Chapter 6
Cross-Sectional Imaging for the Evaluation of Thyroid Nodules and Cancer

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Introduction

Cross-sectional imaging is routinely used for most solid tumors in all phases of therapy: as part of the initial workup, preoperative planning, disease monitoring, and surveillance. Thyroid nodules and suspected thyroid cancers differ from other solid organ malignancies in several key aspects that diminish the utility and need for cross-sectional imaging: (1) The superficial anatomic location allows for comprehensive imaging with neck ultrasound alone in most cases, (2) detection of distant disease in patients with thyroid cancer is accomplished with radioiodine scanning following total thyroidectomy, and (3) the presence of distant metastases preoperatively does not alter initial management, which consists of total thyroidectomy in almost all cases. Furthermore, neck ultrasound can be done in the outpatient setting by the endocrinologist or endocrine surgeon, has lower cost compared to

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cross-sectional imaging, and does not involve radiation or intravenous contrast. This chapter reviews the circumstances when supplemental cross-sectional imaging is useful and also how to manage thyroid lesions found incidentally on cross-sectional imaging.

Initial Evaluation of Thyroid Nodules

In patients with palpable thyroid disease, the American Thyroid Association (ATA) 2015 guidelines for the management of thyroid nodules and thyroid cancer recommend routine initial diagnostic thyroid ultrasound [1, 2]. All subsequent workup depends on ultrasound findings. If neck ultrasound is negative, no further imaging is required. Suspicious findings on ultrasound may prompt serum TSH testing, fine needle aspiration biopsy, and/or radioiodine scanning to evaluate for lesion for the risk of malignancy. Cross-sectional imaging does not further inform the indication for these tests and procedures. Moreover, cross-sectional imaging should not be substituted for neck ultrasound unless there is an absence of ultrasound expertise. In clinical scenarios where ultrasound expertise is lacking, patients should be referred to higher volume centers for management of their thyroid disease when feasible.

Incidentally Detected Thyroid Nodules

With the rising utilization of CT, MRI, and PET scanning, an increasing number of thyroid nodules are discovered incidentally. Incidental thyroid lesions are detected in up to 16 % of CT and MRI scans and 2 % of PET scans [3–5]. Cross-sectional imaging alone is currently not sufficient for thyroid lesions. Neck ultrasound is still indicated. Cross-sectional imaging alone underestimates multi-nodularity when compared to neck ultrasound [6]. Consequently, the official recommendation by the ATA is to obtain thyroid ultrasound for all thyroid nodules incidentally detected on cross-sectional imaging [1, 2]. In addition, obtaining a fine needle aspiration biopsy (FNAB) at the time of ultrasound should be strongly considered because the rate of malignancy in incidentally discovered thyroid nodules is significant; the malignancy rate in thyroid nodules detected on neck CT and MRI ranges from 4 to 11 %, and the malignancy rate among hypermetabolic lesions seen on PET/CT can be as high as 42 % [6–8]. Of note, diffuse thyroidal uptake seen on PET scanning likely represents an inflammatory thyroiditis rather than a thyroid nodule; a thyroid ultrasound is still indicated to survey for thyroid nodules.

Indeterminate Thyroid Nodules

A significant number of thyroid nodules are cytologically indeterminate (Bethesda categories 3 and 4). Surgical excision has generally been recommended for indeterminate thyroid nodules despite the fact that the prevalence of malignancy is relatively low, ranging from 5 to 30 % [9]. Recently, molecular testing has gained considerable attention as a means of risk stratifying indeterminate thyroid nodules. That said, considerable interest remains in using PET for the same purpose. A meta-analysis by Wang et al. in 2013 determined that PET imaging could predict benign versus malignant disease in indeterminate thyroid nodules with a high negative predictive value and moderate positive predictive value [10]. However, due to limited and conflicting evidence, the ATA guidelines do not recommend routine PET imaging for thyroid nodules with indeterminate cytology [2].

