

Solitary thyroid nodules: Surgical Approach.

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Background

- 5% of population have a palpable solitary thyroid nodule
- 50% of population have solitary nodule identifiable at autopsy
- If all nodules were removed less than 10% would prove to be malignant
- Thyroid surgery is not without complications
- Need selective surgical excision policy for thyroid nodules
- Conservative management is appropriate if malignancy can be reasonably excluded



Indications for excision of thyroid nodule

- Proven or suspected cancer
- Obstructive symptoms
- Patient anxiety
- Hyperfunctioning nodules resulting in hyperthyroidism
- Cosmesis



Assessment of thyroid nodules

History

- Rapid painless growth suggests malignancy
- Sudden painful growth suggests haemorrhage into degenerating colloid nodule
- Family history - 20% medullary carcinomas are familial associated with MEN 2 Syndrome



Thyroid nodule Risk Assessment

- History of radiation exposure
- Exposure to ionizing radiation has been shown to increase the risk of malignancy for a thyroid nodule to approximately 40%
 - In 1940s to 60s large numbers of children exposed in USA to low dose irradiation
 - Used in Rx of tonsillar hypertrophy, acne, thymus enlargement
 - In Israel Rx of Tinea Capitis with Radiation.
 - Increased incidence of thyroid malignancy - usually papillary
 - Most occult (<1.5 cm diameter) and multifocal
 - Usually good prognosis



Thyroid nodule Risk Assessment

- Medullary thyroid cancers (MTCs) may be familial 20% of the time, occurring in the multiple endocrine neoplasia (MEN) syndromes.

Some of the conditions associated with differentiated thyroid cancer include:

- familial adenomatous polyposis (FAP)
- phosphatase and tensin homolog hamartoma tumor syndrome (PHTS).
- Carney complex
- Werner syndrome.
- papillary renal cell carcinoma.



- Cold nodules found on radionuclide scan in patients with Graves' disease may be malignant 15% to 38%.
- Complex cysts may also have an associated malignancy approximately 17%.
- A nodule of >4 cm should undergo diagnostic thyroid lobectomy; (FNA) in this group of have up to a 34% false-negative rate.
- 40% of indeterminate lesions diagnosed on FNA were found on histologic section to be malignant



Thyroid Nodules in Children

- Thyroid nodules occur in children in an average of 1% of the population.
- The rate of malignancy in children with a nodule varies among studies at between 20% and 50%.



Risk Assessment Table

6 Section I • Thyroid

TABLE 1-1. Suspicious Clinical Characteristics of Thyroid Nodules

High Risk
Family history of medullary thyroid cancer or MEN syndrome
Rapid growth, especially during levothyroxine therapy
Hard or firm nodule
Fixation of the nodule to adjacent structures
Cervical lymphadenopathy
History of head or neck irradiation

Moderate Risk
Age younger than 20 years or older than 60 years
Male gender
Nodule >4 cm
Complex cystic nodule
Mass effect symptoms (dysphagia, voice change, dyspnea, cough)

MEN = multiple endocrine neoplasia.

Examination

- 80% solitary thyroid nodules occur in women
- The risk of malignancy is increased three fold in men
- Malignancy more common in children and >60 years
- Assess whether true solitary or dominant nodule within goiter
- True solitary nodule have 10% risk of malignancy
- Dominant nodule in multinodular goiter has 2-5% risk of malignancy



Examination

- Evidence of fixation or nodal involvement suggests malignancy
- Most patients will be clinically and biochemically euthyroid
- Obstructive signs - stridor, tracheal deviation, neck vein engorgement
- Hoarseness and vocal cord paralysis suggests recurrent laryngeal nerve palsy
- 50% solitary thyroid nodules in children are cancers
- 70% will have cervical and 15% pulmonary metastases on presentation
- Childhood tumors have good prognosis with greater than 80% 10 year survival



Investigation

Biochemical assessment

- Thyroid functional status - Free T4 and TSH
- Thyroid Antibodies - anti-thyroglobulin and anti-microsomal
- If positive family Hx → possibility of medullary carcinoma – calcitonin and CEA
- If of MEN2 Syndrome suspected: 24 hr urinary catecholamine estimations to exclude pheochromocytoma prior to surgery



Isotope scanning

- ^{131}I , ^{123}I or $^{99\text{Tc}}$ scanning provides functional assessment of thyroid
- Nodules classified as cold, warm or hot
- Unable to differentiate benign and malignant nodules
- Most solitary thyroid nodules are cold
- Most cancers arise in cold nodules
- Risk of cancer in a cold nodule is 10-15%
- Risk of tumor in a hot nodule is 1-2%
- Thyroid scan is of minimal use in evaluation of solitary thyroid nodules (except in HyThy)



Investigation

Standard radiography

- Chest radiography and thoracic inlet views if obstructive symptoms

Ultrasound

- Will define solitary and dominant nodules
- Will distinguish solid and cystic lesions
- Cancer can occur in the wall of a cystic lesion
- No reliable criteria to distinguish benign and malignant lesions



Computed Tomography, Magnetic Resonance Imaging and Positron Emission Tomography Scanning

- CT → limited but important role. CT is best used in advanced thyroid pathology when retrosternal, intrathoracic, or retrotracheal extension of the gland is present.
- It is essential to avoid administering iodinated contrast because it may complicate adjuvant
- radioactive iodine therapy if the thyroid nodule requiring resection is diagnosed as malignant.



