Langerhans cell histiocytosis involving the temporal bone with destruction and subsequent reossification of the bony labyrinth boundaries

Langerhans-Zell-Histiozytose mit Beteiligung des Schläfenbeins mit Zerstörung und anschließender Reossifikation der knöchernen Labyrinthgrenzen

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ABSTRACT

Purpose With an incidence between 1–9/100 000 per year, Langerhans cell histiocytosis (LCH) is a rather rare disease from the hemato-oncologic disease spectrum (Hayes et al. 2009). The tumorlike disease with proliferation of histiocytic cells may manifest as localized to one organ or disseminated with infiltration of a wide variety of organs. Approximately 25–30 % of these cases show involvement of the temporal bone (Ni et al. 2017).

Case Description With vertigo persisting for three years, chronic mastoiditis, and acute progressive hearing loss bilaterally (r > l) for three weeks, a 41-year-old woman presented at an emergency department. The DVT showed extensive bony destruction of large parts of the temporal bone on both sides, involving the vestibular organ, the cochlea, and the internal auditory canal. To confirm the suspicion of a systemic inflammatory process, a PE was performed from the mastoid with bioptic confirmation of an LCH. Systemic therapy was initiated. Post-therapeutic imaging showed almost complete remission with reossification of the preexisting defect zones and the internal auditory canal and labyrinth structures again showed bony margins. Clinically, there was an improvement of the vegetative symptoms with remaining bilateral sensorineural hearing loss.

Discussion LCH of the temporal bone is a rare and often misdiagnosed disease due to its nonspecific clinical presentation. Awareness of temporal bone LCH and its occurrence in adults is essential for accurate and consistent diagnosis.

Key Points:
- LCH is a rather rare disease from the hemato-oncological spectrum
- Affection of the temporal bone, especially such an extensive one (as in this case report), is rather atypical in adulthood
- Use of systemic therapy resulted in remission
- There was complete reossification of the osseous structures post-therapy
- A cochlear implant was able to be implanted to compensate for hearing loss

ZUSAMMENFASSUNG

Ziel Mit einer Inzidenz zwischen 1–9/100 000 pro Jahr ist die Langerhans-Zell-Histiozytose (LCH) eher ein Kolibri im hämato-onkologischen Krankheitsspektrum (Hayes et al. 2009). Die tumorähnliche Erkrankung mit einer Proliferation histiozytärer Zellen kann sich lokalisiert auf ein Organ oder disseminiert mit Infiltration einer Vielzahl von Organen manifestieren. In etwa 25–30 % der Fälle ist das Schläfenbein betroffen (Ni et al. 2017).

Fallbeschreibung Eine 41-jährige Frau stellt sich mit einem seit drei Jahren anhaltenden Schwindel, einer chronischen Mastoiditis und einem akut progredienten Hörverlust beidseitig (r > l) seit drei Wochen in einer Notaufnahme vor. Die DVT zeigte das Bild einer ausgedehnten knöchernen Destruktion weiter Anteile des Schläfenbeins beider Seiten unter jeweiliger Beteiligung des Vestibularorgans, der Cochlea und des inneren Gehörgangs. Um den Verdacht auf einen systemischen Entzündungsprozess zu bestätigen, wurde eine PE aus dem Mastoid mit bioptischem Nachweis eines LCH durchgeführt. Eine systemische Therapie wurde eingeleitet. Die posttherapeutische Bildgebung zeigte eine fast vollständige Remission mit Reossifizierung der zuvor bestehenden Defektzonen, Auch die zuvor destruierten Strukturen des inneren Gehörgangs und des Labyrinths wiesen wieder knöcherne Substanz auf. Klinisch kam es zu einer Verbesserung der vegetativen Symptome bei verbleibendem beidseitigem sensorineuralem Hörverlust.

Diskussion LCH des Schläfenbeins ist eine seltene und aufgrund ihres unspezifischen klinischen Erscheinungsbildes häufig fehldiagnostizierte Erkrankung. Die Kenntnis von LCH des Schläfenbeins und ihres Auftretens bei Erwachsenen ist für eine genaue und konsequente Diagnose unerlässlich.

Wichtige Punkte:

- LCH ist eine eher seltene Erkrankung aus dem hämatoonkologischen Spektrum.
- Ein Befall des Schläfenbeins, insbesondere ein so ausgedehnter (wie in diesem Fallbericht), ist im Erwachsenenalter eher untypisch.
- Einleitung einer Systemtherapie führte zur Remission.
- Vollständige Reossifikation der knöchernen Strukturen nach der Therapie.
- Ermöglichte die Implantation eines Cochlea-Implantats und glich den Hörverlust aus.

