

# GI Grand Rounds

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Moderator: Dr. Lukens

# History

*CC:* Solid food dysphagia

*History:*

- 80 yr old woman presents with solid food dysphagia since '04.
- EGD disclosed a lower esophageal stricture. This was dilated with a balloon ('04 and '05). Biopsies disclosed normal esophageal mucosa. She was placed on PPI.
- She presents now with symptom recurrence . She refers weight loss of 10 lbs over the past 2 mo.

# History

- PMH: HTN, HL, GERD, Breast Ca dx 2005, Hypothyroidism
- PSH: Thyroidectomy, Right Breast Mastectomy
- FAM HX: Mother with Breast Cancer; Father with HTN
- Social : Retired, widowed lives alone. Worked in college administration. 40 pack yr hx of tobacco quit 25 yrs ago. Four alcoholic beverages/month.

# History

- Medications: Arimidex ,Simvastatin, Verapamil, Omeprazole 20 mg BID
- All: Codeine-difficulty swallowing
- ROS: Dysphagia for past two to three months with wt loss of 10 lbs, + vomiting with undigested food, shortly after swallowing. No abdominal pain. No heartburn. No hematemesis. + Sensation of food getting stuck in her chest.

# Physical Exam

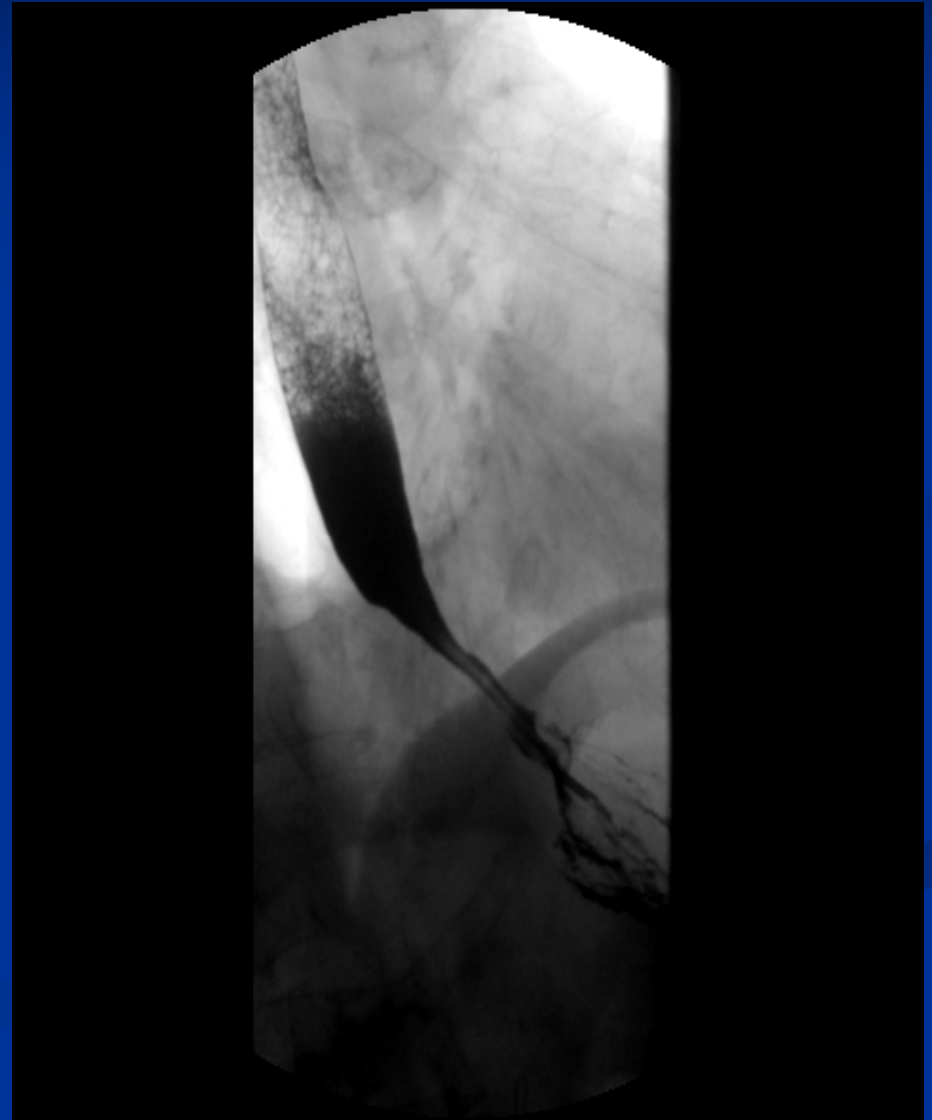
- GEN:NAD, AAOx3
- HEENT: No scleral icterus, PERRLA, EOMI, normal oropharynx
- Neck: No LAD, no JVD, scar from thyroidectomy
- Card: RRR, no M/R/G
- Lungs: CTABL
- Abdomen: Soft, NT, positive for ascites, +BS
- Extremities: No edema

# LABS

<b>WBC:</b> 7	<b>HGB:</b> 12	<b>HCT:</b> 36.7	<b>PLT:</b> 270
Na: 144	K: 4.3	Cl: 106	CO2: 25
BUN: 28	Creat: 1.7	Alb: 3.5	ALT: 14
TB: 0.4	ALK: 94	Amy: 138	Lip: 62

# Imaging:

- There is tapered narrowing of the distal esophagus to the level of the GE junction, and extending approximately 3 or 4 cm above the esophageal hiatus. The liquid barium was noted to hang up above this narrowing, with delayed passage into the stomach. Mild gastroesophageal reflux was demonstrated in the prone position.
- Contrast passed through the stomach and readily into the duodenum.



