

## CASE REPORT

# Langerhans Cell Histiocytosis of the Thyroid: A Diagnostic Odyssey

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## ABSTRACT

Langerhans cell histiocytosis (LCH), characterized by its enigmatic origin, is a rare disease often cloaked in misdiagnosis and delayed identification. Affecting adults at a mere 1-2 cases per million, LCH's infiltration of the thyroid gland represents an even rarer and diagnostically confounding scenario. Due to its infrequent occurrence, it can easily mask itself as a more common thyroid pathology, demanding a heightened level of suspicion. This necessitates accurate diagnosis for appropriate treatment and avoiding the pitfalls of mistaking LCH for other conditions. This challenging case highlights the potential for misdiagnosis of LCH presenting as thyroid swelling in a woman in her early 60s. The cytological smears mimicked medullary and giant cell type of anaplastic carcinoma of the thyroid. This emphasizes the need for comprehensive diagnostic approaches beyond cytological smears.

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## INTRODUCTION

Langerhans cell histiocytosis (LCH) is a complex spectrum of disorders affecting individuals of all ages [1]. It is characterized by the abnormal proliferation of Langerhans cells, specialized immune cells. It presents with diverse clinical manifestations and poses unique diagnostic and therapeutic challenges [1-3]. While most are diagnosed in children, emerging evidence suggests that LCH in adults, though less frequent, is not as rare as previously thought. Estimates range from 1-2 cases per million adults annually [2], highlighting the need for increased awareness and improved understanding of this disease in this population. Unlike in children, where bone involvement dominates, adult LCH exhibits a distinct clinical profile. Notably, thyroid gland involvement of adults in LCH can occur as an isolated disease or as a part of a multisystemic disease where multiple organs are affected at diagnosis [3,4]. This unique presentation emphasizes the crucial role of a comprehensive diagnostic approach to accurately identify and manage LCH in adults, particularly when thyroid involvement is suspected.

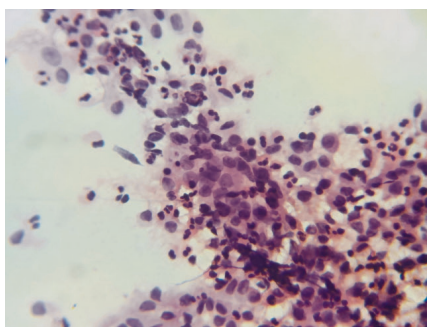
## CASE PRESENTATION

A 60-year-old woman with no significant past medical history presented with a three-month history of progressive swelling in the anterior neck, which significantly accelerated in size over the past month, and also complained of loss of weight. A positive family history of hyperthyroidism was noted in the patient's sister. Examination revealed a soft-to-firm diffuse swelling in the anterior neck measuring 4 x 3 cm.

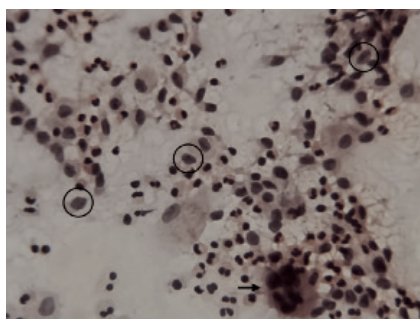
Standard blood investigations including thyroid function test revealed no abnormalities except for elevated fasting blood sugar (141 mg/dL) and HbA1c (8.2%) pointing towards impaired glucose regulation. The specific gravity of urine was within normal limits (1.005). CECT of the neck confirmed bilateral enlargement of the thyroid lobes (right lobe more than left lobe) with heterogeneous echotexture.

