ESOPHAGEAL ADENOCARCINOMA
DIAGNOSIS, STAGING, AND SURVEILLANCE

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Our patient: JS

- 68 yo woman who presented with progressive dysphagia, nausea, and vomiting
- Associated symptoms: weight loss, increasing fatigue
Differential Diagnosis: Dysphagia

- Functional obstruction
  - Motility disorders
    - Scleroderma
    - Achalasia
    - Chagas disease
    - Diffuse esophageal spasm
    - Diabetes

- Esophagitis
  - Reflux
  - Infections
  - Corrosive
  - Alcoholism

- Mechanical Obstruction
  - Luminal
    - Foreign body
  - Wall
    - Benign tumors
    - Malignant tumors
    - Strictures
    - Congenital webs and rings
    - Diverticuli
  - Outside
    - Vascular anomalies
    - Lymphadenopathy
Standard Menu of Tests for Imaging Dysphagia

- Barium swallow (Ba SW)
  - single contrast for lumen diameter
  - double contrast for mucosal detail

- Chest CT

- Endoscopic esophageal ultrasound (EUS)

- PET
Newer Imaging Modalities

- Optical coherence tomography (OCT)
- Virtual CT endoscopy

Routine endoscopy and biopsy is used commonly for diagnosis
Our patient: Ba SW

Report

- Irregular narrowing of the esophagus over 5 cm from the tracheal bifurcation
- Shelf-like edges to narrowed segment
- Irregular mucosa
- Proximal dilated esophagus with hold-up of barium
- Small, reducible hiatal hernia with evidence of reflux
- Impression: Esophageal Cancer

Endoscopic biopsy showed adenocarcinoma
Adenocarcinoma on Ba SW

Classic Appearance

• **Early adenocarcinoma** - Focal nodularity, small polyps, plaque-like lesions, sometimes within pre-existing peptic stricture

• **Advanced disease**
  • Infiltrating: long area of irregular narrowing, mucosal nodularity, ulceration, shelf-like borders
  • Polypoid: fungating intraluminal masses, irregular areas of ulceration
  • Ulcerative: large ulcer with tumor rim, can be confused with benign ulcer
  • Varicoid: less common, serpiginous, fixed submucosal defects that mimic varices on still films
Adenocarcinoma on Barium Swallow (contd.)

Associated Features

- Hiatal hernia (80%)
- Gastroesophageal reflux (48%)
- Peptic stricture (20%)
Let’s review the appearance of different forms of esophageal cancer on barium swallow from four different patients.
Patient 1

INfiltrative Adenocarcinoma

Courtesy of Dr. Norman Joffe
Patient 2

Infiltrative adenocarcinoma

Courtesy of Dr. Norman Joffe
Patient 3

Polypoid Adenocarcinoma

Courtesy of Dr. Norman Joffe
Patient 4

VARICOID ADENOCARCINOMA

Note serpiginous filling defects (long, tortuous black areas)

Courtesy of Dr. Norman Joffe
Our original patient JS needs imaging for staging. To better understand this, let’s cover some core information on esophageal adenocarcinoma.
Esophageal Adenocarcinoma

• Epidemiology

Incidence - annual rate of <10/100,000

Recent trends: Adenocarcinomas used to account for 1-4% esophageal cancers. Since the 1970s, however, incidence has shown dramatic increase; they now constitute 50% of new cases, demonstrating an acceleration rate greater than that of any other cancer in the U.S.

Mortality - annual rate is 11,200, which is close to incidence rates.
Risk Factors

• Age
  Rare under the age of 40, and increases steadily afterward, with a median in the sixth decade of life.

