

Thyroid Nodules

Assessment & Management



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Introduction

- Prevalence of thyroid nodules :
 - 4-7% of population esp. 30-49yo
 - Common in female (4:1 = female : male)
 - Frequency increases with age
 - 5% malignant
 - Thyroid cancer – 0.4% of all cancer deaths

Types of thyroid nodule

1. Colloid nodules
2. Cystic nodules
3. Hyperplastic nodules
4. Inflammatory
 - e.g. lymphocytic thyroiditis, Reidel thyroiditis, viral (de Quervain's) thyroiditis, Hashimoto's
5. Neoplastic
 - Thyroid adenomas / carcinomas
 - secondary

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- Common causes:
 - simple colloid nodules
 - degenerative cysts
 - follicular adenomas
 - nodular thyroiditis

Importance

- To distinguish benign from malignant nodules
 - Hx
 - Exam
 - USS
 - FNA
 - Operative

Case Scenario

- 28yo female
- 4-5/52 lump in neck
- Asymptomatic (no pain/ breathing/ swallowing difficulties)
- No symptoms of hyper / hypothyroidism
- No family / personal Hx of cancer / thyroid disease
- No previous Hx of irradiation



History suggestive of thyroid cancer

1. male
2. <14 or > 65yo
3. Rapidly enlarging nodule
4. Pain, hoarseness, stridor / dysphagia
5. Previous exposure to ionizing radiation
6. Previous Hx of thyroid cancer
7. Family Hx of thyroid cancer (papillary / medullary)
 - PTC : auto dom, diagnosis at 30-40yo
 - Medullary : MEN II
8. Gardner's syn, FAP, Cowden syn (multiple hamartoma syn)

Previous exposure to ionizing irradiation

- Thyroid nodule - 40% chance malignancy
- 70-95% papillary cancer
- Kikuchi, et al 2003
 - Higher chance of multifocal CA
 - FNA = ^ false negative rate

Previous exposure to ionizing radiation

- esp. during infancy / childhood
 - Rx of enlargement of thymus, tonsils, adenoids and lymph nodes, acnes and tinea capitis
 - Japanese atomic bombing, Chernobyl power station
 - Radiation to head and neck and also for Hodgkin's lymphoma, cervical cancer, intra-abdominal / thoracic tumors
- Relative risk:
 - increases 5 to 10 yrs after exposure
 - peaks at 15 to 20 yrs then decreases
 - yet remain at 40 yrs

Case Scenario

- O/E
 - Euthyroid
 - No hoarseness
 - Firm, single nodule (3-4cm) of R lobe of thyroid
 - No cervical lymphadenopathy
 - Pemberton's –ve



Clinical examination

- Hard, fixed thyroid nodule – suspicious but not always cancer
- diffusely enlarged gland, with multiple nodules is more likely to be benign
- Cervical lymphadenopathy
- Hoarseness

Case Scenario

- Ix
 - TFT = normal
 - USS thyroid
 - 3.5 x 2cm predominantly solid nodule of the right lobe of thyroid gland
 - Rest of thyroid gland = normal
 - FNA
 - Non-diagnostic but suspicious of a papillary lesion



