

THYROID NODULE

Background

1. Definition

- Focal enlargement of thyroid tissue
 - Solitary nodule
 - Dominant nodule with other nodules present
 - Multiple nodules, none dominant

2. General info

- Commonly asymptomatic
- Found on physical exam performed for other reasons
- Found on ultrasound or CT scan done for other reasons
 - Controversy about how and when to evaluate
- About 5% malignant
- More common in women

Pathophysiology

1. Pathology of disease

- Focal enlargement due to adenoma, cyst, cancer, autoimmune process

2. Incidence, prevalence

- Nodules very common
 - On palpation 1.5-6.5%
 - Ultrasound 20-76%
 - Autopsy 37-57%

3. Risk factors

- Head and neck irradiation as child or adolescent
- Family history of thyroid cancer
- Age
 - Nodule in a child
 - Age >60 and <30 at presentation increase risk of cancer
- Male sex
 - Nodules in men twice as likely to be cancer as those in women
- Dysphagia or hoarseness with thyroid nodule

4. Morbidity, mortality

- No cancer--no significant morbidity or mortality
- Cancer --related to cancer type and metastatic status

Diagnostics

1. History

- Sx of hyperthyroidism
- Sx of hypothyroidism
- Head and neck radiation
- Family Hx of thyroid cancer
- Prior thyroid cancer

2. Physical exam

- Thyroid palpation
 - Solitary nodule-- large > 4cm, hard, firm, irregular or fixed nodules=higher risk for cancer
 - Dominant nodule with other nodules present

- Multiple nodules, none dominant (thyroid enlargement/ goiter)
 - Exam of neck for nodes, other masses
- 3. Diagnostic testing
 - TSH¹
 - Low TSH, High T4 and/or T3= hyperactive thyroid (benign hyperfunctioning nodule) and no significant risk for thyroid cancer – radioactive iodine uptake and scan
 - Normal TSH – proceed to FNA
 - High TSH – proceed to FNA, free T4, anti thyroid peroxidase antibody to look for Hashimoto’s thyroiditis
 - FNA, ultrasound guided (US) FNA generally recommended^{1,2,3}
 - Non -palpable nodules found on imaging (eg, CT, U/S) and palpable nodules less than 1.5 cm^{1,2,4}
 - controversy exists about proper approach, majority recommend US on all^{1,2,4}
 - Nodules are common on these studies (perhaps 50%)
 - Guidelines vary on recommendations for US FNA, see US FNA below

4. FNA

Decisions about FNA and use of US guided FNA needs to be discussed with local experts who perform FNA and US. Individual local experts will have their own practice for FNA performance and US criteria for malignancy risk

- Fine-Needle Aspiration Biopsy (FNAB)
 - Best diagnostic test
 - Most cost-effective evaluation
 - Requires experience to perform procedure and interpret results
 - Histologic results from FNA, approximately
 - 5 % malignant, require surgery
 - 10 % indeterminate, require further evaluation
 - 70 % benign, require follow-up
 - 15 % nondiagnostic, require further evaluation
- Ultrasound guided FNA
 - Some guidelines recommend US guided FNA on ALL nodules^{1,2,3}
 - Some guidelines recommend US guided FNA on nodules >1.0 or >1.4 cm based on U/S markers of risk⁵
 - Data is unclear on risk of failure to diagnose malignancy in nodules < 1.0 cm but probably very low. Choice to proceed should take into account other risk factors and patient preferences.
 - Some cost effectiveness analysis suggests U/S guided FNA may lead to savings⁶
 - Some U/S features that more likely suggest cancer
 - Hypoechoic
 - Microcalcifications
 - Vascularity—intranodal vascular spots on color doppler
 - nodule longer than wide or AP to transverse diameter > 1.0
 - irregular margins or microlobulated margins
- Calcitonin level
 - Generally reserved for those with family history of medullary carcinoma of thyroid or MEN type 2

Recommended by some experts in evaluating thyroid nodules, especially prior to surgery^{1,7}