- Positron emission computed tomography (PET) scanning is currently being investigated for use in determining malignancy status of thyroid nodules.
- PET scanning is increasingly being used for staging and for surveillance.
- The use of PET CT in other malignancies occasionally detects unsuspected thyroid cancer



Fine needle aspiration cytology

- Should be first line investigation of the solitary thyroid nodule
- With experienced cytologist diagnostic accuracy can be >95%
- Possible cytopathological diagnoses are:
 - Benign
 - Malignant
 - Indeterminate
 - Inadequate



aspiration cytology

- Can distinguish benign and malignant tumors except follicular neoplasms
- Diagnosis of follicular carcinoma depends on criteria that are unavailable in FNA.
- Follicular neoplasm on FNA lesion will require surgical excision.
- False negative rate less than 5% in most institutions. Repeat FNA increases accuracy.



aspiration cytology

Definitive FNA cytology allows:

- **Non-operative treatment with benign disease**
- **Appropriate surgical treatment of thyroid cancers at initial operation**
- **Surgery can be avoided in anaplastic tumors and lymphomas**
- **Reduces total number of unnecessary thyroid lobectomies**
- **Increases yield of thyroid cancers**

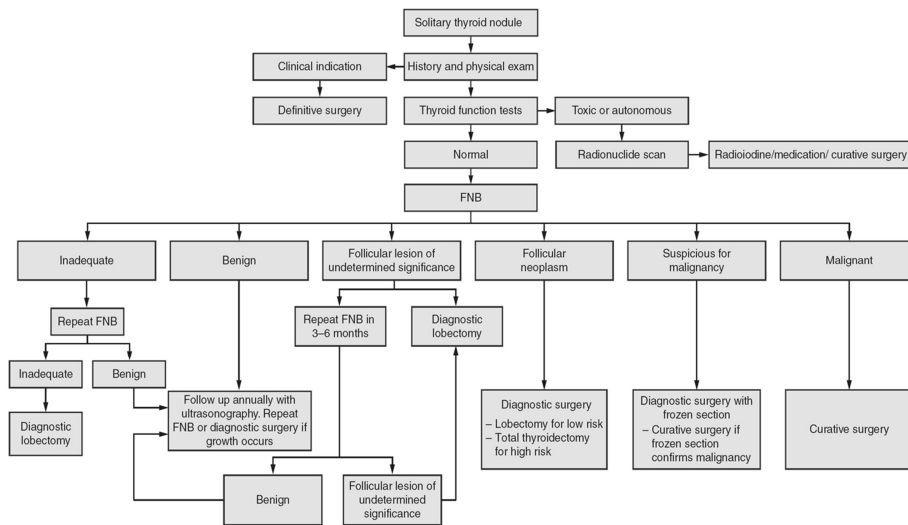


Indications for surgery after FNA cytology

- All proven malignant nodules
- All cytologically diagnosed follicular neoplasms
- All lesions exhibiting an atypical but non-diagnostic cellular pattern on cytology
- Cystic nodules which recur after aspiration
- When on clinical grounds the index of suspicion of malignancy is high even if the cytology report suggests it is benign



Summary Algorithm



Thyroid tumors Benign

- Most are follicular adenomas
- Papillary adenomas are rare
- All papillary tumors should be considered malignant



Follicular adenoma

- Of all follicular lesions - 80% benign and 20% malignant
- They are smooth and discrete lesions with glandular or acinar pattern
- They are encapsulated usually 2-4 cm in diameter
- Adenomas can not be differentiated from carcinoma on FNA cytology
- Requires histological assessment of capsular invasion



Follicular adenoma

- Various histological types are described:
- Embryonal - rudimentary acini. No Colloid
- Fetal
- Simple
- Colloid - Well formed acini. Much colloid
- Macrofollicular
- Microfollicular



Toxic adenoma

- Account for 5% of cases of thyrotoxicosis
- Female : Male ratio 9:1
- Presentation - 54% with a nodule and 37% with thyrotoxicosis
- 95-98 % of toxic adenomas are benign



Toxic adenoma

- Thyrotoxicosis usually not associated with eye signs.
- Hot nodule on scintigraphy.
- Treatment is by enucleation, thyroid lobectomy or I131 ablation.
- Requires post operative Eltroxin until suppressed gland returns to normal



