Management of Invasive Thyroid Cancer

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Well-differentiated thyroid carcinoma (WDTC)
• ~80% of all thyroid cancers
• Multifocal disease common
• Frequent regional lymph node involvement
• Excellent prognosis
• Direct extrathyroidal extension is unusual (10-15%)

Locally invasive WDTC
• Worse prognosis
• Higher local recurrence
• Bulky regional nodes, ECS
• Increased distant metastasis
• More common in older patients, men

Locally invasive WDTC
• Associated with aggressive histologic features
  – Tall cell
  – Trabecular
  – Insular
  – Poorly differentiated thyroid carcinoma
Locally invasive WDTC

- Invades adjacent structures
  - Strap muscles
  - Recurrent laryngeal nerve
  - Larynx
  - Trachea
  - Pharynx
  - Esophagus

Molecular biology of locally invasive WDTC

- WDTC typically have higher propensity for metastasis rather than invasion
- Invasive properties
  - Basement membrane disruption
  - Breakdown of extracellular matrix
  - Loss of adhesion proteins:
    - E-cadherin
    - β-catenin

Pre-Operative Evaluation

- Clinical signs/symptoms suggesting locally invasive thyroid cancer
  - Hoarseness
  - Immobile thyroid mass
  - Stridor
  - Dysphagia
  - Hemoptysis

Pre-Operative Evaluation

- Physical examination
  - Cervical Nodes
  - Central Compartment
  - Endo-laryngeal examination
    - Assess for vocal cord palsy
    - Visible intra-luminal growth?
Pre-Operative Evaluation

• Imaging
  – Ultrasound—excellent for thyroid bed, lateral neck

• Imaging
  – MRI—define tumor invasion of upper aerodigestive tract

• Imaging
  – CT—need to avoid contrast limits utility, but useful especially to evaluate chest

• Fine needle aspiration biopsy
  – Thyroid
  – Nodal metastases
Surgical Management

- Management of aerodigestive tract invasion by thyroid carcinoma has been controversial
  - Complete resection with negative microscopic margins vs.
  - Gross tumor resection (“shave”)

- Complete excision regardless of stage of larygotracheal invasion
- Improved survival compared to incomplete resection
- Low complication rates for tracheal resection with primary anastomosis

Bayles et al (1998)
- Similar survival, but improved local control with complete resection

- Complete resection vs. gross tumor resection (“shave excision”) + RAI have equivalent survival
- Incomplete resection (gross residual disease) has lower survival

Czaja McCaffrey (2006)
- 286 patients with aerodigestive tract invasion by thyroid carcinoma
  - 124 patients with larynx or tracheal invasion
    - 34 complete tumor excision (neg micro margins)
    - 75 shave excision (all gross tumor removed)
    - 15 incomplete excision (gross residual disease)
  - Laryngotracheal invasion—worse prognosis
  - Complete vs shave excision—no difference in survival
  - Gross residual disease—worse survival
Surgical Management

- Czaja McCaffrey (2006)
  - Removal of all gross disease is major factor for ultimate survival
  - Gross intraluminal tumor should be resected completely
  - Shave excision is adequate for minimal invasion of the aerodigestive tract

Surgical Management

- Conflicting results may be related to differing interpretations of “shave” technique
- Definition of “shave” excision
  - All gross tumor is removed
  - There is likely microscopic residual disease

Surgical Management

- “Shave” technique only applicable for partial thickness invasion of aerodigestive tract
- Intraluminal extension of thyroid cancer requires complete resection
  - Attempt conservation surgery, if possible

Surgical Management

- “Shave” technique only applicable for partial thickness invasion of aerodigestive tract
- Intraluminal extension of thyroid cancer requires complete resection
  - Attempt conservation surgery, if possible
  - There is current literature support for use of “shave” technique in select cases of invasive thyroid cancer
Surgical Management

- Strap muscle invasion
  - Most common site of invasion
  - Does not portend worse prognosis
  - Resection of all involved areas with negative margins
- No major morbidity

