First Report of the Coexistence of Langerhans Cell Histiocytosis and Epithelioid Hemangioma of the Larynx

Case Report

Salih Cengiz Meral[1], Levent Yücel[1], Egemen Akıncıoğlu[2], Ömer Günhan[3], Yavuz Fuat Yılmaz[1]

[1]University of Health Sciences Türkiye, Gülhane Training and Research Hospital, Department of Otorhinolaryngology, Ankara, Türkiye
[2]University of Health Sciences Türkiye, Gülhane Training and Research Hospital, Department of Pathology, Ankara, Türkiye
[3]TOBB University of Economics and Technology Faculty of Medicine, Department of Pathology, Ankara, Türkiye

Abstract

Langerhans cell histiocytosis (LCH) is a complex disorder of the mononuclear phagocyte system. Laryngeal epithelioid hemangiomas are rare, benign vascular tumors in adults. Here, we report the first known case of the coexistence of LCH and epithelioid hemangioma in the larynx. A 42-year-old man presented with progressive swelling on the left side of the neck and hoarseness. Endoscopic examination revealed a mass obliterating the left pyriform sinus, false vocal cord, and aryepiglottic fold. Computed tomography (CT) showed a mass destroying the thyroid cartilage, extending to the left false and true vocal cords, and obstructing the airway. Fine-needle aspiration biopsy suggested hemangioendothelioma. However, histopathological examination after total laryngectomy revealed both LCH and epithelioid hemangioma. Positron emission tomography/CT indicated suspected LCH involvement of the pituitary gland and cervical lymph nodes. The patient was treated with chemotherapy. No recurrence was observed at the six-month follow-up. This case highlights the potential association between the mitogen-activated protein kinase pathway, LCH, and epithelioid hemangioma. It also emphasizes the importance of repeating a biopsy in cases of rare laryngeal tumors when initial results are inconclusive.

Keywords: Langerhans cell histiocytosis, epithelioid hemangioma, laryngeal neoplasms, total laryngectomy, case report

ORCID IDs of the authors:
S.C.M. 0000-0003-4220-1911
L.Y. 0000-0001-9045-4636
E.A. 0000-0003-1973-1279
Ö.G. 0000-0002-3712-1469
Y.F.Y. 0000-0003-0668-3263

Cite this article as: *Meral SC, Yücel L, Akıncıoğlu E, Günhan Ö, Yılmaz YF. First report of the coexistence of Langerhans cell histiocytosis and epithelioid hemangioma of the larynx. Turk Arch Otorhinolaryngol. 2025; 63(2): 99-103*

Corresponding Author:
Salih Cengiz Meral, MD;
cengizmeral1994@gmail.com

Received Date: 14.10.2024
Accepted Date: 16.03.2025
Epub: 26.06.2025
Publication Date: 27.06.2025

DOI: 10.4274/tao.2025.2024-10-3

Introduction

Langerhans cell histiocytosis (LCH) is a complex disorder involving the proliferation, differentiation, and aberrant functioning of the mononuclear phagocyte system, and it may present with a wide range of clinical manifestations (1). LCH is observed in individuals under the age of 15 at an annual incidence of 2.6 to 8.9 per million and occurs less frequently in adults, at an incidence of 0.07 per million. Approximately half of the patients present with single-organ involvement, while the rest show multisystem involvement. The most commonly affected sites are the skeletal system, skin, lymph nodes, and visceral organs such as the lungs, liver,

and spleen (2). Lytic bone lesions are the most common finding; however, other features include skin rashes, soft tissue or lymph node swelling, and gingival hypertrophy (3). Laryngeal involvement in LCH is exceedingly rare, with only six previously reported cases (4-9). Epithelioid hemangioma (EH) presents as angioma-like nodular lesions, frequently occurring in the skin, muscle, or bone tissue, and more rarely in the salivary glands, oral mucosa, and various visceral organs (10,11). Here, we report a unique case of a patient who underwent total laryngectomy due to the coexistence of LCH and EH in the larynx.

