THYROID CANCER

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Grand Rounds Presentation
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History

- 1812: Gay-Lussac discovered iodine as a cause of goiter.
- 1833: Boussingault prescribed iodized salt for prevention and treatment of goiter.
- 1836: T.W. King presented anatomical descriptions of thyroid gland.
- 1870: Fagge described sporadic and congenital cretinism.
History

1882 - 1917: Theodor Kocher (Bern) introduced techniques of thyroidectomy (>5000 cases). His mortality rate at the end of 19th century is as low as 1.8%

1880s: Billroth suggested bilateral partial thyroidectomy to prevent hypothyroidism.
History

- 1880: Williams S. Halsted: developed his thyroidectomy techniques in the US.
- Thyroid cancer was first described by Halsted by the terms “sarcomatous degeneration”, “thyroid tumor” or “thyroid cancer cells”
Embryology

- 4<sup>th</sup> week: thyroid gland appears.
- 5<sup>th</sup> week: break down of the thyroglossal duct, thyroid gland continue descending
- 7<sup>th</sup> week: thyroid gland migrates to its position, anterior to the trachea
- 10<sup>th</sup> week: thyroglossal duct disappears
Anatomy

- Locate deep to the sternohyoid muscle, from level C5 to T1 vertebrae or anterior to the 2\textsuperscript{nd} and 3\textsuperscript{rd} tracheal rings.
- Thyroid gland is attached to the trachea by the lateral suspensory (Berry) ligaments.
Anatomy

- Thyroid gland includes 2 lobes and isthmus.
- Isthmus: conical or pyramidal shape.
Anatomy

- Blood supply: sup. & inf. thyroid arteries
- Anatomy variant: thyroid ima artery, in 1.5% to 12%, in front of the trachea.
- Lymph vessels: drain to prelaryngeal, pretracheal and paratracheal nodes.
- Innervation: superior, middle, and inferior sympathetic ganglia.
Anatomy

- Venous supply
  - Superior and middle thyroid v. drain into the IJ
  - Inferior thyroid v. drains into the brachiocephalic trunk
Anatomy - Recurrent Laryngeal Nerve (RLN)

- Sim’s triangle
  - Carotid artery
  - Trachea
  - Inferior pole of thyroid

- LRLN runs parallel with the TEG

- RRLN runs diagonal with the TEG
Thyroid gland - Histology

- **Follicle:**
  - functional unit
  - Follicular cells
  - Contains colloid

- **Lobule:**
  - 20-30 follicles

- **Parafollicular cell or C-cell**
Euthyroidism control:
1. TRH (thyroid releasing hormone) and TSH (thyroid stimulating hormone)
2. Thyroid gland: synthesis, storage, secretion of thyroxine (T4), triiodothyronine (T3)
3. Peripheral control metabolism of T3, T4
Thyroid Nodule Statistics

- 3%-7% population, female is 6.5%; male is 1.5%
- 4% of these nodules are malignant, 1% of all cancers
- Male have a higher risk of being cancer
- Single nodule is more likely malignant than multiple nodules
- Nodules in children and the elderly have a higher risk of malignancy
History Taking

- Age, gender
- Thyroid mass or nodule (time coarse, growth)
- Associated symptoms
  - Pain, hoarseness, dysphagia, dyspnea, stridor, hemoptysis
- Radiation, goiter, Hashimoto’s, Grave’s, other cancers.
- Family history of thyroid and other endocrine tumors.
Physical exam

- Complete head and neck exam
  - Bimanual palpation of thyroid gland and cervical chain of lymph nodes

- Laryngoscope:
  - Evaluate for vocal cord mobility and symmetry
Diagnosis

Needle biopsy:

- Core needle biopsy:
  - Adequate tissue for diagnosis
  - Disadvantages
    - more difficult
    - more traumatic
    - more complications
Diagnosis

- Fine needle aspiration (FNA):
  - Easy to perform, less morbidity.
  - FN: 0.3-10%; FP: 0-2.5%
  - Disadvantages
    - less tissue for diagnosis
    - limit in differentiation of certain types of thyroid cancers
      - Follicular adenoma vs. carcinoma
      - Hurthle cell adenoma vs. carcinoma
Diagnosis-FNA
Diagnosis

Blood test:

- T4, T3, TSH (thyroid function tests)
- Ca, P (hyperparathyroidism asso. with TC)
- TG (increase in recurrent WDTC)
- Calcitonin (increase in MTC)
Diagnosis – U/S

- Sensitive (80%)
- Detect nodule 2-3 mm
- F/u cystic asp., re-collection of fluid
- FNA guide.
Diagnosis - Imaging

- **CT:**
  - Detect tracheal invasion
  - Evaluate for cervical metastasis

- **MRI**
  - Useful to detect residual, recurrent and metastatic carcinoma.
  - T2 differentiates tumor and fibrosis.

