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Case Report

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# Successful treatment of temporal bone langerhans cell histiocytosis with oral steroids: A case report

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ABSTRACT

Langerhans cell histiocytosis (LCH) is a rare disease; treatment recommendations are based on organ involvement and the extent of the disease. We present a patient with a solitary lesion of LCH with BRAF-V600K mutation which was successfully managed with systemic steroids and followed up for a long time. A 39-year-old man presented with persistent right otitis media with effusion despite treatment. LCH was diagnosed by punch biopsy, and temporal computed tomography (CT) showed an invasive, enhancing soft tissue mass extending from the malleolus to the epitympanic recess. Due to the patient's young age and the localization of the lesion, radiation and surgery were not considered. The patient was treated with systemic methylprednisolone. The patient's symptoms resolved after treatment and the tumor regressed completely. The case had a good prognosis in the 5-year period.

This is the first report of a LCH case with the BRAF-V600K mutation, highlighting a unique aspect of the disease. The successful therapy of the temporal bone LCH with systemic steroids alone, underscores the potential effect of this treatment for the management of unifocal lesions in critical locations. Further studies and case reports are needed to expand our understanding of LCH and explore optimal therapeutic approaches for different mutation subtypes.

Keywords: Langerhans cell histiocytosis, BRAF-V600K, Temporal bone, Steroid

## 1. INTRODUCTION

The incidence of Langerhans cell histiocytosis (LCH) is 2.6 to 8.9 cases per million per year in children and 0.07 cases per million per year in adults [1]. LCH is characterized by abnormal proliferation of dendritic cells derived from myeloid lineage cells in the bone marrow. While, the exact etiology and pathogenesis of LCH remain elusive, dysregulation of the immune system and genetic mutations in the affected cells are believed to contribute to its development. LCH affects the bone, skin, lungs, liver, and lymph nodes [2]. The temporal bone is the most commonly involved site, accounting for 15-61% of cases [3]. Specifically, the mastoid region is frequently affected, followed by the squamous part, external ear canal, middle ear, and petrous apex [4]. Temporal bone involvement may lead to symptoms such as otorrhea, post-auricular swelling, hearing loss, and otalgia [4-6]. Due to the resemblance of otologic symptoms with other conditions, particularly mastoiditis, misdiagnosis during the early stages is not uncommon [6].

Accurate diagnosis of LCH relies on the clinician's suspicion, and the gold standard is a biopsy. Histologically, Langerhans cells exhibit a characteristic cleaved nuclei (kidney-shaped) and demonstrate positive staining with S-100, CD1a, CD68, and/or Langerin (CD207). Additionally, the identification of Birbeck granules through electron microscopy further supports the diagnosis [7-9]. BRAF-V600E mutations observed in nearly half of the patients are associated with increased treatment failure and relapse, thereby contributing to a poor prognosis [8]. The presence of BRAF-V600E expression may correlate with the clinical risk profile and the number of lesions [10,11].

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Here, we present a 39-year-old male patient with a solitary lesion of LCH in the temporal bone which was successfully managed with corticosteroids. This highlights the unique aspect of complete disease recovery when treated with systemic steroids, which is a relatively rare occurrence in the literature.

## 2. CASE REPORT

A 39-year-old man was admitted to the hospital with complaints of hearing loss and buzzing in the right ear for the past three months. He had been treated with the diagnosis of effusion in the middle ear for three months.

The otoscopic examination revealed a pale and vascular appearance of the right eardrum, on which a small, irregular, and erythematous bulge was also observed. Audiological tests demonstrated mild conductive hearing loss. Temporal computed tomography (CT) revealed an invasive soft tissue mass in the middle ear, eroding the bony wall of the right internal carotid artery and the tympanic segment of the facial nerve canal. However, the mass was not spreading widely outside the middle ear (Figure 1.a.b.). A punch biopsy of the lesion was performed under local anesthesia. LCH was diagnosed histopathologically with the identification of Langerhans cells with characteristic reniform nuclei and abundant eosinophilic cytoplasm and positive immunohistochemical staining of CD1a and S100 (Figure 2.a.b.). A heterozygous BRAF-V600K mutation was identified on the polymerase chain reaction (PCR) test.