Surgical Management

- Recurrent laryngeal nerve invasion
  - Due to involvement of primary tumor or paratracheal lymph nodes
  - If paralyzed preoperatively, the nerve should be sacrificed
  - If working preoperatively, nerve preservation should be attempted

Surgical Management

- Recurrent laryngeal nerve invasion
  - All gross tumor must be removed, even if this requires nerve sacrifice
  - However, leaving microscopic disease on nerve does not lead to decreased survival or increased local recurrence

Surgical Management

- Laryngeal invasion
  - 3 pathways of invasion
    - Anteriorly through cricothyroid membrane or cricoid cartilage
    - Laterally through thyroid cartilage lamina
    - Posteriorly around the back of thyroid cartilage into paraglottic space
Surgical Management

• Laryngeal invasion
  – If no intraluminal involvement, “shave” excision (all gross tumor removed) while preserving laryngeal framework
  – If there is intraluminal extension, consider partial laryngectomy
    • Total laryngectomy for more extensive intraluminal disease

• Tracheal invasion
  – 2 pathways of invasion
    • Anteriorly through tracheal cartilage rings
    • Laterally through intercartilaginous space
  – Airway mucosa is poor barrier
    • Tracheal mucosa ulceration frequent

• Esophageal invasion
  – Esophageal musculature may be involved
  – Esophageal mucosa is tough barrier to tumor spread
    • Penetration of esophageal mucosa rare
Surgical Management

- Esophageal invasion
  - Wide resection of involved muscularis layer, without reconstruction
  - Esophagectomy for intraluminal extension

- 45 year-old man with 2 month history of voice changes and suprasternal anterior neck mass

- Exam: Bulky bilateral and central neck masses, enlarged firm thyroid; right vocal cord paralysis

- Ultrasonography revealed abnormal bilateral cervical lymphadenopathy involving right level II - IV, left level III-IV, and central compartment; abnormal thickening of a heterogeneous thyroid gland

MRI
• MRI suggested right-sided cricoid cartilage and superior tracheal invasion by tumor; a plane between the tumor and the esophagus could not be identified

• Total thyroidectomy, central and bilateral neck dissections, tracheal resection, possible esophageal resection

• Bronchoscopy and esophagoscopy performed at start of procedure
  – Friable lesion noted in anterolateral trachea at level of thyroid gland
    • Frozen section: Papillary Thyroid Carcinoma
    – Esophageal mucosa without lesions

• Intraoperative findings:
  – Extensive bulky cervical adenopathy, invading left jugular vein and phrenic nerve
  – Surgery was staged—Total thyroidectomy, central neck dissection and tracheal resection performed 1 week after bilateral modified radical neck dissections
• Intraoperative findings:
  – Bulky central compartment nodes removed
  – Left thyroid lobe removed with preservation of left recurrent laryngeal nerve
  – Right thyroid lobe removed en bloc with segmental tracheal resection including inferior right cricoid cartilage
Adjuvant Therapy

- All patients should receive radioactive iodine post-operatively
  - Microscopic local residual disease
  - Microscopic metastatic disease

Adjuvant Therapy

- Post-operative external beam radiation therapy should be considered for invasive WDTC
- Definite indications for XRT
  - RAI resistant disease, not amenable to further surgery
  - Gross residual disease
  - WDTC that has transformed to poorly differentiated or anaplastic subtype

Adjuvant Therapy

- Chemotherapy
  - Standard combination chemotherapy agents
    - Cisplatin, adriamycin
  - Investigational drugs include targeted agents
    - Kinase inhibitors (Sorafenib)

Summary

- Most WDTC’s are not locally invasive
- Locally invasive thyroid cancer follows a more aggressive course
- Locally invasive thyroid cancer is best identified preoperatively
Summary

• Surgical management includes removal of all gross disease, while preserving upper aerodigestive tract function
• Post-operative adjuvant therapy is indicated for invasive thyroid cancer