Fine needle aspiration of the right thyroid lobe yielded hemorrhagic material. Microscopy revealed a cellular smear showing few sheets and clusters of follicular epithelial cells mixed with lymphocytes, foamy and pigment-laden macrophages, and few cells showing hurthle cell change. Few plasmacytoid cells with anisonucleosis having an eosinophilic cytoplasm (Fig. 1). Few cells with abundant pale to granular eosinophilic

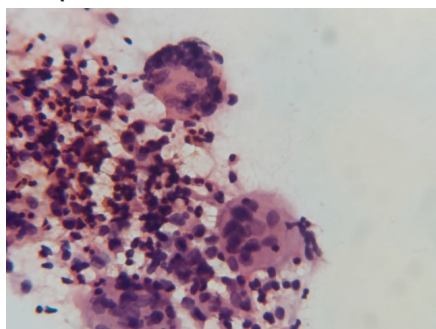
cytoplasm showing nuclear grooving, cleaving, and lobated nuclei (Fig.2) are also noted. Numerous giant cells (osteoclastic type) (Fig.3) and mitosis are also seen, in a background of eosinophils, lymphocytes, and neutrophils. Based on the clinical presentation, imaging findings, and FNAC, a broad differential diagnosis encompassing Medullary carcinoma of the thyroid, Anaplastic carcinoma of the thyroid, and Langerhans cell histiocytosis and further workup to establish a definitive diagnosis was deemed necessary. Surgical oncologist's opinion was sought and an ultrasound-guided trucut biopsy of the thyroid and Serum Calcitonin test level was recommended. The serum calcitonin level was within normal limits (6.1pg/mL). Ultrasound-guided core needle biopsy of the thyroid was performed. Histopathological examination revealed features of Langerhans cell histiocytosis.



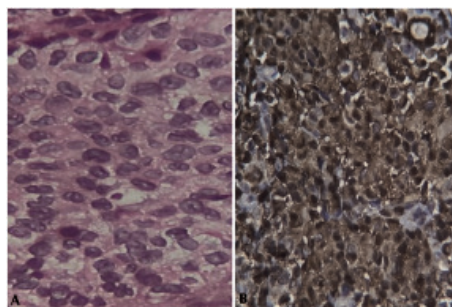
**Fig. 1:** Smear showing clusters of cells with plasmacytoid appearance showing anisonucleosis infiltrated with inflammatory cells predominately showing eosinophils and few neutrophils.



**Fig. 2:** Smear showing singly scattered cells with abundant eosinophilic cytoplasm with few cells having nuclear grooves (circled), and also seen is a giant cell (arrow) in the background of scattered eosinophils.



**Fig. 3:** Smear showing osteoclastic type of giant cells infiltrated by eosinophils, neutrophils, and few lymphocytes.



**Fig. 4:** Trucut biopsy of the thyroid (H&E) showing features of LCH. **A.** Cells having abundant eosinophilic cytoplasm with nuclear grooves **B.** S100 positivity.

## DISCUSSION

Langerhans cell histiocytosis (LCH) denotes a rare pathological entity marked by the clonal expansion of Langerhans cells, which are specialized antigen-presenting cells residing in the epidermis, bronchial epithelium, and mucosal surfaces. This disorder manifests through the infiltration of these cells into various organs and tissues [5], with prevalent afflictions including the skin, bones, lungs, and pituitary gland. Although the involvement of the thyroid in LCH is infrequent, it is noteworthy as it usually arises within the framework of multi-systemic involvement. LCH in adults is an uncommon event, but its occurrence in the thyroid is more frequent in adults compared to children, as reported in numerous studies [4]. This intriguing trend warrants further investigation into the underlying mechanisms. LCH commonly is more frequent in men [2]. Interestingly, females appear to be slightly more susceptible to thyroid LCH than males, with a reported ratio of 1.27:1 [5].

Langerhans cell histiocytosis affecting the thyroid gland often presents with a lack of clearly defined clinical signs and symptoms. This non-specificity in the presentation can make diagnosis challenging. It exhibits a spectrum of clinical courses, ranging from isolated involvement of a single organ to fulminant multisystemic disease with rapid progression. Unifocal involvement often has a better prognosis when compared to multisystemic involvement [4]. LCH presents a unique diagnostic hurdle due to the absence of specific clinical, radiographic, and pathologic features. When presenting clinically, LCH of the thyroid often mimics other thyroid disorders, commonly manifesting as swelling, much like a goitre or nodule [5]. This resemblance presents a diagnostic complexity, often prompting fine needle aspiration cytology (FNAC) as the initial investigative step. Unfortunately, even FNAC poses difficulties in definitively diagnosing LCH due to the shared features with other thyroid neoplasms.

