Esophageal Cancer A Case Report
KAOM  4/12/2012
Steven Ballard DO
Initial Presentation

64 year old Schizophrenic white male with HTN, Tobacco Abuse, and Alcoholism presents with dysphagia that had been present over past few weeks. He felt like the food was getting caught about half way down. NO problems with swallowing liquids, dysphonia, odynophagia or other related complaints. His dysphagia was for solids only.

- Also of note - denied history of GERD, Barrett’s, or family history of cancer.
HISTORY

Past Medical History
- HTN
- COPD
- Schizophrenia
- Depression
- ETOH
- Tobaccoism
- Insomnia

Medications
- HCTZ
- Atenolol
- Proair
- Abilify
- Crestor
- Trazadone
HISTORY CONT.

Family History

- Negative Family history and no Family history of Cancer.

ROS: All other 12 pt ROS neg.

No weight loss, black or bloody stools, odynophagia or other complaints.

Social

- Chronic ETOH and Tobacco use
Physical Exam

- Vitals: VSS Afebrile
HEENT, Lymph, CV, LUNGS, SKIN all normal.
ABD: Soft, no masses, non-tender
Psych: paranoid, anxious, Denial.
Initial Plan

- EGD—Pt refused several times but agreed to Barium swallow.
- Never showed up for Barium—rescheduled and did not show up again with understanding might have cancer.
- Did not come in for follow up visits
- Pt finally followed up after we would no longer refill his other medications and mailed multiple letters.
- Upon follow up he continued to have dysphagia and now GERD symptoms.
Follow up

- Pt saw a different provider and again refused EGD but agreed to Barium swallow which was done and showed:
  - 5 cm irregular stricture distal esophagus suspicious for neoplastic infiltration. Recommended endoscopy.
- Pt scheduled for EGD and Bx of mass with surgery and followed through.
- Path showed Poorly Differentiated Adenocarcinoma.
Follow up Continued

- Pt had resection by surgery of esophageal mass.
- Revealed Invasive Grade II Adenocarcinoma at GE junction. Margins clear. 9/28 nodes had metastatic grade II Adenocarcinoma.
- Staged T3N3
- Pt was sent to Oncology by Surgery after resection for Chemo and Radiation.
Esophageal CA Facts

- 95% are either Squamous cell carcinoma (SCC) and Adenocarcinoma’s.
- During the 20\textsuperscript{th} Century SCC dominated but now almost equal incidence of both in western countries.
- 16,980 in 2011 with 14,710 deaths in US
- Internationally rates 16 fold higher and usually Squamous Cells. Causes unknown. However more attributable to smoking and ETOH.
Facts continued

- Smoking and alcohol are major risk factors for SCC
- GERD, obesity, smoking and Barrett's esophagus with adenocarcinoma
- US and Westernized -- Smoking and ETOH contribute to 90% of cases
- Bisphosphonates contraindicated in Barrett’s by FDA. UK study showed no evidence supporting link. (3)
- Reflux strongest individual risk factor
- Risk Factors: Smoking, Increased BMI, genetics, poor diet, ETOH, Males, Whites, hiatal hernia, Age >50
- Metastasis: Liver, lung, bone, and adrenals
# Epidemiology of esophageal cancer in the United States

<table>
<thead>
<tr>
<th></th>
<th>Squamous cell</th>
<th>Adenocarcinoma</th>
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<tbody>
<tr>
<td>New cases per year</td>
<td>6000</td>
<td>6000</td>
</tr>
<tr>
<td>Male-to-female ratio</td>
<td>3:1</td>
<td>7:1</td>
</tr>
<tr>
<td>Black-to-white ratio</td>
<td>6:1</td>
<td>1:4</td>
</tr>
<tr>
<td>Most common locations</td>
<td>Middle esophagus</td>
<td>Distal esophagus</td>
</tr>
<tr>
<td>Major risk factors</td>
<td>Smoking, alcohol</td>
<td>Barrett's esophagus</td>
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</table>
Barrett’s

- GERD then Metaplasia to Dysplasia to Cancer
- Metaplastic Columnar epithelium replaces stratified squamous epithelium due to chronic GERD
- Management involves 3 components
  1. Treat GERD
  2. Endoscopic Surveillance to detect dysplasia
  3. Treat Dysplasia
Treat GERD

- Same treatment for GERD as Barrett’s but many sources recommend PPI initially. Goal to prevent Cancer development. Efficacy not established in clinical trials. Aggressive GERD treatment debated.