Zitierweise

- Döring K, Ivanyi P, Lanfermann H et al. Langerhans cell histiocytosis involving the temporal bone with destruction and subsequent reossification of the bony labyrinth boundaries. Fortschr Röntgenstr 2024; 196: 1063–1067

ABBREVIATIONS

cMRI	cranial magnetic resonance imaging
CRP	C-reactive protein
CT	computed tomography
DVT	digital volume tomography
ENT	ear, nose, and throat
LCH	Langerhans cell histiocytosis
MS-LCH	multi-system Langerhans cell histiocytosis
PET	positron emission tomography
SS-LCH	single-system Langerhans cell histiocytosis
VA	vertebral artery

Background

Langerhans cell histiocytosis (LCH), characterized by clonal proliferation of mononuclear cells, so-called Langerhans cells, bone marrow lymphoid dendritic cells with antigen-presenting function [1] occurs with an incidence between 1–9/100 000 per year [2]. Approximately 25–30 % of these cases show involvement of the temporal bone [3]. In 30 %, bilateral infiltration is detectable [4], although bilateral temporal bone LCH is quite rare as an initial finding [5]. LCH of the temporal bone predominantly affects males [6] and children (75–90 %), with a peak incidence between the ages of 1 to 3 years [7, 8]. LCH is divided into two groups according to the status of the organic affection pattern: Single-system disease (SS-LCH) and multi-system disease (MS-LCH).

Fewer than 40 adult cases with an isolated LCH manifestation at the petrous bone have been described in the literature [9, 10].

Possible therapy regimens depend on the spread and severity: Thus, the prognosis of SS-LCH is excellent. It is not uncommon to observe spontaneous remission of preexisting osteolysis without therapeutic intervention. If multifocal bone involvement is present in SS-LCH, post-therapeutic reactivation of LCH is observed in up to 20 % of patients – recurrences usually occur within 2 years and remain isolated to the skeleton [11].

People affected by MS-LCH have to expect a significantly higher recurrence rate of 30–50 %. Depending on the involvement of organs at risk, mortality is up to 10–15 %. A response to therapy 6 weeks after treatment initiation is an independent and meaningful predictor of a positive outcome. In the absence of response, survival is only 30–50 % [11].

The following presents a rare case of LCH at the petrous bone in an adult patient. The presented case includes not only the epidemiological background, for example, the affected patient is female and is to be categorized in the group of “single-system disease”, but also the clinical response after initiation of systemic therapy by the Department of Hematology and Medical Oncology. CT-morphologically complete remission with almost complete remodeling of the temporal bone could be demonstrated.

Case Presentation

A 41-year-old female patient presented at the emergency department with a history of vertigo for three years, a history of chronic mastoiditis, and acute hearing loss on both sides (right > left) for three weeks. At the same time, there were disturbances in balance, murmur on both sides, intermittent holocephalic pressing, ibuprofen-sensitive cephalgia (NRS 4/10), and otorrhea. Emesis and photophobia were denied.

The history of psychomotor slowing and delayed or prolonged response latencies was remarkable. The clinical history is bland, with the exception of a Graves' disease and a dissection of the VA.

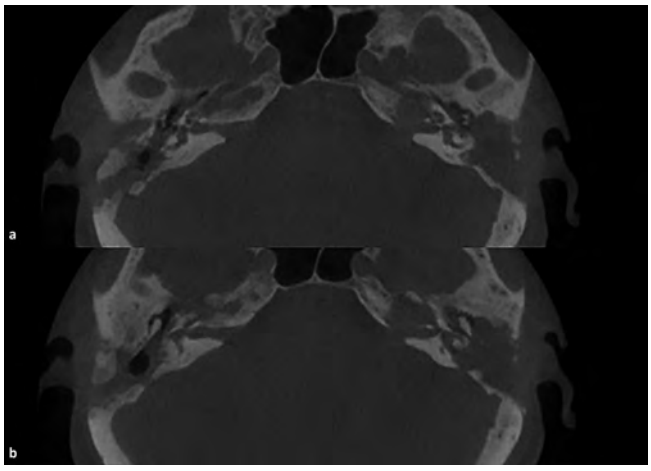
No evidence of a focal neurological deficit or meningitis was found by a neurologic examination. A recommendation was made for inpatient admission, lumbar puncture, and prompt contrast-enhanced cMRI.