Case Presentation

A 42-year-old man presented to University of Health Sciencess Türkiye, Gülhane Training and Research Hospital, with a two-month history of progressive swelling on the left side of his neck and hoarseness. His medical history included hypertension and obesity, and he had a 25-pack-year smoking history. On physical examination, a 5 cm firm, immobile mass was palpated in the left lateral neck. Flexible endoscopic examination revealed a mass obliterating the left pyriform sinus, false vocal cord, and aryepiglottic fold, with significantly limited movement of the left vocal cord.

Computed tomography (CT) revealed a cystic-necrotic mass with calcifications in the left neck, which had completely destroyed the thyroid cartilage and extended to the left false and true vocal cords, causing airway obstruction (Figures 1a, 1b). Magnetic resonance imaging (MRI) showed a 50×53×36 mm heterogeneous mass with diffusion restriction, hypointense on T1-weighted and hyperintense on T2-weighted sequences (Figures 1c, 1d). As there was no apparent involvement of the laryngeal mucosa, fine-needle aspiration biopsy (FNAB) was recommended. Cytological evaluation revealed polygonal cells with distinct intracytoplasmic vacuoles, suggestive of hemangioendothelioma. Core and excisional biopsies were discussed with the patient, who opted for an excisional biopsy.

During surgery, a limited left neck dissection was performed to expose the mass and larynx. Intraoperatively, invasion of the left pyriform sinus and thyroid cartilage precluded a partial laryngectomy, necessitating a total laryngectomy (Figure 2). The pharynx was closed using a primary T-closure technique with continuous sutures. Oral intake was initiated one week postoperatively, and a voice prosthesis was placed on postoperative day 10. The patient was discharged without complications.

Histopathological evaluation of the laryngectomy specimen revealed two distinct lesions (Figure 3a). The first consisted of capillary-sized vessels lined with epithelioid endothelial cells, positive for immunohistochemical stains CD34 (Figure 3b) and ETS-related gene. The second lesion was composed of histiocytoid cells with convoluted nuclei and slightly eosinophilic cytoplasm, accompanied by eosinophils, eosinophilic microabscesses, and multinucleated giant cells. These cells tested positive for Langerin (Figure 3c), CD1a

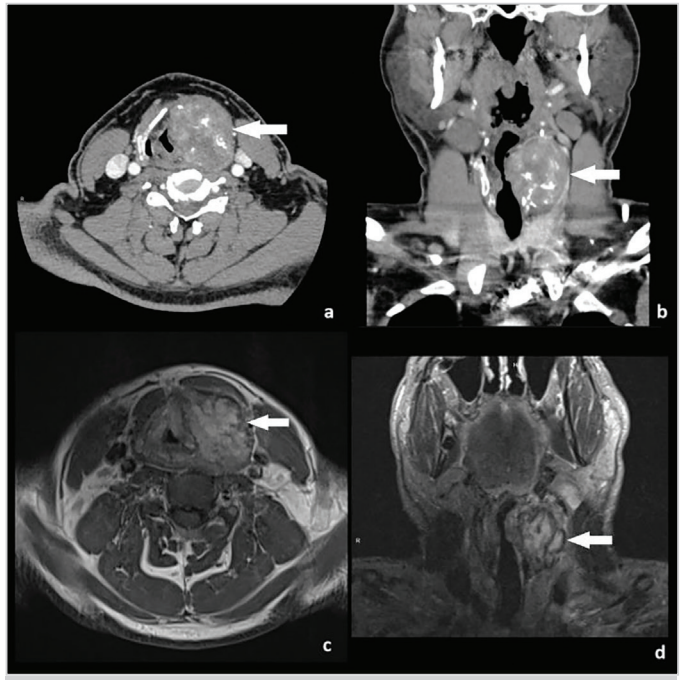

Figure 1. a, b) Axial and coronal computed tomography sections of the neck demonstrate a mass in the left side with cystic-necrotic components and calcifications, completely destroying the thyroid cartilage and extending to the left false and true vocal cords, resulting in airway obstruction.
c, d) Axial T1-weighted and coronal T2-weighted magnetic resonance imaging show a heterogeneous mass in the same region (Arrows indicate the mass.)