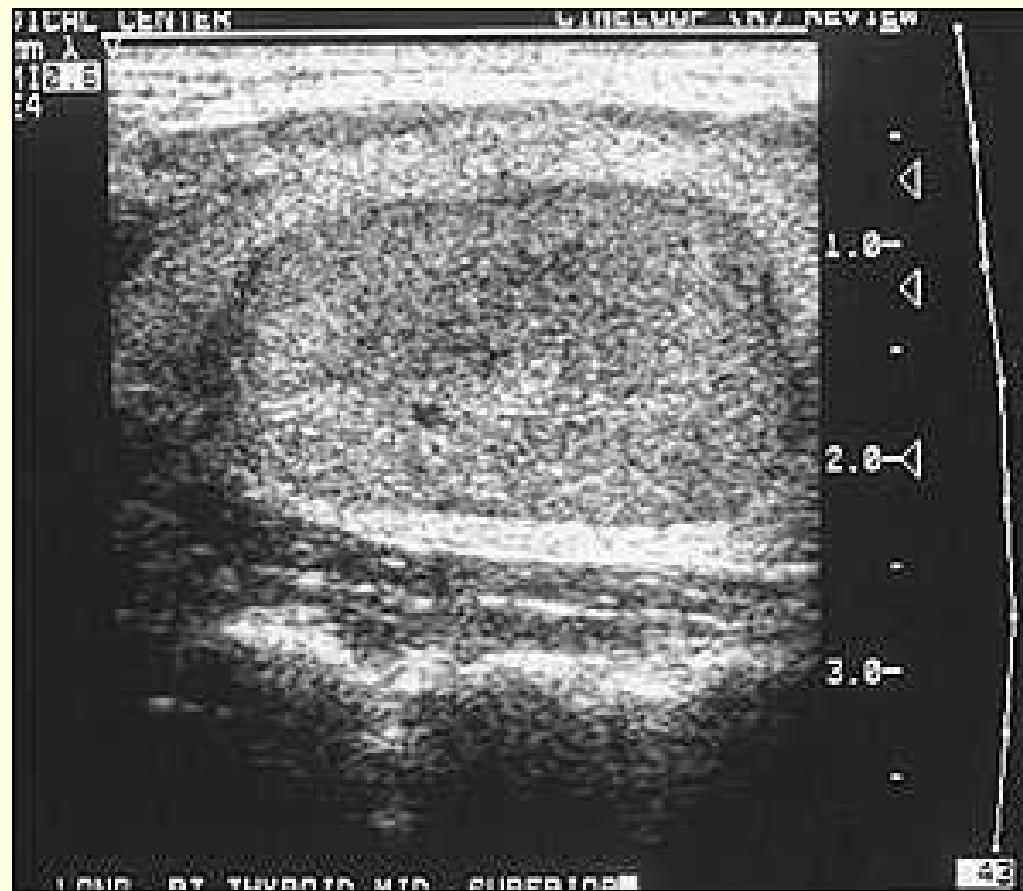
Ix

- TFT
- USS
- FNA
- CT / MRI
- ^{99m}Tc scan / ^{123}I

TFT

- Most patients with thyroid cancer are euthyroid
- Calcitonin
 - only measured if family Hx of medullary thyroid CA / MEN II
- Anti-thyroid Ab
 - *not* useful because it can be abnormal in both benign and malignant disease

USS



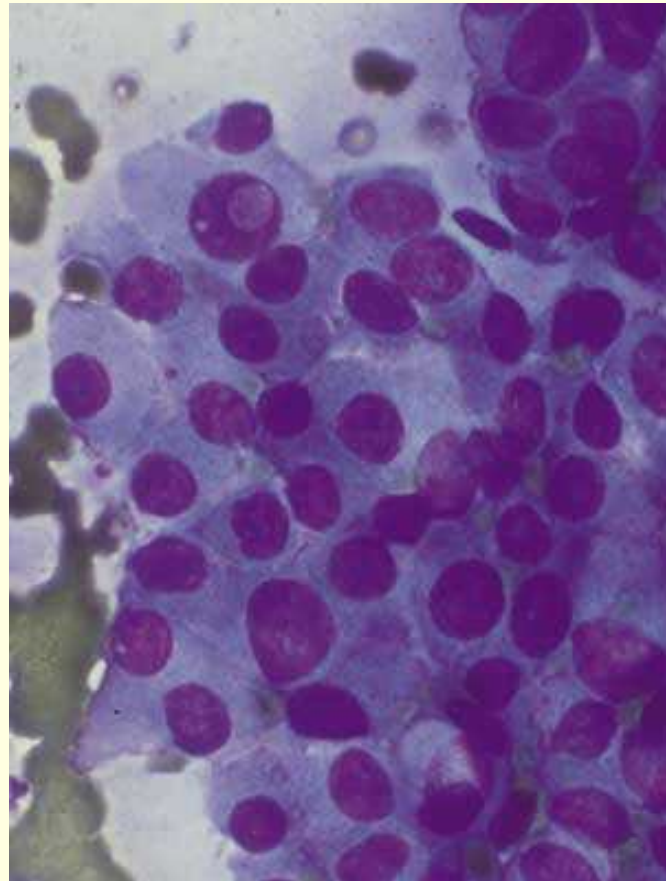
USS

- useful in assessing nodule's size, volume & characteristics, and to measure changes during F/U
 - not reliable in distinguishing benign from malignant nodules