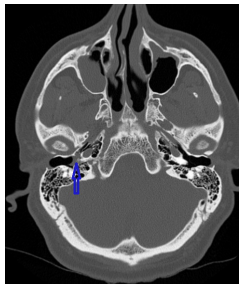

***Figure 1.a.*** *Before treatment axial CT scan (thin blue arrow)*

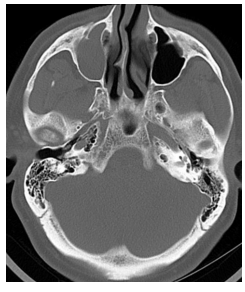

***Figure 1.b.*** *5 years after treatment axial CT scan*

Magnetic resonance imaging (MRI) demonstrated soft tissue with lobulated contours containing heterogeneous hypo-hyperintense areas on T2 scan, heterogeneous on T1 post-contrast scan with enhancement on the lateral (Figure 3.a.c.). Technetium-99m pertechnetate scintigraphy and 18F-FDG positron emission tomography confirmed that the rest of the body was free of disease. Complete blood count, blood chemistry, liver functions, and coagulation studies were normal.

The multidisciplinary council opted for systemic corticosteroid therapy (1 mg/kg/day) and close monitoring of the patient. The dose was gradually reduced by one tablet (16 mg) per week until it was stopped after 6 weeks. Surgical intervention or radiotherapy was not considered appropriate, due to the unifocal nature of the lesion and its localization in a high-risk area. Given the surgical risks, a conservative approach with corticosteroid therapy was preferred as the first-line treatment.

At the end of the treatment, the patient's hearing loss and tinnitus had improved significantly. Follow-up MRI imaging at regular intervals revealed a gradual regression of the lesion, with complete resolution noted at the final follow-up (Figure 3.b.d.). A whole-body MRI performed after treatment, confirmed the absence of residual or recurrent disease. Laboratory parameters remained within normal limits throughout the follow-up period. The patient was monitored for five years post-treatment, during which no recurrence of the disease was observed.

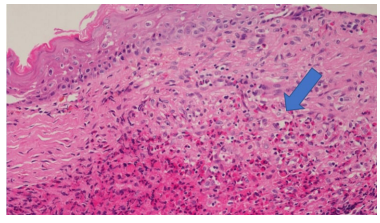

***Figure 2.a.*** *Granulomas made up of Langerhans giant cells (thick blue arrow)*

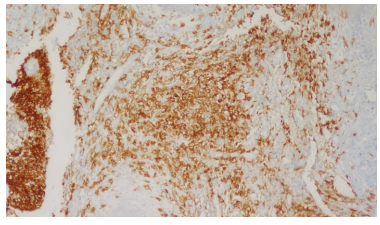

***Figure 2.b.*** *Positive immunohistochemistry stain for CD1a*

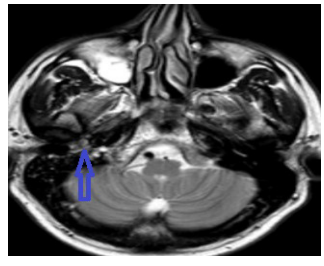

***Figure 3.a.*** *Before treatment T2 axial MRI scan (thin blue arrow)*


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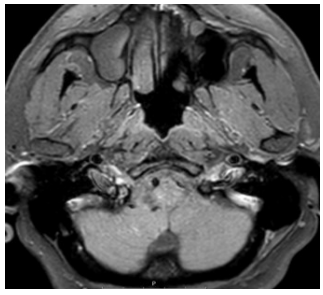

***Figure 3.b.*** *5 years after treatment T2 axial MRI scan*

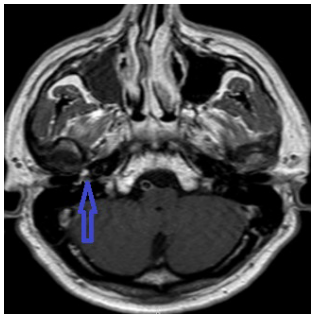

***Figure 3.c.*** *Before treatment T1 postcontrast axial MRI scan (thin blue arrow)*

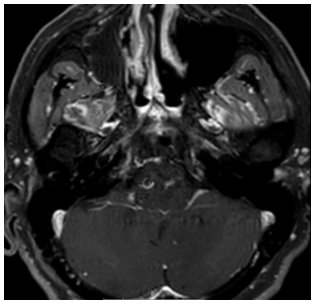

***Figure 3.d.*** *5 years after treatment T1 axial MRI scan*

## 3. DISCUSSION

Langerhans cells histiocytosis shows the features of both inflammatory and neoplastic diseases [12]. Temporal bone involvement causes otologic and neurotologic symptoms, such as otalgia, otorrhea, vertigo, hearing loss, and tinnitus very frequently, according to the site involved by the lesion(s) [4-6,9,13]. In the case presented here, tinnitus and hearing loss were the initial symptoms. Thus, it is crucial for patients with early-onset one-sided tinnitus and hearing loss to undergo a thorough examination, including audiological evaluation and imaging.

