Thyroid Cancer

- Thyroid carcinoma currently represents 1.5% of all newly diagnosed cancers in the US
- 17,000 new cases are diagnosed annually
- Locally invasive presentation of well differentiated thyroid carcinoma occurs in less than 5% of cases
- Invasive thyroid carcinoma refers to disease which protrudes beyond the capsule
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.
Anatomy

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

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

- Left RLN runs parallel with the tracheoesophagel groove

- Right RLN runs diagonal with the TEG
History

- Time course and growth of thyroid mass or nodule
- Associated symptoms
  - Pain, hoarseness, dysphagia, dyspnea, stridor, hemoptysis (these symptoms may be associated with malignancy)
- Goiter
History

Risk factors

• Thyroid exposure to irradiation
  - low or high dose external irradiation (40-50 Gy [4000-5000 rad])
  - especially in childhood for:
    - large thymus, acne, enlarged tonsils, cervical adenitis, sinusitis, and malignancies
  - Up to 5% of pts with history of low-dose radiation exposure develop a thyroid malignancy
  - When patients present with a solitary nodule and history of radiation exposure, 40% of these nodules will harbor carcinoma
History

- **Risk factors**
  - **Age and Sex**
    - Age less than 15 or greater than 45 places a patient at greater risk for having carcinoma
    - Benign nodules occur most frequently in women 20-40 years
    - Men have a higher risk of a nodule being malignant
History

- Family History
  - History of family member with medullary thyroid carcinoma
  - History of family member with other endocrine abnormalities (parathyroid, adrenals)
Physical exam

- Complete head and neck exam
  - Bimanual systematic palpation of thyroid gland and cervical chain of lymph nodes
    - Metastatic adenopathy commonly found:
      - in the central compartment (level VI)
      - along middle and lower portion of the jugular vein (levels III and IV)

- Indirect or fiberoptic laryngoscopy
  - vocal cord mobility
  - evaluate airway
  - Pyriform or subglottic extension
  - preoperative documentation of any unrelated abnormalities
Physical exam

- Examination of the thyroid nodule:
  - consistency - hard vs. soft
  - size – < 4cm
  - Multinodular vs. solitary nodule
    - multi nodular - 3% chance of malignancy
    - solitary nodule - 5%-12% chance of malignancy
  - Mobility with swallowing
  - Mobility with respect to surrounding tissues
  - Well circumscribed vs. ill defined borders
Diagnosis

- Initial step in evaluating the routine patient with a thyroid nodule should include a thyroid stimulating hormone level (TSH).
- If normal then the next step involves ultrasound examination of the thyroid to assess the number and characteristics of the nodules and then performing a fine needle aspiration (Wein and Weber, Otolaryngol Clin N Am 38 (2005) 161-178).
Diagnosis

- If the TSH is high, treatment with thyroid replacement therapy should be initiated and FNA should be performed when the patient is considered euthyroid.
- Individuals with low TSH, may have hyperfunctioning nodule and should be evaluated with thyroid scan. These lesions have low likelihood of malignancy (Wein and Weber, Otolaryngol Clin N Am 38 (2005) 161-178).
Diagnosis – U/S

- Sensitive (can detect nodule 2-3 mm)
- Nodules ≥ 1 cm, in 2 dimensions are considered biologically significant
- FNA guide.
Diagnosis – U/S

- **Advantages**
  - Sensitive procedure for identifying lesions in the thyroid (2-3mm)
  - Can detect the presence of lymph node enlargement and calcifications
  - Noninvasive and inexpensive

- **Disadvantages**
  - Unable to reliably diagnose true cystic lesions
  - Cannot accurately distinguish benign from malignant nodules
Diagnosis

- **Fine needle aspiration (FNA):**
  - Easy to perform
  - Less morbidity
  - **Disadvantage**
    - Limit in differentiation of certain types of thyroid cancers (evidence of capsular or vascular invasion necessary for diagnosis)
      - Follicular adenoma vs. carcinoma
      - Hurthle cell adenoma vs. carcinoma
  - **Pathologic results are categorized as:**
    - Positive
    - Negative
    - Indeterminate
Diagnosis- Imaging

