Cytological Features of a Lymphoepithelial Cyst Collected from Fine Needle Aspiration of the Thyroid Gland That Mimicked Papillary Thyroid Carcinoma: A Case Report

In Ho Choi, Sun-Wook Kim, Jee Soo Kim, Young-Lyun Oh

1Department of Pathology, Soonchunhyang University Seoul Hospital, Soonchunhyang University College of Medicine, Seoul; Departments of 2Medicine, 3Surgery, and 4Pathology, Samsung Medical Center, Sungkyunkwan University School of Medicine, Seoul, Korea

Since its first description in 1989, lymphoepithelial cyst of the thyroid gland (LEC-T) has been generally considered a branchial cleft derivative similar to its presentation in other sites, including thymus, parathyroid, and pancreas. However, its characterization has mainly focused on histologic and sonographic findings, and cytological findings are generally described simply or left out entirely. Fine needle aspiration cytology (FNAC) of our case showed large tissue fragments of epithelial cells on a background of lymphocytes. Some areas showed sheets or small nests of squamoid cells, which were closely admixed with clusters of lymphoid cells. Squamous cells contained relatively moderate to large amounts of eosinophilic cytoplasm and vesicular nuclei with occasional nuclear grooves that lacked intranuclear inclusions. Some cells demonstrated keratinization and nuclear atypia. Herein, we describe FNAC findings of LEC-T and review other possible diagnoses.

Keywords: Thyroid gland; Branchioma; Cyst; Cell biology

INTRODUCTION

The lymphoepithelial cyst of the thyroid gland (LEC-T) has been generally considered as a branchial cleft derivative, and it has been unusual occurring site like other unusual sites such as the thymus, oral cavity, parotid gland, and pancreas [1]. Since the first report of a LEC-T in 1989, its histological resemblance to branchial cleft cysts and embryological branchial cleft derivatives in the thyroid, thymus, and parathyroid have led to general consensus of its branchial origin [2]. Although there have been several reports of histological and immunohistochemical findings of LEC-T [1], its cytological characteristics have been described in only a few reports [3-5]. Herein, we describe the cytological findings on fine needle aspiration cytology (FNAC) of a 54-year-old woman with LEC-T mimicking papillary thyroid carcinoma (PTC).

CASE REPORT

1. Patient history

A 54-year-old woman with no previous medical problems visited hospital due to a palpable neck mass. Laboratory findings showed increased microsomal antibody (1,175.4 μ/mL; normal, 0-60 μ/mL) but normal findings in other thyroid function test, parathyroid hormone, and calcitonin. Sonographically, the mass was a 1.6-cm, irregular, calcified, hypoechoic nodule (Fig. 1A) in the inferior pole of the right thyroid with multiple hypoechoic lesions in bilateral cervical lymph nodal enlargement. Due to suspicion for malignancy, sono-guided FNAC and BRAF study (result: not detected) were performed. Computed tomography revealed a 1.4-cm, mildly enhancing soft-tissue mass in the right thyroid lobe (Fig. 1B) with multiple suspicious metastatic nodes. Total thyroidectomy was performed due to concern for thyroid cancer.
2. Cytological findings of lymphoepithelial cyst of the thyroid gland

FNAC of LEC-T showed large tissue fragments of epithelial cells on a background of lymphocytes (Fig. 2A). Most of these syncytial fragments demonstrated overwhelming cellularity with no noticeable architectural configuration. However, focal areas showing a

Fig. 1. Radiologic findings of a lymphoepithelial cyst of the thyroid gland. (A) Ultrasonography reveals a 1.6-cm, irregular, hypoechoic nodule in the inferior pole of the right lobe and multiple hypoechoic lesions in the mid and superior poles. (B) Computed tomography reveals a 1.4-cm, mildly enhanced soft-tissue mass in the right lobe and heterogeneous attenuation in the parenchyma of both lobes.

Fig. 2. Fine needle aspiration cytology of the lymphoepithelial cyst of the thyroid gland. (A) Syncytial tissue fragments are present in the lymphocytic background. (H&E, ×12.5). (B) Cellular fragments show papillary-like configuration with fibrovascular stroma (H&E, ×40). (C) Area suggesting squamous metaplasia is identified in the tissue fragments (H&E, ×100). (D) Squamous components (left side) and clusters of lymphoid cells (center and superior side) are closely blended (H&E, ×200). (E) Some areas of squamous cells show unorganized arrangement and mild cellular atypia (H&E, ×400). (F) Several small solid cell nests and detached cells are intermingled with lymphocytes (H&E, ×400).
papillary-like configuration with fibrovascular stroma (Fig. 2B) and suggesting squamous metaplasia were also noted (Fig. 2C). Sheets of squamous cells were closely admixed with clusters of lymphoid cells (Fig. 2D). These cells contained relatively moderate to large amounts of eosinophilic cytoplasm and vesicular nuclei, which varied in size from micro- to macronucleoli. Nuclear grooves were occasionally present, but intranuclear inclusions were not identified. Some cells demonstrated keratinization and nuclear atypia (Fig. 2E). Small solid nests and single squamoid cells were dispersed on the background of lymphocytes (Fig. 2F). Scattered lymphocytes showed polymorphous features without atypia, but eosinophils were not easily recognized. FNAC was interpreted as suspicious for PTC on a background of Hashimoto’s thyroiditis.