USS

- Findings suggestive of malignancy
 - Microcalcifications
 - Irregular / microlobulated borders
 - Tall shape
 - Marked hypoechogenicity
 - Complex cysts

FNA



FNA

- Very useful in determining nature of thyroid nodule
- 5 diagnostic categories:
 - Benign
 - Malignant
 - Suspicious
 - Inconclusive (Follicular / Hurthle neoplasm)
 - non-diagnostic

FNA

- If result = **malignant / benign**

- 90% accuracy rate
- 1-10% false negative
- 2% false positive

- If result = **suspicious**

- 40-45% rate of malignancy

(Amrikachi, et al 2001¹)

- Trained cytologist

FNA

- USS guided FNA (Weiss, et al 2002²)
 - Sensitivity = 85.5% (USS guided vs 89.8% clinical FNA)
 - Specificity = 87.9% (USS guided vs 86.7% clinical FNA)
 - But unsatisfactory sample = 7.1% (vs 18.2%)
- Conclusion
 - USS guided FNA does not improve the result of FNA but decreases the rate of inadequate sampling

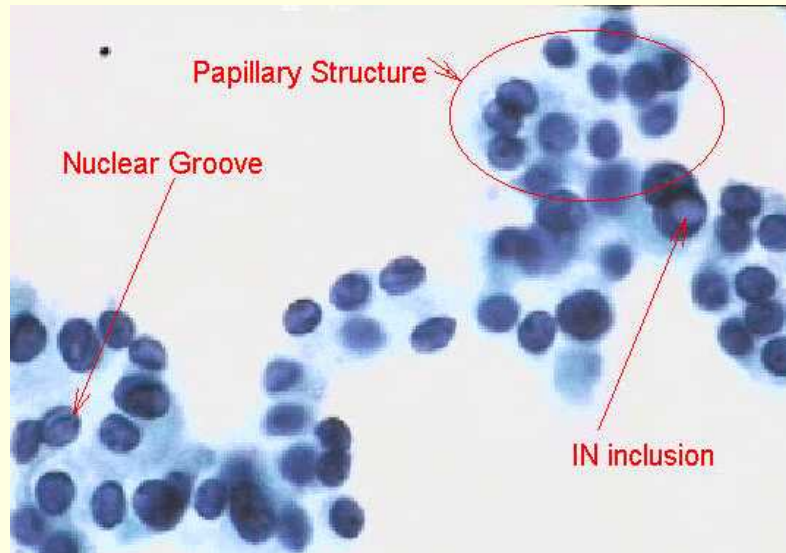
Pitfalls in FNA

- Follicular & Hurthle cell carcinoma cannot be distinguished from adenoma on FNA
 - Because capsular / lymphatic / vascular invasion is the criteria which is only seen on histology

