

Langerhans Cell Histiocytosis in the Thyroid and Draining Lymph Nodes: A Case Report

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A 53-year-old woman was presented with several 0.3-0.6 cm-sized nodules within the right lobe of the thyroid. Histologic sections of the thyroid demonstrated multiple papillary microcarcinomas in the background of lymphocytic thyroiditis, with a small focus of Langerhans cell histiocytosis (LCH). Small LCH nodules were also found in the draining cervical lymph nodes. 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 rare. (*Endocrinol Metab* 27:138-141, 2012)

Key Words: Langerhans cell histiocytosis, Thyroid papillary carcinoma, Thyroid gland

INTRODUCTION

Langerhans cell histiocytosis (LCH) is a rare disorder characterized by proliferation of abnormal clusters of differentiation 1a-positive (CD1a) dendritic cells [1]. It may cause local or systemic effect [1,2]. LCH may be associated with Hodgkin's disease, non-Hodgkin's lymphomas, carcinomas and other solid tumors [3,4]. A limited number of thyroid LCH with co-existing papillary carcinoma has been reported in the literature. Involvement of the thyroid gland can be focal or diffuse, and results in organ involvement, occasionally accompanied by nodular goiter, lymphocytic thyroiditis, or papillary carcinoma [5,6]. Moreover, LCH occurring in lymph nodes draining thyroid papillary carcinoma is extremely rare. We report a very rare case of thyroid LCH with papillary carcinoma and co-existing LCH of draining lymph nodes.

CASE REPORT

A 53-year-old woman presented with a progressively enlarging thyroid over 5 years. Laboratory studies including thyroid function tests, chemistry profile, complete blood cell count with differential, platelet count, red blood cell distribution width, and prothrombin

and partial thromboplastin times were all within the normal limits. Thyroid function studies disclosed free T₄ and T₃ levels were within the normal limits.

Ultrasonography revealed three calcified masses measuring 0.6, 0.4, and 0.3 cm. Fine needle aspiration was performed several times but failed due to inadequate specimen.

The patient underwent right thyroid lobectomy with right lymph node dissection. Pathologic examination of the right lobe revealed multiple calcified nodules measuring up to 0.6 cm in the greatest dimension.

Microscopic examination of the nodules revealed papillary microcarcinomas (Fig. 1). The remainder of the thyroid tissue showed lymphocytic thyroiditis and a separate, incidental, 0.5 cm-sized nodule (Fig. 2A). Microscopic examination of this nodule revealed poorly circumscribed proliferation of large cells effacing the follicular architecture of the thyroid. The cells comprising the nodules were arranged in sheets and small cluster, and exhibited abundant eosinophilic cytoplasm and bean-shaped, folded nuclei admixed with eosinophils (Fig. 3). Immunohistochemical stain for S100 was strongly positive in the large cells with folded nuclei, while pancytokeratin was negative (Fig. 2B, C). Although immunohistochemical stain for CD1a and electron microscopy were not performed,

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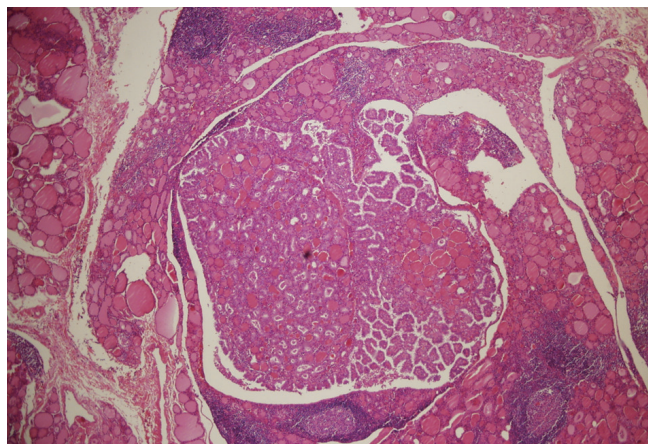


Fig. 1. Papillary microcarcinoma of the thyroid in the background of lymphocytic thyroiditis (H&E stain, $\times 40$).

