Thyroid Cancer

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Table of Contents

Introduction ........................................ 2
Papillary Thyroid Cancer ............................ 2
Follicular Neoplasm ................................. 4
Medullary Thyroid Cancer ......................... 6
Anaplastic Thyroid Cancer ......................... 9
Benign Nodule .................................... 10
Conclusion ........................................ 11
References .......................................... 11
Thyroid Cancer

David F. Schneider, MD, MS, and Rebecca S. Sippel, MD, FACS

INTRODUCTION

Surgery is the mainstay of treatment for almost all types of thyroid cancers. Thyroid cancer occurs in a variety of histologic forms and presents with a spectrum of disease severity. The most common type is papillary thyroid cancer, comprising 70% to 80% of all thyroid tumors. Follicular thyroid cancer is the second most common type of differentiated thyroid cancer, making up 15% to 20% of all thyroid cancers. Medullary thyroid cancer is often hereditary and constitutes 5% to 10% of all thyroid cancers. Finally, anaplastic thyroid cancer is a rare but lethal form of thyroid cancer where surgery plays a limited role. A unique set of diagnostic and treatment options exist for each type of thyroid cancer, and the surgeon must understand these nuances to offer the patient the appropriate surgical therapy to prevent recurrence or facilitate adjuvant therapy.

PAPILLARY THYROID CANCER

CASE 1 PRESENTATION

A 54-year-old man presents to the clinic after noticing a mass in his neck while shaving. On exam, the 2.5-cm nodule is located 2 fingerbreadths below the cricoid cartilage and 1 cm to the right of midline. It is firm, mobile, and nontender. There are no other masses in the neck and no lymphadenopathy. The remainder of his physical exam is unremarkable. His history is notable for acid reflux and hypertension, but he denies any history of radiation to the neck or family history of thyroid malignancy, parathyroid problems, or adrenal tumors. He denies any symptoms of hyperthyroidism or hypothyroidism.

What are the next steps in evaluating this thyroid nodule?

As part of a detailed history for newly discovered thyroid nodule, the physician must establish risk factors for thyroid cancer. The 2 main risk factors for thyroid cancer are a history of head or neck radiation and a family history positive for thyroid malignancy or other endocrine tumors. It is also important to inquire about symptoms of hyperthyroidism and compressive symptoms such as hoarseness, cough, dysphagia, or breathing problems, as these may signify rapid growth or invasion and can increase the suspicion for malignancy.

Laboratory evaluation of a new thyroid nodule should include a thyroid-stimulating hormone (TSH) level to determine if the patient has unrecognized hyperthyroidism or hypothyroidism. A suppressed TSH level can be followed up with thyroid scintigraphy to distinguish between Graves disease, a solitary toxic nodule, or toxic multinodular goiter. Ultrasound is an important tool in evaluating thyroid nodules as it is used to measure the size and determine the features of the nodule, and it can also identify additional nonpalpable nodules or lymphadenopathy in the central or lateral compartments.

Fine-needle aspiration (FNA) biopsy is the most important tool for evaluating thyroid nodules. FNA biopsy results are classified according to the Bethesda criteria, which indicate the risk of malignancy (Table 1). Even though this patient’s nodule was palpable, it is best to evaluate it with an ultrasound-guided FNA biopsy. Ultrasound guidance can confirm the nodule is actually being sampled as well as help to target the most suspicious portions of the nodule in order to maximize the accuracy of the FNA.

Aside from assisting with FNA biopsy, ultrasonography is also the best modality for imaging the thyroid and neck lymph nodes. Although highly operator-dependent, ultrasound is noninvasive and does not involve any radiation or contrast risk to the patient. Ultrasound characteristics concerning for malignancy include hypoechoigenicity, microcalcifications, irregular margins, and chaotic vascular patterns. High-resolution ultrasound can also demonstrate extracapsular invasion and lymph node involvement.

CASE 1 CONTINUED

The patient undergoes a workup of his thyroid nodule. His TSH level is within normal limits. Ultrasound evaluation demonstrates a 2.5-cm hypoechoic nodule in the mid portion of the right neck.
lobe of the thyroid with some internal microcalcifications (Figure 1). Additionally, suspicious lymph nodes are seen in the central neck and level IV in the lateral neck. (See Figure 2 for an illustration of the anatomy of the lymph node compartments in the neck.) FNA biopsy results of his thyroid nodule are consistent with papillary thyroid cancer.