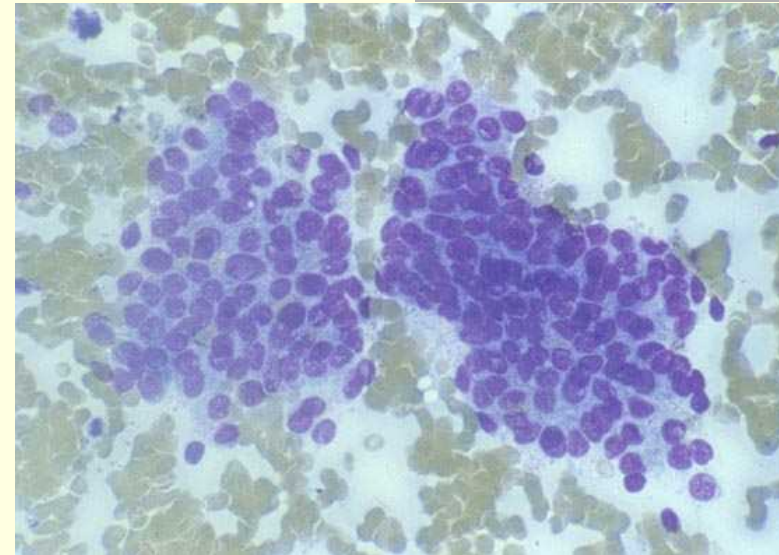
Other pitfalls in FNA

- Papillary CA – usually accurate diagnosis
- Medullary and Anaplastic CA – could be difficult to differentiate
- Lymphocytic lesions (lymphocytic thyroiditis vs. lymphoma)
- Cysts (difficulties with degenerative nodules)

FNA

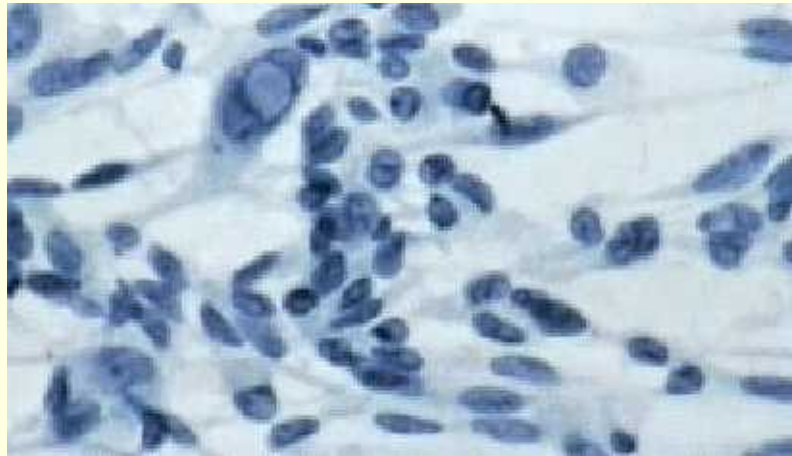


■ Papillary CA

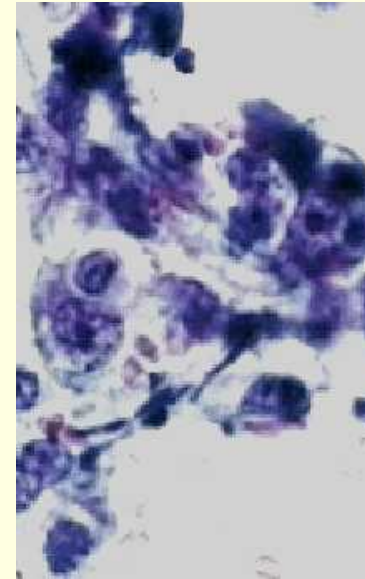


■ Follicular CA

FNA



■ Medullary CA



■ Anaplastic CA

CT



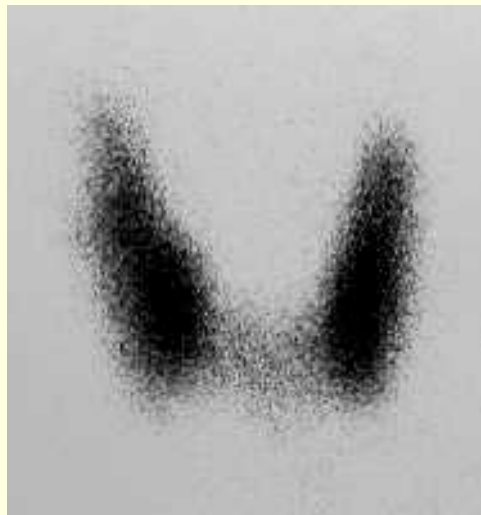
CT

- Assess:
 - Degree of retrosternal extension
 - Relation to trachea
 - Extracapsular spread / Invasion into surrounding structures
 - Local / distant metastasis

