GBMC Head & Neck Grand Rounds

5/7/2010
Ian Smith
Topic: Hypopharyngeal Cancer
58 YEAR OLD MALE

- Presented 9/4/2008
- CC: Sore throat
- HPI: 58 year old with odynophagia, dysphagia, left otalgia, no weight loss
- Meds: plavix, asa 81, lipitor, metoprolol, cilostazol, lisinopril
- All: NKDA
- PMH: CAD, PVD
- PSH: 5vCABG, right iliac stent
58 YEAR OLD MALE

- Taken for DL/Bx
58 YEAR OLD MALE

- Jan 2009 completed RT
- 3/3/2010 DL Bx aborted due to brady/hypotension
- 3/23/2010 DL Bx Inv Squamous Cell Ca
- Rsstaged T2N0M0
- 4/7/2010 TL, paratracheal node dissection, left II-IV, pectoraslis MF
PATHOLOGY
Poorly Differentiated Squamous Cell Carcinoma
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CLINICAL MANAGEMENT OF HYPOPHARYNGEAL CANCER

GBMC- Head & Neck Grand Rounds

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PGY3 – Otolaryngology Head & Neck Surgery
May 7, 2010
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GBMC- Head & Neck Grand Rounds
May 7, 2010

NEEDS ASSESSMENT:

Of all subsites of head and neck squamous cell carcinoma, patients with hypopharyngeal carcinomas as a group fare the worst in terms of oncologic outcome. These patients tend to present at a later stage with a paucity of symptoms compared with other types of head and neck cancers. Providers who participate in the care of head and neck cancer patients must recognize the clinicopathologic features and be educated on optimal management of these tumor types.

LEARNING OBJECTIVES:

- To describe the clinical and histopathologic features important in defining the disease process of hypopharyngeal cancer.
- To discuss the treatment options including surgical management, chemotherapy, and radiation.
- To discuss the efficacy and outcomes of surgical and non-surgical organ preservation approaches for the treatment of this disease.
- To discuss follow up and ongoing surveillance of patients with this disease.
Anatomy of Hypopharynx

- Extends from the oropharynx superiorly to the cervical esophagus inferiorly.
  - Superior extent at the level of the hyoid bone or at the level of the pharyngoepiglottic folds.
  - Inferiorly, the hypopharynx tapers to the esophageal introitus at the cricopharyngeus muscle (lower boarder of cricoid cartilage).
  - Anteriorly bordered by the larynx
  - Posteriorly by the retropharyngeal space.

- Subdivided into 4 regions: the pyriform sinuses, the postcricoid region, and the lateral and posterior pharyngeal walls.

- Hypopharyngeal cancers are often named for their location based on these subregions.
Overview of Hypopharyngeal CA

- Associated with the poorest survival of all head and neck primary sites.
- Behavior differs greatly from that of Laryngeal CA.
  - usually poorly differentiated
  - patients are usually asymptomatic
  - early presentations uncommon (T1 N0 cases account for only 1-2% of all patients seen)
  - nodal involvement present in 50-70% of cases at presentation (70% Stage III at presentation)
  - Tend to have significant submucosal extent and skip lesions making the estimation of the extent of disease difficult
Overview of Hypopharyngeal CA

- Following treatment, 50% of patients develop recurrence in less than 1 year.
- Most mortality in the first 2 years following diagnosis is due to locoregional recurrence.
- The 5-year survival rate with small (T1-T2) lesions is about 60%.
- With T3-T4 lesions or multiple node involvement, survival falls to 17-32%.
- Five-year survival for all stages is approximately 30%.
Overview of Hypopharyngeal CA

- Represents approximately 4-7% of all cancers of the upper aerodigestive tract.
- ~95% SCC (others include lymphomas, neuroendocrine tumors, adenocarcinomas, and sarcomas)
- Most arise in the pyriform sinus. In the United States and Canada, 65-85% of hypopharyngeal carcinomas involve the pyriform sinuses, 10-20% involve the posterior pharyngeal wall, and 5-15% involve the postcricoid area.
- Male-to-female ratio of 3:1 (women have a higher incidence of postcricoid cancers related to nutritional deficiencies such as Plummer-Vinson Syndrome)
- The mean age at presentation is 65 years.
Etiology and Biology

- The causal relationships among alcohol and tobacco intake, genetic predisposition, diet, and socioeconomic conditions in the development of squamous cell cancers of the head and neck apply as well to hypopharyngeal cancer.