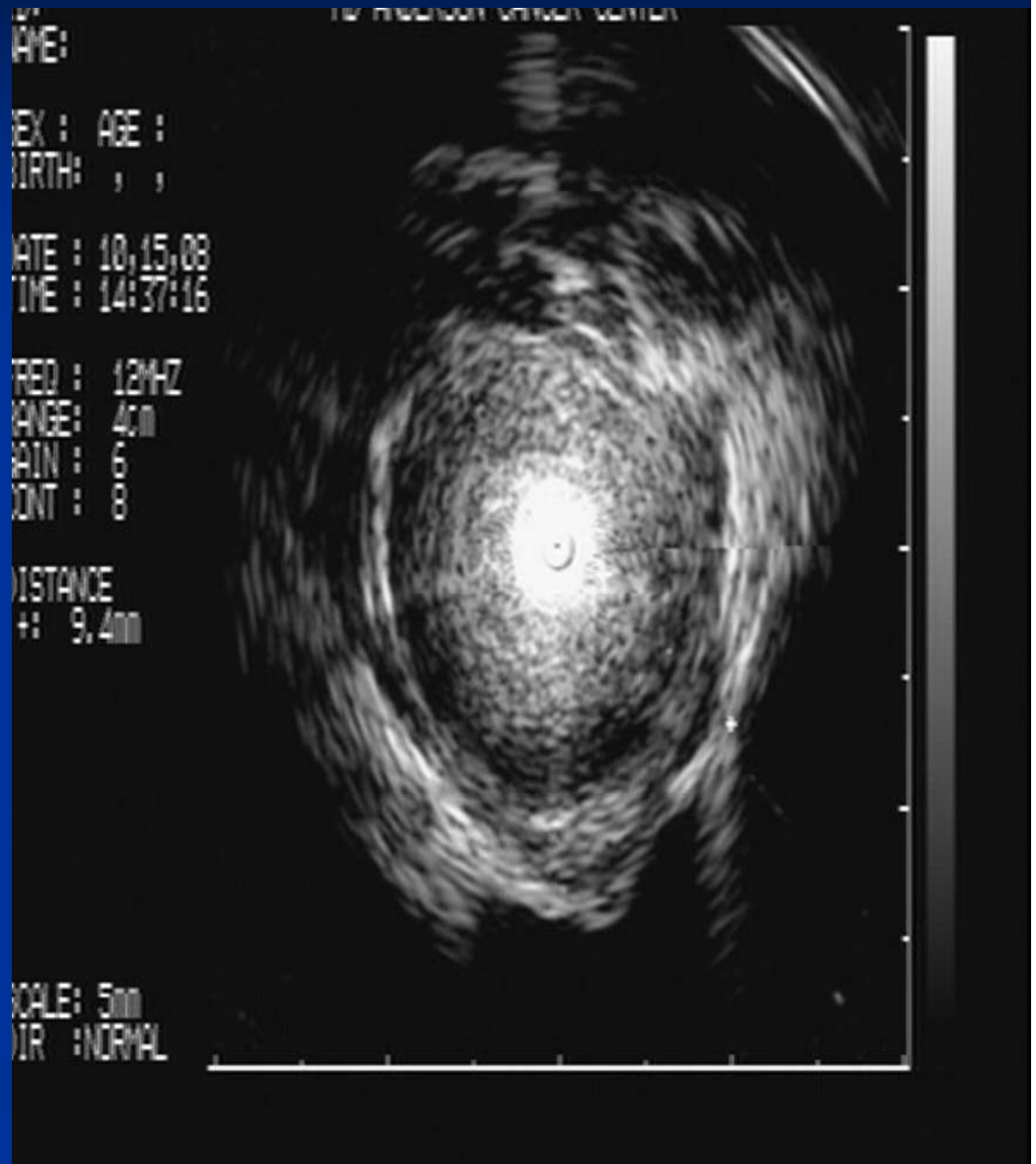
# Endoscopy

- A smooth stricture was seen 35 cm from the incisors with normal appearing mucosa. The standard adult endoscope was unable to traverse the stricture.



# EUS

- A 12 MHz miniprobe was passed through the upper endoscope into the stricture and that showed the esophageal wall to be thickened to about 10mm. Lack of echo pattern was consistent and highly suspicious for a malignant infiltrative process.

