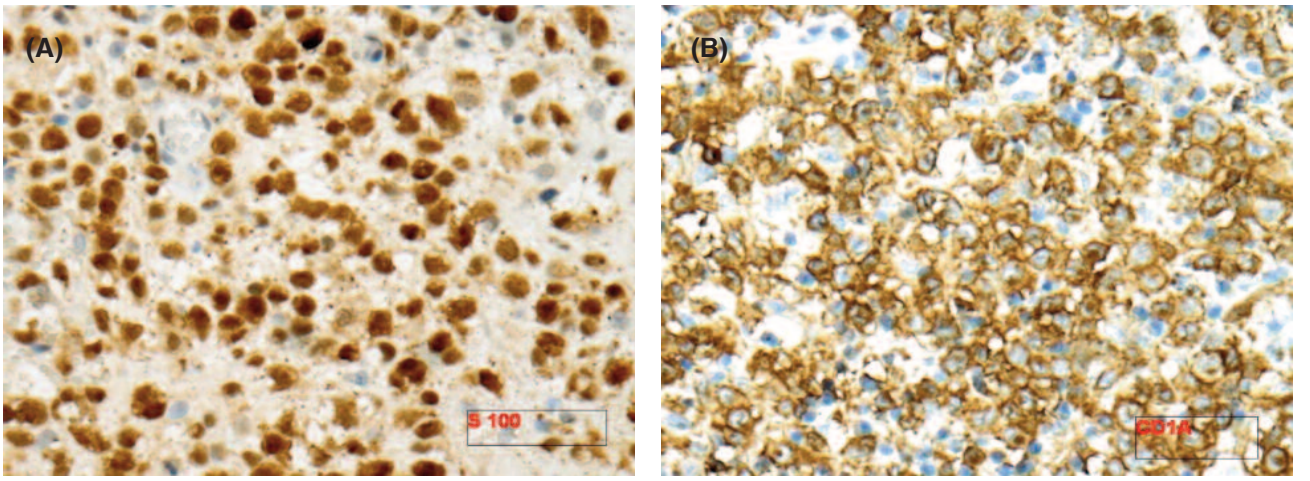

Figure 5. Eosinophils and Langerhance cells were demonstrated in the biopsy from the left mastoid. **(A)** Eosinophils (in blue) and Langerhance histiocytes(in brown). S-100 protein, (x200). **(B)** Langerhance cells cytoplasma painted in brown. CD1-A (x200).

and CD- 1A. Given the medical history and the histopathology results, the patient was diagnosed with LCH. During the next few months there was a clear improvement in his gait and the conductive part of the hearing loss had decreased

The patient underwent further workup, including skeletal scanning, and chest CT, which revealed defused interstitial changes, consistent with pulmonary involvement**.** Under the care of the hematology service, a systemic-multifocal bone disease protocol was induced. This treatment included IV vinblastin and oral prednisolone for three months protocol and later a supplement course of methotrexate and 6-MP for fifteen months. During the course of treatment there were bouts of unsteadiness, and temporary facial paraesthesia. A repeated MRI, five months after initializing the later course, showed a decreased signal in the temporal bone, representing local response (Figure 3b). There were two incidences of recurrence. One was two years after the treatment in the left hip and a year later in both hip joints. Both were treated with radiation with additional seven ARA C protocols until March 2009. Since then all his vestibulopathic and neuropathic symptoms resolved. His lung lesions subsided and he is still receiving Aredia once a month for bone involvement prevention.

Discussion

LCH is a rare entity with several subtypes, of which carry different clinical manifestation and prognosis[4]. Eighty percent of diagnosed cases of LCH are related to EG- the unifocal form. Because some of these lesions are asymptomatic, the disease may be under diagnosed (multifocal or systemic disease presenting as unifocal disease). Otologic manifestations are commonly the initial and only site of LCH, with and overall incidence of 15%-61%[2].

Diagnosis and workup

The most common signs of LCH in the temporal bone include granulation tissue or aural polyps in the external auditory canal. Other manifestations include otorrhea, followed by postauricular swelling, conductive and sensorineural hearing loss and Vertigo. Classically, the clinician confronts destructive ear disease [1] or an inflammatory disorder of the middle ear and mastoid that do not respond to routine antibiotic therapy[5, 6].

In our case, the patient presented with two clinical signs. The first was middle ear effusion and external otitis. The second was bilateral vestibular loss, due to labyrinthine involvement. Labyrinthine involvement caused by spread of the granulomatous process from the middle ear and mastoid into the semicircular canals is a very unusual finding, especially when it is bilateral[7].

As in our case, the clinical suspicion increases when medical history reveals a previously confirmed diagnosis of LHC.

When such clinical suspicion arises, temporal bone imaging studies are of major diagnostic importance. The

high resolution CT scan of the temporal bone, as well as MRI may demonstrate destructive lesions of the temporal bone and calvarium. The differential diagnosis of such lesions in the temporal bone include cholesteatoma, and osteomyelitis, as well as malignancies such as squamous cell carcinoma, Ewing's sarcoma, lymphoma, leukemia, and metastasis [8].

Naturally, the next diagnostic step following exam and imaging is tissue biopsy with immune- histochemistry. The goal of mastoidectomy, in our case, was for diagnosis purposes only, and unlike in the case of a true tumor or cholesteatoma, it did not require complete curative removal. However, surgery of the mastoid has also been found to have a therapeutic effect [9].

Management: Management of LCH is based on stratification of the patients according to severity of the disease and other risk factors [2]. Mild isolated bone involvement may occasionally heal spontaneously [10] or after percutaneous needle biopsy. When there is a limited number of isolated bone lesions, good response to surgical curettage is commonly seen [9]. Some reports have shown good results with local resection, or a combination of resection and low dose radiotherapy (10-20 Gy) [2, 3, 9] as well as Intralesional injections of methylprednisolone for residual tissue, when complete excision is not possible [11, 12]. Brisman et al [13], based on a limited follow-up analysis, recommended an open biopsy and curettage, followed by stereotactic radiotherapy for residual tumor, persistent symptoms, or recurrence.

In patients with multiple bone lesions the use of chemotherapy significantly decreases recurrences [14]. Chemotherapy is especially indicated in cases of multisystem disease. The majority of current protocols use a combination of multiple chemotherapeutic agents. Despite treatment, approximately 20% of patients with multisystem LCH disease do not respond and have a poor prognosis with high mortality.

Conclusion

1. Although it is not possible to diagnose LCH on clinical grounds alone, the following points are suggestive of the disease and warrant further imaging studies and biopsies:

- A previous history of EG
- Diabetes insipidus
- "Unusual course" or unresponsiveness of otologic conditions, such as otalgia, otorrhea, hearing loss, vertigo, local swelling, the presence of granulation tissue and a new onset hearing loss.

2. LCH is primarily a disease of children but may occasionally be seen in adults. A high index of suspicion based on the manifestations listed above, will enable prompt diagnosis and delivering local treatment, as well as systemic treatment like chemotherapy for multifocal or systemic disease.

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