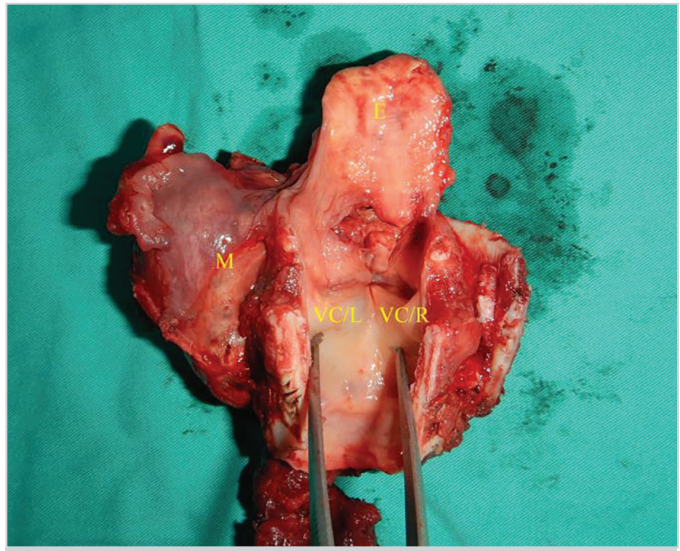

Figure 2. Total laryngectomy specimen, posterior view. The tumor invades the left laryngeal ventricle, false vocal cord, aryepiglottic fold, and cricoarytenoid unit

E: Epiglottis; M: Mass, CV/L: Left vocal cord, CV/R: Right vocal cord

(Figure 3d), and S100, supporting a diagnosis of LCH. LCH involvement was also identified in cervical lymph nodes (Figures 4b-4d).

To assess for systemic involvement, positron emission tomography/CT (PET/CT) was performed, revealing suspected LCH involvement in the pituitary gland and some cervical lymph nodes. Bone scintigraphy was normal. Laboratory investigations showed elevated thyroid-stimulating hormone (144 mLU/mL) and normal prolactin (15.24 ng/mL) and other hormone levels. The patient was referred to hematology and endocrinology. Chemotherapy with cytarabine (100 mg/m^2/day for five days per cycle, over six monthly cycles) was administered. At the six-month follow-up, no recurrence was noted.

Written informed consent was obtained from the patient for publication of this case report.

Discussion

Involvement of the ear, nose, and neck in LCH most commonly affects the mastoid, middle ear, and external auditory canal (12). Temporal bone involvement can mimic otitis media or mastoiditis, especially in pediatric patients. Other noninfectious conditions that may resemble acute mastoiditis include acute myeloid leukemia, rhabdomyosarcoma, and lymphoma (13). Awareness of these differential diagnoses is critical to avoid delays in treatment.

Laryngeal involvement in LCH is extremely rare. Of the six prior reported cases, four occurred in adults (4). Symptoms depend on the site of involvement and may include dyspnea, hoarseness, cough, cervical mass, sore throat, and stridor. A broad differential diagnosis, including benign and malignant laryngeal tumors, should be considered. CT and MRI are essential for evaluating the extent of disease before biopsy or surgery. CT is useful for identifying bony destruction, while MRI can reveal soft tissue involvement and contrast enhancement. Although Guo et al. (12) recommend CT as the initial imaging modality, we believe MRI should also be performed in all cases to fully assess potential laryngeal involvement.

FNAB may lead to misdiagnosis, as in our case. If a laryngeal mass is clearly visualized, direct laryngoscopy with biopsy is preferable. Previous reports also indicate that multiple biopsies may be necessary for a definitive diagnosis of LCH (4). In our case, the coexistence of EH and LCH may have contributed to the initial diagnostic difficulty. This case emphasizes the importance of considering repeat biopsy and maintaining close communication with pathologists when evaluating rare laryngeal tumors.