Initial Preoperative Evaluation for Thyroid Cancer

For patients with suspected or biopsy-proven thyroid cancer undergoing preoperative evaluation, the 2015 ATA guidelines on imaging for thyroid cancer do not recommend routine cross-sectional imaging prior to initial surgery [11]. Neck ultrasound can provide sufficient information about the primary lesions and regional lymph nodes for preoperative planning in the vast majority of cases. Unlike most other solid tumors, staging and screening for distant metastases is performed postoperatively using serum thyroglobulin and/or functional radioiodine imaging instead of preoperative cross-sectional imaging [1]. This is because the detection of distant metastases prior to initial surgery does not obviate the need for total thyroidectomy. Even patients with metastatic disease need total thyroidectomy to properly receive radioactive iodine therapy, and thyroidectomy also allows disease monitoring using serum thyroglobulin. The minority of patients that may benefit from supplemental cross-sectional imaging are patients with clinical or sonographic evidence of locally advanced disease. Specific considerations and indications for each cross-sectional imaging modality (CT, MRI, PET) are described below.

Computed Tomography

Supplemental CT scanning in addition to ultrasound should be considered when there is an advanced primary tumor, bulky lymphadenopathy, or signs and symptoms of local invasion. The specific indications for preoperative CT scanning for

Fig. 6.1 Axial (**a**) and coronal (**b**) images from CT chest with intravenous contrast demonstrating a multi-nodular goiter with an enlarged thyroid gland, thyroid nodules with calcifications, and extension into the mediastinum

initial surgery for thyroid surgery are listed in Box 6.1. Sonographically, extrathyroidal extension and invasion of local structures will appear as a blurry or indistinct border (see Fig. 6.1). Locoregionally advanced disease is present in approximately 10–15 % patients with well-differentiated thyroid cancer [12, 13]. However, at our academic practice, only 5 % or less of patients with thyroid cancer require supplemental cross-sectional imaging in addition to neck ultrasound.

Box 6.1. Indications for Preoperative CT for Initial Surgery for Thyroid Cancer

- Clinical evidence of local invasion:
  - Hoarseness, voice changes
  - Stridor
  - Dysphagia
  - Fixed mass on exam
- Sonographic evidence of invasion of aerodigestive or vascular structures
- Large primary tumor and/or mediastinal extension
- Extensive nodal extension into:
  - Mediastinum
  - Deep structures of neck
- Lack of thyroid ultrasound capability/expertise

CT scanning allows better visualization of structures in the deep/posterior neck and mediastinum, i.e., those areas that lie at the limits of the acoustic window accessible by ultrasound. When extracapsular extension is suspected, CT scanning is reported to be 29–78 % sensitive and 91–99 % specific for invasion of the trachea,

esophagus, carotid artery, internal jugular vein, or recurrent laryngeal nerve [14]. Additionally, CT scanning carries the advantages of being widely available, reproducible, and user independent.

Assessment of the primary tumor and lymph nodes should include scanning from the skull base to the mediastinum. Intravenous contrast is needed to facilitate visual differentiation of tissues and should be used in all cases unless specifically contraindicated by allergy or renal insufficiency.

Iodinated contrast interferes with the uptake of radioactive iodine, an important component of thyroid cancer treatment. Thus, postoperative radioactive iodine ablation should be delayed for at least one month after the administration of iodinated contrast [15]. Because of this interaction, it is important to only obtain CT scanning when indicated. Finally, if CT scanning is performed, the decision to do so should be communicated clearly between surgeon and endocrinologist.

Magnetic Resonance Imaging

MRI is principally used for patients with an indication for cross-sectional imaging that have a contraindication for CT scanning, typically patients who have a known allergy to iodinated CT contrast. Since the gadolinium contrast used with MRI scanning does not interact with radioactive iodine, MRI may also be considered in patients with a strong, urgent indication for radioactive iodine therapy. The drawbacks to MRI include long image acquisition times, which can lead to motion artifact or feelings of claustrophobia, and increased risk of nephrogenic systemic fibrosis in patients with renal failure [16].

MRI images with and without contrast should be obtained. Thyroglobulin produced in lymph node metastases is hyperintense on T1-weighted scans (see Fig. 6.2). Papillary thyroid cancer typically has lower mean T2 signal intensity ratio (SIR) and apparent diffusion coefficient (ADC) than benign nodules; using T2 SIR and ADC combined, MRI has 93 % sensitivity and 93 % specificity for discrimination between PTC and benign nodules [17].