• Race and Gender
  White:black ratio - 4:1
  Male:female ratio - 7:1

• Barrett’s esophagus
• Scleroderma, achalasia s/p myotomy - increased risk of Barrett’s esophagus
• ? Tobacco, alcohol
Clinical Features

• Typical patient: 60 yo white male
• Symptoms:
  - Dysphagia, odynophagia, nausea, vomiting
  - Anorexia, weight loss, debility
  - H/o chronic reflux esophagitis or Barrett’s esophagus
• Complications:
  - Obstruction
  - Haemorrhage
  - Perforation
  - Fistula formation
• Often dx late because symptoms tend to manifest with advanced disease
Pathology and Spread

• Distribution
  90% in distal esophagus, may extend into gastric cardia

• Features
  Grossly, can be fungating polypoid, varicoid, superficial raised, flat, depressed, infiltrating, and/or ulcerated. Size: 1-10+ cm
  Resemble adenocarcinomas of gastric cardia, usually moderate-well differentiated, with adjacent areas of high-grade dysplastic/ columnar epithelium

• Spread
  Direct extension - fistulae into trachea, bronchi, aorta
  Lymphatic spread - regional and distant nodes
  Hematogenous spread - lung, liver, adrenals, and bone
Staging

Multimodality approach to therapy requires accurate staging to assess tumor resectability

- **Whole-body scan**: CT, bone scan, PET

- **Regional staging** (depth of wall invasion): EUS > CT (most accurate before any form of therapy)

- **Adjuvants to surgery**: laparoscopy, thoracoscopy, bronchoscopy
**TNM Staging System**

<table>
<thead>
<tr>
<th>T - Primary Tumor</th>
<th>Stage grouping</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tis Carcinoma in situ</td>
<td>Stage 0  Tis   N0   M0</td>
</tr>
<tr>
<td>T1 Tumor invades mucosa or submucosa</td>
<td>Stage I    T1    N0   M0</td>
</tr>
<tr>
<td>T2 Tumor invades muscularis</td>
<td>Stage IIA  T2    N0   M0</td>
</tr>
<tr>
<td>T3 Tumor invades adventitia</td>
<td>Stage IIB  T1    N1   M0</td>
</tr>
<tr>
<td>T4 Tumor invades adjacent structures</td>
<td>Stage III  T3    N1   M0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>N - Regional Lymph Nodes</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>N0 No regional nodes</td>
<td>Stage 0 Tis N0 M0</td>
</tr>
<tr>
<td>N1 Regional node metastasis</td>
<td>Stage I T1 N0 M0</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>M - Distant Metastases</th>
<th>Stage grouping</th>
</tr>
</thead>
<tbody>
<tr>
<td>M0 No distant metastases</td>
<td>Stage IIA T2 N0 M0</td>
</tr>
<tr>
<td>M1 Distant metastasis</td>
<td>Stage IIB T1 N1 M0</td>
</tr>
</tbody>
</table>

Stage IV Any T Any N M1
Radiologic Staging: CT

- Technique:
  - 7-10 mm collimation, contrast-enhanced CT
  - Contiguous slices from thoracic inlet (or cricoid cartilage) through liver

- Overall accuracy of staging is 64%
Radiologic Staging: CT

• Evaluation criteria:
  • Involvement of esophageal wall - focal or circumferential thickening
    T1, 2 - thickness 5-15 mm
    T3 - thickness >15mm with irregular outer contour
  
  • Extension to paraesophageal fat and surrounding structures - T4
    Tracheo-bronchial invasion - indentation/displacement of airway, focal loss of fat plane
    Aortic involvement - interface arcs >90deg suggest invasion
    Other: pericardial thickening or effusion, loss of crural fat planes
Radiologic Staging: CT

- Evaluation criteria:
  - Regional lymph nodes >10 mm - N1
  - Distant metastases (nodes, organs) - M1
    - Hepatic mets - low-density lesions, with ill-defined borders
    - Adrenal mets - enlarged heterogeneous gland

CT Staging: Limitations

- Wall thickness varies with distention of the esophagus
- Cannot distinguish T1 from T2
- Great variance in reported sensitivities and specificities for local extension
- Easy to miss micro-invasion of lymph nodes, and small nodes adjacent to large tumor mass
Our patient JS’ Chest CT

Dilated esophagus proximal to tumor
Aortic arch
Trachea

4x3cm mass in sub-carinal area
Descending aorta
Ascending aorta
SVC
Left PA
JS: CT Staging - T3, N0, ?M

Hiatal hernia

Right adrenal mass
? adenoma, ? met

Slight fullness of left adrenal
• Chest CT should be the first-line imaging modality for staging. If it shows obvious metastases or invasion through the esophageal wall, an EUS is not indicated.