- What surgical treatment would you recommend for this patient’s papillary thyroid cancer?

Surgical treatment of papillary thyroid cancer recognized on FNA biopsy should consist of a total thyroidectomy, as this facilitates the use of postoperative radioactive iodine ablation and long-term follow up with thyroglobulin testing. Incidentally discovered papillary thyroid cancers <1 cm in size may be adequately treated with thyroid lobectomy. The need for lymph dissection is guided by preoperative and intraoperative findings. On ultrasound this patient had suspicious lymph nodes in both the central and lateral neck. Therefore, prior to surgery the patient should undergo an ultrasound-guided FNA biopsy of the largest suspicious node. If nodal involvement is confirmed, then the optimal surgical treatment would be a total thyroidectomy with a right central and lateral neck dissection.

Nodal dissection should be compartment-oriented, and if lateral neck nodal involvement is identified it should be assumed that there is also central neck nodal involvement and both areas should be cleared. Any uncertainty regarding suspicious lymph nodes seen by ultrasound or intraoperatively that cannot be resolved with FNA biopsy preoperatively can be clarified with intraoperative frozen section.

A central neck dissection involves the removal of level VI lymph nodes, and a lateral neck dissection removes a minimum of levels III and IV and may include levels II and V (Figure 2). The central neck (level VI) is defined by the area between the carotid sheaths and from the hyoid bone to the innominate vessels. Clearance of nodes in this region involves dissection of the tracheoesophageal groove, putting the recurrent laryngeal nerve at risk for injury. Another risk of central compartment lymph node dissection is hypoparathyroidism, as these glands or their blood supply may be either inadvertently removed or damaged during this dissection. Often, the inferior glands must be autotransplanted after central compartment lymph node dissection.9,10

A modified radical neck dissection involves removing all nodes within the anterior cervical triangle, whose borders are the anterior border of the sternocleidomastoid muscle, the inferior border of the mandible, and the midline of the neck (includes the central compartment). To perform a modified radical neck dissection, the collar incision used for thyroidectomy is carried laterally and superiorly along the medial border of the sternocleidomastoid muscle. The surgeon gains access to the lateral neck by either retracting or disconnecting the sternocleidomastoid muscle from its insertion on the clavicle. Lymph nodes removed lie between the superficial and prevertebral fascia, preserving the carotid artery, jugular vein, vagus nerve, spinal accessory nerve, sternocleidomastoid muscle, and phrenic nerve. Additional nerves placed at risk during a lymph node dissection in this area include the hypoglossal and glossopharyngeal nerves. The marginal mandibular nerve is at risk if dissection is carried close to the mandible. Injury to the thoracic duct can occur when dissection is carried down near the clavicle or anterior mediastinum on the left side.1,11

Level V lymph nodes are located in the posterior cervical triangle whose borders are defined by the posterior border of the sternocleidomastoid muscle anteriorly, the trapezius muscle posteriorly, and the clavicle inferiorly. Papillary thyroid cancer rarely metastasizes to these

### Table 1. The Bethesda System for Thyroid Cytopathology

<table>
<thead>
<tr>
<th>Category</th>
<th>Risk of Malignancy (%)</th>
<th>Recommended Management</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nondiagnostic or Unsatisfactory</td>
<td>1–4</td>
<td>Repeat FNA with US guidance</td>
</tr>
<tr>
<td>Benign</td>
<td>0–3</td>
<td>Clinical follow-up</td>
</tr>
<tr>
<td>Atypia of undetermined significance (AUS) or Follicular lesion of undetermined significance (FLUS)</td>
<td>5–15</td>
<td>Repeat FNA*</td>
</tr>
<tr>
<td>Suspicious for malignancy</td>
<td>60–75</td>
<td>Lobectomy ± frozen section or total thyroidectomy</td>
</tr>
<tr>
<td>Malignant</td>
<td>97–99</td>
<td>Total thyroidectomy</td>
</tr>
</tbody>
</table>

FNA = fine needle aspiration; US = ultrasonography.