- Radionuclide imaging
 - Can tell if hot or cold but does not r/o cancer.
 - Not cost-effective as first evaluation, useful in hyperthyroid conditions

Differential Diagnosis

1. Cysts
2. Adenomas
3. Thyroid cancer
4. Multinodular goiter
5. Hashimoto thyroiditis
6. Primary thyroid lymphoma
7. Metastatic carcinoma of thyroid and neck

Therapeutics

Management based on results of FNAB

- Malignant cytopathology--Follicular, papillary or medullary thyroid carcinoma (~5%)
 - Refer to local expert
 - Thyroidectomy is usual course, but requires staging and workup
- Indeterminate cytopathology (sufficient cells, uncertain diagnosis)
 - US guided FNA, if not done initially
 - Repeat US guided FNA at clinically appropriate interval
 - Surgery without further evaluation
- Benign cytopathology (most common finding, ~65%)
 - Nodule suppression to limit further growth has limited impact, and is not generally recommended⁸
 - Repeat periodic evaluation—interval of exam one month to one year, depending on clinical scenario
 - If enlarging consider repeat FNA
 - Repeat U/S at 6 to 18 months¹
 - If nodule stable, repeat in 3-5 years¹
 - Repeat TSH periodically
 - Evaluate for hyper or hypothyroid based on TSH results
- cytopathology (insufficient cells for diagnosis)
 - Repeat FNA recommended first, consider U/S-guided FNA
 - Consider surgery if:
 - Nodule large (e.g.>2.5 cm)
 - Repeat FNA is nondiagnostic
- Management of cold area (nodule) on Grave's disease radioisotope scan
 - FNA generally recommended¹
- Management of hot nodule on radioisotope scan with low TSH
 - Radioactive iodine ablation treatment
 - Thyroid lobectomy
 - Younger patients
 - Those with larger nodules

- Nodules with significant hemorrhage or cystic components
 - Any patient who prefers surgery
- Management of benign functioning nodule on radioisotope scan with normal TSH
 - Radioactive iodine ablation is an option
 - Periodic clinical and TSH follow-up needed
- Management of cystic benign nonfunctioning nodule
 - Simple aspiration is an option (limited data)
 - Aspiration, instillation and flushing with 99% ethanol is an option^{1,9}

Prognosis

1. Non-cancerous lesions: no change in morbidity/ mortality
2. Cancer prognosis depends on type of cancer and metastases

Patient Education

1. http://www.thyroid.org/patients/brochures/Nodules_brochure.pdf (Accessed 10.5.2010)
2. <http://familydoctor.org/online/famdocen/home/articles/742.html> (Accessed 10.5.2010)

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4. Christopher R, J Decision Analysis of Discordant Thyroid Nodule Biopsy Guideline Criteria, Clin Endocrinol Metab, August 2008, 93(8):3037.
5. Management of Thyroid Nodules, Ultrasound Consensus Conference Statement, Radiology 2005 237; 794.
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8. Richter B, Pharmacotherapy for thyroid nodules: a systematic review and meta-analysis, Endocrinol Metab Clin North Am. 2002 Sep;31(3):699-722.
9. Bennedbaek FN, Treatment of Recurrent Thyroid Cysts with Ethanol, J Clin End & Metab 2003, 88(12):5773-5777.
10. Cibas ES, Fine-Needle Aspiration in the Work-Up of Thyroid Nodules, Otolaryngol Clin of North Am. 2010 Apr;43(2):257-271.
11. Lim S, Gibbons V, Conaglen JV. Assessment and Management of Thyroid Nodules in General Practice. New Zealand Family Physician 2007; 34(4):274-277.
<http://www.rnzcp.org.nz/assets/documents/Publications/Archive-NZFP/Aug-2007-NZFP-Vol-34-No-4/LimAugust07.pdf> Accessed 10.5.2010.

Evidence-Based Inquiries

1. What is the best way to evaluate thyroid nodules less than 1 cm in size?

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