When dynamic contrast MRI was compared to US-guided FNAB in the evaluation of multinodular goiter for underlying thyroid cancer in 26 consecutive patients, Tunca et al. reported 100 % sensitivity and 100 % NPV compared to 71.4 % and 91.7 % sensitivity and NPV, respectively, for US-FNAB [18].

Positron Emission Tomography

The images generated by PET are low resolution and not suitable for operative planning. Similar to other solid organ malignancies, the primary use of PET scans is to evaluate for the presence of distant metastases (see Fig. 6.3). However, for the initial

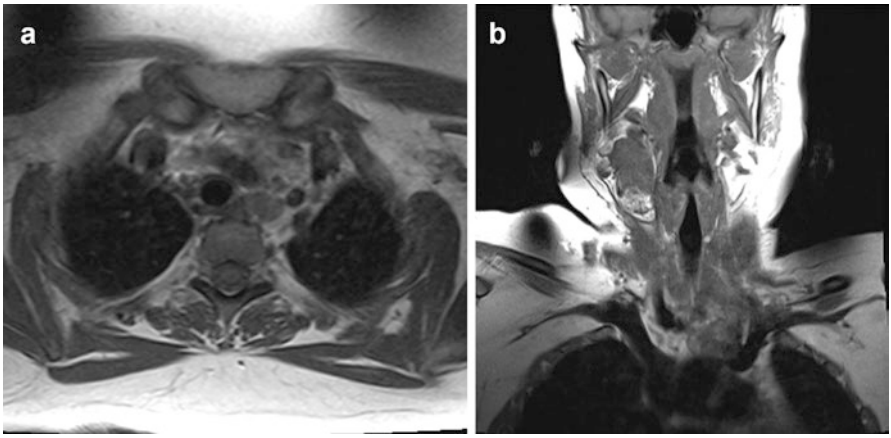

Fig. 6.2 T1 weighted axial (**a**) and coronal (**b**) images of MRI demonstrating paratracheal and neck lymphadenopathy in a patient with recurrent papillary thyroid carcinoma after total thyroidectomy

evaluation of thyroid cancer, this is achieved postoperatively with radioactive iodine scanning. Moreover, given their relatively low metabolic activity, most primary thyroid tumors and up to 70 % of metastases are non-FDG avid [19–22]. Thus, there is no role for PET or combined PET/CT scans for the initial evaluation of thyroid cancer.

Surveillance for Persistent or Recurrent Thyroid Cancer

Following surgery for thyroid cancer, patients should be assessed for persistent or recurrent disease using serum thyroglobulin (either on thyroid hormone therapy or after stimulation with recombinant human TSH) in combination with a neck ultrasound at 6–12 months postoperatively. The presence of disease as indicated by serum thyroglobulin or neck ultrasound may prompt further imaging. In patients who have undergone less than a total thyroidectomy or did not undergo radioiodine ablation, the absolute value of thyroglobulin is less meaningful, but an elevation in serum thyroglobulin from baseline should raise suspicion.

Conceptually, persistent/recurrent thyroid cancer can be classified as being either cervical or extracervical, with the former usually being managed surgically and the latter often being managed nonsurgically. The degree of thyroglobulin elevation provides some guide as to the anatomic location of persistent/recurrent disease, with the most common presentation being a small-volume locoregional lymph node recurrence associated with a thyroglobulin level in the single digits [23]. For such cases, ultrasound imaging alone is adequate. Patients with suspected extracervical disease may be evaluated with (1) diagnostic whole body scanning with radioactive iodine, (2) thin-cut non-contrast chest CT, or (3) 18 F-FDG PET scanning.