- Fundoplication option—does not appear to be more effective than med mgmt. (3)
Surveillance

- AGA recommends
- NO dysplasia - then EGD every 3-5 years
- Low grade dysplasia 6-12 months
- High grade dysplasia in absence of eradication therapy: every 3 months
- Endoscopic evaluation using white light endoscopy, four quadrant Bx every 2cm, specific Bx specimens of any mucosal irregularities separately. If known or suspected dysplasia then four quad Bx every 1cm. (3)
Treatment of Dysplasia

- Depends on low grade vs high grade and recommends 2 pathologists opinions.
- High grade: Endoscopic eradication therapies:
  - radiofrequency ablation
  - photodynamic therapy
  - EMR (not electronic medical records) Endoscopic Mucosal Resection

EMR Recommended for patients who have dysplasia in Barrett’s associated with visible mucosal irregularity to determine T stage of neoplasia. (3)
Diagnosis of Cancer

- Barium swallow/upper GI can be helpful and suggest cancer
- However, diagnosis is confirmed by Endoscopic Biopsy

- “Endoscopic visualization of a large mucosal mass is nearly pathognomonic of esophageal cancer; biopsy must be performed to confirm the diagnosis” (1)
More biopsies the better

- Studies have shown that the more biopsies are taken the more accurate the diagnosis.
- 1 biopsy — 93 percent
- 4 biopsies — 95 percent
- 7 biopsies — 98 percent
- “The addition of brush cytology specimens to seven biopsies increased the accuracy to 100 percent.” (1)
- Some are using chromoendoscopy with Lugol’s iodine to stain for directing Bx in suspected SCC but limited data to support
Squamous vs Adenocarcinoma

**SCC**
- Tobacco and ETOH
- Declining in US
- Arise 10 years earlier
- Increased perioperative risk due to location
- Recurrence more common locally

**Adenocarcinoma**
- GERD and Obesity
- Increasing in US
- Distal location makes easier to resect and less risk.
- Recurrence more common distant
- Prognosis thought to be better due to lower lymphatic spread rates (4)
Squamous vs Adenocarcinoma
Importance of Histology

“However, it remains unclear as to whether and how histology should dictate the therapeutic approach. Future studies in esophageal cancer should analyze and report separately the results of therapeutic strategies according to histology” (4)
Early Superficial Esophageal Cancer

- Early cancers look like superficial plaques, nodules, or ulcerations
Advanced lesions

Malignant Stricture

Ulcerating mass
Advanced lesions

- Circumferential mass
Prognosis

- 19% survival at 5 years according to US Surveillance, Epidemiology and End Results (SEER) Program (01-07)
- Strongly associated with Staging (SCC or Adenocarcinoma)
- “TNM staging system of the American Joint Committee on Cancer (AJCC) and the International Union Against Cancer (UICC) for esophageal cancer is used universally” (2) A major change between the 2002 and the 2010 editions was separating staging based on histology.
- “In addition, tumors at the EGJ and proximal 5 cm of the stomach that extend into the EGJ or esophagus as staged as esophageal cancers while all other tumors with an epicenter in the stomach >5 cm from the EGJ, or those within 5 cm or the EGJ without extension into the esophagus are staged as gastric cancers.” (1)
- The new recommendations from AJCC in 2010 was based on group (worldwide data on 4627 patients) who had esophagectomy alone and no chemo or radiation. As a result prognosis associated with those who have had pre-op chemo or radiation is controversial.
Staging and follow up

- Preoperative staging is important in management and usually starts with CT chest and abdomen for position of tumor and metastatic disease. However being replaced by PET scans due to increased sensitivity for small metastasis. Both have limited use for local staging.
- Preoperative PET scans change management and 20% can avoid unnecessary surgery.
- Integrated PET/CT scans are used to detect metastatic disease who are surgical candidates.
- Local staging: Endoscopic ultrasound (EUS)—most accurate for local-regional disease and can assist with management. Can also include FNA to increase accuracy of dx.
Staging Continued

- “The role of staging laparoscopy is controversial, and there is no consensus on this issue. While a few patients may avoid an unnecessary laparotomy and hospitalization, most patients will not have any abnormality found at laparoscopy.” (1)

- “NCCN (National Comp Cancer Network) guidelines suggest that diagnostic laparoscopy is optional for patients with no evidence of metastatic disease and tumor location at the EGJ. Other clinicians (including one of the authors [MG]) advocate diagnostic laparoscopy for patients with adenocarcinomas arising within the intraabdominal portion of the esophagus or at the EGJ, or if there is suspicion for intraperitoneal metastatic disease that cannot otherwise be confirmed.” (1)

- “Preoperative bronchoscopy with biopsy and brush cytology is indicated for patients with locally advanced nonmetastatic tumors that are located at or above the level of the carina.” (1)
Endoscopic Ultrasound
### TNM staging of esophageal squamous cell cancer (SCC)

#### Primary tumor (T)*
- **TX**: Primary tumor cannot be assessed
- **T0**: No evidence of primary tumor
- **Tis**: High-grade dysplasia
- **T1**: Tumor involves lamina propria, muscularis mucosae, or submucosa
  - **T1a**: Tumor involves lamina propria or muscularis mucosae
  - **T1b**: Tumor involves submucosa
- **T2**: Tumor involves muscularis propria
- **T3**: Tumor involves adventitia
- **T4**: Tumor involves adjacent structures
  - **T4a**: Resectable tumor involving pleura, pericardium, or diaphragm
  - **T4b**: Unresectable tumor involving other adjacent structures, such as aorta, vertebral body, trachea, etc.