A DVT of the temporal bone and inner ear was performed immediately. DVT showed extensive osseous destruction of large portions of the petrous bone on both sides (▶ **Fig. 1, 2**). The vestibular organ and the cochlea as well as the ventral and superior wall of the internal auditory canal were involved to different extents with corresponding bony dehiscence to the intracranial space. Further evaluation by cMRI corroborated the findings in intermodal comparison and raised the suspicion of granulomatous inflammation (▶ **Fig. 3**). In addition, pachymeningeal enhancement could be seen (▶ **Fig. 4**).

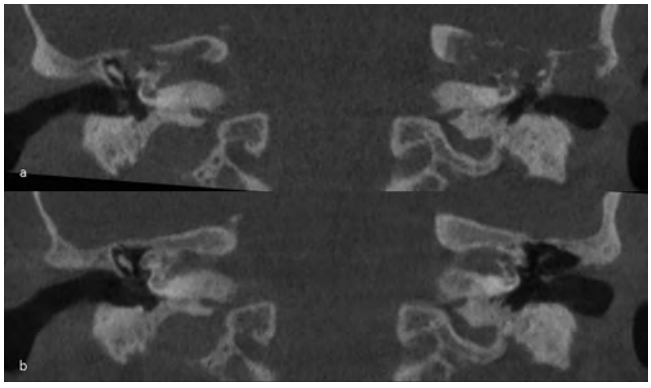
This was followed by an immunological consultation. In the presence of elevated inflammatory parameters (CRP 49.4 mg/dl), an interdisciplinary sampling of the mastoid was considered under the suspicion of a systemic inflammatory process.

This revealed Langerhans cell histiocytosis, whereupon, after performing further imaging studies using CT plasmacytoma status, systemic therapy with Cladribine was initiated by the Department of Hematology and Medical Oncology.

The last imaging and clinical control, one year after the initial diagnosis and initiation of systemic therapy, revealed stable disease: the area of missing bone and dehiscence of the internal auditory canal and labyrinth structures on the previous images showed bone density again (▶ **Fig. 2–4**). The bony limitation of the lateral semicircular canal was again visible. Intralabyrinthine sclerosis, especially on both sides of the basal turn near the oval window, was new compared to the previous examination. Clinically, there was improvement of vegetative symptoms with remaining bilateral sensorineural hearing loss. In the meantime, the patient has already been fitted with a cochlear implant on the left side. The opposite side is still pending.



▶ **Fig. 1** DVT of the temporal bone – axial. **a**, **b** show the extent of bony destruction due to LCH infestation. The extensive osseous destruction encompasses large parts of the temporal bone on both sides. The vestibular organ and the cochlea as well as the ventral and superior wall of the internal auditory canal were involved to different extents with corresponding bony dehiscence to the intracranial space.



▶ **Fig. 2** DVT of the temporal bone – coronary. **a** Findings of Langerhans cell histiocytosis before initiation of systemic therapy. **b** Reossification of the bony boundary of the inner ear after implementation of system therapy.

