

Thyroid Langerhans cell histiocytosis and papillary thyroid carcinoma

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Abstract: A 27-year-old female, married with two children, presented to our clinic with a 1-year history of thyroid swelling and pressure symptoms on lying backward and bilateral cervical lymphadenopathy. The patient was a known case of panhypopituitarism for 5 years. Comprehensive patient evaluation including FNAC with papillary thyroid cancer result then she underwent total thyroidectomy and bilateral neck dissection and final histologic examination confirmed papillary thyroid carcinoma in the background of lymphocytic thyroiditis, associated with Langerhans cell histiocytosis (LCH). The draining cervical lymph nodes were also involved by LCH and metastatic papillary thyroid carcinoma. Although the association of LCH with papillary thyroid carcinoma in the thyroid has been reported, their co-existence with LCH in the draining lymph nodes is very uncommon.

Keywords: Langerhans cell histiocytosis (LCH); papillary thyroid carcinoma (PTC); panhypopituitarism

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Introduction

Langerhans cell histiocytosis (LCH) is a clinically variable proliferative disease characterized by accumulation in organs of cells which share phenotypic characteristics with Langerhans' cells (1,2). LCH may be focal, involve one organ system, or be systemic, affecting multiple organ-systems. Children are the most commonly affected age group, however young adults and especially smokers are at risk of LCH (1-3). Involvement of the pituitary gland is described in about 25% of cases, however concurrent involvement with the thyroid gland is rare (1). We report a rare case of multisystem LCH involving the pituitary and thyroid glands with concurrent papillary thyroid carcinoma metastatic to draining cervical lymph nodes which are also affected by LCH.

Case presentation

A 27-year-old female, married with two children presented

to our clinic with a 1-year history of a neck swelling and pressure symptoms on lying backward. The patient had been known as a case of panhypopituitarism for the past 5 years. She initially presented with diabetes insipidus, followed by hyperprolactinemia, secondary amenorrhoea, hypothyroidism and hypogonadotrophic hypogonadism due to a pituitary mass centered in the hypothalamic, sellar and suprasellar regions. She was treated with hormonal replacement therapy. Her clinical course was complicated by an attack of right facial palsy (Ramsay hunts syndrome) which resolved with treatment. She also tested positive for anti-CMV IgM and demonstrated allergies to sulfa-drugs.

Clinical examination revealed a firm, painless, diffusely enlarged thyroid gland, and mobile on swallowing. Laryngoscopy did not identify any structural or functional abnormality of the vocal folds

Blood tests revealed RBC 3.8, Hgb 9.1 gm/dL, Hct 28.4%, Plt 83 and a normal creatinine level. Thyroid

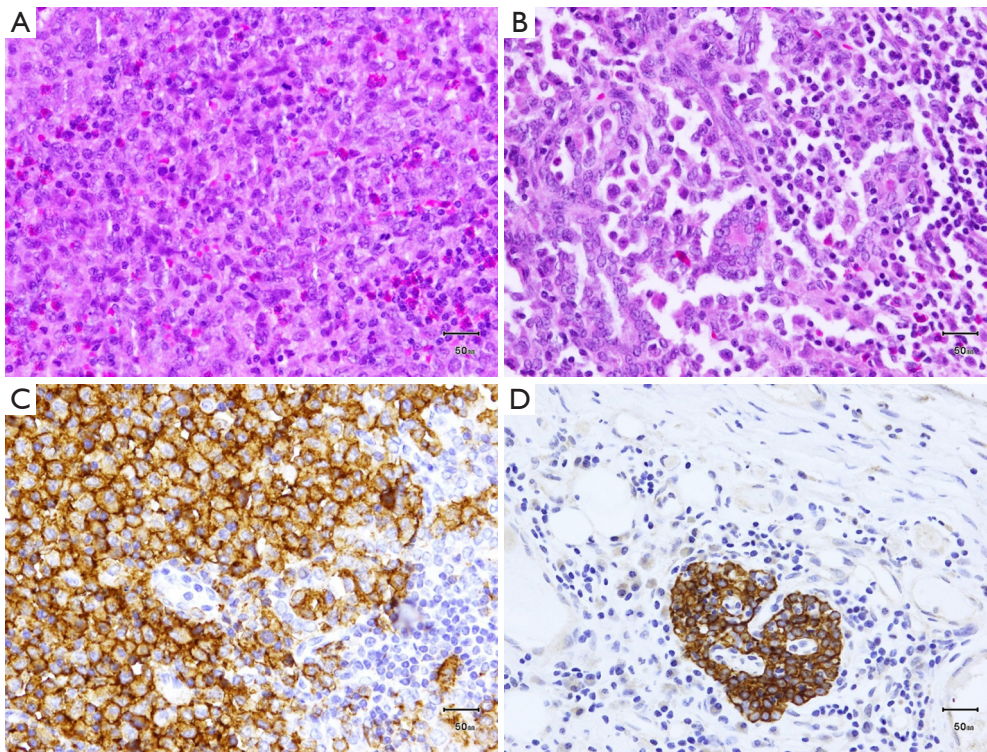


Figure 1 Slide description. (A) Sheets of epithelioid Langerhans histiocytes efface majority of thyroid and draining cervical lymph nodes. Background lymphocytes and eosinophils are present (H&E, 400×); (B) papillary clusters of atypical follicular cells prominently obscured by histiocytic and inflammatory infiltrate (H&E, 400×); (C) CD1a immunostain highlights Langerhans histiocytic cells (400×); (D) CKAE1/AE3 immunostain highlights metastatic foci of papillary thyroid carcinoma (400×).

function tests revealed secondary hypothyroidism: thyroid stimulating hormone (TSH) level 0.01 mIU/L, free T_4 of 13.7 pmol/L, and free T_3 of 3.1 pmol/L. She was placed on thyroid hormone replacement therapy. Additional laboratory tests revealed: AST 62 U/L, ALT 29 U/L.