*Lobectomy can also be considered depending on clinical or sonographic characteristics.
nodes, and level V dissection is usually only performed for known lymph node metastases in this area.8,12

• **What postoperative treatment would you recommend for this patient?**

Postoperatively, the patient will be treated with radioactive iodine ablation. Four to 5 days after the radioactive iodine treatment, a $^{131}$I whole body scan (WBS) will be obtained to detect metastatic disease. Preparation for radioactive iodine treatment can be done by withdrawing the patient from thyroid hormone for 3 to 4 weeks or by administering recombinant TSH. Once patients have completed radioactive iodine treatment, they need to be placed on thyroid hormone supplementation. One of the most important components of adjuvant therapy in thyroid cancer is L-thyroxine suppressive therapy.2,13

**FOLLICULAR NEOPLASM**

**CASE 2 PRESENTATION**

A 42-year-old previously healthy woman presents for routine physical examination. A 3-cm nodule is palpated in the right lobe of the thyroid.

There is no lymphadenopathy palpable, and the remainder of her physical exam is normal. She has no family history of thyroid cancer or neck irradiation. Her TSH level is 1.5 mIU/L. Ultrasound demonstrates a large, highly vascular nodule with hypoechoic areas in the mid portion of the right thyroid lobe without any central or lateral lymphadenopathy (Figure 3). FNA biopsy of this lesion is read as “follicular neoplasm.”

• **What is the next step in treating this patient?**

Follicular neoplasms are identified in 15% to 20% of all FNA biopsies.14 Of these, 15% to 30% prove to be malignant. Cytology cannot distinguish benign from malignant follicular lesions; the histopathologic hallmarks of follicular carcinoma include capsular and vascular invasion.14 Therefore, this patient should undergo a diagnostic left lobectomy. The Bethesda system classifies FNA biopsy results and provides estimated risk of malignancy and management recommendations for each result (Table 1).

**CASE 2 CONTINUED**

While the patient is recovering from a right thyroid lobectomy and isthmusectomy, the

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Figure 1. Neck ultrasound image demonstrating a nodule in the upper portion of the left lobe of the thyroid. The nodule has internal calcifications and irregular contours, making it suspicious for carcinoma.

Figure 2. Lymph node compartments of the neck. Levels VI and sometimes VII are included in a central neck dissection, while a lateral neck dissection for thyroid cancer usually includes levels II to IV and rarely V. (Adapted with permission from Doherty GM, Haugen BR, Kloos RT, et al. Revised American Thyroid Association management guidelines for patients with thyroid nodules and differentiated thyroid cancer. Thyroid 2009;19:1167–1214.)
final pathology proves to be follicular carcinoma. Two weeks after surgery, the patient’s incision is well healed, but her voice is hoarse. The patient is quite anxious about her diagnosis and has many questions about the need for additional surgery.

- **What is the next step in the management of this patient?**

  The patient will need a completion thyroidectomy, but her voice changes are concerning for a recurrent laryngeal nerve injury. In this setting, it would be dangerous to proceed with completion thyroidectomy, exposing the contralateral recurrent laryngeal nerve to potential injury, before documenting that the left recurrent nerve is functioning.

**AVOIDING NERVE INJURY DURING THYROIDECTOMY**

Understanding the anatomy and development of the recurrent laryngeal nerve is crucial to preventing injury to the nerve during thyroidectomy. The recurrent laryngeal nerve develops from the same primordial bundle as the vagus nerve and is associated with the sixth branchial pouch. As the neck elongates during development, the laryngeal nerve becomes recurrent, passing under the aortic arch on the left or the subclavian artery on the right and then reascending along the trachea in the tracheoesophageal groove. When it reaches the mid portion of the thyroid gland, the nerve may divide into 2 or more branches. Here, the nerve can pass either anterior or posterior to the inferior thyroid artery. The 3 most common configurations are: (1) nerve anterior to the artery, (2) nerve between a bifurcation in the artery (50% of patients on the right), or (3) nerve posterior to the artery (50% of patients on the left). At this critical area, the nerve is immediately posterior to the superior parathyroid gland. The recurrent nerve is usually found within the tracheoesophageal groove within 2 to 3 cm of the entry point into the larynx at the cricothyroid articulation on the posterior border of the cricothyroid muscle.