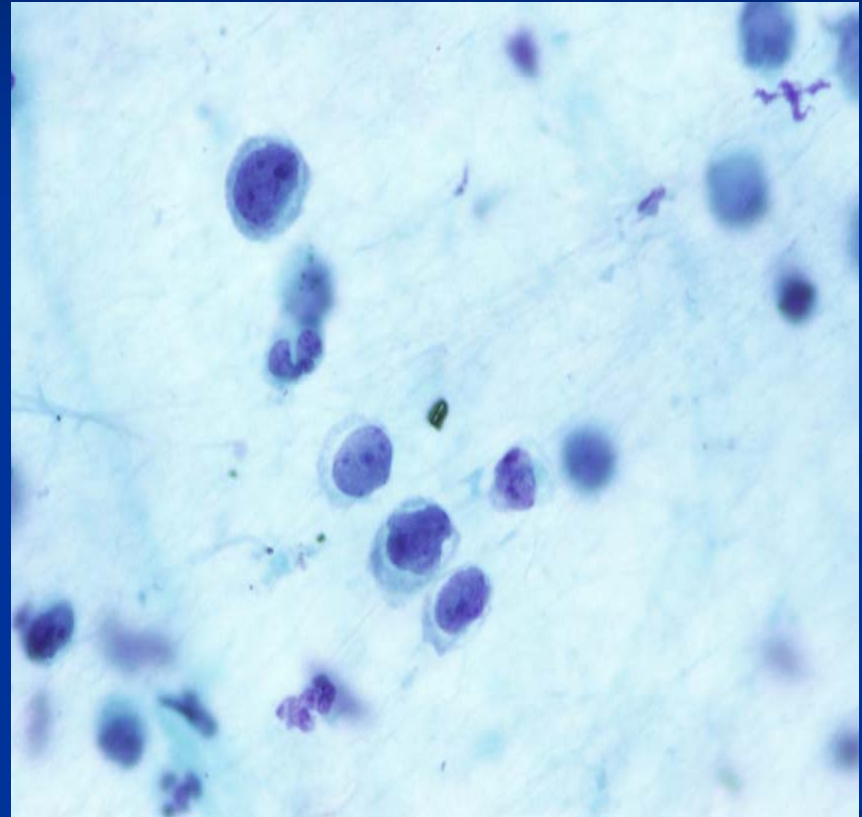
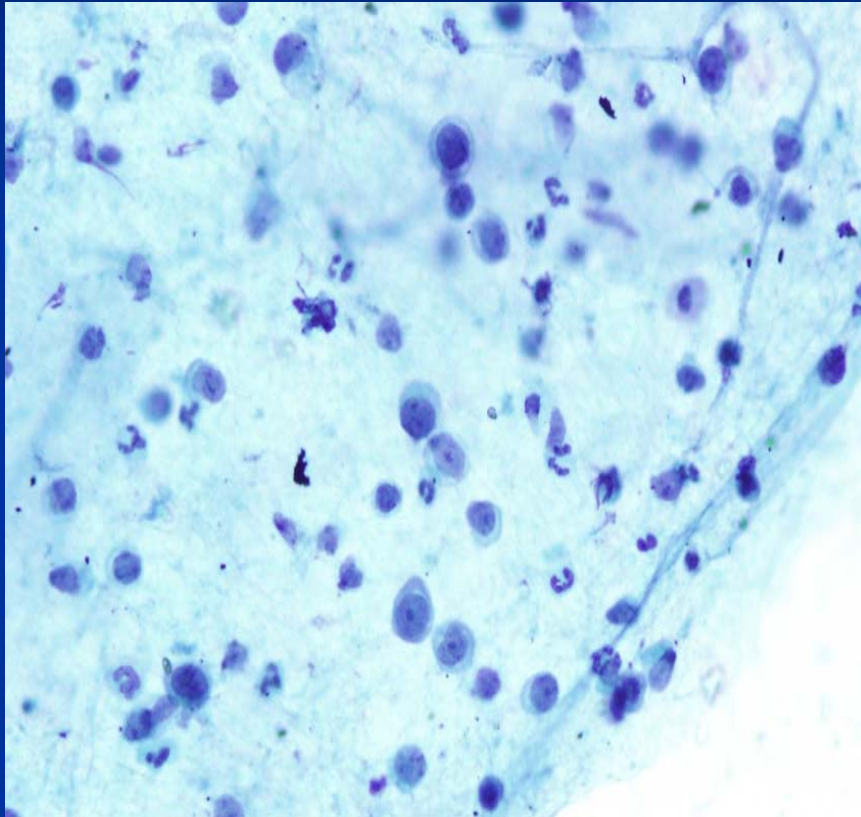


# EUS-Linear

- The linear echoendoscope was passed to the level of the stricture and it also showed thickened esophageal wall consistent with an infiltrating process involving all the layers and penetrating into the adventitia.

