

Thyroid Cytopathology: Evaluation of a Thyroid Nodule

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Abstract

The thyroid specialist frequently evaluates thyroid nodules because they may represent malignancy. Nodules are typically found on physical exam or incidentally when other imaging studies are performed. Malignant or symptomatic nodules that compress nearby structures warrant surgical excision. Yet, the majority of thyroid nodules are asymptomatic and benign, so the thyroid surgeon must rely on diagnostic studies to determine when surgery is indicated. Ultrasound is the preferred imaging modality for thyroid nodules, and the ultrasound guided fine needle aspiration biopsy (FNAB) is the preferred method of tissue sampling. Nodules one centimeter or larger, or nodules with suspicious sonographic appearance warrant cytologic analysis to better quantify the risk of malignancy. Molecular biomarkers are a powerful adjunct to cytology, as detecting malignancy pre-operatively allows total thyroidectomy in a single operation without the need for frozen section or a second operation for completion thyroidectomy if malignancy is found during the initial thyroid lobectomy.

Keywords

Thyroid nodule, Thyroidectomy, Biopsy, Thyroid cancer.

Introduction

The thyroid nodule is a common entity. While autopsy data indicate a 50% prevalence of thyroid nodules larger than one centimeter in patients without clinical evidence of thyroid disease, the prevalence of palpable nodules is only 4 to 7%, (1, 2). Ultrasonography is far more sensitive than palpation, as it detects nodules of any size in up to 67% of the general population (3). Thyroid nodules warrant removal when they are large enough to be symptomatic, or if there is a concern for malignancy. The majority of nodules are asymptomatic, and with only 5 to 10% of nodules being malignant, the decision to operate is made on therapeutic or diagnostic grounds (4, 5). Ultrasound imaging studies and cytology from fine-needle aspiration are the main tools used by the clinician to decide whether surgical excision of a thyroid nodule is warranted. Molecular genetic biomarker analyses are now being used to increase the accuracy of fine needle aspiration biopsies, and appear to substantially alter the clinical decision-making process as they become more widely available and more thoroughly evaluated.

Clinical Assessment

Patients most often present with a large palpable nodule in the neck or report of an incidental nodule found on imaging studies performed for another reason. A single dominant or solitary nodule is more likely to represent carcinoma than a single nodule within a multinodular gland, with an incidence of malignancy from 2.7 to 30% and 1.4 to 10% respectively (6). Yet, the overall risk of malignancy within a gland with a solitary nodule is approximately equal to that of a multinodular gland due to the additive risk of each nodule (7). Important elements in the patient's history which increase the likelihood of malignancy include prior head and neck irradiation (especially during childhood, with a relative risk of 8.7 at 1 Gy for x-rays and gamma-radiation), reports of rapid growth, dysphagia, dysphonia, male gender, presentation at extremes of age (less than 20 years or more than 70 years), and a family history of medullary thyroid carcinoma or multiple endocrine neoplasia (8, 9).

Physical exam findings that increase the concern for malignancy include:

- Nodules larger than 4 cm in size (19.3% risk of malignancy (10))
- Firmness to palpation
- Fixation of the nodule to adjacent tissues
- Cervical lymphadenopathy
- Vocal fold immobility

Imaging studies

Ultrasonography

Ultrasonography is the imaging study of choice for thyroid nodules. It can identify nodules too small to be palpated, the presence of multiple nodules, central, or lateral neck lymphadenopathy, and provides accurate measurements of nodule diameter for interval monitoring. Additionally, it allows characterization of nodules by sonographic features which suggest malignancy. Solid appearance (or hypoechogenicity), increased vascularity, microcalcifications, irregular margins, and the absence of a halo are features that have been consistently associated with malignancy

Fine-needle aspiration biopsy

Fine needle aspiration biopsy (FNAB) is the most important step in the workup of the thyroid nodule, as cytology is the primary determinant in whether thyroidectomy is indicated. FNAB is widely available and well tolerated, with a low risk of complications. Its use has dramatically decreased the number of thyroidectomies performed, and improved the yield of malignancy in glands that have been extirpated (27). FNAB can be performed with or without ultrasound guidance, but diagnostic accuracy is improved using sonographic needle localization due to a decreased number of inadequate specimens and false negative results (28).

Patients with lesions classified as follicular or oncocytic neoplasm, or suspicious for malignancy should be offered a diagnostic lobectomy in situations where molecular testing is not available.

Where diagnostic testing with BRAF and RAS mutations is available, finding one of these mutations in an indeterminate FNA specimen predicts malignancy with a 100% specificity and positive predictive value according to a recent prospective study (36). A 100% specificity for BRAF has been confirmed by a second prospective study (39). Finding one of these mutations in an indeterminate FNA specimen may be considered an indication for total thyroidectomy in some medical centers. Caution is advised, as a false positive BRAF mutation has been described. In this case, the final pathology was of atypical nodular hyperplasia which may be a premalignant lesion (37). Surgical excision of any RAS mutated cytology specimen in the form of lobectomy regardless of cytopathology must also be considered as it has an 87.5% risk of malignancy (36).

Conclusion

Thyroid nodules are common entities that a thyroid surgeon must evaluate. Nodules are found through physical exam, or incidentally through imaging modalities performed for other reasons. The majority of thyroid nodules are benign, but they warrant surgical excision when they are large enough to be symptomatic or if there is concern for malignancy. Ultrasound is the primary study by which the thyroid gland is imaged. Nodules one centimeter or larger or sonographically suspicious subcentimeter nodules warrant cytologic analysis through fine-needle aspiration biopsy (FNAB) to determine the risk of malignancy. Molecular biomarkers have shown great promise in their ability to detect malignancy in FNAB specimens, and are serving as a powerful adjunct to cytology where they are available. Detecting malignancy pre-operatively allows total thyroidectomy in a single operation without the need for frozen section or removal of the thyroid remnant in a second surgery. Cytology and molecular biomarkers are the primary diagnostic modalities a surgeon utilizes to determine the extent of thyroid surgery.

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