The recurrent nerve may divide before penetrating the larynx. Only the anterior branch is motor, innervating all the intrinsic muscles of the larynx except the cricothyroid. The posterior branch provides sensory innervation to the subglottic area and the proximal trachea.

A unilateral recurrent laryngeal injury leads to hoarseness, while a bilateral injury leads to adducted cords and an occluded airway. In experienced hands, the incidence of permanent recurrent laryngeal nerve injury is 1% or less. Approximately 10% of patients will experience transient nerve paresis, and most of these will recover a normal voice within 6 to 8 weeks. If the voice has not recovered by 6 months, it is likely that the injury will be permanent. Therefore, this patient’s voice should be evaluated again in 4 weeks. Regardless of the quality of her voice, the patient should have a direct laryngoscopy before her completion thyroidectomy.

Another nerve that could potentially be injured during thyroidectomy is the external branch of the superior laryngeal nerve. The superior laryngeal nerve also originates from the vagus nerve near the jugular foramen. It descends posterior and medial to the internal carotid artery toward the larynx. When it reaches the hyoid bone, this nerve divides into an internal branch and external branch. The external branch turns medially, typically running behind the superior thyroid artery. Given its orientation to the superior thyroid pole, it is also at risk of injury during ligation of the superior vessels. The external branch of the superior laryngeal nerve provides motor input to the inferior constrictor and cricothyroid muscles. Injury to this nerve typically affects both the pitch and strength of the voice. Since this patient mainly has hoarseness without changes in pitch, a recurrent laryngeal nerve injury is more likely.

**CASE 2 CONTINUED**

The patient’s voice recovers by the next clinical visit, and preoperative laryngoscopy dem-
Thyroid Cancer

A 10-year-old boy presents with his parents after they noticed a lump in his neck. On further questioning, you find that his father and several other members of the family have had a thyroidectomy at a young age. On physical exam, there is a centimeter-size firm nodule in the right thyroid with palpable lymphadenopathy in the lateral neck. Ultrasound-guided biopsy of the thyroid nodule and a lymph node reveals spindle-shaped cells that stain positive for calcitonin. The patient is diagnosed with medullary thyroid cancer (MTC).

- Why is the patient’s family history important?

MTC constitutes 5% to 10% of all thyroid cancers and may be sporadic or familial. Familial types are the multiple endocrine neoplasia (MEN) type 2A and 2B and familial medullary thyroid cancer (FMTC). Each type of familial MTC is associated with characteristic germline mutations of the RET gene.

- MEN-2 carriers confer a 50% risk of transmitting the gene to their offspring since gain-of-function RET mutations are inherited in an autosomal dominant fashion. The clinical behavior of the MTC can be reliably predicted by the specific RET codon mutation. For example, MEN-2B patients expressing the 918 codon mutation exhibit the most aggressive form of MTC, with early presentation during infancy. A wide spectrum of codon mutations exist for MEN-2A and FMTC, and the specific genotype-phenotype correlations are important for helping families decide on the appropriate timing of treatment. In general, patients with FMTC have mutations that exhibit less aggressive forms of the disease that present later in life. In the MEN syndromes, the specific codon mutations are also associated with different rates of pheochromocytoma. For example, pheochromocytoma is detected in 50%
# Thyroid Cancer