- No proven advantage with MRI

Nuclear Scintigraphy

- radioisotope scans are not very useful in determining treatment of solitary thyroid nodules

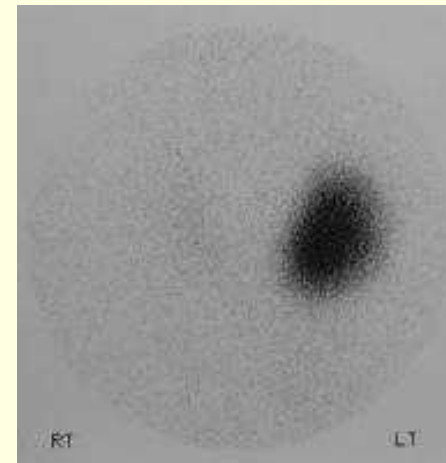


Nuclear Scintigraphy

- Nodules are classified according to their ability to take up isotope
- ^{99m}Tc
 - Trapped by thyroid gland but not organified
- ^{123}I
 - Trapped by thyroid gland then organified

Nuclear Scintigraphy

- cold nodule : 20% malignant
- warm nodule : 10% malignant
- hot nodule : 5% malignant



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- Occasional use with radioisotope scans
 - if cold nodule is shown up in patient with graves' disease, then surgery would strongly favoured over medical / radionuclide therapy
 - To show an hyperfunctioning nodule in hyperthyroid patient

Case Scenario

- Non-diagnostic FNA
- ? papillary lesion

- Treatment
 - Right Hemithyroidectomy



Treatment

Suspicious

Cystic

Benign

Malignant

Treatment of *suspicious thyroid nodules*

- Surgery is strongly recommended
 - Hemithyroidectomy
- Role of intra-operative frozen section
 - Not shown to be beneficial

Treatment of *cystic thyroid nodules*

- 70% adequately treated by FNA aspiration alone
 - cysts < 4cm and without solid components
 - less than 1% risk of CA (vs complex cysts = 15%)
 - but for cysts > 4cm, complex or recurrent (>3 asp)
 - Surgery



Treatment of *benign thyroid nodules*

- Repeat USS + follow-up
 - 6/12 then if no change in nodule, D/C

- ? Medical:
 - Suppressive therapy : short course (6/12 - 3yrs) of thyroid hormone medication
 - Not proven to be beneficial
 - Risks: osteoporosis, CVS side effects & thyrotoxicosis