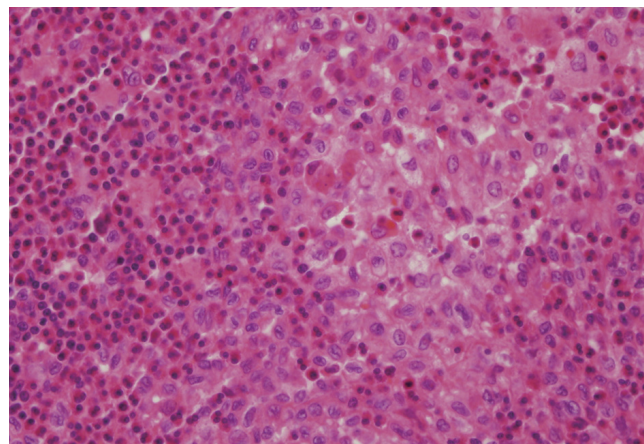


Fig. 3. Sheets of Langerhans cells with eosinophils (H&E stain, $\times 400$).

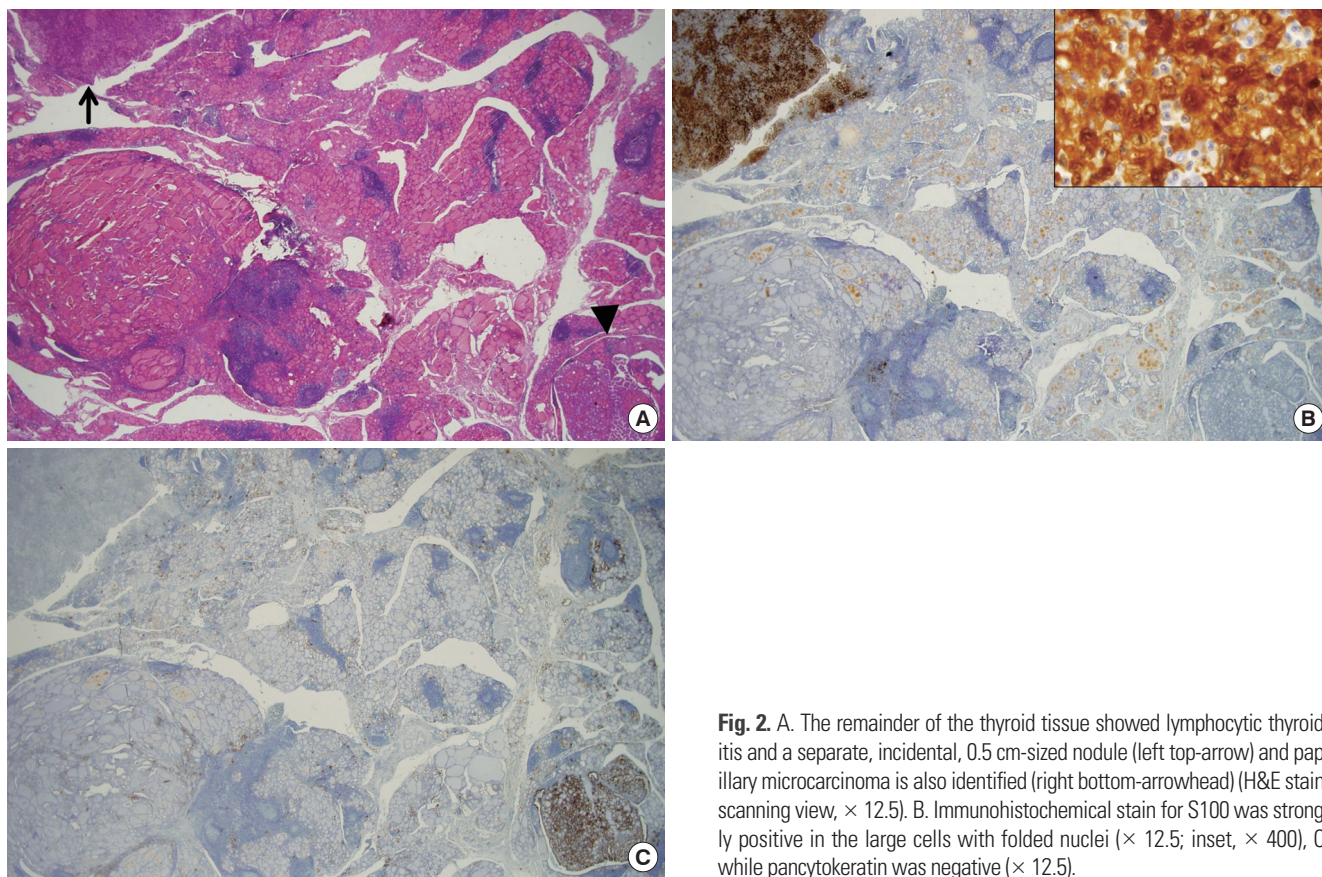


Fig. 2. A. The remainder of the thyroid tissue showed lymphocytic thyroiditis and a separate, incidental, 0.5 cm-sized nodule (left top-arrow) and papillary microcarcinoma is also identified (right bottom-arrowhead) (H&E stain, scanning view, $\times 12.5$). B. Immunohistochemical stain for S100 was strongly positive in the large cells with folded nuclei ($\times 12.5$; inset, $\times 400$). C. while pancytokeratin was negative ($\times 12.5$).

the diagnosis of LCH of the thyroid gland was made based on microscopical and immunohistochemical results. Examination of the right paratracheal lymph nodes revealed incidental, small nodules measuring up to 0.2 