The osteolytic bone lesion caused by LCH has characteristic imaging findings typically seen as a soft tissue mass on CT scan and an enhancing hypointense mass on T1-weighted and hyperintense on T2-weighted images on MRI. The hypointense T2 lesion on the MRI of this case may be explained by the presence of blood or deposition of hemoglobin degradation products secondary to the biopsy procedure or may be due to air containment [14]. It is helpful to use CT scan as the initial imaging modality to define temporal LCH lesions and exclude other possible osteolytic etiologies. However, MRI is superior for assessing central nervous system (CNS) involvement, soft tissue, and post-treatment monitoring [7].

To differentiate a Langerhans cell lesion from other possible causes, a biopsy is necessary. The identification of the histopathological features of Langerhans cells, as well as the demonstration of immunochemical staining with CD1a and S-100 protein, confirms the diagnosis of LCH. Additionally, a PCR test identified a heterozygous BRAF-V600K mutation in our case.

The missense mutation in our case replaced the valine with a lysine residue. It is important to note that valine is typically replaced by glutamate in the majority of the V600E expression variants. Li et al., reported higher c-Kit protein and KIT gene expression in the V600K mutation, which may be attributed to the catalytic lysine effect [15]. In a study by Heritier et al., patients with the BRAF V600E mutation were reported to be at higher risk of LCH reactivation [11]. Although, the case we presented here had a good prognosis in the 5-year period following therapy, we believe patients with the BRAF-V600K mutation require extended follow-up due to the potential risk for recurrence. As there is no other similar case report in the literature, the association of this mutation with recurrence and the effect on prognosis are not known.

The treatment of LCH in the temporal bone depends on the extent and severity of the disease, as well as the age and overall health of the patient. Treatment of temporal bone LCH in adults is more challenging due to lacking a standardized treatment protocol and limited case reports. Surgical resection, curettage, or corticosteroid injection are the recommended treatment options for isolated lesions [3,5,7]. Radiotherapy may be used as adjuvant therapy or for recurrent disease [5]. Chemotherapy (vinblastine-steroid regimen) is a better option for patients with multifocal disease. In adult patients with multifocal single-system involvement, it has been emphasized that systemic treatment is significantly effective [16]. Vemurafenib has been reported to be a powerful therapy agent in patients with multisystem LCH. However, it has also been emphasized that many side effects occur during treatment [17]. In children with LCH, the presence of BRAF V600E expression has been shown to be associated with a weak response to chemotherapy [11]. Systemic steroids combined with other therapy is preferred for LCH areas in the vicinity to CNS; such as mastoid, sphenoid, orbital, ethmoid, or temporal bone [4]. A patient with the combination of LCH and Rosai-Dorfman Disease who developed clinical cervical lymphadenopathy-hepatomegaly was reported to have been treated with low-dose steroids only [18]. To the best of our knowledge, there is no information in the literature about whether the presence of the BRAF-V600K mutation has an effect on treatment.


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Considering the placement of the tumor, which made the surgical resection risky, and the potential complications of radiotherapy, we opted for systemic steroid treatment in this case. Fortunately, the patient's complaints improved shortly after the treatment, and the tumor regressed completely in several years without any sequel.

## Conclusion

To our knowledge, this is the first report of a LCH case with the BRAF-V600K mutation, highlighting a unique aspect of the disease. The successful treatment of temporal bone LCH with systemic steroids alone underscores the potential of this treatment in managing unifocal lesions in critical locations. Further studies and case reports are needed to expand our understanding of LCH and explore optimal therapeutic approaches for different mutation subtypes.

## Compliance with Ethical Standards

**Ethical standards:** This work was conducted ethically in accordance with the World Medical Association's Declaration of Helsinki.

**Patient consent:** The patient gave his consent for clinical information and images relating to his case to be reported in a medical publication.

**Conflict of interest:** The authors declare that they have no conflict of interest.

**Author contributions:** MBA and MIS: Interpreted the results and contributed to manuscript writing, NT, SD and OC: Prepared the figures, SD, O C and MIS: Cared for the patient and revised the manuscript. All authors designed the study, read and revised the manuscript.

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