A key hurdle lies in the cytopathological findings of LCH. While nuclear grooving is a characteristic feature,

the presence of eosinophils and multinucleated giant cells in the smears can readily lead to misdiagnosis as inflammatory lesions. This case highlights the inherent difficulty in definitively diagnosing LCH of the thyroid through cytology alone, particularly when distinguishing it from other aggressive malignancies like medullary and anaplastic thyroid carcinomas. While classical LCH cytology features histiocytoid cells with abundant cytoplasm and characteristically folded, convoluted, and grooved nuclei amidst eosinophils, our case presented with an additional layer of complexity. The presence of plasmacytoid cells with abundant, well-defined cytoplasm and eccentric nuclei mimicked the cytological features of medullary carcinoma. This diagnostic dilemma stemmed from the atypical presentation of LCH in our case. While the folded and grooved nuclei of the histiocytoid cells pointed towards LCH, the plasmacytoid cells with features mimicking medullary carcinoma introduced significant ambiguity. Although LCH presents with an osteoclastic type of giant cells, the presence of numerous osteoclastic giant cells was noted to mimic anaplastic carcinoma of the thyroid giant cell type. This ambiguity emphasizes the limitations of cytology in the definitive diagnosis of LCH, especially when atypical presentations are involved.

Due to its infrequency and potential for misdiagnosis, diagnosing LCH in the thyroid on FNAC requires careful consideration. This case serves as a reminder of the challenges in definitively diagnosing LCH of the thyroid, particularly when faced with atypical presentations and potential mimics like medullary carcinoma and giant cell type of anaplastic carcinoma of the thyroid. Surgical resection of the thyroid (total thyroidectomy) is the primary treatment for medullary carcinoma of the thyroid, followed by close surveillance for the detection of recurrent disease. However, Anaplastic carcinoma being a highly aggressive tumor with a property to invade usually presents as an unresectable mass even at the time of presentation in most cases. In such cases, chemoradiation can be a preferred management. For patients with disseminated Langerhans cell histiocytosis (LCH), chemotherapy may be the preferred course of treatment. In instances of LCH confined to a single organ system, surgical resection offers a more definitive approach. Given the propensity of thyroid LCH to manifest with multisystem disease, a thorough systemic

evaluation is warranted upon diagnosis [5]. As the management for each of the mentioned conditions differs, care should be taken to confirm the diagnosis histopathologically before a definitive diagnosis is established on cytological smears.

## CONCLUSION

FNAC, a commonly used diagnostic tool in thyroid disorders, has demonstrated limited effectiveness in definitively diagnosing LCH involvement within the thyroid as it may mimic many inflammatory and malignant conditions. The presence of plasmacytoid cells and numerous multinucleated giant cells of the osteoclastic type in thyroid cytology may not be limited to the medullary and giant cell type of anaplastic carcinoma of the thyroid as LCH involving the thyroid may also mimic such a picture. Employing a holistic approach, including detailed clinical history, cytomorphological expertise, and judicious use of ancillary tests, is essential for accurate diagnosis and optimal patient management.

## ACKNOWLEDGEMENT

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## REFERENCES

1. Ben Nacef I, Mekni S, Mhedhebi C, Riahi I, Rojbi I, Nadia M, Khiari K. Langerhans cell histiocytosis of the thyroid leading to the diagnosis of a disseminated form. *Case Reports in Endocrinology*. 2020 Mar 17;2020.
2. Lian C, Lu Y, Shen S. Langerhans cell histiocytosis in adults: a case report and review of the literature. *Oncotarget*. 2016 Apr 4;7(14):18678.
3. Rodriguez-Galindo C. RARE SYSTEMIC HEMATOLOGIC DISORDERS Langerhans cell histiocytosis. *Blood REVIEW*. 2020 Apr 16;135(16).
4. Dursun A, Pala EE, Ugurlu L, Aydin C. Primary langerhans cell histiocytosis in thyroid. *Acta Endocrinologica (Bucharest)*. 2020 Oct;16(4):501
5. Zhang J, Wang C, Lin C, Bai B, Ye M, Xiang D, Li Z. Spontaneous thyroid hemorrhage caused by langerhans cell histiocytosis: A case report and literature review. *Frontiers in Endocrinology*. 2021 May 19;12:610573.