Malignant thyroid tumors

- Differentiated thyroid cancer accounts for 80% of thyroid neoplasms
- Female : Male 4:1
- Usually presents as solitary thyroid nodule in young / middle age adult
- Nodule more likely to be malignant in man or child
- Papillary and follicular tumors are biologically very different



Comparison of papillary and follicular tumours

Papillary tumors	Follicular tumors
Multifocal	Solitary
Unencapsulated	Encapsulated
Lymphatic	Hematogenous
	spread
Metastasize to regional nodes	Metastasize to lung, bone and brain



Papillary and mixed tumors

- 50% tumors are less than 2 cm diameter at presentation
- Tumors less than 1 cm diameter regarded as minimal or micro-papillary lesions
- Psammoma bodies and 'orphan Annie' nuclei are characteristic histological features
- 30 - 50% are multi-centric with simultaneous tumor in contra-lateral lobe
- Early spread occurs to regional lymph nodes



Papillary Tumors

- 'Lateral aberrant thyroid' almost always metastatic papillary carcinoma
- Thyroid lobectomy adequate for minimal lesions
- Total thyroidectomy is otherwise surgery of choice
- Radioactive Iodine ablation is the default completion Rx.
- Many tumors are TSH dependent
- TSH suppression with post-operative thyroxine appropriate
- Thyroxine reduces recurrence and improves survival



Papillary Tumors: L.N. Dissection??

- 80% of nodes have microscopic involvement
- Role of prophylactic lymph node dissection at time of initial surgery unclear
- Lymph node dissection does not improve survival
- Alternative is to sample the lymph nodes (functional LN dissection)
- If negative - no further surgery
- If positive - modified neck dissection



Follicular tumors

- **Can not differentiate follicular adenoma and carcinoma on FNA cytology**
- **Treatment of all follicular neoplasms is thyroid lobectomy with frozen section**
- **If frozen section confirms carcinoma - Total thyroidectomy**
- **If frozen section confirms adenoma - No further surgery required**
- **Total thyroidectomy allow detection of metastases using 123I Scanning during follow up**
- **All patients require suppressive thyroxine therapy**



Follow up of thyroid carcinoma:

- Annual ¹²³I scanning to detect asymptomatic recurrence
- Treatment of such recurrence can still be curative
- Need to be off T4 for at least one month with high level of TSH
- Serum Thyroglobulin - increasing levels often first sign of recurrence
- May allow detection of recurrence without inconvenience of scintigraphy



Anaplastic carcinoma

- Accounts for < 5% thyroid malignancies
- Occurs in elderly and is usually an aggressive tumor
- Local infiltration causes dyspnea, hoarseness and dysphagia
- Thyroidectomy seldom feasible
- Incision biopsy should be avoided as it often causes uncontrollable local spread
- Radiotherapy and chemotherapy important modes of treatment
- Death usually occurs within 6 months



Thyroid lymphoma

- Accounts for 2% of thyroid malignancies
- Often arises with Hashimoto's thyroiditis or non-Hodgkin's B-cell lymphoma
- Presents as a goiter in association with generalized lymphoma
- Diagnosis can often be made by CNBx
- Chemotherapy with/without Radiotherapy is treatment of choice
- Prognosis is good - often more than 85% 5 year survival



Medullary carcinoma of the thyroid

- Accounts for 8% of thyroid neoplasms
- Arises from para-follicular C-cells
- 20% of cases are familial
- Autosomal dominant inheritance with almost complete penetrance
- Can occur as part of MEN IIa and MEN IIb syndromes
- 80% of cases are sporadic



MTC

- Sporadic cases usually unilateral
- 50% have lymph nodes at presentation
- Familial cases often multifocal and bilateral
- Tumors metastasize to nodes and systemically to bone, liver and lung
- They produce calcitonin, calcitonin gene related peptide and CEA
- Total thyroidectomy is the treatment of choice
- Calcitonin and CEA can be used in follow up for the presence of metastatic disease



PRACTICAL PEARLS

- Nodule formation in the presence of a history of ionizing radiation exposure carries a 40% risk of malignancy and warrants excision via total thyroidectomy.
- Thyroid cancer rarely, if ever, forms from benign nodules, but because of the false-negative rate of FNA nodules, it requires yearly follow-up with ultrasonography and physical examination.
- Atypical or follicular lesions may be treated by thyroid lobectomy because their risk of malignancy is low; however, discussion with the patient regarding a completion thyroidectomy should be done preoperatively because the pathology may demonstrate malignancy.

- Some patients do not prefer the possibility of an interval completion thyroidectomy. If contralateral nodularity is present, the patient may initially be offered a total thyroidectomy.
- Nodules with a high risk of malignancy should be treated via total thyroidectomy.
- Curative surgery for malignancy generally includes total thyroidectomy with ipsilateral central lymph node dissection on the side of the malignancy.
- Although rare, children with clinically detected thyroid nodules are at higher risk of malignancy than adults and as such warrant careful workup and evaluation.