**Table 2.** American Joint Committee on Cancer (AJCC) TNM Staging for Thyroid Cancer

<table>
<thead>
<tr>
<th>Primary Tumor (T)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>TX</td>
<td>Primary tumor cannot be assessed</td>
</tr>
<tr>
<td>T0</td>
<td>No evidence of primary tumor</td>
</tr>
<tr>
<td>T1</td>
<td>Tumor ( \leq 2 ) cm, limited to the thyroid</td>
</tr>
<tr>
<td>T1A</td>
<td>Tumor ( \leq 1 ) cm, limited to the thyroid</td>
</tr>
<tr>
<td>T1B</td>
<td>Tumor ( &gt;1 ) cm but ( &lt; 2 ) cm, limited to the thyroid</td>
</tr>
<tr>
<td>T2</td>
<td>Tumor ( &gt;2 ) cm but ( &lt; 4 ) cm, limited to the thyroid</td>
</tr>
<tr>
<td>T3</td>
<td>Tumor ( &gt;4 ) cm, limited to the thyroid or minimal extrathyroid extension (sternothyroid or perithyroid soft tissues)</td>
</tr>
<tr>
<td>T4A*</td>
<td>Tumor of any size extending beyond thyroid capsule to invade subcutaneous soft tissues, larynx, trachea, esophagus, or recurrent laryngeal nerve</td>
</tr>
<tr>
<td>T4B</td>
<td>Tumor invades prevertebral fascia or encases carotid artery or mediastinal vessels</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Regional Lymph Nodes (N)</th>
<th></th>
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<tbody>
<tr>
<td>NX</td>
<td>Regional lymph nodes cannot be assessed</td>
</tr>
<tr>
<td>N0</td>
<td>No regional lymph node metastasis</td>
</tr>
<tr>
<td>N1</td>
<td>Regional lymph nodes metastasis</td>
</tr>
<tr>
<td>N1A</td>
<td>Metastasis to level VI lymph nodes</td>
</tr>
<tr>
<td>N1B</td>
<td>Metastasis to unilateral, bilateral, or contralateral cervical (levels I, II, III, IV, or V) or superior mediastinal (level VII) lymph nodes</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Distant Metastasis (M)</th>
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</thead>
<tbody>
<tr>
<td>M0</td>
<td>No distant metastasis</td>
</tr>
<tr>
<td>M1</td>
<td>Distant metastasis</td>
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</tbody>
</table>

### Stage Grouping

**Differentiated Cancers† <45 years old**

<table>
<thead>
<tr>
<th>Stage I</th>
<th>T1</th>
<th>N0</th>
<th>M0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage II</td>
<td>T2</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>Stage III</td>
<td>T3</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T1</td>
<td>N1A</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T2</td>
<td>N1A</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T3</td>
<td>N1A</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IVA</td>
<td>T4a</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T4a</td>
<td>N1A</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T1</td>
<td>N1B</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T2</td>
<td>N1B</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T3</td>
<td>N1B</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T4A</td>
<td>N1B</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IVB</td>
<td>T4B</td>
<td>Any N</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IVC</td>
<td>Any T</td>
<td>Any N</td>
<td>M1</td>
</tr>
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</table>

**Medullary Carcinoma**

<table>
<thead>
<tr>
<th>Stage I</th>
<th>T1</th>
<th>N0</th>
<th>M0</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage II</td>
<td>T2</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td>Stage III</td>
<td>T3</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T1</td>
<td>N1A</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T2</td>
<td>N1A</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T3</td>
<td>N1A</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IVA</td>
<td>T4A</td>
<td>N0</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T4A</td>
<td>N1A</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T1</td>
<td>N1B</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T2</td>
<td>N1B</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T3</td>
<td>N1B</td>
<td>M0</td>
</tr>
<tr>
<td></td>
<td>T4</td>
<td>N1B</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IVB</td>
<td>T4B</td>
<td>Any N</td>
<td>M0</td>
</tr>
<tr>
<td>Stage IVC</td>
<td>Any T</td>
<td>Any N</td>
<td>M1</td>
</tr>
</tbody>
</table>

**Anaplastic Carcinomas‡**

| Stage IVA | T4A| Any N | M0 |
| Stage IVB | T4B| Any N | M0 |
| Stage IVC | Any T| Any N | M1 |


*All anaplastic tumors are considered T4 tumors.

†Papillary and follicular carcinomas are considered differentiated thyroid cancers.

‡All anaplastic carcinomas are considered stage IV.
of patients with 634 and 918 mutations but is much less frequent in patients with mutations in codons 609, 611, or 620.28

Primary hyperparathyroidism occurs in 20% of patients with MEN-2A. It is most commonly associated with codon 634 mutations, and the disease is often mild. A common finding in MEN-2A is normal calcium and parathyroid hormone (PTH) levels but slightly enlarged gland(s) found at the time of thyroidectomy. While only 1 or 2 glands may be enlarged, the histopathology in MEN-2A hyperparathyroidism is nodular parathyroid chief cell hyperplasia. Grossly, this translates into asymmetric hyperplasia. The operative strategy is to preserve enough tissue for parathyroid function. It is recommended to remove enlarged glands even if the patient is eucalcemic at the time of thyroidectomy as the underlying disease will develop over time. In general, patients with MEN-2A should be treated with parathyroidectomy, removing only enlarged glands found at the time of operation. If hyperplasia is found, then a subtotal parathyroidectomy is needed, leaving part of the most normal-appearing gland in-situ with an intact pedicle. Because hyperparathyroidism in a young patient is quite morbid, treatment trends have shifted toward preserving parathyroid tissue rather than performing a subtotal parathyroidectomy as the initial operation if the other glands appear grossly normal.28–30

• What further testing should be undertaken at this time?

