Locally advanced asymptomatic papillary thyroid cancer presenting with retropharyngeal lymph node metastasis symptoms

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Abstract: Papillary thyroid cancer (PTC) rarely metastasizes to the retropharyngeal lymph nodes. Managing patients with locally advanced primary PTC and metastasis located in distant anatomical areas is challenging. Herein, we report a 56-year-old patient with locally advanced asymptomatic PTC, who presented with obstructive airway symptoms due to the metastatic retropharyngeal lymph node. The patient underwent simultaneous total thyroidectomy, central lymph node dissection, en bloc resection of strap muscle and left laryngeal nerve via cervical approach and transoral resection of the metastatic retropharyngeal lymph node. Metastatic PTC should be included in the differential diagnosis of a retropharyngeal masses. Simultaneous total thyroidectomy of the primary thyroid cancer via a cervical approach and transoral resection of an isolated retropharyngeal metastasis is safe and feasible.

Keywords: Papillary thyroid cancer (PTC); retropharyngeal lymph node metastasis; clinical presentation; diagnosis; surgery

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Introduction

Papillary thyroid cancer (PTC) is the most common type of thyroid cancers. Patients with PTC are usually asymptomatic. However locally advanced thyroid carcinoma can manifest with dysphagia, dyspnea, and dysphonia because of involvement of esophagus, trachea and recurrent laryngeal nerve (1). It primarily metastasizes through the lymphatic system to the first echelon—central compartment (level VI) lymph nodes then to the lateral (levels II, III, IV, and V) neck compartments (2). PTC metastasis to the retropharyngeal space is rare with only a few reported cases (Table S1) (4,6-9).

The surgical approach for metastatic retropharyngeal lymph node can be challenging. There are several approaches for excision of retropharyngeal masses, including, transcervical, transmandibular and transoral.

In this article, we report a patient with locally advanced asymptomatic PTC, who presented with obstructive airway symptoms due to a metastatic retropharyngeal lymph node.

Case presentation

A 56-year-old female presented to the primary care provider with snoring, obstructive sleep apnea and dyspnea. On physical exam, a mass was noted on the posterior oropharyngeal wall. Computed tomography (CT) scan revealed an enhancing low density 2.1 cm x 1.3 cm mass, associated with asymmetrical soft tissue thickening in the left posterior pharynx just above the upper epiglottis (Figures 1-4). There was also a suspicious, low density 1.6 cm left thyroid nodule, with calcification (Figures 3,4). No other pathological lymphadenopathy, and no salivary glands pathology were reported.

After that the patient was referred to our clinic for evaluation of a posterior pharyngeal wall mass and an incidental left thyroid nodule. Physical examination revealed...
a bulging firm mass of the posterior oropharynx. Neck was supple, with palpable, mobile, non-tender 2 cm left thyroid nodule. Trachea was midline and no palpable cervical lymphadenopathy was noted. Flexible laryngoscopy showed a posterior pharyngeal wall mass at the hypopharynx-nasopharynx junction. Both vocal cords were mobile bilaterally.

Thyroid US revealed a left thyroid nodule 5.4x3.7x2.4 cm³ with calcification and minimal vascularity, the mass appeared to invade the strap muscle (Figures 5, 6). No discrete nodules were noted in the right thyroid lobe. Ultrasound-guided fine needle aspiration (FNA) of the left thyroid nodule was...
We decided to perform simultaneous transoral excision of the retropharyngeal mass, and total thyroidectomy via the transcervical approach. First, the parapharyngeal mass was excised through a transoral 1.5 cm vertical incision over the mass and the cystic-appearing firm lymph node was dissected circumferentially safely. Then cervical incision was performed. We identified that the strap muscle was invaded by the left thyroid mass. The left recurrent laryngeal nerve was completely encased by the mass. We performed total thyroidectomy with en bloc resection of the strap muscles and en bloc resection of the left recurrent laryngeal nerve with central lymph node dissection (level IV).