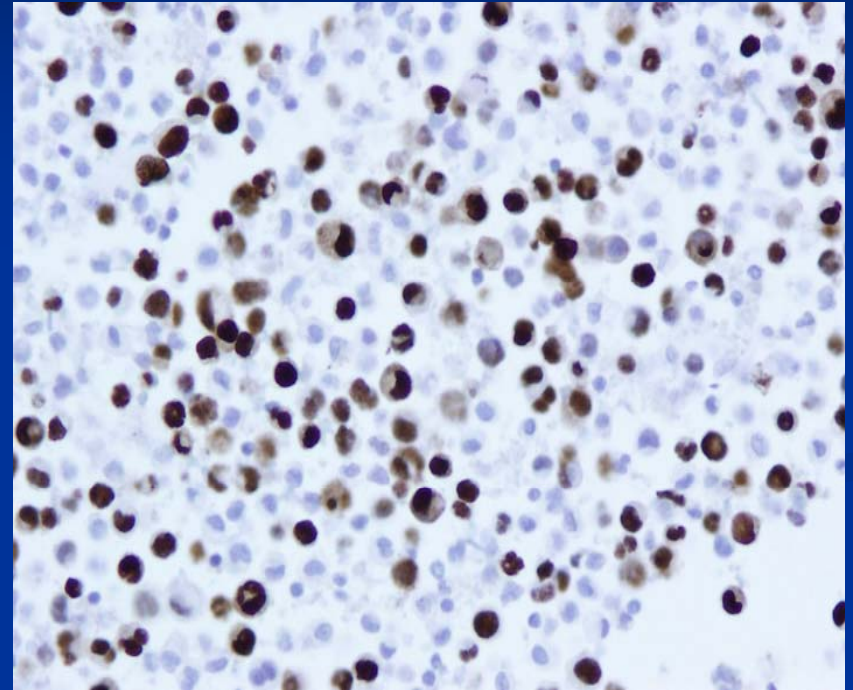
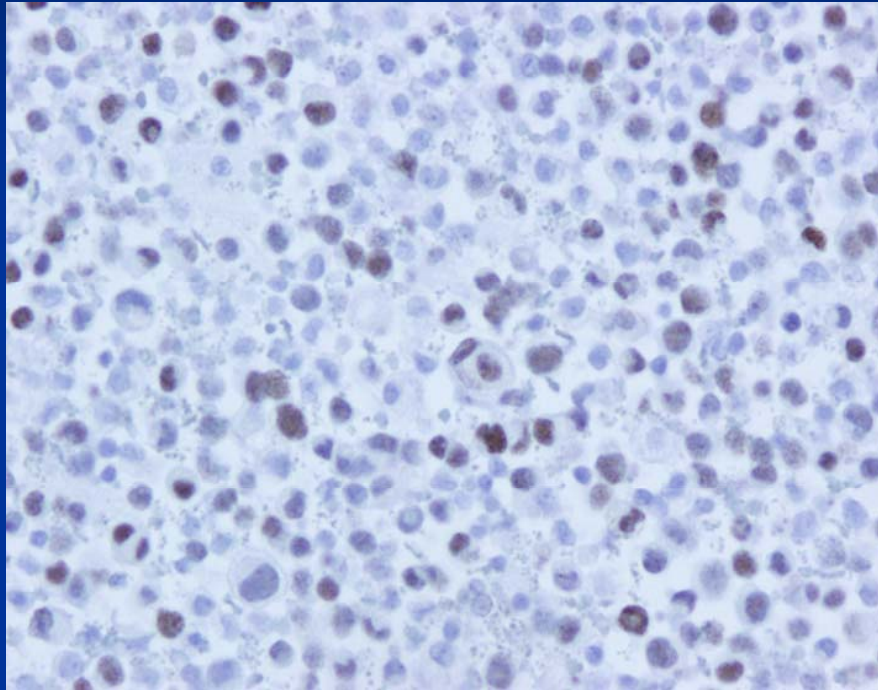


# Path



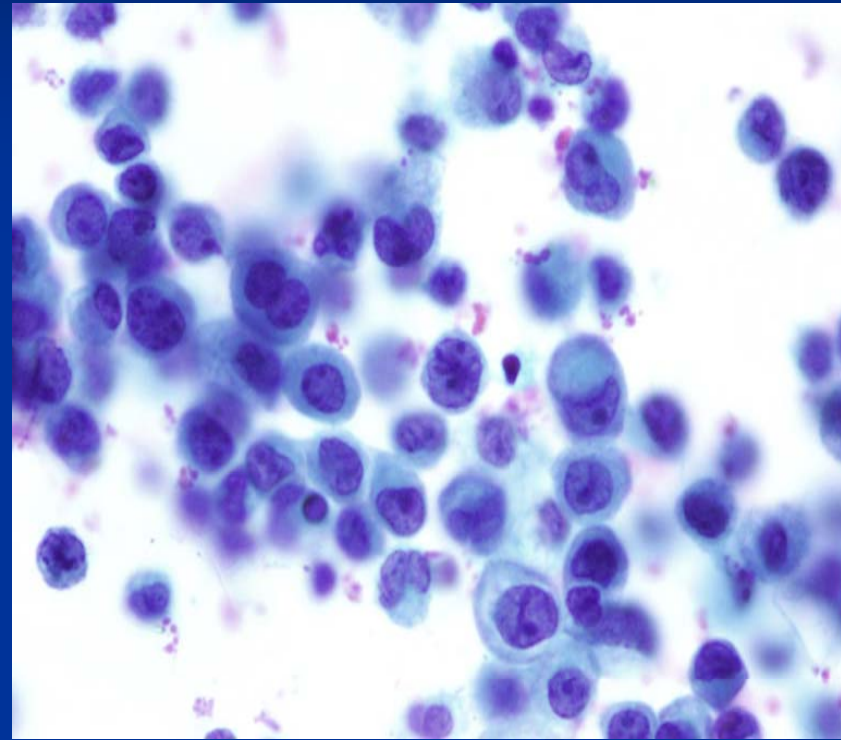
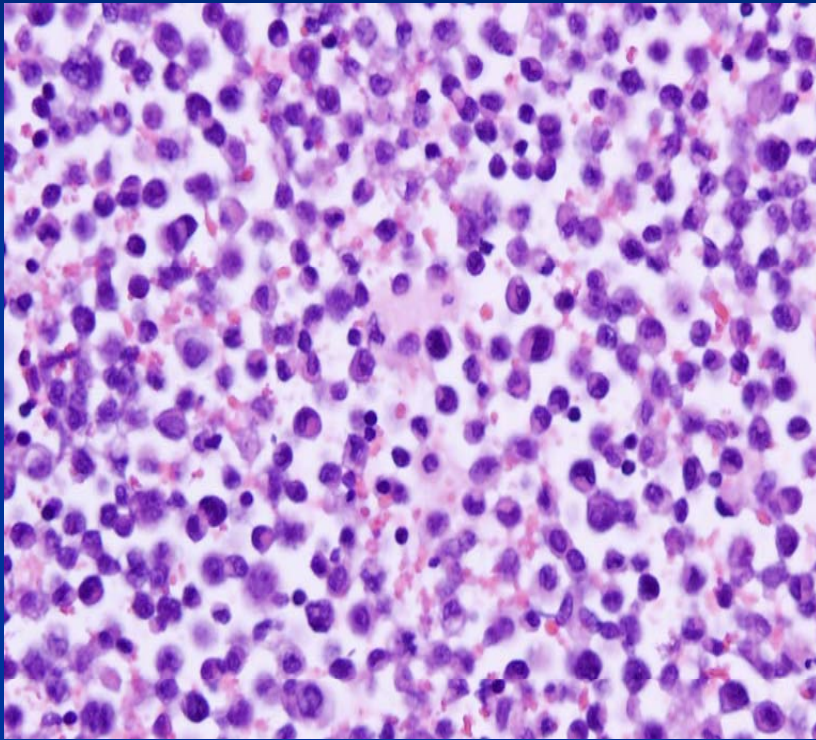
- Features were consistent with breast primary.