- **CXR:**
  - Tracheal deviation, airway narrowing, lung metastasis.
Diagnosis – thyroid scan

- Radioactive iodine or technetium uptake
- Before FNA – test of choice for initial w/u
- Uses today
  - Indeterminate FNA
  - Large benign nodules (> 4cm)
Thyroid Cancer

Classification:

1. Well-differentiated malignant neoplasms (85% of thyroid cancer)
   * Papillary thyroid carcinoma (PTC)
   * Follicular thyroid carcinoma (FTC)
   * Hurthle cell carcinoma (HCC)
2. Poor differentiated malignant neoplasms
   * Medullary thyroid carcinoma (MTC)
   * Anaplastic thyroid carcinoma (ATC)
   * Insular thyroid carcinoma (ITC)

3. Other malignant tumors:
   * Lymphoma
   * Metastatic tumors
Papillary Thyroid Carcinoma (PTC)

- Most common WDTC - 75%-85%
- 80%-90% of radiation-induced TC
- Peak incidence: 30s-40s
- 10 year-survival: 84%-90%
- Female:male ratio is 3:1
PTC – pathology Variants

- Microcarcinoma
- Macrocarcinoma
- Encapsulated
- Follicular
- Oncocytic
- Solid
- Diffuse Follicular
- Diffuse Sclerosing
- Tall Cell
- Columnar
- Dedifferentiated
PTC - pathology

**Gross**

- Non-encapsulated
- Central necrosis with fibrosis or hemorrhage
- Cystic degeneration in large tumors
- Multicentricity in 75% of tumors
- High rate of metastasis to regional lymph nodes (50%)
PTC - pathology

- Histology
  - Psammoma bodies
  - Columnar thyroid epithelial
  - Well-formed fibrovascular cores
PTC - pathology

- **Histology**
  - Papillary projections
  - Nuclei
    - Vesicular and ground-glass “Orphan Annie” appearance
    - High N:C ratio
    - Mitotic figures
Follicular Thyroid Carcinoma (FTC)

- 5%-10% of thyroid cancers, 15% of WDTC
- Peak in 50s
- Female:male ratio is 3:1
- 10-year survival rate: 86% in non-invasive tumors, 44% in invasive tumors
FTC - pathology

Gross
- Well-encapsulated
- Cystic degeneration, calcification, hemorrhage
- Tendency invade the thyroid capsule and blood vessels.
FTC - pathology

- Histology
  - Follicular pattern with vesicular nucleolus cells
FTC - pathology

- Histology
  - Capsular and vascular invasion
Hurthle Cell Carcinoma (HCC)

- Most aggressive type of WDTC
- About 5% of WDTC
- High incidence of bilateral thyroid lobe involvement
- High incidence of recurrence and high mortality
Medullary Thyroid Carcinoma (MTC)

- Account for 5% to 10% of all thyroid cancers
- Tumor of the calcitonin-producing parafollicular or C-cells
MTC

- Sporadic
  - 80% of MTC
  - Poorer prognosis
  - Unifocal
  - Not associated with other endocrine tumors
  - Peak in middle age to elderly
MTC

- Familial
  - 20% of MTCs
  - Autosomal dominant inheritance
  - Associated with C-cell hyperplasia
  - Associated other endocrine tumors
  - Peak in 30s.
MTC Family traits

- Sipple’s syndrome (MEN II a)
  - MTC
  - Pheochromocytoma
  - hyperparathyroidism

- 2. Wermer’s syndrome (MEN II b)
  - MTC
  - pheochromocytoma
  - mucosal neuromas
  - marfanoid habitus.
MTC

- 50% have regional metastases to lymph nodes.
- Distant metastasis include: lung, liver, adrenal glands, and bone (osteoblastic)
Medullary carcinoma

- **Gross**
  - gray to yellow, firm, well-circumscribed or invasive with bilateral multicentric involvement.

- **Histology**
  - Hyperplastic C-cells contain immunoreactive calcitonin
Anaplastic Thyroid Carcinoma (ATC)

- Undifferentiated differentiated CA
- 3% of thyroid cancers
- Most aggressive, poorest prognosis
- Uncapsulated, extension outside the gland
- Death in several months due to airway obstruction, vascular invasion, distant metastasis.
- Higher incidence in pre-existing multi-nodular goiter
Anaplastic Carcinoma

- **Gross**
  - fleshy, tan-white appearance, with hemorrhagic and necrotic areas.