Given the patient’s strong family history of thyroid cancer and the young age of presentation, the child should undergo genetic testing.31 Ideally, a prophylactic thyroidectomy should be performed for patients known to carry RET mutations. Children with MEN-2A should undergo thyroidectomy by age 5 years, while children with MEN-2B should have a prophylactic thyroidectomy during infancy.32,33 Again, the specific codon mutation helps determine the appropriate timing of thyroidectomy.

Further testing would also include a baseline serum calcitonin level, as this will be used to monitor for recurrence after his initial treatment. Carcinoembryonic antigen is an additional tumor marker for MTC, but it is not specific for MTC.34 Since pheochromocytoma and hyperparathyroidism are part of the MEN-2 syndromes, serum or urinary catecholamines and a serum calcium should be checked prior to any operation.35 If this patient has biochemical evidence of pheochromocytoma, the localization and resection of that tumor should occur prior to any other operation, as surgery in the setting of untreated pheochromocytoma can be life-threatening.

CASE 3 CONTINUED

The boy undergoes genetic testing and is found to have a RET mutation. His baseline calcitonin level is 235 pg/mL. His serum calcium is normal and his plasma free metanephrines are within normal limits.

• What operation should be performed for this patient?

MTC should be treated with a total thyroidectomy and bilateral central cervical lymph node dissection. Lymph node metastases in the lateral neck are also common in medullary cancer.28 Neck ultrasound can be used to evaluate the extent of lymph node involvement. FNA preoperatively can confirm lymph node metastases. Since he has palpable disease in the right lateral neck, this patient should also undergo a modified radical neck dissection on the right side; if ultrasound reveals disease on the contralateral side, he may need a bilateral lateral neck dissection.

CASE 3 CONTINUED

The child is treated with a total thyroidectomy, bilateral central cervical lymph node dissection, and right modified radical neck dissection. The procedure is complicated by postoperative hypocalcemia. He is complaining of peri-oral numbness and his serum calcium level is 7.5 mg/dL.

• How would you treat this problem and what is the likelihood of this being a permanent problem?

HYPOPARATHYROIDISM AND HYPOCALCEMIA

Hypocalcemia after total thyroidectomy is due to hypoparathyroidism. Permanent hypoparathyroidism occurs in less than 3% of cases, whereas 10% of patients experience transient hypoparathyroidism.36 Knowledge of parathyroid development and anatomy can help the surgeon avoid damaging or inadvertently removing the parathyroid glands during thyroidectomy and thus prevent the development of hypoparathyroidism. The development of the parathyroid glands dictates their potential locations, and they can be found anywhere along their course of descent. The superior glands are typically located in the tracheoesophageal groove on the posterior aspect of the thyroid. Most upper glands are found close to the inferior thyroid artery; they are often at the cricothyroid junction or behind the upper or middle aspects of the thyroid lobe. More rarely, a superior gland can
be found above the upper pole or the retropharyngeal or retroesophageal space.36,37

Inferior parathyroids can normally be found on the posterolateral aspect of the inferior pole of the thyroid. Often, they are contained in the thyrothymic ligament or within the thymus itself. Other ectopic locations include the carotid sheath, the anterior mediastinum, or within the thyroid. The orientation of the parathyroid glands to the recurrent laryngeal nerve can serve as a guide for locating ectopic glands. Superior glands will lie posterior and lateral to the nerve, while inferior glands will be anterior or medial to the nerve.36

Surgical technique can help prevent hypoparathyroidism during thyroidectomy. The inferior thyroid artery should be ligated at its terminal branches close to the thyroid capsule rather than at its main trunk. The surgeon should also avoid thermal coagulation near the parathyroids, extensive mobilization, or accidental removal of parathyroids with the specimen. In this case, the patient underwent a total thyroidectomy with a central compartment lymph node dissection. It is difficult to preserve the lower parathyroids during this lymph node dissection, and they often require autotransplantation.38