- Radiologic imaging for regional spread of carcinoma can include CT or MRI.
- Diagnostic imaging criteria for CT or MRI include:
  - Recurrent disease
  - Clinical lymph node metastasis
  - Vocal cord paralysis
  - Fixation of the tumor mass to adjacent anatomy
  - Presence of upper aerodigestive symptoms suggestive of invasive disease
Diagnosis - Imaging/Endoscopy

- **CT:**
  - Readily accessible, but may delay RAI postoperatively
  - Detects tracheal invasion and evaluate for cervical metastasis

- **MRI:**
  - Excellent soft tissue evaluation for findings such as cervical esophageal invasion with the use of contrast material that will not conflict with potential future treatments
  - Useful to detect residual, recurrent and metastatic carcinoma.
  - T2 differentiates tumor and fibrosis.

- **CXR:**
  - Tracheal deviation, airway narrowing, lung metastasis.

- **Panendoscopy:**
  - May be considered in certain patients before surgical resection to assess and reconstruction for intraluminal spread of tumor and aid in planning for surgery
Classification of Malignant Thyroid Neoplasms

- Papillary carcinoma
  - Follicular variant
  - Tall cell
  - Diffuse sclerosing
  - Encapsulated
- Follicular carcinoma
  - Overtly invasive
  - Minimally invasive
- Hurthle cell carcinoma
- Anaplastic carcinoma
  - Giant cell
  - Small cell

- Medullary Carcinoma
- Miscellaneous
  - Sarcoma
  - Lymphoma
  - Squamous cell carcinoma
  - Mucoepidermoid carcinoma
  - Clear cell tumors
  - Plasma cell tumors
  - Metastatic
    - Direct extension
    - Kidney
    - Colon
    - Melanoma

- Direct extension
- Kidney
- Colon
- Melanoma
Papillary Thyroid Carcinoma (PTC)

- Most common well differentiated thyroid carcinoma (WDTC) – 60-70%
- 85%-90% of radiation-induced thyroid carcinoma
- Peak incidence: 30s-40s
- Female: male ratio is 2:1
- Lymph node involvement is common
PTC - pathology

- Gross
  - Unencapsulated but often have a pseudocapsule
  - Central necrosis with fibrosis or hemorrhage
  - Cystic degeneration in large tumors
  - High rate of metastasis to regional lymph nodes (50%)
PTC - pathology

**Histology**
- Papillary projections
- Psamomma bodies
- Well-formed fibrovascular cores

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

- 10% of thyroid cancers
- Mean age is 50 years
- Female: male ratio is 3:1
- Occur more frequently in iodine deficient areas
- Less likely to spread via lymphatic pathways, but may spread through local extension and hematogenous spread
- Distant metastasis is more common than in papillary, especially at presentation.
FTC - pathology

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

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

- Most aggressive type of WDTC
- About 3% of thyroid malignancies
- High incidence of bilateral thyroid lobe involvement
- High incidence of recurrence and high mortality
Hurthle Cell Carcinoma (HCC)

- Fine needle aspiration typically demonstrates hypercellularity and the presence of eosinophilic cells.
- Cytologic differentiation between adenoma and malignant tumor is extremely difficult.
- Histologic findings of capsular or vascular invasion confirm the presence of Hurthle cell carcinoma.
Medullary Thyroid Carcinoma

- Account for 5% to 10% of all thyroid cancers
- Tumor of the calcitonin-producing parafollicular or C-cells
- Sporadic
  - 70% of MTC
  - Poorer prognosis
  - Unifocal
  - Not associated with other endocrine tumors
  - Peak in middle age to elderly
Medullary Thyroid Carcinoma

- Familial
  - 30% of MTCs
  - Autosomal dominant inheritance
  - Associated with C-cell hyperplasia
  - Associated other endocrine tumors
  - Peak in 30s.
Medullary Thyroid Carcinoma

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

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

- **Histology**
  - spindle or giant multinucleated cell are present
6th edition of the AJCC TNM staging system for thyroid cancer has undergone revision

Some specific changes include:

- T1 now includes all tumors ≤ 2 cm
- N1a nodes now refer to metastasis in Level VI (pretracheal, paratracheal, and prelaryngeal/Delphian) lymph nodes, and N1b nodes now refer to metastasis to unilateral, bilateral, or contralateral cervical or superior mediastinal lymph nodes.
- T4a tumors refers to those cancer with extracapsular spread, that are resectable, and T4b tumors refer to those that have unresectable extension.
All anaplastic carcinomas are T4.
- T4a refers to those tumors that are surgically resectable, intrathyroidal anaplastic carcinoma
- T4b refers to those that are surgically unresectable extrathyroidal anaplastic carcinoma