• However, if the CT demonstrates only localized involvement, EUS is indicated to more accurately assess the depth of invasion through the esophageal wall.

• Combined CT and EUS provides a higher accuracy rate overall (86%) than either method alone.
Radiologic Staging: EUS

- **Technique:**
  - Ultrasound transducer, at 7.5 MHz or 12 MHz, introduced into esophageal lumen
  - 360 degree view, 3-10 cm depth penetration
  - Higher frequencies improve clarity at expense of penetration
  - Image quality enhanced by use of water-filled balloon or direct wall contact

- **Anatomy**
  - Characteristic 5-layer wall
  - Normal thickness 2-3 mm when distended
  - Primary cancer usually seen as hypoechoic disruption of those layers
Normal EUS Anatomy

- Mucosa
- Muscularis mucosae
- Submucosa
- Muscularis propria
- Adventitia
Example of EUS
ESOPHAGEAL CANCER

Distal esophageal adenocarcinoma associated with Barrett’s esophagus

Thickening of mucosa and submucosa
T2, N1 lesion

8mm lymph node
Radiologic Staging: EUS

- **Evaluation criteria:**
  - **Degree of involvement of esophageal wall**
    - 85% accurate compared to surgical pathology
  - **Local extension**
    - Bronchoscopy or CT provides better assessment of invasion of the tracheobronchial tree
  - **Regional lymph nodes >10mm - N1**
    - Lower accuracy of 75%
    - Malignant nodes have sharp, rounded borders, and are more hypoechoic than benign nodes
EUS Staging: Limitations

- Tumor stenosis may prevent passage of the endoscope
- Easy to miss micro-invasion of lymph nodes
- Difficult to assess supraclavicular and celiac axis nodes
- Cannot evaluate distant metastases
- Limited availability; academic / research centers
Radiologic Staging: PET

Primary advantage is greater accuracy (86%) compared to CT (73%) for evaluation of extra-mural disease.

Limitations

- Cost
- Restricted availability; academic/ research centers
- Inadequate for local staging (T1-3)
Example of PET Staging:

**LOCAL DISEASE**

[Image of PET scan]

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[Links to resources]

Journal.med.edu/v.4_n.2/11/v42reed.htm

Www.ctsnet.org/journal/ats/68/1133
PET
Distant metastases
Establish treatment objective (cure, prolongation of survival, or palliation) based on stage of disease, age, social situation, and needs of patient

**Options:**

- **Surgery:**
  - 20% of lesions are resectable. However, multiple complications can occur - anastomotic leak, torsion, gangrene etc. Also, survival rates are poor: 25% at one year, 10% at 5 years post-op

- **Radiation therapy:**
  - External beam and intraluminal radiation can be palliative or rarely, curative; mean response is 3 months, with 3-year survival in localized disease around 10%
Treatment (contd.)

• **Chemotherapy:**
  - Agents include combination cisplatin / 5-fluorouracil, gemcitabine, paclitaxel

• **Multimodality therapy:**
  - Combined modality (chemo + radiation therapy), alone or followed by surgery, may increase cure rate and prolong survival, but has high morbidity and expense

• **Palliation of dysphagia:**
  - Peroral dilation and stents
  - Electrocautery, Argon plasma coagulator, Nd:YAG laser for ablation of superficial tumor
  - Photodynamic therapy uses Photofrin (porphyrin compound) and low-power laser to sensitize, then ablate superficial cancer
Palliative stent

Www.mindspring.com/~atlsouthgastro/es_mt_03.html
Treatment: JS

- **Esophagectomy based on T3, N0 staging:**
  - Mass removed was 4 x 2 x 1.8 cm adenocarcinoma, moderately-poorly differentiated, with adventitial invasion
  - 13 regional lymph nodes were negative but radial margin was positive for tumor

- **Chemotherapy:**
  - 5 cycles of cisplatin / 5-fluorouracil
  - Trials of Xeloda, Gemcitabine, and Taxotere
  - JS developed multiple subcutaneous nodules, increasing SOB, and cough
Follow-up surveillance

- Response to therapy (evaluation of residual tumor) can be performed with EUS, which is superior to endoscopy with biopsy.