- Tobacco and ethanol are the principle carcinogens responsible and act synergistically.

- In examining these factors, three specific components appear to be more closely associated with hypopharyngeal cancer:
  - Alcohol intake appears to be more common in patients with hypopharyngeal cancer when compared with laryngeal cancer.
  - A condition specifically associated with postcricoid carcinoma is the Plummer-Vinson or Paterson-Brown-Kelly syndrome, which primarily affects women (85% of the cases).
    - This syndrome represents the combination of dysphagia, iron deficiency anemia, and hypopharyngeal and esophageal webs.
  - Gastroesophageal or laryngotracheal reflux (postcricoid)
Larger lesions are required to produce symptoms making the time between initial symptoms and diagnosis longer than that for laryngeal tumors or other tumors of the head and neck.

Symptoms: dysphagia, odynophagia, globus sensation or referred otalgia (CNX)

Cervical LN occurs as presenting symptom in ~ 50% of cases.
Work up

- Consists of an initial history and physical examination, including a well conducted flexible fiberoptic endoscopic examination.
- Labs: CBC, CMP, thyroid
- Imaging: CT, MRI, PET, PET/CT
- Panendoscopy (for biopsy)
Patient presenting with hoarseness and dysphagia. CT scan demonstrates bulky right pyriform sinus tumor (white arrows) eroding through thyroid cartilage, with displacement of supraglottic airway.
An understanding of the site of initiation and patterns of spread of hypopharyngeal carcinoma is critical in the management of these tumors.

Medial wall pyriform sinus tumors usually spread along the mucosal surface to the aryepiglottic folds and can invade into the larynx by involving the paraglottic space.

Tumors of the lateral wall and apex commonly invade the thyroid cartilage.

Once the tumor penetrates the constrictor muscle, it can spread along the fascial planes to the base of skull.

Because of the abundant lymphatics in the region and the extent of the primary tumor at diagnosis, metastasis to the regional lymph nodes is common.
Tumor Spread

- Hypopharyngeal carcinomas metastasize primarily to the superior jugular and midjugular nodes.
- However, metastasis to the retropharyngeal nodes, paratracheal nodes, paraesophageal nodes, and parapharyngeal space nodes may be present.
AJCC Staging (T stage)

- **T1** Tumor is limited to one subsite or 2cm or less.
- **T2** Tumor invades more than one subsite of the hypopharynx or an adjacent site, or measures more than 2cm but no more than 4cm without fixation of the hemilarynx.
- **T3** Tumor measures more than 4cm or with fixation of the hemilarynx.
- **T4a** Tumor invades thyroid/cricoid cartilage, hyoid bone, thyroid gland, esophagus, or central compartment of soft tissue (strap mm).
- **T4b** Tumor invades prevertebral fascia, encases the carotid artery or involves mediastinal structures.
AJCC Staging (N stage)

- **N0**: no regional LN
- **N1**: single ipsilateral LN less or equal to 3cm
- **N2a**: single ipsilateral LN 3-6cm
- **N2b**: multiple ipsilateral LNs all less than 6cm
- **N2c**: bilateral or contralateral LNs all less than 6cm
- **N3**: any LN more than 6cm
<table>
<thead>
<tr>
<th>Stage</th>
<th>TIS</th>
<th>N0</th>
<th>M0</th>
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<tbody>
<tr>
<td>Stage 0</td>
<td>TIS</td>
<td>N0</td>
<td>M0</td>
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<tr>
<td>Stage I</td>
<td>T1</td>
<td>N0</td>
<td>M0</td>
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<td>M0</td>
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<tr>
<td>Stage III</td>
<td>T3</td>
<td>N0</td>
<td>M0</td>
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<td>T1</td>
<td>N1</td>
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<tr>
<td>Stage IVB</td>
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</tr>
<tr>
<td>Stage IVC</td>
<td>Any T</td>
<td>Any N</td>
<td>M1</td>
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Treatment Overview

- Historically, the standard therapy focused on radical surgery followed by radiation or radiation alone.