Any ischemic or inadvertently removed parathyroid gland(s) can either be reimplemented in the sternocleidomastoid muscle, or the gland can be reimplemented into the brachioradialis muscle of the nondominant forearm. The forearm procedure avoids another neck operation and eases localization should the transplanted gland become hyperplastic. Resection of a recurrence in the forearm can be performed under local anesthesia. Regardless of the location, parathyroid autotransplantation involves the same basic steps. First, the parathyroid is cleaned of its associated fat. Next, it is minced with fine scissors. A pocket is created within the muscle, and the minced gland is inserted into the pocket. A single figure-of-eight stitch is used to close the pocket. Before cutting the sutures, several clips are placed to mark the site.

Postoperative hypocalcemia should be managed with oral calcium supplementation as this provides longer-lasting symptom relief and sustained elevation in serum calcium levels. Intravenous calcium gluconate can be administered for severe symptoms or electrocardiogram changes, but oral calcium should be given concomitantly since the intravenous calcium preparation will not last very long. In addition to measuring serum calcium, PTH or phosphate can also be measured to evaluate the degree of hypoparathyroidism. Activated vitamin D can be added to oral calcium supplementation when the PTH level is less than 10 pg/mL or the phosphate is above the normal limits.

CASE 3 CONTINUED

Postoperatively, the patient’s calcium normalizes in 5 days. In addition, his calcitonin level is undetectable. While still in the hospital, the patient’s mother asks if her son will receive radioactive iodine ablation.

- What is the role of radioactive iodine for MTC?

MTC arises from the parafollicular C cells and not the thyroid follicular cells. Since these cells do not concentrate iodine, radioactive iodine is not effective for MTC. For these reasons, surgical treatment is the mainstay of initial therapy and recurrence.31

ANAPLASTIC THYROID CANCER

CASE 4 PRESENTATION

A 77-year-old female presents with a rapidly growing, firm neck mass extending from the midline to the lateral neck. Her family says that her voice has become hoarse over the last 3 weeks, and she has also developed dysphagia but denies any dyspnea. Her primary care physician ordered a computed tomography scan of the neck that demonstrates a heterogeneous mass arising from the right thyroid but extending to the lateral neck, encasing the right common carotid artery and invading the internal jugular vein. FNA biopsy of this mass reveals pleomorphic, large, bizarre cells.

- What is the diagnosis and how should you counsel the family?

Anaplastic thyroid cancer is a poorly differentiated tumor that carries a very poor prognosis. All patients with this diagnosis are considered to have stage IV disease and usually die within months of diagnosis. It is subclassified into small or large cell types. Clinically, it is recognized by a hard mass with rapid progression and extension into local structures.1,39

- What treatment options are available?

If the disease is diagnosed early and the tumor is locally confined, then a total thyroidectomy should be performed. This scenario, however, occurs very rarely and the most common surgical procedure indicated for this type of thyroid cancer is a tracheostomy because the tumor directly invades the trachea. A combination of external beam radiation therapy
with doxorubicin-based chemotherapy is the standard treatment for anaplastic cancer. Dedifferentiation is associated with loss of the sodium-iodide transporter, so anaplastic thyroid cancer is unresponsive to radioactive iodine ablation.

This patient clearly has local invasion into the lateral neck, but does not appear to have invasion of the trachea. Therefore, multimodal therapy with chemotherapy and radiation would be the most appropriate treatment for this patient.

**CASE 5 PRESENTATION**

A 38-year-old female presents with a long-standing right thyroid nodule. She thinks it has been present since her mid 20s. She relates that she has had trouble swallowing lately. This is especially true for foods like bread and rice. Her TSH level is normal, and a recent ultrasound shows a 4.4-cm right thyroid nodule, slightly larger than a year ago when it was 4.2 cm. FNA biopsy of this nodule is consistent with a benign colloid nodule.

- **Would you recommend surgery at this time?**

This patient is experiencing compressive symptoms due to a large thyroid nodule. Compressive symptoms can include neck pain or pressure, dysphagia, or dyspnea. One or more of these symptoms in conjunction with a goiter or large nodule is an indication for thyroidectomy. Since this patient does not have any nodules on the left side, a right thyroid lobectomy should be recommended at this time.