- Local recurrence can be followed with EUS > CT

- Distant spread can be evaluated with CT, PET, and bone scans.
JS: Follow-up CT

Left and right posterior sub-carinal masses
Obviously, esophageal cancer is difficult to treat when diagnosed in its advanced stages. Let’s discuss how we might screen and survey patients to pick up the disease early on, when it has a better prognosis for long-term survival.
Screening

Mass screening using abrasive balloon cytology can be applied to high-risk areas (e.g. China), but is not cost-effective for low-incidence areas like the U.S.

Consider screening high-risk individuals only:
Barrett’s esophagus, scleroderma, ?chronic reflux esophagitis (especially older white males)
Screening Methods

Endoscopy:

• with Lugol’s iodine staining (abnormal areas do not stain dark brown and should be biopsied)

• With OCT (optical coherence tomography) - uses infrared light to produce high resolution images of tissue microstructure; may enhance sensitivity of screening by pre-selecting dysplastic areas for biopsy
OCT

**(Optical Coherence Tomography)**

- Non-invasive cross-sectional optical imaging technique
- Similar to EUS, but uses light instead of acoustic signal
- Used as an adjunct to endoscopy
- Provides 10-fold higher resolution than clinically available EUS: ~10µm via longitudinal transverse scan
- Limited depth of field - few millimeters (here: 5.5mm x 2.5mm depth)
- Normal esophagus: can visualize 5 layers up to inner circular muscularis propria
- OCT provides morphological and diagnostic information for Barrett’s esophagus and adenocarcinoma
OCT: Normal esophagus

From Bouma et al. Gastrointestinal Endoscopy 51(4):April 2000

Five-layered architecture of wall:

- ep – epithelium
- lp – lamina propria
- mm – muscularis mucosa
- sm – submucosa
- mp – muscularis propria, inner circular layer
OCT: Barrett’s Esophagus

From Bouma et al. Gastrointestinal Endoscopy 51(4):April 2000
OCT: Adenocarcinoma

From Bouma et al. Gastrointestinal Endoscopy 51(4):April 2000
Surveillance

- Periodic testing of high-risk individuals with confirmed Barrett’s esophagus
  
  **Methods:**
  - UGI endoscopy q1-2 years, complemented by 4-quadrant biopsy. Sensitivity may be enhanced using OCT, as previously described.
  - Virtual CT endoscopy

  **Management:**
  - Medical therapy with antacids and antireflux agents for mild dysplasia
  - Prophylactic esophagectomy for high-grade dysplasia
Although non-radiologic, esophagoscopy is so important to the work up of esophageal pathology that we include some examples of the classic endoscopic appearance of such pathology, including Barrett’s esophagus and esophageal cancer.
Endoscopy:
NORMAL ESOPHAGUS

Squamo-columnar junction

Www.mindspring.com/~atlsouthgastro/es_ge_01.html
Endoscopy:
Reflux Esophagitis

Www.mindspring.com/~atlsouthgastro/es_es_02.html
Endoscopy: 
**Barrett’s Esophagus**

Columnar epithelium

Ulcerated area

Raised lesion

Www.mindspring.com/~atlsouthgastro/es_ba_01.html  
Www.mindspring.com/~atlsouthgastro/es_ba_02.html  
Www.mindspring.com/~atlsouthgastro/es_ba_05.html
Endoscopy:
ADENOCARCINOMA

Www.mindspring.com/~atlsouthgastro/es_mt_02.html
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- BIDMC
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