Discussion

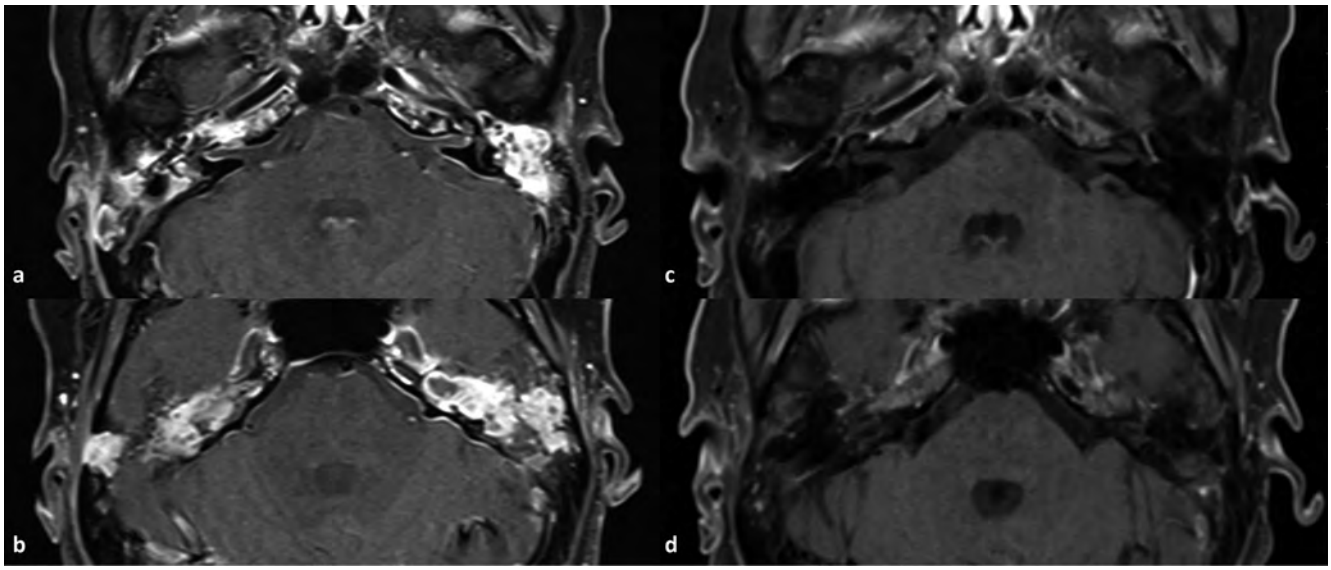
While single-system LCH is defined by the involvement of a single organ system at the time of diagnosis, multi-system LCH involves two or more organ systems. Unifocal single-system disease is the most common form of LCH, with an incidence of 70 % of cases [12].

The multisystem category is divided into low-risk and high-risk variants depending on the organs affected. High-risk organs include the liver, lung, and spleen. Involvement of one or more of these organs is associated with higher risk and mortality [13]. The etiology of LCH is poorly understood, with arguments in favor of an autoimmune, neoplastic, or reactive origin of the disease.

Due to its initial nonspecific clinical presentation, LCH isolated to the temporal bone at the time of initial presentation is easily misdiagnosed: otorrhea, otalgia, postauricular rash, hearing loss, and tissue swelling are often clinically leading. In addition, LCH mimics other otologic pathologies, including otitis media or mastoiditis and temporal abscess [14].

Suspicion should arise from unusual findings on imaging. Extensive, often bilateral osteolytic changes and soft tissue compaction manifesting around the bone lesion may provide initial clues in this regard [3]. MRI is considered second-line imaging and is indicated to assess disease spread (both extracranial and intracranial) or to further characterize soft tissue involvement. However, the final diagnosis can only be confirmed by biopsy, either by fine needle aspiration or excisional biopsy.

Histologically, LCH consists of multinucleated Langerhans cells from a conglomerate of various eosinophils, neutrophils, and lymphocytes [2, 7]. However, definitive diagnosis of LCH requires immunohistochemistry demonstrating positivity for CD1a and/or langerin (CD207), two components of immature dendritic cells



▶ **Fig. 3** cMRI of the temporal bone – axial. **a**, **b** show the extensive granulomatous inflammation (strong contrast enhancement of all structures) of the temporal bone at the time of diagnosis. After successful therapy, a markedly regressive contrast agent accumulation is evident on imaging, see also **c**, **d**.

[7]. Electron microscopy reveals characteristic tennis ball-shaped organelles known as Birbeck granules, but these may also be present in physiological Langerhans cells. Treatment of temporal bone LCH depends on the severity and stage of the disease [2].

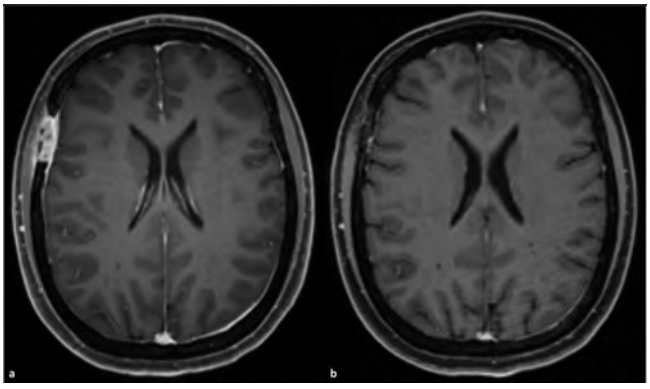
According to the guidelines, the initiation of systemic therapy is recommended in SS-LCH with unifocal bone involvement involving so-called "special site" lesions – these include craniofacial bones (e. g. orbita, temporal bone, mastoid, os sphenoidale, etc.). The reason for this is the risk of neurodegenerative LCH and a possible affection of the pituitary gland and consecutive diabetes insipidus (DI) associated with the involvement of craniofacial bones. With an incidence of 15–50 %, DI is the most commonly observed endocrinopathy of LCH.