cm in the greatest dimension, and the nodules showed clusters of cells with abundant eosinophilic cytoplasm and bean-shaped, folded nuclei admixed with eosinophils (Fig. 4A). The

diagnosis of LCH in draining lymph nodes was made. Immunohistochemical stain for S100 was strongly positive in the large cells with folded nuclei (Fig. 4B).

Evidence of LCH multi-focality was not confirmed because follow-up studies, such as bone marrow aspiration and biopsy, bone scan, and computed tomography of the neck, chest, abdomen, and

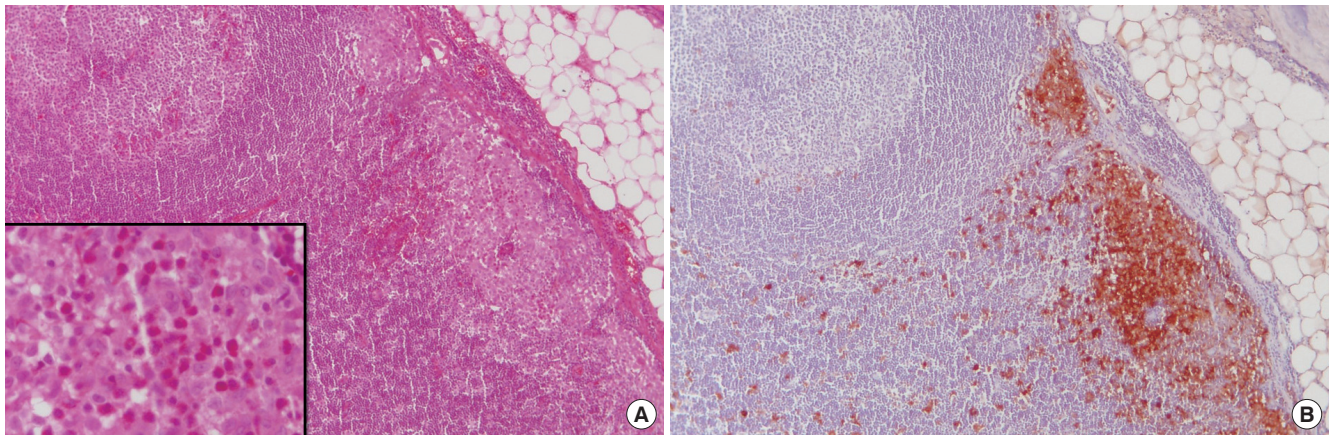


Fig. 4. A. Low-power photograph of a lymph node showing aggregates of pale staining cells (H&E stain, $\times 100$; inset, $\times 400$). B. Sections stained with antibody to S100 protein. There is intense nuclear and cytoplasmic staining of Langerhans cells.