# Ascitic fluid Path



- Immunohistochemical studies performed on cell block sections show that the tumor cells are positive for ER, PR and negative for calretinin supporting the diagnosis of Breast cancer.

# Path H and E, Cytology



- Consistent with patient's history of Invasive Lobular Carcinoma with ER, PR and Her2/neu weakly positive (40%).

# Discussion

- Metastatic spread to esophagus from breast cancer has been estimated to 0.4% of all cases of symptomatic esophageal obstruction.

- Toreson WE. Secondary carcinoma of the esophagus as a cause of dysphagia. Arch Pathol. 1944;38:82-84.
- Borst MJ, Ingold JA. Metastatic patterns of invasive lobular versus invasive ductal carcinoma of the breast. Surgery 1993. 114(3):637-41.

- Autopsy studies shown up to 6% of breast cancer patients have metastasis to the esophagus.

- Asch MJ et al. Gastrointestinal metastases from carcinoma of the breast: autopsy study and 18 cases requiring operative intervention. Arch Surg. 1968;96:840-843.
- Abrahms HL, et al. Metastases in carcinoma: Analysis of 1000 autopsied cases. Cancer 1950;3:74-85.
- Graham, WP et al. Gastrointestinal metastasis from carcinoma of the breast. Ann Surg 1964;159:477-480.

- The most common malignancy to spread to the esophagus is breast carcinoma.

- Herrera JL, et al. Benign and metastatic tumors of the esophagus. Gastroenterol Clin North Am 1991;20:775-89.

# Discussion

- Patients present with dysphagia, the most common symptom.
- Other associated symptoms are weight loss, anorexia, aspiration, or dysphonia.
- Achalasia and dysmotility have also been reported.
- Significant proportion also suffer from laryngeal nerve paralysis.

- Nazareno J et al. Metastatic breast cancer to the gastrointestinal tract: A case series and review of the literature. World J Gastro. 2006 12(38):6219-6224

Nazareno reported in his case series review of 6 patients showed metastases from breast cancer can present as stricture, dysmotility, or pseudoachalasia.

-Nazareno J et al. Metastatic breast cancer to the gastrointestinal tract: A case series and review of the literature. *World J Gastro.* 2006 12(38):6219-6224.

Table 1 Summary of gastrointestinal presentations of metastatic breast cancer

Site	Presentation	Reference
Oropharynx	Oropharyngeal dysphagia	(Case 2)
	Tongue lesion	11
Esophagus	Stricture	(Case 3), 8, 13, 32-45
	Achalasia	(Case 1), 9, 10
	Non-specific dysmotility	31
Stomach	Linitis plastica	(Case 4), 5, 6, 46-53
	Obstruction/Stenosis	(Case 5), 19, 46
	Polyp	46, 54, 55
	Ulcer/Erosion	19, 46, 56, 57
	Perforation	58
Small intestine	Obstruction/Stenosis	(Case 4), (Case 6), 20, 59-62
	Multiple strictures/ Diffuse infiltr.	(Case 5)
Colon	Obstruction/Stenosis	25, 60, 63-66
	Asymptomatic abdominal Mass	19
	Multiple strictures/ Diffuse infiltr.	(Case 6), 67
	Polyp	68
	Rectum	Obstruction/Stenosis
	Linitis plastica	48

**Table 1** Clinical data of the patients

Patient	Age (years)	Tumor location and endoscopic features	Symptoms and duration (weeks)	Treatment	Status	Survival time (months)
1	79	Lower esophageal mass	Dysphagia (8)	Stent and hormonal therapy	Dead	4.13
2	77	Lower esophageal stricture	Dysphagia (9)	Dilatation and stent	Alive	12.00
3	66	GEJ mass	Dysphagia (72)	Stent and hormonal therapy	Dead	96.63
4	57	Gastric cardiac mass	dyspepsia (26)	Hormonal therapy	Dead	19.97
5	75	Gastric body mass	Anemia and weight loss (6)	Chemotherapy	Dead	10.10
6	75	Diffuse gastric body mass	Anemia and abdominal pain (2)	Palliative care only	Dead	21.37
7	64	Ulcerated pyloric mass	Anemia (4)	Palliative care only	Dead	7.33
8	60	Obstructing pyloric mass	Vomiting and abdominal pain (1)	GJ and chemotherapy	Alive	12.67
9	90	Stenotic pyloric mass	Vomiting (12)	Stent and hormonal therapy	Dead	2.07

*GJ* gastrojejunostomy; *GEJ* gastroesophageal junction

Ayantunde review of nine patients revealed patient presented with symptoms for minimum of 2 mos prior to presentation when the lesion in the lower esophagus.