An ultrasound of the abdomen showed hepatosplenomegaly.

An ultrasound of the neck reported bilateral heterogeneous enlarged thyroid lobes and bilateral abnormal suspicious appearance of the cervical and supraclavicular lymph nodes sized between 1.8 to 3.5 cm rounded and hypoechoic.

FNA cytology from the dominant hypoechoic lesion with irregular margins 20 mm in diameter localized in the lower portion of the right thyroid lobe showed papillary thyroid carcinoma in a background of lymphocytic thyroiditis. The patient underwent total thyroidectomy and neck dissection in the form of bilateral central (level VI) + bilateral radical modified lateral neck dissection (levels II–V).

Gross examination of the thyroid gland revealed abnormal dark color and diffuse enlargement due to an

infiltrative process with areas of necrosis and hemorrhage occupying both lobes, measuring up to 7 cm in the greatest dimension in each lobe and an enlarged isthmus.

Microscopic examination demonstrated a thyroid with diffuse effacement and infiltration by sheets of epithelioid histiocytic cells with prominent associated lymphoid and eosinophilic component. These cells were identical in morphology to those involving and effacing cervical lymph nodes. The thyroid also demonstrated multiple foci of atypical follicular cells arranged in papillary clusters with prominent nuclear enlargement, overlapping, intranuclear inclusions and grooves. The epithelioid histiocytic component largely obscured the papillary follicular structures which were identifiable as small clusters scattered throughout both lobes of the thyroid.

Immunohistochemical studies demonstrated that the epithelioid histiocytic cells were positive for CD1a, S100, CD68, and CD45. Immunohistochemical stains also helped identify small CKAE1/AE3 positive, TTF1 positive metastatic papillary follicular clusters within pericortical

Table 1 Clinicopathologic features of previously reported cases showing thyroid papillary carcinoma associated with LCH in lymph nodes

Case (ref.)	Year	Age/Sex	Side	Tumor size	Gross	Tumor type	Lymphocytic thyroiditis	LN meta	LCH in thyroid	LCH in LN
1 (7)	1992	55/M	Lt	5 cm	Ill-defined, firm, white	PTC	None	Yes	None	Yes
2 (8)	1997	51/M	Rt	0.3 cm	Firm, dark brown	PTC	None	Yes	None	Yes
3 (9)	1998	22/F	Lt	ND	ND	PTC	ND	None	None	Yes
4 (6)	2012	53/F	Rt	Up to 0.6 cm	Multiple, calcified	PTC	Yes	Yes	Yes	Yes
Present case	2016	27/F	Bilateral	>7 cm each lobe	Dark colour and enlarged both lobes	PTC	Yes	Yes	Yes	Yes

F, female; LCH, Langerhans cell histiocytosis; LN, lymph node; Lt, left; M, male; ND, not described; PTC, papillary thyroid carcinoma; Rt, right.

regions of cervical lymph nodes (*Figure 1*).

Tumor size was 4 cm in 7 cm lobe and final pathological staging is pT4aN1bMx according to AJCC.

Patient received radioiodine [1-131] adjuvant therapy post-operative.

Following discussion of the case at a multidisciplinary team meeting, the decision was made for continuous treatment with prednisone and chemotherapy.

Discussion

As LCH in the thyroid gland is already considered rare, there are only very few cases reported in the English literature of LCH in the thyroid gland associated with papillary thyroid carcinoma (4-6) (summarized in *Table 1*).

LCH may present as a tumour, skin rash, lytic bone lesions, pneumothorax, interstitial lung disease, diabetes insipidus (DI), or present as multiple affected organ systems within the human body as shown in our case in the pituitary and thyroid glands (10).

The etiology of LCH remains unknown. Uncertainty persists as to whether this disorder is primarily neoplastic, immunodysregulatory, or reactive with neoplastic and immunodysregulatory characteristics (6,11).

The increased incidence of papillary carcinoma of the thyroid is well established in inflammatory conditions such as Hashimotos/autoimmune lymphocytic thyroiditis and possibly in Grave's disease (12,13).

The concurrent findings of LCH and papillary carcinoma in the patient presented here adds to the growing body of literature that suggests that LCH as a neoplastic condition with a prominent inflammatory component may also increase risk of papillary carcinoma in the thyroid

adding to the paradigm of inflammation induced neoplasia.

It should also be noted that many papillary carcinomas of the thyroid seem to induce a heavy lymphocytic infiltrate, and on occasion a prominent infiltrate of Langerhan's type histiocytes, both within the thyroidal parenchyma as well as in draining lymph nodes. It will be interesting to postulate that this induced inflammatory infiltrate may further develop into a neoplastic transformation into LCH (14,15).

We believe that our patient carrying worse prognosis because of co-morbidity than similar patient with the same disease and stage, however no available data comparing the long term prognosis because of the disease rarity.

In conclusion, the clinical varieties of LCH range from a curable, solitary, destructive lesion of bone to a lethal leukemia-like disorder, depending upon the sites and extent of involvement, which primarily affects infants (16). The mainstay of diagnosis of this rare condition is through careful clinic-radiologic and histopathologic analysis supplemented by immunohistochemical staining (S-100, CD1a) (17). Finally, when LCH involves the thyroid gland, careful investigation for co-existent papillary carcinoma should also be performed, as is the case for inflammatory conditions of the thyroid such as Hashimotos thyroiditis and Graves disease.

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Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

Informed Consent: Written informed consent was obtained from the patient for publication of this manuscript and any accompanying images.

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