Histopathology of the left thyroid lobe revealed a 2.5 cm × 2.0 cm papillary carcinoma, classic type, stage pT4aN1aM0, BRAFV600E mutant, and the left retropharyngeal lymph node was also positive for metastatic PTC. There was extrathyroidal extension present but the surgical margins were uninvolved by carcinoma. Nine of the twelve lymph nodes of the left central compartment were positive for metastatic PTC.

Postoperative period was uneventful except for hoarseness. Her voice was strong subjectively and objectively. The patient received radioactive iodine postoperatively and continued to show no evidence of recurrence after 2 years of follow-up.

Discussion

Papillary thyroid carcinoma is the most common and fortunately the least aggressive type of thyroid cancers. It usually grows slowly and has a favorable prognosis (14). However, PTC can be locally aggressive, and directly invading the nearby tissues. PTC most commonly metastasizes into the central compartment (level VI) lymph nodes, then the lateral (levels II, III, IV, and V) compartment nodes (2). Metastasis of PTC to the retropharyngeal lymph nodes (RPLN) is very rare and few cases are reported in the literature (Table S1).

There are three possible scenarios to identify metastatic PTC to the retropharyngeal lymph nodes. In the first scenario, initially a RPLN mass is detected and there is no evidence of a primary thyroid neoplasm (6). After removing the RPLN and getting a histologic confirmation of metastatic PTC, an occult primary thyroid carcinoma is identified 1 to 6 months later (3,5,10,11,13). Probably this occurs due to a lymphatic pathway, described by Rouviere, connecting the posterior surface of the thyroid gland to the retropharyngeal lymphatic system (15). In the second scenario, recurrence of PTC can present with retropharyngeal lymph node metastasis (4,6-9). It is proposed that the lymphatic flow direction could become retrogradely after total thyroidectomy and neck dissection, leading to the RPLN metastasis (6). In the third scenario, both the primary thyroid tumor and the RPLN metastasis are diagnosed at the same time (3,6,9,12). Our case fits into the third scenario.

Recurrent cases of retropharyngeal PTC metastasis in most cases are clinically asymptomatic, whereas initial metastasis can manifest with various symptoms like swelling of the tonsils, snoring, fullness sensation in the throat, neck mass, or temporomandibular joint syndrome (3-13). In our case, the patient had both primary thyroid cancer...
and retropharyngeal metastasis. Despite the extensive local invasion, the primary thyroid cancer was asymptomatic and was found incidentally on CT scan as a benign thyroid nodule. Whereas the metastatic retropharyngeal lymph node manifested with obstructive symptoms: snoring, obstructive sleep apnea, and dyspnea. Our patient also had the BRAF mutation, which probably contributed to the aggressiveness of the cancer with the local invasion and the retropharyngeal lymph node metastasis.

Patients presented with recurrent disease in RPLN can be diagnosed with either CT or magnetic resonance imaging (MRI) (3-8,11-13). In our case, the physical exam and the flexible laryngoscopy were able to detect the retropharyngeal mass.

Transcervical ultrasound is not reliable in detecting retropharyngeal lymph nodes, although it is useful in revealing thyroid nodules and cervical lymphadenopathy. High serum thyroglobulin levels in recurrent cases of RPLN metastasis can also direct the clinician towards the diagnosis of metastatic PTC. FNA of the RPLN can be done either transcervically or transorally under CT or US guidance (3,4,6,7,12). However, FNA is not always accurate: non-diagnostic samples or even benign cytology has been reported with a proven metastatic disease (3). Our patient had both, a thyroid nodule and a RPLN, and we only biopsied the thyroid nodule because it was easily accessible. In cases of recurrent RPLN metastasis, FNA can be done transorally under US-guidance (4). In most cases of initial RPLN metastasis, histologic diagnosis is only established after resection of the mass. In our case, both the primary PTC and the retropharyngeal lymph node metastasis were diagnosed preoperatively.

PTC is a differentiated thyroid cancer with good prognosis. Excision of the primary tumor and neck dissection of the metastases provides a long-term disease-free and overall survival benefit (16-18). The ATA 2015 guidelines lack the nodal size threshold and the surgical management recommendations for retropharyngeal lymph node metastasis (18). This is because RPLN metastasis of PTC is very rare.