- Ayantunde A. A. Esophagogastric Cancers Secondary to a Breast Primary Tumor Do Not Require Resection. *World J Surg* 2007 31:1597-1601.

- Rampado reported in his case series and review of 25 patients, largest case series to date, that majority of the lesions are located in the mid-esophagus.
- Median length of stricture was 5 cm. Longest was 7 cm.
- Endoscopic biopsies were negative in 17/19 (89%). 24 out of 25 had normal appearing mucosa.

**TABLE 2. Level of Esophageal Stricture**

Level of Stricture	% (No.)
Upper esophagus	20 (5/25)
Mid esophagus	52 (13/25)
Lower esophagus	28 (7/25)

**TABLE 1. Details of Prior Breast Cancer Treatment**

Patient No.	Age (yr)	Disease-Free Interval (yr)	Type of Surgery for Breast Cancer	Adjuvant Therapy
<b>1980–1990</b>				
1	52	9	Mastectomy	No
2	56	9	Mastectomy	No
3	46	8	Mastectomy	Telecobalt therapy + chemotherapy
4	75	22	Mastectomy	No
5	56	20	Mastectomy	Telecobalt therapy
6	71	8	Mastectomy	Radiotherapy
7	69	4	Mastectomy	Telecobalt therapy
8	53	9	Mastectomy	Radiotherapy + chemotherapy
9	67	10	Mastectomy	Chemotherapy
10	58	16	Mastectomy	Telecobalt therapy
11	45	4	Mastectomy	No
<b>1991–2006</b>				
12	65	17	Mastectomy	Radiotherapy + chemotherapy
13	63	2	Quadrantectomy	Radiotherapy + chemotherapy + hormone therapy
14	70	14	Mastectomy	No
15	51	21	Mastectomy	Chemotherapy + hormone therapy
16	58	9	Quadrantectomy	Radiotherapy
17	56	1.5	None	Radiotherapy + chemotherapy
18	87	11	Mastectomy	Radiotherapy + hormone therapy
19	56	20	Mastectomy	Hormonal therapy + radiotherapy
20	75	9	Quadrantectomy	Radiotherapy + chemotherapy
21	53	14	Mastectomy	Radiotherapy
22	58	10	Quadrantectomy	Radiotherapy
23	64	17	Mastectomy	Hormone therapy
24	56	17	Mastectomy	Radiotherapy + chemotherapy + hormone therapy
25	62	3	Mastectomy	Radiotherapy + chemotherapy + hormone therapy
Total	58	10	—	—

Mean period between diagnosis of cancer and onset of symptoms due to esophageal metastases is around 8-10 years; longest reported interval is 24 yrs.

# Discussion

- Most patients are post-menopausal

- Anaya D et al. Esophageal perforation in a patient with metastatic breast cancer to esophagus. *Ann Thorac Surg* 2006;81:1136-8.

- Only has been 11 cases where the esophagus has been the first recurrent site.

- Only three cases in the literature where mucosal layers of the esophagus presented with breast metastasis.

- Wada Y et al. Esophageal metastasis of breast carcinoma. *Breast Cancer* 2009 16:151-156.

# Mechanism

- Esophageal spread from breast cancer has been proposed from periesophageal LN through intramammary lymphatics which can cause esophageal obstruction, at the level of the carina. Cancerous lymph nodes may become fixed to the surrounding structures, thereby compressing the esophageal lumen.
- Tumor may infiltrate intramurally within the esophagus and disrupt motility by obliterating nerve plexuses as well as the normal architecture of the esophagus.

- Rampaddo S. Mediastinal Carcinosis Involving the Esophagus in Breast Cancer: The Breast-Esophagus Syndrome. *Ann Surg* 2007;246: 316-322.

# Lobular versus Ductal

- Metastatic patterns of invasive lobular and invasive ductal carcinoma differ with regards to gastrointestinal metastasis.
- Ductal carcinomas are composed of well formed glandular structures while Lobular carcinomas are non-cohesive small cells dispersed in fibrous stroma.
- Down-regulation or loss in expression of the cell to cell adhesion molecule E-cadherin in lobular carcinomas is believed to be reason for difference.

- Gujral D. An unusual case of dysphagia in ductal breast cancer due to submucosal oropharyngeal metastatic spread: a case report. *Cases Journal* 2009. 2(3)1-4.

**Table 2** Clinicopathological data of the patients

Patient	Histology	Other sites of metastases	Ascites	ER status (biopsy of the metastasis)	CK7	EMA	CA153	Time between primary and secondary cancers (years)
1	Ductal	Lung	No	+ve	-ve	+ve	210	4.51
2	Lobular	Lymph nodes (LN)	No	+ve	+ve	+ve	321	6.52
3	Lobular	Bone and peritoneum	Yes	+ve	+ve	+ve	126	19.78
4	Lobular	Liver and bone	Yes	+ve	+ve	+ve	233	32.75
5	Ductal	Brain	No	-ve	+ve	-ve	16	11.50
6	Lobular	Peritoneum, bone and LN	No	+ve	+ve	+ve	48	2.83
7	Lobular	Peritoneum, bone, and brain	No	+ve	+ve	+ve	598	5.52
8	Lobular	Bone	Yes	+ve	+ve	+ve	357	5.33
9	Lobular	Peritoneum, bone, and LN	No	+ve	+ve	+ve	52	10.48

*ER* estrogen receptor; *CK* cytokeratin; *EMA* epithelial associated membrane antigen; *CA153*, carcinoma antigen (0–35 KU/l); +ve positive; -ve negative

## Lobular versus Ductal

Ayantunde case series revealed invasive lobular carcinoma is more likely to have gastrointestinal metastasis over ductal carcinoma.