#### Regional lymph nodes (N)Δ
- **NX**: Regional lymph node(s) cannot be assessed
- **N0**: No regional lymph node metastasis
- **N1**: Metastasis in 1-2 regional lymph nodes
- **N2**: Metastasis in 3-6 regional lymph nodes
- **N3**: Metastasis in seven or more regional lymph nodes

#### Distant metastasis (M)
- **M0**: No distant metastasis
- **M1**: Distant metastasis

#### Histologic grade (G)
- **GX**: Grade cannot be assessed - stage grouping as G1
- **G1**: Well differentiated
- **G2**: Moderately differentiated
- **G3**: Poorly differentiated
- **G4**: Undifferentiated - stage grouping as G3 squamous

### Anatomic stage/prognostic groups

#### Squamous cell carcinoma

<table>
<thead>
<tr>
<th>Stage</th>
<th>T</th>
<th>N</th>
<th>M</th>
<th>Grade</th>
<th>Tumor location $S$</th>
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<tbody>
<tr>
<td>O</td>
<td>Tis (HGD)</td>
<td>N0</td>
<td>M0</td>
<td>1, X</td>
<td>Any</td>
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<tr>
<td>IA</td>
<td>T1</td>
<td>N0</td>
<td>M0</td>
<td>1, X</td>
<td>Any</td>
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<tr>
<td>IB</td>
<td>T1</td>
<td>N0</td>
<td>M0</td>
<td>2-3</td>
<td>Any</td>
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<td></td>
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<td>N0</td>
<td>M0</td>
<td>1, X</td>
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<td>2-3</td>
<td>Lower, X</td>
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<td>N1-2</td>
<td>M0</td>
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<td>Upper, middle</td>
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<td>N3</td>
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Note: cTNM is the clinical classification, pTNM is the pathologic classification.
* At least maximal dimension of the tumor must be recorded and multiple tumors require the T(m) suffix.
* High-grade dysplasia (HGD) includes all noninvasive neoplastic epithelia that was formerly called carcinoma in situ, a diagnosis that is no longer used for columnar mucosae anywhere in the gastrointestinal tract.
* Number must be recorded for total number of regional nodes sampled and total number of regional nodes with metastasis.
* Or mixed histology including a squamous component or NOS.
* Location of the primary cancer site is defined by the position of the upper (proximal) edge of the tumor in the esophagus.

Used with the permission of the American Joint Committee on Cancer (AJCC), Chicago, Illinois. The original source for this material is the AJCC Cancer Staging Manual, Seventh Edition (2010) published by Springer New York, Inc.
TNM staging of esophagogastric junction (EGJ) adenocarcinoma

<table>
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<th>Primary tumor (T)*</th>
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<td>TX</td>
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<td>Tis</td>
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<td>T3</td>
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<td>T4</td>
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<tr>
<td>T4a</td>
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<tr>
<td>T4b</td>
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<tr>
<th>Regional lymph nodes (N)A</th>
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<tbody>
<tr>
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<tr>
<td>N1</td>
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<th>Distant metastasis (M)</th>
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<td>M1</td>
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<th>Histologic grade (G)</th>
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<th>Grade</th>
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<tbody>
<tr>
<td>0</td>
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<td>M0</td>
<td>1, X</td>
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<td>1-2, X</td>
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<tr>
<td>III</td>
<td>T3</td>
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<td>M0</td>
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<td>T4a</td>
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<td>M0</td>
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<tr>
<td>IIIb</td>
<td>T3</td>
<td>N2</td>
<td>M0</td>
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<tr>
<td>IIIc</td>
<td>T4a</td>
<td>N1-2</td>
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<td>IV</td>
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Treatment

- Over the last 15 years, Treatment has changed and usually consists of combined therapies, however optimal management is still controversial.
- Differences histologically between SCC and Adenocarcinoma now staged separately but lack of data on specific treatments for each so treatment is similar for both.
- Recommendations based on location of the Cancer and Stage.
Thoracic Esophageal Cancer