- **Histology**
  - spindle or giant-cell
Malignant Lymphoma

- 2%-5% of thyroid cancers
- Increase in Hashimoto’s or endemic goiter areas
- Most common in > 50s
- Prognosis factors: cell types and stages
Malignant Lymphoma

- **Gross**
  - large, yellow-tan, scaly with hemorrhagic and necroptic areas

- **Histology**
  - small cell non-cleaved type (MC) and large cell non-cleaved follicular
Metastatic carcinoma

- Found in 2%-4% of patients who died of cancer
- MC from: malignant melanoma, lung, kidney, breast, colon.
- Mets. by lymphatic or vascular deposits of tumor emboli
## THYROID GLAND

**TX:** Primary tumor cannot be assessed

**T0:** No evidence of primary tumor

**T1:** Tumor 1 cm or less in greatest dimension limited to the thyroid

**T2:** Tumor more than 1 cm but not more than 4 cm in greatest dimension limited to the thyroid

**T3:** Tumor more than 4 cm in greatest dimension limited to the thyroid

**T4:** Tumor of any size extending beyond the thyroid capsule

### Summary of Stage Groupings

#### Papillary of Follicular

#### Under 45 Years

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#### 45 Years and Over

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#### Medullary

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#### Undifferentiated

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Management of the Thyroid Nodule

Serial exam

- Physical examination
  - Benign
  - Asymptomatic palpable nodule

- U/S
  - F/u a benign, nonpalpable nodule
  - F/u a cystic nodule for reaccumulation
Management of the Thyroid Nodule

- Trial of suppression of TSH
  - Benign or indeterminate FNA (controversial)
  - Maintain TSH level between 0.1 and 0.5 mlU/L per day
  - Decrease tumor volume up to 50% in 40% pts.
  - A shrinking tumor is not likely malignant
Management WDTC

Surgical options

- Total thyroidectomy
- Thyroid lobectomy
  - benign or inconclusive frozen section
- Near total thyroidectomy
  - Preserve minimal thyroid tissue, RLN, parathyroid glands.
- +/- Neck dissection
  - N0 – Elective neck dissection is not indicated for WDTC
  - N+ - Level II-V and VI neck dissection
    Level I if clinically + nodes - rare
Adjuvant therapy:

- **Post-op radioactive iodine**
  - Total body scan to evaluate for residual and mets
  - If positive, I-131 ablation performed
  - Pts should be hypothyroid (TSH > 50 mU/l) prior to scan
  - Patients are followed with yearly scanning X 5 years

- **External beam radiation therapy**
  - Advanced locoregional WDTC with gross residual
  - Tumors that do not pick up I-131
  - Unresectable bone mets
  - More sensitive in follicular & papillary vs. Hurthle cell
Management of HCC

- Tx of choice is thyroidectomy
- Thyroid lobectomy
  - Adequate with benign frozen section
  - Completion thyroidectomy for indeterminate frozen section malignant on final pathology
- Tumors are unresponsive to external beam radiation or I-131
- Post-op thyroid suppression is indicated because tumors have TSH receptors.
Management MTC

- Surgery: Thyroidectomy and SLND (level II, III, IV), anterior compartment ND (include level VI, and/or VII).
- 10-year survival rate is 90%
- Recurrent MTC: resistant to chemo and XRT
Management ATC

- Dx: FNA or open biopsy
- Usually unresectable
- Tracheotomy for airway obstruction
- Tx with the combination:
  * Surgery: thyroidectomy/ND, debulking surgery
  * Chemotherapy: Adriamycin and Cisplatin
  * XRT: only external beam, tumor does not concentrate I-131,
Surgical complications

Non-metabolic complications

- **Nerve injury**
  - SLN (laryngeal sensation) – up to 5% incidence
    - Unstable voice
    - Diff. high pitch,
    - Dysphagia and aspiration
    - Laryngoscopy: bowing of VCs, ipsilateral rotation or displacement of affected VC.
  - RLN up to 1-2% incidence
    - Unilateral – no treatment vs medialization procedure
    - Bilateral: re-intubate, tracheotomy
Surgical complications

Non-metabolic complications:
- Hemorrhage: thru the drains, neck swelling
- Airway obstruction
  - Hematoma
  - Laryngeal edema
  - Bilateral RLN injury
- Chyle leak
- Pneumothorax
Surgical complications

Metabolic complications:

- **Hypocalcemia: 5% of thyroidectomy**
  - Prevention - autotransplantation of parathyroid glands
  - Treatment – IV vs PO calcium replacement and Vit. D

- **Thyroid storm**
  - More common in pts. with hyperthyroidism or chronic systemic diseases
    - Tx. supportive
    - Beta blockers
    - Muscle relaxants
Prognostic factors

- Histology: is an important factor
- Age: is a significant factor, e.g. WDTC
- Sex: female have more risk of thyroid nodule; males have more risk of thyroid cancer
- Size: tumor > 1.5 cm has poorer prognosis
- Extracapsular, vascular invasion or metastases disease are poor prognosis factors
- History of radiation: high risk of papillary CA
Prognostic factors

- Mayo clinic: “AGES” including age, grade, extracapsular tumor, and size.
- Lahey clinic: “AMES” including age, metastasis, extracapsular tumor, and size.
Conclusion

- Thyroid cancer is relatively rare (1% of all cancers), one of the most curable cancer.
- Surgery is the treatment of choice for most of thyroid cancers
- Preservation of the RLN and normocalcemia are the goals for a successful thyroidectomy
- Surgical complications are preventable and treatable