3. Histological findings of lymphoepithelial cyst of the thyroid gland

Grossly, the resected specimen showed a multinodular, yellowish-gray, solid lesion (Fig. 3A, arrowhead) in the inferior pole of the right thyroid lobe. The surrounding parenchyma of both lobes showed multiple tiny, patchy lesions. Microscopically, the lesion consisted of labyrinth-like cystic spaces lined by squamous epithelial cells with florid lymphoid hyperplasia forming follicles and germinal centers (Fig. 3B, C). Some squamoid cells had solid or pseudopapillary architectures (Fig. 3D, E), and several necrotic foci with cholesterol

![Fig. 3. Macroscopic and microscopic findings of the lymphoepithelial cyst of the thyroid gland. (A) Grossly, the specimen has a multinodular, yellowish-gray, solid lesion (arrowhead). (B-F) The lesion is a labyrinth-like cystic lesion lined by squamous epithelial cells with florid lymphoid hyperplasia and focal desquamating keratin. The epithelial components show solid and papillary architecture. Some damaged cellular lesions show lymphocytic and eosinophilic infiltration (H&E stain; B, ×12.5; C, ×100; D&E, ×400; F, ×400). (G) The p63 is positive in the squamous components (×200). (H) Ki-67 proliferation index is less than 2% (×200). (I) Opposite lobe contains a 0.2-cm papillary microcarcinoma, follicular variant (H&E, ×200).](http://jsms.sch.ac.kr)
crystals and calcification were also noted. Some damaged areas of the squamous epithelium demonstrated cellular atypia and an infiltration of lymphocytes and eosinophils (Fig. 3F). The squamous elements showed positivity for p63 (Fig. 3G). Indeed, Ki-67 proliferation index of these squamous elements was less than 2%, suggesting a benign lesion (Fig. 3H). No atypical lymphoid tissue was identified. The surrounding parenchyma showed lymphocytic infiltration with lymphoid aggregation. Incidentally, a minute PTC (0.2 cm), follicular variant was found in the opposite lobe but was not detected during preoperative radiologic examinations (Fig. 3I). No lymph node metastasis was noted.

**DISCUSSION**

LEC-T has been postulated to originate from solid cell nests of the thyroid gland, which are derivatives of the embryonic ultimobranchial body [6], and are associated with chronic or Hashimoto’s thyroiditis. Previous reports about LEC-T focused on its histological and sonographic findings, and almost all cases demonstrated benign sonographic findings with rare calcification [4,5]. Otherwise, previous reports of cytological features of LEC-T on FNAC were sparsely documented and simple, despite the practical usefulness of FNAC today [3-5].

The key feature of the present case is squamous metaplasia with a lymphocytic background. Large syncytial clusters or small solid nests of squamous epithelial cells and clusters of lymphoid cells were closely mixed (Fig. 2C-F). A variety of thyroid lesions can exhibit squamous differentiation, and it is problematic and challenging to differentiate metastatic from neoplastic origin. Nodular, tumor-like squamous metaplasia can appear as an evolution of Hashimoto’s thyroiditis and nodular goiter [7,8]. However, extensive squamous metaplasia is rarely present on thyroidal FNAC and requires a thorough approach to diagnosis and treatment [7].

Given squamous metaplasia with lymphocytic background on cytology, several other entities can be considered in the differential diagnosis, including mucoepidermoid carcinoma, squamous cell carcinoma, and Warthin-like variant of PTC. High-grade mucoepidermoid carcinoma can exhibit malignant cells similar to squamous or anaplastic carcinoma. In particular, sclerosing mucoepidermoid carcinoma with eosinophilia often occurs on the background of Hashimoto’s thyroiditis, and its cytological findings are characterized by tissue fragments of squamous cells with varying degrees of differentiation. Mucoepidermoid carcinoma of the thyroid gland is known to show mucin-producing cells, intermediate cells, and squamous cells on FNAC, consistent with salivary gland origin. However, the present case showed no glandular differentiation or eosinophilia.

Most cases of squamous cell carcinoma of thyroid are present with primary papillary carcinoma or anaplastic carcinoma of thyroid, remaining rare cases with pure squamous cell carcinoma (less than 1% of all thyroid cancer). Consequentially, the aspiration cytology of squamous cell carcinoma in thyroid, whether the pure form or the combined form with papillary or anaplastic carcinoma, can show large sheets of squamous epithelium. However, it usually shows marked nuclear atypia, frequent mitoses, and necrotic background comparing to LEC-T; therefore, absence of these atypical findings may help identify the true diagnosis of LEC-T.

Among the other neoplasms, squamous metaplasia is occasionally seen in PTCs (range, 20% to 40%), including conventional and Warthin-like variant (W-PTC) [9]. If syncytial tissue fragments of epithelial cells with abundant cytoplasm with or without papillary architecture are closely admixed with lymphoid tissue, a specimen can be mistaken for W-PTC. Our case showed squamoid syncytial fragments closely intermingled with lymphoid tissue, matching histological findings showing the squamous epithelium and subepithelial lymphoid aggregates (Figs. 2D, 3C). W-PTC can show predominant cystic change, but it usually occurs in the lateral lobe and is composed of Hurthle cells [10], which is opposed to present case having no oncocytic cells on FNAC. Indeed, no case of the Warthin-like variant of PTC with extensive squamous metaplasia has been reported in literature of thyroid FNAC.

Although some authors have insisted that LEC-T should be considered for solid thyroidal masses with respiratory epithelium on FNAC [5], cases without respiratory cells and extensive lymphocyte and squamous tissue fragments may still be malignant, especially when some cells show PTC-like nuclei. Additionally, microscopic findings with mild nuclear atypia squamous metaplasia on lymphocytic background and the additional radiologic findings suspicious for lymph node metastasis like present case led to the misdiagnosis of PTC, in spite of the first impression of lymphocytic thyroiditis with extensive squamous metaplasia.

To conclude, it is important to know the cytological pitfalls of LEC-T, which may hinder correct diagnosis and prevent appropriate conservative management. Identifying the definite cytological atypia of squamous cells and nuclei of PTC may help cytopathologists to make the diagnosis of LEC-T as opposed to malignancy.
REFERENCES