RPLN can be surgically excised via transcervical, transmandibular or transoral approaches (3-13). The transcervical approach provides a wide exposure of the retropharyngeal space, but the morbidity of such an extensive approach is rarely justified in the treatment of a metastatic differentiated thyroid cancer. This approach can cause injuries to the major vascular structures, lower cranial nerves, and the sympathetic chain. The transmandibular approach allows a significant exposure but can cause complications like pharyngocutaneous salivary fistula, poor healing of an osteotomy, damage to the teeth, and temporomandibular joint dysfunction.

The transoral approach is less invasive and allows adequate access for the excision of an isolated metastatic RPLN from an oncological point and avoids the potential morbidity of other approaches (7). Well-differentiated thyroid cancer LN metastasis doesn't require excision with wide margins.

Goepfert et al. 2015 proposed transoral robot-assisted surgical excision of an isolated retropharyngeal thyroid metastasis. They report that robot-assisted approach offers a safe and effective dissection through the improved visualization and the dexterity in a small working space. Limitations of the transoral robotic approach are the cost, the availability of the machine, the need for extra training, and the loss of tactile feedback (4).

Our case is unique because the patient had both locally advanced primary tumor and an isolated RPLN metastasis. Because those lesions were in distant different anatomical regions, the retropharyngeal mass located high in the oropharynx and the primary thyroid tumor located in the lower neck with substernal extension, we performed simultaneous transoral and transcervical approaches for their excision. We believe that trying to access both lesions from single cervical approach would have done more harm than benefit in this case, by unnecessarily extending the surgical trauma by a very long incision, and risking injury to vital blood vessels and nerves.

The presence of BRAF<sup>V600E</sup> mutation is associated with a significantly higher risk of recurrence than BRAF wild-type tumors. Our patient had a BRAF<sup>V600E</sup> mutation and it probably contributed to the local aggressiveness of the primary tumor and the unusual retropharyngeal metastasis.

Conclusions

The possibility of metastasis from a papillary thyroid carcinoma in the differential diagnosis of lymph node swelling in the retropharyngeal space should be considered. Simultaneous transoral and transcervical approaches to the metastatic retropharyngeal lymph nodes and the primary differentiated thyroid tumors are feasible and safe.

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Footnote

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

Informed Consent: The authors were not able to reach the patient for the consent. However, none of the images used in the manuscript can be used to identify the patient.

References

18. Haugen BR, Alexander EK, Bible KC, et al. 2015 American Thyroid Association Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer: The American Thyroid Association Guidelines Task Force on Thyroid Nodules and Differentiated Thyroid Cancer. Thyroid 2016;26:1-133.

### Table S1: A review of the literature of retropharyngeal and parapharyngeal metastasis from differentiated thyroid cancer