- Ayantunde A. A. Esophagogastric Cancers Secondary to a Breast Primary Tumor Do Not Require Resection. *World J Surg* 2007 31:1597-1601.

TABLE 4. Sites and histological findings of gastrointestinal metastases

Histological finding	Site of involvement				Overall, n (%)
	Esophagus	Stomach	Small intestine	Colon and rectum <sup>a</sup>	
GI metastasis (group 1)					
Lobular	2	6	2	8	18 (34)
Ductal	0	4	2	3	9 (17)
Mixed	0	0	0	0	0
Unknown	0	0	0	1	1 (2)
GI metastasis and carcinomatosis (group 3)					
Lobular	2	4	4	6	16 (30)
Ductal	0	1	2	5	8 (15)
Mixed	0	0	0	1	1 (2)
Unknown	0	0	0	0	0
Overall (groups 1 and 3)					
Lobular	4	10	6	14	34 (64)
Ductal	0	5	4	8	17 (32)
Mixed	0	0	0	1	1 (2)
Unknown	0	0	0	1	1 (2)
Total, n (%)	4 (8)	15 (28)	10 (19)	24 (45)	53

GI, gastrointestinal.

<sup>a</sup> One patient had a rectal metastasis of ductal origin.

McLemore et al. findings in their retrospective review of 73 patients from 1985-2000 that lobular carcinoma had a greater propensity to metastasize to the GI tract, and peritoneum.

# Radiographic Findings

- Barium swallow usually shows a smooth concentric mid-esophageal stricture.
- Endoscopy typically shows normal overlying mucosa due to metastatic lesions being submucosal. Endoscopic biopsies are usually nondiagnostic.
- CT may show diffuse wall thickening throughout the length of the stricture and sometimes the presence of adenopathy.

# Management

- First line of treatment are hormonal therapy, systemic chemotherapy, and/or radiation.

-- Wada Y et al. Esophageal metastasis of breast carcinoma. Breast Cancer 2009 16:151-156.

- Esophageal dilatation has shown high risk of perforation, as high as 26% in case series.

--Varanasi R et al. Breast Carcinoma Metastatic to the Esophagus: Clinicopathological and Management Features of Four cases, literature review. The Amer J Gastro. 1995;90:(9)1495-1499.

- Palliative therapy with expansile stenting. If unsuccessful, placement of feeding tube should also be considered.

# Cases which resulted in Perforation after dilation.

*Reports in the English Literature of Dysphagia from Metastatic Breast Cancer Managed with Endoscopic Dilation*

Author (ref)	n	Age (yr)	Disease-free yr	Level of Stricture	Dilation Technique	Perforation
Varanasi	4	63	8	Mid	Balloon	Yes
		64	22	Mid	Balloon/Savary	Yes
		78	8	Mid	Maloney	Yes
		67	20	Mid	Balloon	No
Holyoke (5)	1	44	4	Mid	Unknown	Yes
Boccardo (10)	1	66	5	Mid	Endoprosthesis	No
Stallone (17)	1	74	19	Mid	Endoscope	Yes
Atkins (21)	5	Unknown	Unknown	Mid	Unknown	Yes
		69	11	Mid	Unknown	Yes
		77	7	Mid	Maloney	Yes
		Unknown	Unknown	Upper/mid	Unknown	No
		67	3	Mid	Maloney	No
Phadke (23)	1	49	8	Distal	Unknown	Yes

# Rampado reports in this table the survival of the 25 cases.

**TABLE 3. Clinicopathologic Characteristics, Treatment, and Survival**

Patient No.	Level of Stricture	Duration of Dysphagia (mo)	Other Sites of Metastases	Endoscopic Biopsy/Brush Cytology	EUS	Therapy	Status (mo)
1980–1990							
1	Mid	12	Bone	Positive	No	Prosthesis*	Dead, 2
2	Mid-lower	6	Liver	Negative	No	Laparoscopy, dilation, prosthesis, chemotherapy	Dead, 3
3	Upper-mid	5	No	Negative	No	Dilation	Dead, 19
4	Mid	6	Liver	Negative	No	Dilation	Dead, 1
5	Lower	3	Skin	Negative	No	Chemotherapy	Dead, 39
6	Upper	5	Bone	Negative	No	Dilation <sup>†</sup>	Dead, 12
7	Lower-cardia	2	Liver	Negative	No	Laparoscopy, dilation <sup>‡</sup>	Dead, 1
8	Upper	14	Pulmonary, lymph nodes	NA	No	Gastrostomy	Dead, 7
9	Mid	3	Liver, bone	Negative	No	Dilation, prosthesis	Dead, 2
10	Mid	7	No	Negative	No	Dilation, prosthesis	Dead, 19
11	Upper	2	Bone	Negative	No	Gastrostomy, chemotherapy	Dead, 1
1991–2006							
12	Mid	14	No	Negative	No	Dilation, hormone therapy	Alive, 67
13	Mid	5	Bone, lymph nodes	NA	Yes	Hormone therapy, chemotherapy	Dead, 16
14	Mid	8	No	Negative	Yes	Thoracoscopy, radiotherapy, hormone therapy	Dead, 26
15	Mid	9	No	Negative	No	Radiotherapy, hormone therapy	Alive, 75
16	Lower	12	bone	Negative	Yes	Thoracoscopy, dilation, prosthesis	Dead, 34
17	Mid	1	Skin, bone	Negative	No	Dilation	Dead, 1.5
18	Upper	2	Skin	Positive	No	Dilation, hormone therapy	Dead, 3
19	Upper-mid	15	Skin	Negative	No	Dilation, prosthesis, <sup>§</sup> hormone therapy	Alive, 40
20	Mid	11	No	Negative	Yes	Thoracoscopy, hormone therapy	Alive, 19
21	Cardia	24	No	NA	No	Laparoscopy, gastrostomy, hormone therapy	Alive, 28
22	Mid-lower	10	No	NA	Yes	Thoracoscopy, hormone therapy, chemotherapy	Alive, 1
23	Mid	8	No	Negative	No	Thoracoscopy, hormone therapy, chemotherapy	Alive, 1
24	Upper	10	Skin	NA	No	Prosthesis, chemotherapy	Alive, 1
25	Cardia	24	No	NA	Yes	Myotomy, hormone therapy	Alive, 1
Total	—	7.5	—	—	—	—	—