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

Case	Year	Age/Sex	Side	Tumor size	Gross	Tumor type	Lymphocytic thyroiditis	LN meta	LCH in thyroid	LCH in LN
1 (14)	1990	55/M	Lt	5 cm	Ill-defined, firm, white	PC	None	Yes	None	Yes (draining LN)
2 (13)	1996	51/M	Rt	0.3 cm	Firm, dark brown	PC	None	Yes	None	Yes (draining LN)
3 (12)	1998	22/F	Lt	ND	ND	PC	ND	None	None	Yes*
Present case	2010	53/F	Rt	Up to 0.6 cm	Multiple, calcified	PC	Yes	Yes	Yes	Yes (draining LN)

* This patient re-presented with a painful LN measuring 1.2 cm in the left posterior triangle (distant LN) 2 months later.

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

pelvis were not performed in this patient.

1. Materials and methods

Hematoxylin-eosin-stained sections were examined. Immunohistochemical studies were conducted on formalin-fixed, paraffin-embedded, 4 μ m-thick tissue sections. The primary antibodies used were murine monoclonal anti-pancytokeratin (prediluted; AE1/AE3, Dako, Glostrup, Denmark), and S-100 (prediluted; Dako). Tissue sections were deparaffinized three times in xylene for a total of 15 minutes and subsequently rehydrated. Immunostaining was performed using a Bond-max autoimmunostainer (Leica Biosystem, Melbourne, Australia) with ER1 or ER2 retrieval buffers and a Bond Polymer refine detection system DS9800 (Vision Biosystems, Melbourne, Australia).

DISCUSSION

Even though limited numbers of thyroid LCH with co-existing papillary carcinoma has been reported in the literature [6-10], asso-

ciation with papillary thyroid carcinoma is more often described [11]. However, LCH is very rarely found in lymph nodes draining papillary carcinoma of the thyroid. To the best of our knowledge, only three cases had been reported in the English literature to date [12-14], and this is the first case to be found in Korea [15]. Clinicopathologic features of previously reported cases were described in Table 1. Although one Korean case with multifocal LCH in the thyroid gland has been reported, that case did not show papillary carcinoma of the thyroid. Moreover, our case is unique because LCH is identified in the thyroid gland and the draining lymph nodes simultaneously. In three previously reported cases, thyroid LCH was not co-existing [12-14].

The etiology of LCH remains unknown. Ambivalence persists as to whether this disorder is primarily neoplastic, immunodysregulatory, or reactive with neoplastic and immunodysregulatory characteristics [16,17]. Many reported cases of LCH of the thyroid have been associated with lymphocytic thyroiditis [3,18]. Coexistence of thyroid LCH and LCH in draining lymph nodes in our case appears to be an incidental finding, even though there remains a possibility

that the LCH arose in response to carcinoma and lymphocytic thyroiditis. However, thyroid carcinoma developed years after LCH diagnosis has been made [3]. Thus, thyroid LCH should raise the possibility of other associated disorders.

It has been suggested that LCH cells may alter their migratory properties through the expression of various cytokine receptors and by releasing inflammatory chemokines, causing not only retention of lesional Langerhans cells but also recruitment of eosinophils and T lymphocytes, as well as resultant development of lymphocytic thyroiditis. Lindley et al. [12] reported a very interesting case, which showed that one patient with history of left thyroid lobectomy for papillary carcinoma re-presented with a painful lymph node in the left posterior triangle showing LCH without metastasis two month later. This case suggests that Langerhans cell proliferation may be a reactive phenomenon, probably through the expression of cytokine or chemokine receptors.

In conclusion, LCH associated with papillary thyroid carcinoma and lymph nodes is uncommon. However, it should be borne in mind that LCH in the thyroid gland or lymph nodes can be associated with papillary carcinoma, because LCH may present a diagnostic challenge to the unsuspected pathologist, especially when dealing with aspirates from cervical lymph nodes for metastatic work-up.

요 약

53세 여자 환자가 갑상선 우엽에서 0.3-0.6 cm 크기의 다양한 종괴가 발견되어 내원하였다. 조직소견상 림프구성 갑상선염 배경 하에, 갑상선미세유두암 여러 개가 관찰되었으며, 작은 랑게르한스 세포조직구증식증이 주위에서 관찰되었다. 혈액경부림프절에도 랑게르한스 세포조직구증식증이 관찰되었다. 갑상선에서 갑상선미세유두암과 랑게르한스 세포조직구증식증이 함께 동반하는 것은 드물지만 가끔 보고되고 있다. 하지만, 혈액경부림프절에서도 랑게르한스 세포조직구증식증이 발견되는 것은 매우 드물다.

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