<table>
<thead>
<tr>
<th>Author</th>
<th>Cases</th>
<th>Age, sex</th>
<th>Presenting symptoms/how was detected</th>
<th>Physical exam/laryngoscopy</th>
<th>RP or PP</th>
<th>Preoperative workup</th>
<th>Surgical approach/surgery</th>
<th>Identification of RP/PP LN/metastasis</th>
<th>Previous/following surgeries, previous RAI Rx of the primary cancer</th>
<th>Stage</th>
<th>Postoperative RAI treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lombardi et al. 2004 (5)</td>
<td>#1 40 M</td>
<td>Swelling of the left tonsil for 2 months</td>
<td>Mild displacement of the left tonsillar fossa and nasopharyngeal wall</td>
<td>PP</td>
<td>CT, MRI left PP mass, hypodense and cystic, FNA: non-diagnostic</td>
<td>Transcervical excision of PP mass</td>
<td>Initial</td>
<td>TT w/o ND 3 weeks after removing RP mass</td>
<td>pT2aN1aM0</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>#2 52 F</td>
<td>Asymptomatic, PP mass detected on physical exam</td>
<td>Soft mass 6 cm between the angle of mandible and ant border of the sternocleidomastoid muscle; endoscopy: displacement of the left pharyngeal wall</td>
<td>PP</td>
<td>CT and MRI PP mass, cystic; frozen sections: PTC</td>
<td>Transcervical excision of PP mass + TT + bilateral SND (levels 2–4, 6)</td>
<td>Concurrent</td>
<td>None</td>
<td>pT4aN1aM0</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Shellenger et al. 2007 (4)</td>
<td>#1 46 F</td>
<td>Asymptomatic, RP mass detected on CT, had high TG</td>
<td>NA</td>
<td>RP</td>
<td>CT: isolated 2 cm right lateral RPLN</td>
<td>Transoral excision of RPLN</td>
<td>Recurrent</td>
<td>23 months earlier TT + right SND (levels 2–6); RAI Rx 2×</td>
<td>NA</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>#2 36 M</td>
<td>Asymptomatic, PR mass detected on MRI</td>
<td>NA</td>
<td>RP</td>
<td>MRI: left level 5, bilateral paratracheal, superior mediastinal and left RPLN, US-FNA of jugular node: + cancer</td>
<td>Transcervical excision of left RPLN + transcervical bilateral neck, paratracheal and mediastinal dissection</td>
<td>Recurrent</td>
<td>13 months earlier TT with CLND and left MRND; 2nd left ND</td>
<td>NA</td>
<td>No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>#3 56 F</td>
<td>Asymptomatic, RP mass detected on US, had elevated TG</td>
<td>Normal</td>
<td>RP</td>
<td>CT: recurrence in the left lateral neck, bilateral paratracheal, and left RPLN; US-FNA of RPLN: PTC</td>
<td>Transcervical excision of left RPLN + bilateral paratracheal, superior mediastinal and left neck dissection</td>
<td>Recurrent</td>
<td>18 years earlier TT; two ND; RAI Rx</td>
<td>NA</td>
<td>No</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aygenc et al. 2007 (3)</td>
<td>#1 47 M</td>
<td>Intraoral, painless mass +4 months, snoring and fullness sensation in the throat</td>
<td>Left submucosal mass with marked medial displacement of the tonsillar fossa. No thyroid pathology</td>
<td>MRI: non-vascular neoplasm, no thyroid pathology. Occult primary tumor detected 3 months after surgery; scintigraphy showed: left thyroid nodule; FNA: PTC</td>
<td>Transcervical resection of PP mass</td>
<td>Initial</td>
<td>TT with MRND 3 months after surgery</td>
<td>NA</td>
<td>NA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>#2 13 F</td>
<td>Asymptomatic, PP mass detected on MRI</td>
<td>NA</td>
<td>RP</td>
<td>MRI: multiple lymphadenopathy on right neck and PP mass 3 cm</td>
<td>Transcervical excision of PP mass + MRND</td>
<td>Recurrent</td>
<td>2 years earlier TT; RIA Rx</td>
<td>NA</td>
<td>NA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kainuma et al. 2011 (6)</td>
<td>#1 68 M</td>
<td>Asymptomatic, RP mass detected on CT and MRI</td>
<td>Normal</td>
<td>RP</td>
<td>CT and MRI: bilateral RPLN</td>
<td>Transcervical approach: resection of bilateral RPLN + bilateral SND (levels 1–2)</td>
<td>Recurrent</td>
<td>1 year earlier TT + right SND (levels 3–6); RAI Rx 3×</td>