Stage groupings for patients with papillary and follicular carcinomas > 45 has been revised, recognizing that pts > 45 with differentiated thyroid cancer do not do as well

Stage III disease refers to those patients with minimal extrathyroidal extension
Staging

- **Stage IVA**
  - Tumors (any size) extends beyond thyroid capsule, invading subcutaneous soft tissues, larynx, trachea, esophagus, or recurrent laryngeal nerve (RLN)

- **Stage IVB**
  - Tumors invade preverterbral fascia, carotid artery or mediastinal vessels

- **Stage IVC**
  - Advanced tumors with distant metastasis
Prognostic factors

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

- **Histology:** the cell type is one of the most predominant prognostic factor and influences other risk factors.

- **Age:** at the time of diagnosis is a significant effected risk factor, e.g. well-differentiated thyroid carcinoma has a greater tendency to invade the surrounding structures in patients older than 40. Mortality rate increases significantly in patients older than 60.

- **Sex:** females are at a higher risk of developing thyroid nodules, however, males have a higher risk of thyroid cancer. Tumors are more aggressive and the prognoses are poorer in males than those in females.
Prognostic factors

- **Size** of primary lesions: the larger the size of the tumor the greater the risk of vascular invasion or metastatic spread. Tumors greater than 1.5 cm carry a higher risk of recurrence and mortality.

- **Extracapsular** or vascular invasion and *metastatic* disease are poor prognosis factors. Regional metastasis in papillary carcinoma correlates positively with the incidence of local recurrence. Well-differentiated thyroid cancer, which invades and paralyzes the recurrent laryngeal nerve requires a wider resection. Distant metastases are rare in papillary cancers, but more often seen in follicular tumors, and are associated with poorer prognosis.

- **History of radiation** is associated with higher risk of papillary carcinomas requiring more extensive resection to eradicate disease
Treatment Considerations

- When a follicular neoplasm's obtained on FNA, 80% benign, 20% carcinoma
  - Of this 20%, up to 50% have the diagnosis of follicular variant of papillary carcinoma

- For patients with follicular carcinoma the most important prognostic parameter is age, not sex.
  - Patients 45 years of age or older at the time of diagnosis have a worse prognosis than their younger counterparts.

- Individuals with carcinomas greater than 5 cm fare worse, probably because of extracapsular spread.

- Patients with vascular invasion do worse than individuals with capsule invasion.

- Insular carcinoma is also considered to be a variant of follicular carcinoma that presents with more advanced-stage disease at diagnosis, a higher frequency of metastasis, and a decreased survival when compared with pure follicular carcinoma.
Treatment Considerations

- Papillary carcinoma has a number of variants requiring special consideration.
  - The diffuse sclerosing variant is a rare subtype that tends to present in women younger than 25 years of age.
    - Tumor size is large at presentation (mean, 6.9 cm) with 100% of patients developing regional lymph node metastases.
    - Despite these factors, prognosis seems to be favorable when aggressive care is rendered.
  - The tall cell variant, representing approximately 5% of papillary carcinomas, is also considered an aggressive subtype with a worse prognosis.
    - Typical presentation is in the older patient with a large tumor, extrathyroidal extension, and nodal metastases.
  - The follicular variant of papillary carcinoma, representing approximately 24% of cases, is more frequently multicentric but has clinical behavior similar to pure papillary carcinoma.
Treatment Considerations

- Hürthle cell carcinomas, considered by some to be a variant of follicular carcinomas, represent only 3% of all thyroid tumors.
  - Ipsilateral lymph node metastases are present in 25% of patients.
  - In patients with metastases, only 38% of lesions demonstrated uptake of radioactive iodine (RAI)
Invasive Carcinoma

- The locally invasive presentation of well-differentiated thyroid carcinoma occurs in less than 5% of all cases.
- The most common pathology involved is papillary carcinoma.
- There is a male predominance with patients presenting at a higher mean age than those with noninvasive disease.
- Invasive thyroid carcinoma spreads by direct extension from the primary tumor or from extracapsular spread of paratracheal nodal metastasis.
- Tumor at the primary site has the capacity for invasion through the cricothyroid membrane or the thyroid cartilage anteriorly or may extend posteriorly to wrap around the thyroid cartilage and present in the region of the piriform sinus.
Invasive Carcinoma

The goals of treatment for invasive thyroid carcinoma include

- prevention of hemorrhage and airway obstruction
- preservation of a functional upper aerodigestive tract
- prevention of locoregional recurrence
- long-term survival.

