Warthin-like tumor of the thyroid gland: An uncommon variant of papillary thyroid cancer

Harold H. Kim, MD; David Myssiorek, MD; Keith S. Heller, MD; Fazlur Zahurullah, MD; Tawfiqul Bhuiya, MD

Abstract

Several variants of papillary thyroid cancer have been described, including, most recently, Warthin-like tumor of the thyroid gland. To bring attention to this uncommon variant, we review previous reports on this entity and we add 5 new cases to the literature. We retrospectively reviewed the records of all patients who had undergone thyroidectomy at our institution during a 7-year period. Among these cases, we identified 5 patients who had had a Warthin-like tumor of the thyroid. From their charts, we compiled data on age, sex, lymphadenopathy, distant spread, and treatment. Pathologic specimens were reviewed for tumor size, capsular invasion, and vascular invasion. All 5 patients were women (mean age: 51.6 yr). Tumor size ranged from 0.9 to 2.0 cm. Multifocality was seen in 1 of the 5 patients; this patient was also the only one who experienced capsular and vascular invasion. No patient had lymph node spread or distant metastasis. Because the follow-up period among these patients was still short, we were unable to analyze long-term survival data.

Introduction

Papillary carcinoma is the most common primary malignancy of the thyroid gland, and its prognosis is relatively favorable. Several variants of papillary carcinoma of the thyroid have been described. Recognition of these variants is important because different types of tumor have distinct cytologic and nuclear features, and they can follow different clinical courses, some of which (e.g., the tall-cell variant and the diffuse sclerosing variant) necessitate an aggressive treatment plan and close follow-up. Although the predominant cells may vary (e.g., tall cells, clear cells, or oxyphilic cells), all known variants display nuclear grooving and intranuclear pseudo-inclusions that identify them as papillary carcinomas.

In 1995, Apel et al described a subtype of papillary carcinoma of the thyroid that is made up primarily or entirely of Hurthle cells within a lymphocytic stroma; this entity displays a striking resemblance to Warthin’s tumor (papillary cystadenoma lymphomatosum of the salivary gland). This "Warthin-like tumor of the thyroid" (WALTT) usually affects middle-aged women. It is frequently accompanied by lymphocytic infiltration of the tumor and clinical thyroiditis.

Much still remains to be learned about this relatively new subtype of papillary carcinoma. In an effort to add to our knowledge of this variant and to introduce it to the otolaryngology community, we discuss a series of 5 new cases. We also review the pertinent literature that has been previously published.

Patients and methods

We searched the surgical pathology database at the Long Island (N.Y.) Jewish Medical Center and identified all patients who had undergone a thyroidectomy there from July 1995 through June 2002. We paid specific attention to those patients whose surgical pathology revealed a papillary carcinoma of the thyroid. We analyzed those records and identified 5 cases that were consistent with the description of WALTT that was published by Apel et al. We compiled data on these patients’ demographic characteristics, tumor size, capsular and vascular invasion, multifocality,
lymphadenopathy, distant spread, and treatment. We also reviewed each patient’s pathologic slide and description of the gross specimen to assist in the characterization of this entity.

Because this subtype of papillary carcinoma was identified relatively recently, the follow-up period for our 5 patients was short. Papillary thyroid carcinoma is a slowly progressive neoplasm that requires long-term follow-up to fully assess both its behavior and the success of therapeutic endeavors, and we were therefore unable to assess prognosis.

**Results**

All 5 patients whose pathologic features were consistent with WALTT were women (table). Their ages ranged from 33 to 65 years (mean: 51.6). The age and sex of these patients were consistent with those cited in previous reports. Tumor sizes ranged from 0.9 to 2.0 cm. Capsular and vascular invasion and multifocality were seen in only 1 patient. As has been often reported in other cases of WALTT, 4 of our 5 patients had been previously diagnosed with Hashimoto’s thyroiditis. No lymphatic or distant metastasis had occurred in our population.

On gross inspection, all tumors were well circumscribed and either solid or partially cystic. Microscopically, they displayed a similar histologic appearance—that is, a delicate papillary architecture with a prominent inflammatory infiltrate in the stalk of the papillary fronds (figure). The inflammatory cells were predominantly mononuclear and made up of mature lymphocytes admixed with some plasma cells. The cells lining the papillary fronds resembled Hurthle cells in that they displayed well-defined borders and a voluminous granular eosinophilic cytoplasm. A moderate degree of nuclear atypia was also observed, but all specimens also contained areas of typical nuclear enlargement with crowding and overlapping, prominent

### Table. Summary of findings

<table>
<thead>
<tr>
<th>Pt.</th>
<th>Age/sex</th>
<th>Tumor size (cm)</th>
<th>Capsular invasion</th>
<th>Vascular invasion</th>
<th>Multifocality</th>
<th>Other</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>44/F</td>
<td>1.5</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>None</td>
</tr>
<tr>
<td>2</td>
<td>54/F</td>
<td>2.0</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>HT*</td>
</tr>
<tr>
<td>3</td>
<td>62/F</td>
<td>1.0</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>HT</td>
</tr>
<tr>
<td>4</td>
<td>33/F</td>
<td>0.9</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>HT</td>
</tr>
<tr>
<td>5</td>
<td>65/F</td>
<td>2.0</td>
<td>Yes</td>
<td>Yes</td>
<td>Satellite contralateral lobe</td>
<td>HT</td>
</tr>
</tbody>
</table>

* Hashimoto’s thyroiditis.