- Chemotherapy potentially curative option for SCC however high rates of recurrence with chemo alone.
- In General: “inclusion of surgery is preferred for clinically resectable esophageal cancer, particularly for adenocarcinoma” (4)
- “Several trials and meta-analyses support the view that a concurrent trimodality approach (concomitant chemoradiotherapy followed by surgery) provides a survival benefit compared to surgery alone. Further, local control appears to be better with preoperative chemoradiotherapy compared to surgery alone.” (4)
- Also, local failure rates may be lower in patients treated with chemoradiotherapy followed by surgery compared to those receiving either chemotherapy followed by surgery or surgery alone.
- Guidelines: “National Comprehensive Cancer Network (NCCN) recommend preoperative chemoradiotherapy as the primary treatment recommendation for T1bN1, and T2-T4, N0-1 disease, regardless of histology. Definitive chemoradiotherapy is a reasonable approach for patients who are not surgical candidates.” (4)
Treatment continued

- Recommendations are for multidrug chemotherapy rather than single agent usually using Cisplatin and FU in addition to radiation therapy. RTOG 85-01 trial (4)

- RTOG 5-01 Trial Closed due to showed a significant survival advantage for chemoradiotherapy and became the standard of care for patients with inoperable disease. This trial had 90% SCC.

- “Of the five completed randomized trials compared preoperative concurrent chemoradiotherapy versus surgery alone, only two show a statistically significant survival benefit for chemoradiotherapy, three others do not, two of which were underpowered. Of these, the two most important are the Dutch CROSS trial and CALGB 9781.” (4)
Treatment continued

- CROSS Trial—Dutch study with 363 with adenocarcinoma. At a median follow-up of 32 months, median overall survival was significantly better with preoperative chemoradiotherapy (49 versus 26 months, three-year survival rate 59 versus 48 percent).

- CALGB 9781 — ”CALGB 9781 was originally designed as a randomized Intergroup trial of trimodality therapy versus surgery in 500 patients with stages I-III esophageal or EGJ cancer, staged with esophagogastroduodenoscopy, barium esophagram, and CT. Staging EUS and thoracoscopy/laparoscopy were encouraged. Due to poor accrual, the study was closed prematurely with only 56 patients enrolled (42 adenocarcinomas, 14 SCC). Five-year survival was 39 versus 16 percent in favor of trimodality therapy, although the difference was not statistically significant.” (4)

- “Summary — For patients with completely resected node-positive esophageal cancer who have not received neoadjuvant therapy, we typically recommend some form of postoperative therapy. It is difficult to come to any conclusions as to whether there are specific advantages for adjuvant chemoradiotherapy over chemotherapy alone. In our view, either approach is reasonable. Further confirmatory trials, particularly randomized trials, are necessary before specific recommendations can be made.” (4)
Other locations

• EGJ cancers — Most treated with preoperative chemoradiotherapy. However, “these tumors have been included in many of the trials examining the benefit of adjuvant and neoadjuvant chemotherapy for gastric cancer, and institutional practice varies.” (4)

• Cervical esophageal cancer — Close relation to SCC of the head and neck. “Radiation combined with chemotherapy is preferred over surgery for these patients since survival appears to be the same, and major morbidity is avoided in most.” (4)
Summary Continued

- Approach to a patient with Esophageal Cancer should be a multidisciplinary team approach with Oncology, Surgery, GI, and PCP.
- Some studies show that survival is prolonged with trimodal therapy of chemoradiation with surgery but this is controversial. Oncologists on this case did recommend this approach.
- Chemoradiation therapy after surgery seems to be better as well.
- Treatment of GERD and close monitoring with serial EGD and biopsies in management of Barrett’s along with treatment of dysplasia is key to preventing evolution of cancer.
Sources

1. Up to Date. UTDOL.com. Diagnosis and Staging of Esophageal Cancer. Authors: John R Saltzman, MD, FACP, FACGMichael K Gibson, MD, PhD, FACP Section Editors. Douglas A Howell, MD, FASGE, FACG Richard M Goldberg, MD Deputy Editor Diane MF Savarese, MD

Pictures: Early, superficial esophageal cancer seen on endoscopy through Advanced lesions. Courtesy of William Brugge, MD. UTDOL. Article Diagnosis and Staging Esophageal Cancer


3. Up to Date. UTDOL.com. Management of Barrett’s Esophagus

4. Up to Date. UTDOL.com Radiation therapy, Chemoradiotherapy, Neoadjuvant approaches, and Postoperative Adjuvant therapy for Localized Cancers of the Esophagus. Authors: Noah C Choi, MD Michael K Gibson, MD, PhD, FACP Section Editors: Richard M Goldberg, MD Christopher G Willett, MD Deputy Editor: Diane MF Savarese, MD