LCH lesions have been reported in the subglottic area, epiglottis, and false vocal cords (4). In our patient, the

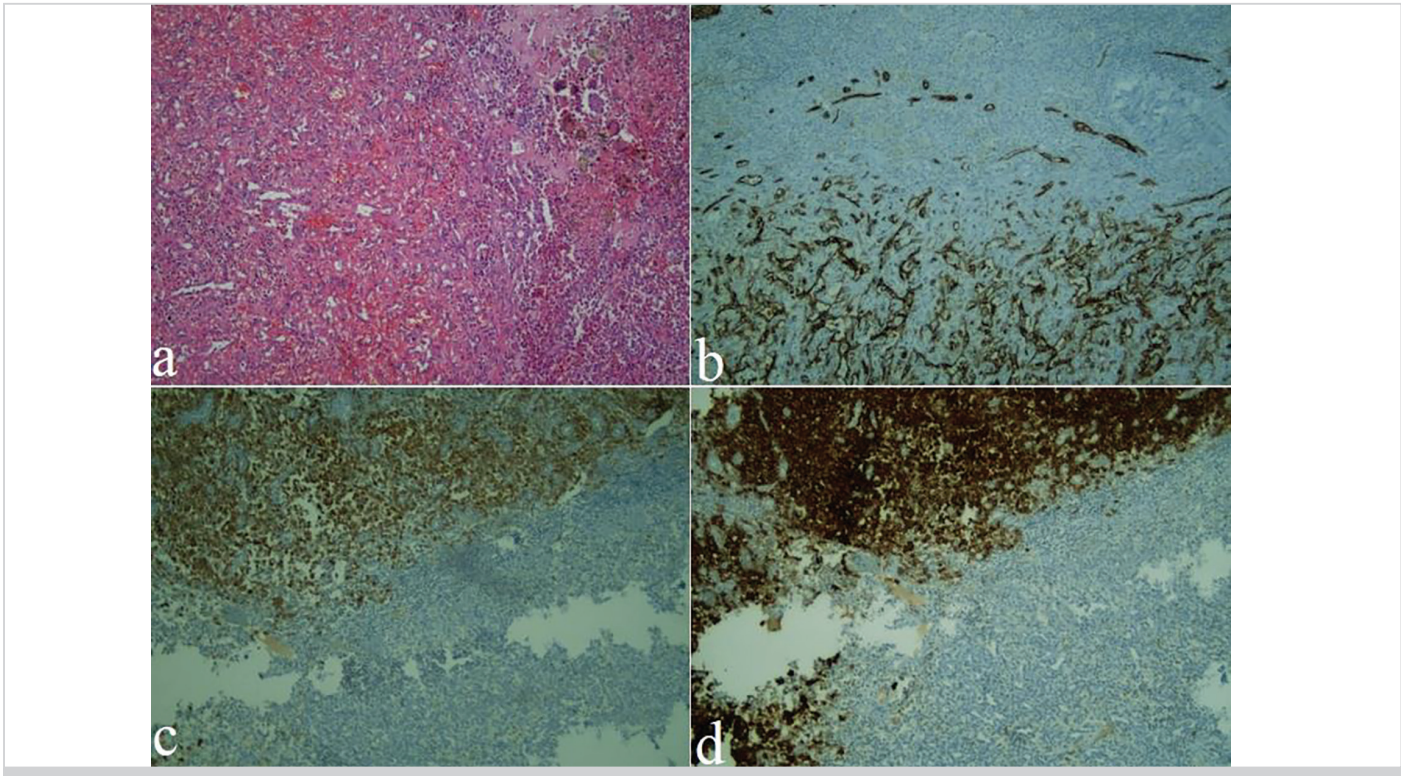

Figure 3. a) Epithelioid hemangioma (left) and Langerhans cell histiocytosis (right) in the larynx (Hematoxylin-Eosin, ×100). **b)** CD34-positive immunohistochemical staining of epithelioid endothelial cells in the larynx (×100). **c)** Langerin-positive immunohistochemical staining of Langerhans cells in the larynx (×100). **d)** CD1a-positive immunohistochemical staining of Langerhans cells in the larynx (×100)