- More conservative procedures for early lesions became possible with the introduction of conservation laryngeal procedures in the 1960s.

- Currently, the goal of hypopharyngeal cancer management is to achieve the highest locoregional control with the least functional injury, preserving respiratory function, deglutination, and phonation.

- Organ-preserving therapy for hypopharyngeal lesions includes nonsurgical concurrent or induction chemotherapy and radiation or surgical options including transoral laser microsurgery, partial Pharyngectomy and supracricoid hemilaryngopharyngectomy.
Recent advances include modern conservative surgical approaches that involve robotic assistance and laser dissection and new radiotherapy techniques such as intensity-modulated radiation therapy (IMRT) for increased conformal irradiation.

Despite these new treatment modalities, an optimal treatment strategy for hypopharyngeal cancers, is difficult to determine because no randomized study comparing outcomes following surgery with outcomes following radiation or chemoradiation has been completed.

Currently, there is no standard of care for these lesions because some institutions use combination chemotherapy and radiation protocols as primary treatment, whereas others continue to use surgery followed by radiation alone or with chemotherapy as the primary modality.
Surgical Management

- Advanced hypopharyngeal tumors requiring surgery routinely involve reconstruction with either microvascular free flaps (fasciocutaneous or jejunum interposition) or gastric pull-ups.

- When primary surgical-based approaches are used, a careful assessment of the tumor extent is critical because hypopharyngeal tumors often have significant submucosal extension, which can significantly affect the planned resection.

- Ultimately, surgery for advanced lesions often necessitates total laryngectomy with partial or total pharyngectomy required in 56% to 79% of patients.
The available surgical options can be divided among the organ-preservation procedures and more radical operations.

- The conservation surgical procedures are limited to T1, T2, or highly selected T3 lesions, except for the endoscopic approach used by Steiner and colleagues.
- The more radical operations typically require extensive reconstruction of the alimentary tract.

### Surgical Options

<table>
<thead>
<tr>
<th>Procedure</th>
<th>T Stage</th>
<th>Reconstruction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Partial pharyngectomy</td>
<td>T1, T2</td>
<td>Primary closure</td>
</tr>
<tr>
<td>Partial laryngopharyngectomy</td>
<td>T1, T2, T3</td>
<td>Regional or free flap</td>
</tr>
<tr>
<td>Supracricoid hemilaryngectomy</td>
<td>T1, T2, T3</td>
<td>Primary closure</td>
</tr>
<tr>
<td>Endoscopic CO₂ laser resection</td>
<td>T1, T2 (possible T3, T4)</td>
<td>Secondary intention</td>
</tr>
<tr>
<td>Total laryngectomy with partial/total pharyngectomy</td>
<td>T3, T4</td>
<td>Primary closure vs. regional or free flap</td>
</tr>
<tr>
<td>Total pharyngo-laryngo-esophagectomy</td>
<td>T4</td>
<td>Gastric pull-up</td>
</tr>
</tbody>
</table>
Non-Surgical Management

- Combined chemotherapy and radiation therapy directed at the primary tumor are the most common nonsurgical approaches for advanced tumors. *(Lefebvre, et al. JNCI, 1996)*

- Best responses are to platinum-based compounds such as cisplatin or carboplatin and/or 5-FU.

- Chemo used alone only for palliation.

- Even when radiation and chemotherapy are used as initial modalities of therapy, great care must be taken to follow patients because the ability to surgically salvage treatment failures is an integral part of the therapeutic regimen.

- Combined chemotherapy and radiotherapy for hypopharyngeal carcinomas leads to a higher rate of stricture and gastrostomy tube dependence compared with other subsites of the head and neck.
Management Based on Stage

- **T1/T2** - Radiotherapy alone (commonly 66-70 Gy) or surgery (possibly with postoperative irradiation, depending on the pathology findings). Larynx preservation therapy is typically possible and is strongly favored.