Few disagree that the goal in treating invasive thyroid carcinoma is to remove all macroscopic disease noted at the time of surgery.

Wein and Weber summarized that

- For individuals with limited tracheal deficits but gross intraluminal spread of tumor, window and sleeve resections are necessary.
- For larger defects, up to one third the circumference of the tracheal, use of sternocleidomastoid and pectoralis major myoperiosteal flaps over T-tubes has been described.
- For larger defects, tracheal resection with re-anastomosis with release procedures while preserving at least one recurrent laryngeal nerve has been described with favorable results.

- Retrospective review of 1200 pts with diagnosis of well-differentiated thyroid carcinoma (EBM rating: C-4)
- 49 pts (5%) showed involvement of an adjacent structure (larynx, trachea, esophagus)
  - 30 female
  - 19 male
- Type of surgery, radiation treatment, radiiodine treatment, and pt demographics evaluated

- Most common pathologic finding was papillary carcinoma (43 pts, 88%)
- Follicular carcinoma, including Hurthle cell carcinoma was noted in 6 pts (12%)
- Anaplastic tumors were excluded

- All patients underwent total thyroidectomy and central neck dissection
- Eighteen also had functional neck dissection (37%)
- For extrathyroidal involvement, two main approaches were used
  - Radical surgery to excise all microscopic disease, with or without adjuvant therapy (n=16)
    - 9 total laryngectomies, 6 partial tracheal resections, 1 partial esophagectomy
  - Surgery for macroscopic disease only, followed by iodine and radiation treatment for microscopic residual disease (n=33)

- Overall 5 year survival for invasive carcinoma was 78%, compared to 93% of noninvasive disease.
- The only statistically significant factor was large tumor size.
- Concluded that conservative procedures followed by radioiodide treatment were associated with similar survival rates aggressive techniques, with less perioperative mortality and lower overall mortality.
Extended Surgical Resection

- Surgical treatment of invasive thyroid carcinoma should remove all gross disease especially in medullary carcinoma.
- Fixation to the thyroid cartilage may require partial or full thickness removal of the thyroid structures.
  - Thyroid cartilage lamina can be removed without major morbidity if the internal thyroid perichondrium is left intact (Cummings, 2005).
- The trachea can be partially resected and repaired to permit en bloc tumor removal with primary anastomosis performed for resections up to 4 tracheal rings (Cummings, 2005).
Extended Surgical Resection

- Tracheal shavings can be performed, leaving the internal mucosa intact
- Isolated full-thickness defect can be repaired with composite mucosal cartilage grafts from the nasal septum
- With more extensive skeletal involvement, partial laryngectomy may be required
- Total laryngectomy should be performed in extreme cases with extensive intraluminal invasion (Cummings, 2005)
  - Typically this would be done after failure of radioiodine treatment, external beam radiation treatment, or both.
- Pharyngeal and esophageal local invasion typically requires resection of the immediate area and primary closure
Management
ATC

- Dx: FNA or open biopsy
- Usually unresectable
- Most have extensive extrathyroidal involvement at the time of diagnosis
  - surgery is limited to biopsy and tracheostomy
- Tracheotomy for airway obstruction
- Treatment with the combination:
  - Surgery: thyroidectomy/ND, debulking surgery for palliation
  - Chemotherapy
  - XRT: only external beam, tumor does not concentrate I-131, palliative
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
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
    - Treatment. supportive
    - Beta blockers
    - Muscle relaxants
Conclusion

- The goal of management for invasive thyroid cancer is to remove all gross disease especially in medullary carcinoma.
- Postoperative treatment with radioactive iodine is generally effective with papillary and follicular carcinoma, less likely with Hurthle cell variant or medullary carcinoma.
- Type of cancer and risk grouping can affect prognosis of cancer and treatment.
References