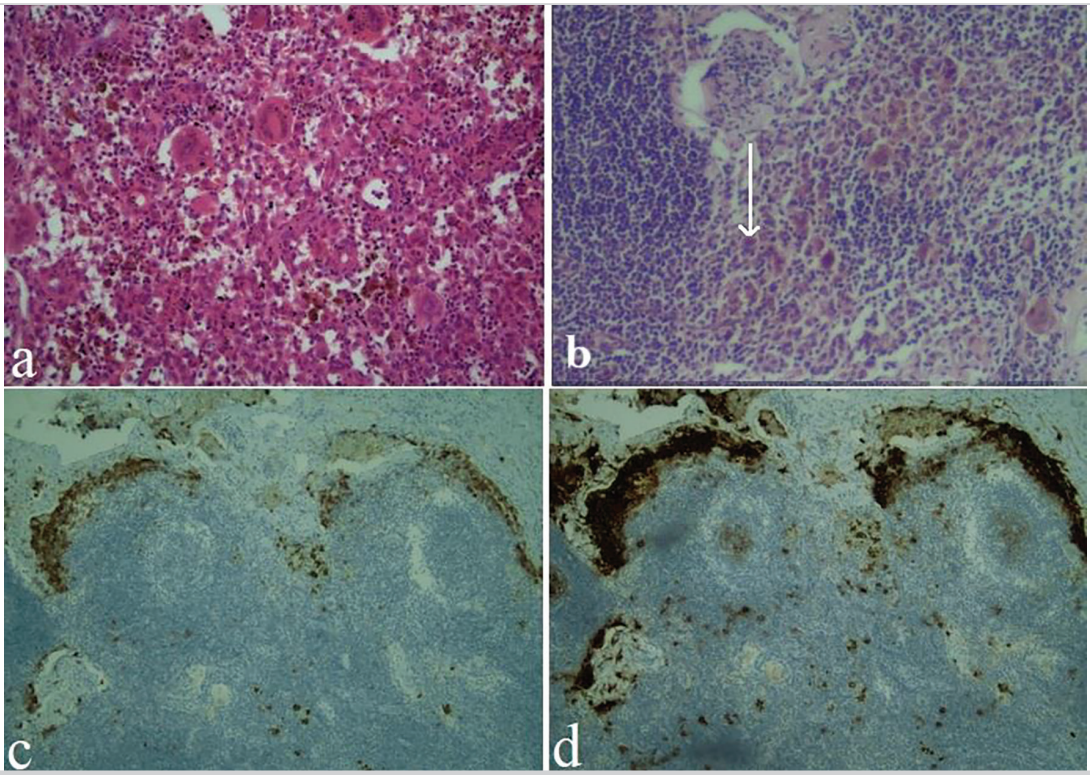

Figure 4. a. Langerhans cells, eosinophils, and multinucleated giant cells in the larynx (Hematoxylin-Eosin, ×200). **b.** Langerhans cells in a cervical lymph node (white arrow) (Hematoxylin-Eosin, ×100). **c.** Langerin-positive immunohistochemical staining of Langerhans cells in the lymph node (×100). **d.** CD1a-positive immunohistochemical staining of Langerhans cells in the lymph node (×100).

mass invaded the thyroid cartilage and obstructed the left pyriform sinus and airway, necessitating total laryngectomy. The preliminary diagnosis was hemangioendothelioma, a borderline tumor.

The coexistence of EH and LCH is highly unusual. We hypothesize that mutations in the mitogen-activated protein kinase (MAPK) pathway, including B-Raf proto-oncogene, serine/threonine kinase (BRAF), may underlie both lesions (1,14). However, the prognostic impact of EH on LCH remains unclear.

Management and prognosis of LCH depend on the location and extent of disease. A multidisciplinary approach is crucial. Comprehensive evaluation, including PET/CT, bone scintigraphy, and endocrine testing, is essential to determine disease dissemination. Surgical resection, radiotherapy, and corticosteroids may be used for isolated lesions, while systemic involvement often requires chemotherapy (1,4). The *BRAFV600E* mutation is found in 25-64% of LCH cases and is associated with increased recurrence risk (14). Targeted therapy such as vemurafenib may be considered in mutation-positive patients.