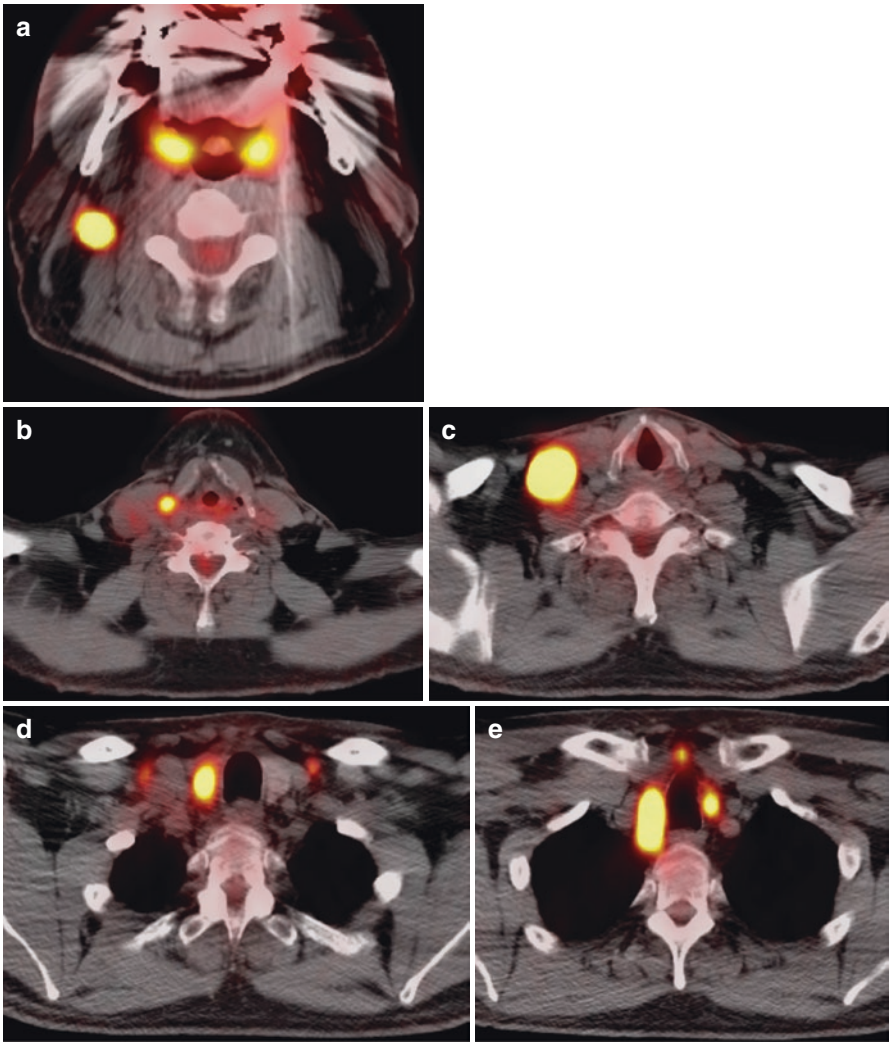

Fig. 6.3 Axial images from an 18-FDG PET/CT demonstrating (**a**, **b**, **c**) hypermetabolic lymphadenopathy in left neck levels II–V and a (**d**, **e**) hypermetabolic right thyroid nodule in patient diagnosed with metastatic papillary thyroid carcinoma

18 F-FDG PET scanning is most strongly indicated in the patient with suspected extracervical disease and negative radioactive iodine imaging [24–27]. The 2015 ATA guidelines recommend PET scanning in patients with negative RAI imaging and thyroglobulin greater than 10 ng/ml [2]. As some high-grade tumors dedifferentiate, they may lose their affinity for iodine and simultaneously become more hypermetabolic on PET scan [28]. The sensitivity and specificity of PET/CT in I^{131}-negative patients with suspicion of persistent or recurrent disease has been reported at 81 and 89 % [29]. The sensitivity of PET/CT may be improved with TSH stimulation [30].

Similar to the indications for chest CT in the initial evaluation for thyroid nodules and thyroid cancer, CT should be considered when there is extensive bulky lymphadenopathy and/or signs and symptoms of local invasion of aerodigestive structures. Additionally, chest CT should be obtained in patients with negative US and high serum thyroglobulin (>10 ng/ml) or rising serum thyroglobulin. While MRI can be considered as an alternative imaging modality for the neck, it is not as sensitive for pulmonary nodules as chest CT.

Conclusion

Cross-sectional imaging is uncommonly indicated in the evaluation of thyroid nodules and thyroid cancer. Supplemental cross-sectional imaging should only be performed in addition to neck ultrasound when there is evidence of extensive disease or invasion of aerodigestive structures. For thyroid cancer surveillance after initial surgery, cross-sectional imaging should be used to evaluate patients with negative neck ultrasound but high or rising levels of thyroglobulin.

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