<td>pT4aN1aM0</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>#2 62 M</td>
<td>Asymptomatic, RP mass detected on CT and MRI</td>
<td>Normal</td>
<td>RP</td>
<td>CT and MRI well-enhanced right cervical LNs and left RPLN</td>
<td>Transcervical approach, resection of left RPLN; left SND (level 1) + right SND (levels 2–5)</td>
<td>Recurrent</td>
<td>27 years earlier subtotal thyroidectomy, TT + right SND levels 2, 4, 5; left SND (levels 2–3); RAI Rx 6×</td>
<td>NA</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>#3 47 M</td>
<td>Right neck mass for 12 months</td>
<td>No thyroid nodule</td>
<td>RP</td>
<td>US: 15 mm in right thyroid lobe; FNA: susp PT; CT and MRI: right cervical LN met and left RPLN</td>
<td>Transcervical resection of right RPLN + TT + right MRND (levels 1–6)</td>
<td>Concurrent</td>
<td>None</td>
<td>pT1N1bM0</td>
<td>NA</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Goepfert et al. 2015 (7)</td>
<td>1 64 F</td>
<td>Asymptomatic, RP mass detected on MRI, had TG elevation</td>
<td>NA,</td>
<td>RP</td>
<td>US: negative; MRI: isolated 2.6 cm left RP mass, PET-CT: hypermetabolic left RPLN and hypermetabolic lung nodule. CT-guided FNA: positive for PTC</td>
<td>Transoral robotic surgery: excision of left RPLN</td>
<td>Recurrent</td>
<td>2 years earlier TT left CLND and lateral ND; RAI Rx</td>
<td>pT3N1b</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Otosuki et al. 2007 (8)</td>
<td>5</td>
<td>Mean age 63 (40–84) pain, dysphagia; 2 were asymptomatic</td>
<td>Displacement of the tonsillar fossa, soft palate, and/or nasopharyngeal wall</td>
<td>RP</td>
<td>PP mass detected on CT or MRI</td>
<td>Transcervical resection of RPLN</td>
<td>Recurrent</td>
<td>Average 174 months (5 months to 30 years)</td>
<td>NA</td>
<td>Yes (3)**</td>
<td></td>
</tr>
<tr>
<td>Le et al. 2007 (9)</td>
<td>6</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Sirotnak et al. 1997 (10)</td>
<td>1 53 F</td>
<td>Right-sided headaches, temporomandibular joint syndrome</td>
<td>Firm, mobile, submucosal 2 cm × 2 cm mass lateral and superior to the tonsillar fossa</td>
<td>PP</td>
<td>X-ray: calcification in PPS; thyroid scan: cold nodule in the right thyroid lobe</td>
<td>Transcervical excision of the mass</td>
<td>Initial</td>
<td>TT + right MND afterwards</td>
<td>NA</td>
<td>No</td>
<td></td>
</tr>
<tr>
<td>Horvath et al. 1991 (11)</td>
<td>1 55 F</td>
<td>Sensation of mass in her left throat for 3 years</td>
<td>Elevation of the left oropharyngeal wall</td>
<td>PP</td>
<td>CT left parapharyngeal mass, fluid density with thick wall</td>
<td>Unknown approach, excision of mass</td>
<td>Initial</td>
<td>TT afterwards</td>
<td>NA</td>
<td>NA</td>
<td></td>
</tr>
<tr>
<td>Ferrario et al. 1995 (12)</td>
<td>1 47 M</td>
<td>Snoring for 3 years</td>
<td>Right tonsil enlargement</td>
<td>PP</td>
<td>MRI 4 cm right tonsil mass; US, CT confirmed the lesion + small right thyroid nodule, R LAD; FNA of mass: PTC</td>
<td>Transcervical excision of PP mass + TT + right ND</td>
<td>Concurrent</td>
<td>None</td>
<td>pT2aN1aM0</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>DiLeo et al. 1998 (13)</td>
<td>1 65 M</td>
<td>Severe obstructive sleep apnea</td>
<td>Fullness of the right palate and lateral pharyngeal wall</td>
<td>RP</td>
<td>MRI: RP mass, polysomnography</td>
<td>Transcervical excision</td>
<td>Initial</td>
<td>TT subsequently</td>
<td>NA</td>
<td>Yes</td>
<td></td>
</tr>
<tr>
<td>Our case</td>
<td>1 56 F</td>
<td>Obstructive sleep apnea, snoring, dysphagia</td>
<td>Bulging firm mass of posterior pharynx; palpable 2 cm left thyroid nodule</td>
<td>RP</td>
<td>CT 2.1 cm left RP mass, 1.6 cm left thyroid nodule 5.4 cm; FNA: PTC</td>
<td>Transcervical excision or RPLN + trans-cervical CLND</td>
<td>Concurrent</td>
<td>None</td>
<td>pT4aN1aM0</td>
<td>Yes</td>
<td></td>
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</table>