Conclusion

We present the first reported case of the coexistence of LCH and EH in the larynx. This case highlights the potential link between the MAPK pathway and both pathologies and underscores the need for careful histopathological evaluation and communication with the pathology team in rare laryngeal tumors.

Ethics

Informed Consent: Informed consent was obtained from the patient for this case report.

Footnotes

Authorship Contributions

Concept: S.C.M., L.Y., Design: S.C.M., L.Y., Data Collection and/or Processing: S.C.M., L.Y., E.A., Analysis and/or Interpretation: S.C.M., L.Y., E.A., Literature Search: S.C.M., L.Y., E.A., Ö.G., Y.F.Y., Writing: S.C.M., L.Y.

Conflict of Interest: There is no conflict of interest to disclose.

Financial Disclosure: The authors declared that this study has received no financial support.

Main Points

- Langerhans cell histiocytosis (LCH) of the larynx is a very rare disease of which only six prior cases have been reported.
- We report a unique case of a patient who underwent a total laryngectomy due to the coexistence of LCH and epithelioid hemangioma (EH) of the larynx.
- The mutations in the mitogen-activated protein kinase pathway, including B-Raf proto-oncogene, serine/threonine kinasemay have a role in the coexistence of EH and LCH.
- Whether EH influences the prognosis of LCH is not known.

References

1. Allen CE, Merad M, McClain KL. Langerhans-cell histiocytosis. N Engl J Med. 2018; 379: 856-68. [Crossref]
2. Rodriguez-Galindo C, Allen CE. Langerhans cell histiocytosis. Blood. 2020; 135: 1319-31. [Crossref]
3. Gulati N, Allen CE. Langerhans cell histiocytosis: Version 2021. Hematol Oncol. 2021; 39: 15-23. [Crossref]
4. Zhou AS, Li L, Carroll TL. Laryngeal Langerhans cell histiocytosis: a case report and literature review. Ann Otol Rhinol Laryngol. 2021; 130: 429-33. [Crossref]
5. Booth J, Thomas R. Histiocytosis X. J Laryngol Otol. 1970; 84: 1123-32. [Crossref]
6. Lhot J, Dvořačkov I. Histiocytosis x of the larynx. J Laryngol Otol. 1975; 89: 771-7. [Crossref]
7. Friedmann I, Ferlito A. Primary eosinophilic granuloma of the larynx. J Laryngol Otol. 1981; 95: 1249-54. [Crossref]
8. Yoshida T, Kuratomi K, Mitsumasu T. Benign neoplasms of the larynx. A 10-year review of 38 patients. Auris Nasus Larynx. 1983; 10(Suppl 1): 61-71. [Crossref]
9. Duynstee M, Verwoerd-Verhoef H, Monnier P, Mooi W. Langerhans cell histiocytosis of the larynx. Int J Pediatr Otorhinolaryngol. 2000; 56: 65-9. [Crossref]
10. Dannaker C, Piacquadio D, Willoughby CB, Goltz RW. Histiocytoid hemangioma: A disease spectrum: Report of a case with simultaneous cutaneous and bone involvement limited to one extremity. J Am Acad Dermatol. 1989; 21: 404-9. [Crossref]
11. Fetsch. JF. Epithelioid haemangioma. Fletcher CD, Unni K, Mertens F, editors. World Health Organization classification of tumours. Pathology and genetics of tumours of soft tissue and bone. IARC press, 2002. p. 159-160. [Crossref]
12. Guo Y, Ning F, Wang G, Li X, Liu J, Yuan Y, et al. Retrospective study of Langerhans cell histiocytosis in ear, nose and neck. Am J Otolaryngol. 2020; 4: 102369. [Crossref]
13. Wong K, Arrighi-Allisan AE, Fan CJ, Wanna GB, Cosetti MK, Perez ER. A review of noninfectious diseases masquerading as acute mastoiditis. Otolaryngology–Head and Neck Surgery. 2022; 167: 901-911. [Crossref]
14. Harmon CM, Brown N. Langerhans cell histiocytosis: a clinicopathologic review and molecular pathogenetic update. Arch Pathol Lab Med. 2015; 139: 1211-4. [Crossref]