**CASE 5 CONTINUED**

She undergoes a thyroid lobectomy and remains in the hospital overnight for observation. Approximately 4 hours postoperatively, she coughs forcefully and then begins complaining of increasing neck pressure and difficulty swallowing and breathing.

- **What is the most likely problem and how would you evaluate and treat it?**

Her history and symptoms are most consistent with a neck hematoma. Neck hematomas can be a life-threatening complication. Diagnosis is based on clinical assessment and exam. Imaging is rarely indicated and can be dangerous to obtain in a person with a potentially expanding hematoma. Neck swelling is often present, but given the deep location of the hematoma, it is not always evident on physical exam. Patients who are stable can be taken to the operating room for evacuation of the hematoma; for unstable patients or those in respiratory distress, it is safest to drain the hematoma at the bedside by reopening the incision prior to transporting them back to the operating room.

**CASE 5 CONTINUED**

After recovering from her re-operation, the patient sees you in clinic for follow-up. Her final pathology report reads “A 4.1-cm benign colloid nodule with an adjacent 0.4-cm single focus of papillary carcinoma. No evidence of extrathyroidal or lymph-vascular invasion.”

- **Should this patient undergo a completion thyroidectomy for this microcarcinoma?**

This patient has an incidental papillary microcarcinoma, defined as any tumor less than 1 cm in size. Despite an extremely low mortality, certain subsets of patients with microcarcinomas are prone to locoregional recurrence, making the optimal surgical treatment and the role of radioactive iodine ablation very controversial. The primary determinants of prognosis in papillary microcarcinoma are size, multifocality, capsular invasion, lymph node metastases, and growth. This tumor was identified incidentally, and therefore the decision to proceed with completion thyroidectomy is not informed by lymph node status or growth. Presumably, there were no obvious central compartment lymph nodes seen during her first operation. This is a unifocal tumor without capsular invasion—2 factors that would favor observation over further surgery. Several studies have tried to establish a cut-off size for recommending completion thyroidectomy. In general, tumors <5 mm rarely metastasize or recur, but this cut-off value has not been confirmed in all studies. Since her tumor is <0.5 mm, unifocal, and without other worrisome histologic features (high grade, insular or tall cell variants), then observation with biannual ultrasound is warranted. To slow or prevent growth of this tumor, TSH suppression with supplemental L-thyroxine can also be considered.

Truly incidental microcarcinomas are associated with decreased recurrence rates and more indolent behavior compared to microcarcinomas identified by preoperative FNA. Therefore, microcarcinomas that are identified preoperatively should be treated with a total thyroidectomy as the initial procedure. Current research in developing molecular diagnostics for thyroid...
cancer may help to clarify the appropriate treatment for incidental papillary microcarcinomas.

CONCLUSION

Thyroid cancer exists in a variety of histologic forms. Each type requires a unique surgical approach. Papillary thyroid cancer is the most common type and can be associated with lymph node metastases. Lymph node metastasis can be detected by ultrasound and FNA, and lymph nodes can be treated with compartment-oriented dissection. Follicular thyroid cancer is the other form of differentiated thyroid cancer; it cannot be differentiated from benign follicular adenomas by cytology alone. Therefore, a diagnostic lobectomy is required so that histology can distinguish benign from malignant follicular lesions. Both papillary and follicular thyroid cancer are considered differentiated thyroid cancer and can be treated with radioactive iodine ablation after surgical resection. MTC occurs in both sporadic and familial forms. Genetic testing is often appropriate, and the specific RET codon mutation helps guide therapy. Anaplastic thyroid cancer carries the worst prognosis. This type of thyroid cancer often presents with advanced disease, and tracheostomy or chemoradiation is frequently required.

The major complications of thyroidectomy are recurrent laryngeal nerve injury and hypoparathyroidism. Familiarity with the anatomy and attention to surgical technique can avoid these complications. Bleeding is a life-threatening complication after thyroidectomy and requires prompt recognition and drainage.

Thyroid cancer therapy continues to evolve. Genetic testing in MTC has already changed our approach and recommendations for prophylactic surgery. Newer molecular diagnostics for differentiated thyroid cancer will add to the information gained from ultrasound and FNA biopsy. This added information will likely translate into more tailored surgical treatment for each individual patient.

REFERENCES


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