- **T3/T4 (resectable)** - Partial or total laryngopharyngectomy, neck dissection, postoperative radiotherapy +/- chemo, or concurrent chemoradiotherapy or participation in prospective clinical trials.

- **Unresectable or medically unstable** - (1) Radiotherapy alone with altered fractionation or concurrent chemoradiotherapy or (2) participation in prospective clinical trials.
The control of regional metastasis is a critical component of the management of hypopharyngeal and cervical esophageal tumors.

As for other sites, the discussion of neck management can be divided between elective neck dissection (for N0 stage necks) and therapeutic neck dissection (for N+ necks).

For necks with positive nodes, the current management is to treat both necks, either with radiation followed by salvage surgery if necessary or surgery followed by radiation.

For the ipsilateral neck that is staged N0, there is compelling evidence to treat both necks for all but the very early lesions where a unilateral neck dissection alone may be adequate.
Recent Studies

  - Retrospective study from the Netherlands, 893 pts over 10yrs
  - Compared radiotherapy alone, combined surgery and radiotherapy and surgery alone.
  - Results: The 5-year disease-free survival after radiotherapy alone was 37%, after surgery alone 41% and **after combined therapy 47%**.
  - Majority of pts were Stage IV, and stage IV showed largest difference b/w tx groups.
  - N-stage is more important for the prognosis than the T-stage.

Table 6. Five-year disease-free survival in different stages of disease after different treatment

<table>
<thead>
<tr>
<th>Treatment</th>
<th>5-year disease-free survival (%)</th>
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<tbody>
<tr>
<td>Stage I</td>
<td></td>
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<tr>
<td>R (n = 27)</td>
<td>54</td>
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<tr>
<td>RS (n = 4)</td>
<td>75</td>
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<tr>
<td>S (n = 6)</td>
<td>60</td>
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<tr>
<td>Stage II</td>
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<td>R (n = 49)</td>
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<td>RS (n = 25)</td>
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<tr>
<td>S (n = 8)</td>
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<td>Stage III</td>
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<tr>
<td>RS (n = 62)</td>
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<td>Stage IV</td>
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<td>R (n = 83)</td>
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</tr>
<tr>
<td><strong>RS (n = 287)</strong></td>
<td><strong>43</strong></td>
</tr>
<tr>
<td>S (n = 27)</td>
<td>22</td>
</tr>
</tbody>
</table>
Recent Studies

  - Sx followed by concomitant chemoradiation therapy (CCRT) versus CCRT followed by early surgical salvage.
  - Retrospective study from Taiwan.
  - 202 pts with HPC
  - The 5-year disease-specific survival rate was 80% for stage I-II, 44.8% for stage III, and 14.3% for stage IV disease.
  - Surgery plus concomitant chemoradiotherapy led to a better survival rate than CCRT plus salvage surgery in patients with stage III-IV HPC.
Follow-up

- Close monitoring is required for these patients
- Reevaluate the disease status due to high risk of recurrence:
  - Perform a neck examination and fiberoptic laryngoscopy every 1-3 months for 1-2 years after the initial treatment and 2-4 times per year thereafter.
  - If PET scan was informative at initial diagnosis, consider repeating not sooner than 4 months after radiation or surgery; prior to this time, the inflammation from treatment may give a false-positive reading.
- Monitor for second primary cancers (incidence of approximately 3% per y) once or twice per year.
- Chest x-ray films for detection of lung cancer or metastases
- Hepatic panel to check for liver metastases
- Thyroid-stimulating hormone (TSH) levels once or twice per year if neck was radiated
Conclusions

- Neoplasms of the hypopharynx are some of the most challenging diseases managed by the head and neck surgeon.

- As with all advanced head and neck cancers, a multidisciplinary approach involving head and neck surgeons, radiation therapists, medical oncologists, and speech language pathologists is used in formulating a treatment plan.

- With advances in reconstructive techniques and organ-preservation protocols, improved options are available for patients.

- Ultimately, prospective, multi-institutional trials together with biomarkers are necessary to delineate the best therapy for individual patients.
Thank You