Surgical treatment of *benign nodules*

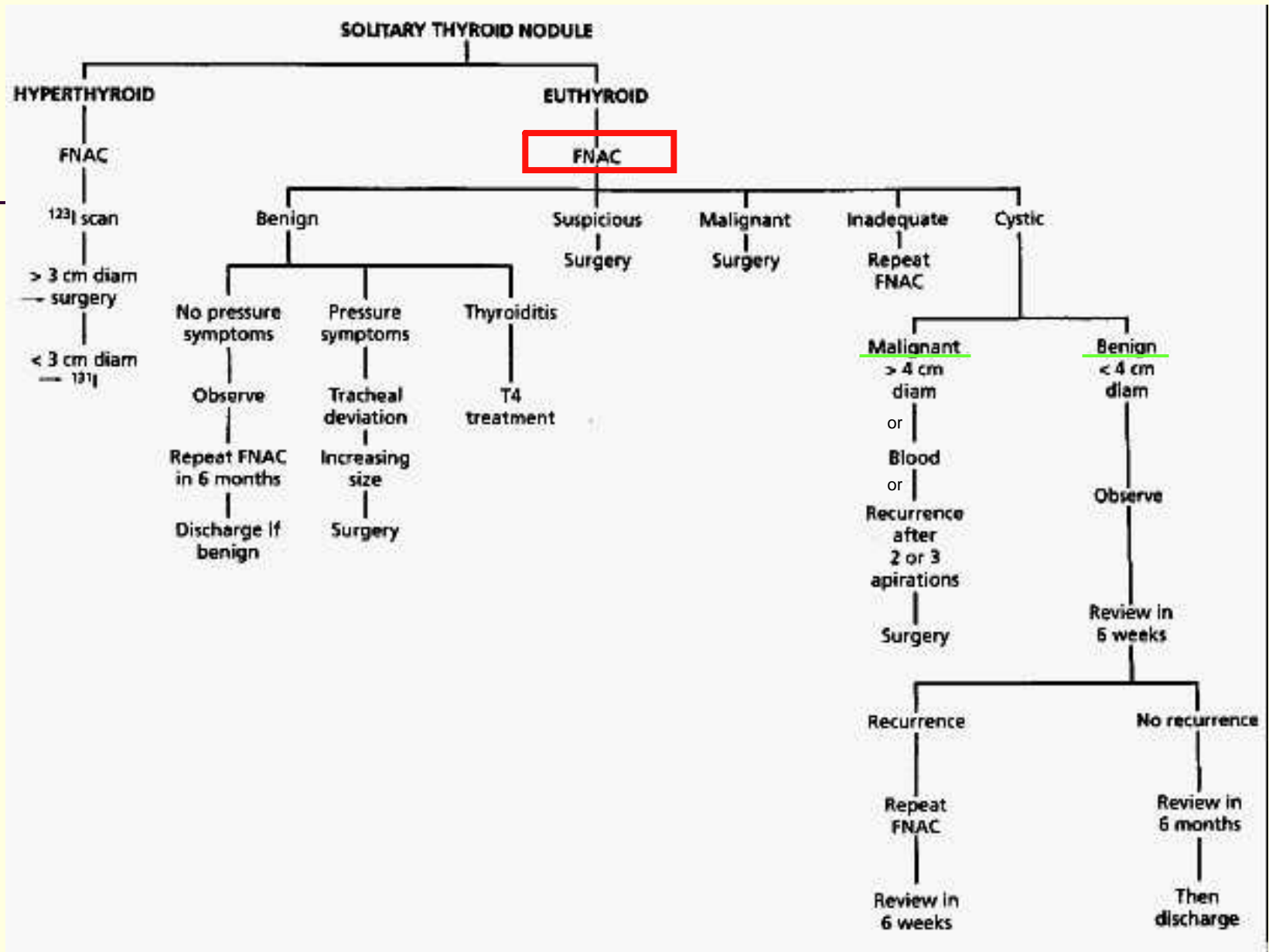
- common indications:
 - Risk of cancer (Hx / FNA)
 - Intrathoracic extension
 - Cosmetic reasons
 - Compressive symptoms
 - Thyrotoxicosis

Surgical Treatment of thyroid nodules

- Benign :
 - Hemithyroidectomy

- Malignant:
 - Hemithyroidectomy Vs Total thyroidectomy

 - post-op ¹³¹I
 - External beam radiation



Wong & Wheeler, WJS 2000³

FNA cytology results & interpretations (1)

(Delbridge et al, 1996⁴)

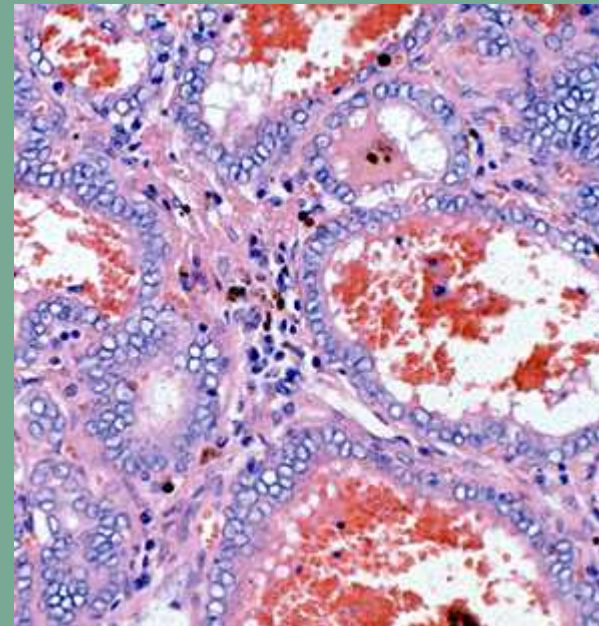
Category	Cytology	Interpretation
Inadequate	Not enough cells / too much blood	Needs to be repeated. If still inadequate treat on clinical grounds
Cystic	Cystic fluid with macrophages etc	Repeat aspiration if cyst recurs. Further recurrence / very large cyst requires surgery
Benign	Normal follicular cells with abundant colloid	Conservative Rx but repeat aspiration at least once in 6/12
Thyroiditis Hashimoto's subacute	Inflammatory cells	Specific therapy for thyroiditis