Therefore, in the present case report, the purine analog cladribine was used as established (1000 mg/m^2 intravenously on days 1–5, every 4 weeks for a maximum of 4 cycles). As mentioned above, successful response to therapy – confirmed by clinical symptom relief and follow-up imaging (in our case a DVT of the petrous bone was performed) – after 6 weeks is considered a decisive prognostic predictor for the overall outcome. In our case, the expected and hoped for positive response to therapy could be evaluated both on imaging (stable disease) and clinically. Peritherapeutic complications did not occur in our patient.

Multifocal disease should be treated with systemic therapy, including vinblastine (6 mg/m^2) as a first-line chemotherapeutic agent with or without concomitant prednisone therapy (40 mg/m^2/day) for 12 months [2].

Close follow-up with surveillance imaging by MRI and/or PET every 6 months is essential, as recurrence can occur in up to 50 % of cases after initial treatment [15].

In a study by Modest et al., 90 % of patients with recurrent LCH survived 42 months after treatment [15], with, as would be expected, a lower mortality rate in patients with localized (12.5 %) versus multifocal (37.5 %) temporal bone LCH.



▶ **Fig. 4** MRI of the same patient. The patient has a primarily osseous manifestation of Langerhans cell histiocytosis. According to the classification, it is therefore referred to as a single-system disease, as only a primary osseous manifestation on the skull could be detected in the staging. Isolated foci of inflammation could thus also be delineated on the cranial calvaria, including the extension of the inflammatory process per continuitatem to the adjacent pachymeninx.

In this context, the imaging findings of initially complete osteolytic destruction of both temporal bones with involvement of the cochlea and vestibular organ and almost complete posttherapeutic remodeling are impressive. Serial imaging examination over one year after cessation of systemic therapy showed unexpected signs of bipetrosal reossification in response to intravenous systemic therapy.

It is empirically established that bone undergoes constant remodeling processes. Both congenital changes and acquired diseases affect the balance of normal bone metabolism.

In view of this, it is particularly noteworthy that the bony borders of the labyrinth were maintained during reossification and

were shown to be re-mineralized on imaging. Thus, fitting of a cochlear implant, as in this case subsequently with remaining surditas, is in principle still possible. The present case suggests that in the context of Langerhans cell histiocytosis, the actual bone matrix is preserved, and complete remission is possible after CTx in the form of bipetrosal remodeling, conservative systemic therapy is always advisable even in advanced stages, and the progress of healing should be monitored by serial imaging.

To our knowledge, this rare phenomenon has not yet been described in this context in the literature. The literature includes Individual case reports, but each one is of different etiopathogenesis. For example, O'Guinn reported a rare case of thoracic vertebral osteomyelitis secondary to pulmonary Blastomyces dermatitidis. Posttherapeutically, vertebral reossification with complete preservation of the former bone boundaries was shown on imaging, which was completely unexpected [16]. Individual cases of reossification have also been described in plasmocytoma patients. In this regard, Ouyang et al. investigated the extent of reossification and prognosis after radiotherapy with and without surgical intervention in a cohort of 39 patients [17]. Here, the importance of significant reossification after radiotherapy could be substantiated. Unless there is neurological impairment, conservative methodologies such as systemic therapy and local radiotherapy should be preferred to surgical interventions. Overall, more attention should be paid to possible reossification.

Conclusion

LCH of the temporal bone is a rare and frequently misdiagnosed condition in adults due to its nonspecific clinical presentation. Imaging techniques can be supportive, but definitive diagnosis depends on tissue biopsy and immunohistochemistry. Treatment, whether in the form of local surgical excision, ± adjuvant radiotherapy for single-system infestation patterns, or by means of systemic therapy for disseminated organ infestation patterns, has a favorable prognosis. However, given the high recurrence rate, close monitoring in the context of "watchful waiting" is required. Increased physician awareness of LCH of the temporal bone, particularly in the adult population, may lead to timely diagnosis and consecutive improvement of treatment outcomes. In the presented case the possible reossification of initially CT-morphologically destroyed bony boundaries of the labyrinth could be demonstrated.

Cross-sectional imaging (CT, MRI) is important for the early detection and follow-up of the condition.

Conflict of Interest

The authors declare that they have no conflict of interest.

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