---

**Figure.** A: Histology reveals papillae with dense lymphoplasmacytic infiltrate in papillary stalks. B: The lining epithelium of the papillae exhibits eosinophilic cytoplasm and elongated, overlapping nuclei with nuclear grooves.
nucleargrooves, occasional intranuclear pseudoinclusions, and foci of optical clearing of nuclei typical of papillary carcinoma of the thyroid. The surrounding parenchyma in 4 of the 5 specimens contained a chronic lymphocytic infiltrate in the pattern typical of Hashimoto’s thyroiditis, a finding that was consistent with the clinical diagnosis in these patients.

Discussion

WALTTs are predominantly populated by oxyphilic cells that display nuclear grooves and intranuclear areas of optical clearing, which is typical of papillary carcinomas of the thyroid.1,2 The results of studies of RET oncogene expression further support the classification of WALTT as a papillary thyroid carcinoma. Normal thyroid follicular cells, follicular neoplastic cells, and thyroid follicular cells in benign nodular hyperplasia do not express the RET proto-oncogene. By contrast, 40% of papillary thyroid carcinoma cells do, particularly the well-differentiated variants.9,10 D’Antonio et al found that WALTT cells also strongly express the RET/PTC gene, further suggesting its identity as a well-differentiated subtype of papillary carcinoma.13

Apel observed that WALTT displays extensive lymphocytic infiltration of the tumor stroma and papillary stalks.8 The lymphocytic infiltrate is made up of a mixed population of B and T cells, and it may provide a protective effect; some authors have suggested that the behavior of this tumor is much more benign than that of some other papillary carcinomas.8,11 Patients with WALTT often display a picture of Hashimoto’s thyroiditis in the rest of the thyroid gland.8,11 Four of our 5 patients had a preoperative clinical diagnosis of Hashimoto’s thyroiditis that was corroborated by histologic findings of lymphocytic infiltrates and Hurthle cell changes in thyroid parenchyma adjacent to the papillary carcinoma.

Because WALTT appears to be benign, preoperative identification would be helpful in preparing patient counseling and a therapeutic plan. The diagnostic study of choice for evaluating a thyroid mass is fine-needle aspiration biopsy (FNAB), which has been reported to be accurate in more than 90% of cases of papillary carcinoma.14,15 Studies of FNAB specimens have shown that a confusing picture often arises, as features suggestive of both papillary thyroid carcinoma and Hashimoto’s thyroiditis may be seen.16 Furthermore, because the tumor is predominantly made up of oxyphilic cells, the possibility of a Hurthle cell or tall-cell variant of papillary carcinoma also arises.

The Hurthle cell variant of papillary carcinoma of the thyroid is not common, accounting for only 1 to 11% of all papillary carcinomas.17,18 FNAB of this entity reveals monolayered cell sheets and papillary cell clusters with cells that contain abundant granular cytoplasm and nuclear characteristics consistent with a papillary carcinoma. Unlike WALTT, the Hurthle cell variant lacks an inflammatory infiltrate.

By contrast, the tall-cell variant of papillary thyroid carcinoma is associated with profound inflammation. Furthermore, its classification as a variant of papillary carcinoma is related to its characteristic nuclear properties. Therefore, cytologic differentiation between the tall-cell variant and WALTT is not reliable. Because FNAB can only suggest the presence of a papillary carcinoma, a definitive diagnosis lies with the surgical specimen. Studies of the role of frozen sections in the diagnosis of WALTT are lacking.

On histologic section, WALTT can still be mistaken for the tall-cell variant of papillary thyroid carcinoma by virtue of its oncocytic cytoplasm. WALTT is distinguished by the absence of elongated oncocytic tumor cells (i.e., cells whose length is twice their width), the presence of prominent nucleoli and granular cytoplasm, and the presence of dense lymphocytic infiltrate.19

Although long-term follow-up data on patients with WALTT are not available, pathologic data do not show that WALTT is any more aggressive than well-differentiated papillary carcinoma. The findings in most cases reported in the literature are consistent with ours—namely that patients had small encapsulated tumors and no extrathyroidal or vascular invasion. Cases with long-term follow-up will have to be reported in the literature before any substantive comments on prognosis can be made. Until then, initial therapy should entail a total thyroidectomy when FNAB suggests the presence of a thyroid papillary neoplasm. Subsequent therapy can be guided by the patient’s risk factors, including age, sex, tumor size, extrathyroidal extension, and metastasis. If findings on pathologic review do not warrant a more aggressive approach, treatment should be similar to the treatment offered to patients with well-differentiated thyroid carcinomas.

References

WARTHIN-LIKE TUMOR OF THE THYROID GLAND: AN UNCOMMON VARIANT OF PAPILLARY THYROID CANCER


References


Continued from page 53

pharyngotomy or midline thyrotomy) to achieve complete tumor removal while preserving laryngeal function and the overlying mucosa.

SCHWANNOMA OF THE TRUE VOCAL FOLD: A RARE DIAGNOSIS