FNA cytology results & interpretations (2)

Category	Cytology	Interpretation
Atypical follicular pattern	Minimal colloid with a cellular microfollicular pattern	Generally indicates either : <ul style="list-style-type: none">■ follicular adenoma■ follicular carcinoma or■ hyperplastic nodule. Surgery is indicated since prevalence of follicular cancer is 20%
Malignant <ul style="list-style-type: none">■ Papillary■ anaplastic■ Medullary■ lymphoma	Cells characteristic of the specific type of malignancy	Surgery is indicated except for lymphoma

Case Scenario

- **Histology** (reviewed on Day 5 post-op)
 - follicular variant of Papillary CA
- **Completion** thyroidectomy (day 7)



Thyroid CA

- Papillary
- Follicular
- Medullary
- Anaplastic
- Others e.g. lymphoma, sarcoma
- Secondary e.g. breast & kidney

Hemithyroidectomy Vs Total Thyroidectomy for malignant disease

- Controversial
- Arguments for *total thyroidectomy*:
 - Multi-focality of disease
 - Ease of using radioactive iodine treatment
 - Use of thyroglobulin for F/U
 - Lower local recurrence rate
 - ?better survival
 - High incidence of complication in re-operative thyroid surgery
 - Low operative complication rate in experienced hands

- *Hemithyroidectomy*

- Lower risk of surgery

- Depending on prognosis

- Low risk patients = hemithyroidectomy

- High risk patients = total thyroidectomy

- For single nodule / non-determined diagnosis

- ?use of FS

Prognosis of Thyroid CA

■ 1979 (Mayo Clinic) – AGES

- Age
- Tumor grade
- Extent
- Size

■ 1988 (Lahey clinic) – AMES

- Age
- Mets
- Extent
- Size

■ 1993 – MACIS

- Metastasis
- Age
- Completeness of resection
- Invasion
- Size

■ GAMES

- Grade
- Age
- Mets
- Extent
- Size

■ TNM

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- Poor prognostic factors
 - Grade: High grade lesion
 - Age: Men >40yo, women >50yo
 - Mets : LN / distant mets
 - Extent:
 - extraglandular involvement
 - residual tumor after surgery
 - Capsular invasion
 - Tracheal invasion
 - Size: papillary >4cm, follicular >2cm

Solitary thyroid nodules in children

- FNA could be difficult to perform
- Incidence of CA is much higher than in adult
~ 30%
 - Papillary CA (85-90%)
 - Follicular CA (10-15%)
 - Thyroid CA = 3% of all childhood CA
 - high incidence of nodal and distant metastasis
 - better prognosis than adult

Summary

- Thyroid nodules are common
- most of thyroid nodules are benign
- Importance is to distinguish benign from malignant nodules

Summary - assessment

- Risk factors: male patients, very young / old age, history of previous irradiation, family Hx of thyroid cancer/ MEN 2
- FNA is the most useful test in determining treatment
- Follicular & Hurthle cell carcinoma cannot be distinguished from adenoma on FNA
- Inadequate samples need repeat FNA

Summary - treatment

- Most benign nodules are treated conservatively with observation, repeat USS & FNA
- Most cystic nodules are treated with aspirations
- Suspicious and malignant lesions need surgical treatment

References

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