\*Esophageal perforation managed conservatively.

<sup>†</sup>Esophageal perforation treated with gastrostomy, cervical drainage, and stent placement to seal the perforation.

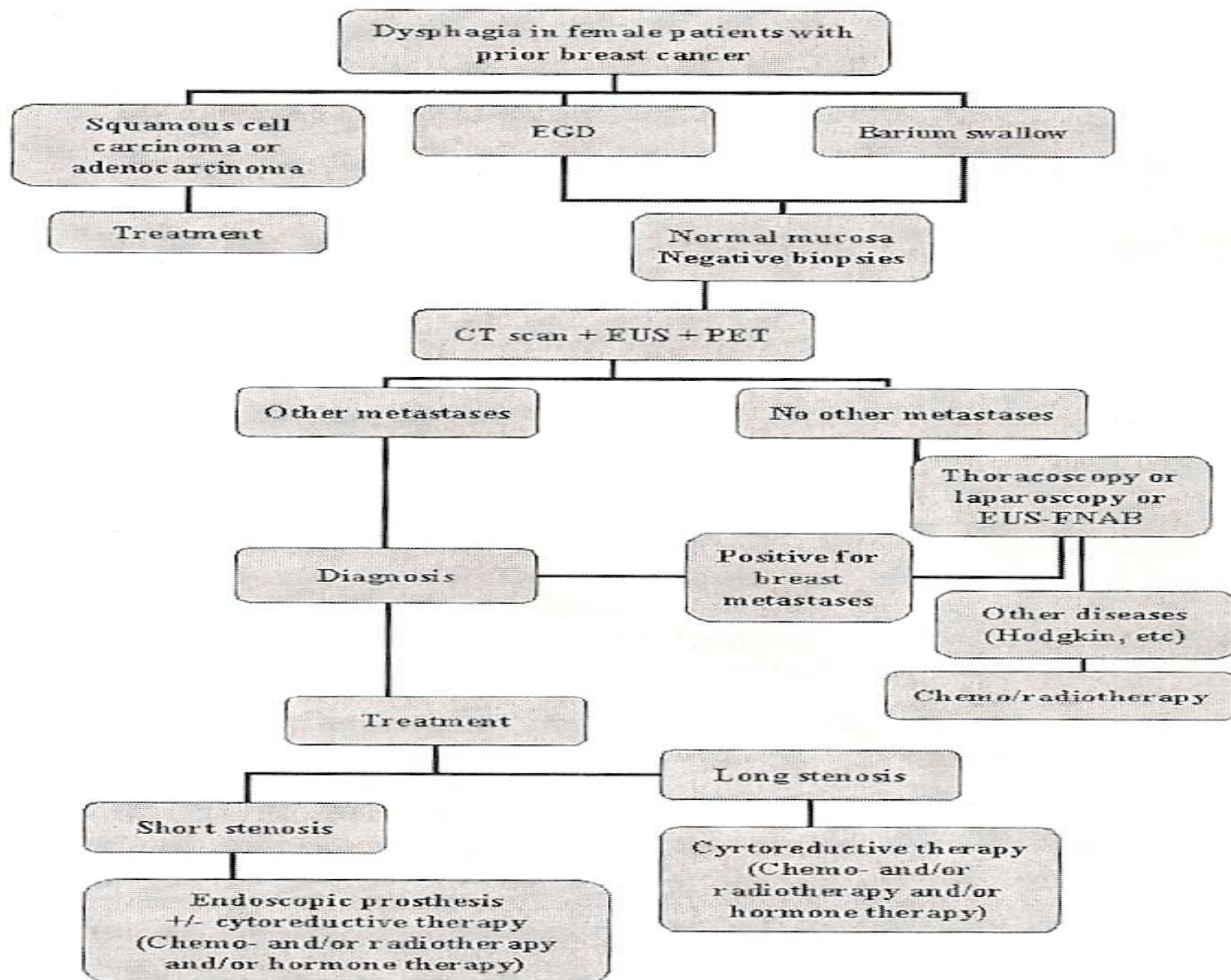
<sup>‡</sup>Esophageal perforation treated with esophagectomy and retrosternal gastric pull-up.

<sup>§</sup>Tracheoesophageal fistula managed with subcutaneous esophagogastric bypass.

<sup>||</sup>Died of respiratory failure during the perioperative period.

NA indicates not assessed; EUS, endoscopic ultrasound.

# Treatment algorithm



# Follow Up

- Patient after completing EGD and EUS had paracentesis performed along with CT which showed carcinomatosis and ascitic fluid consistent with breast cancer.
- Patient also had EGD and stent placement and again began systemic chemotherapy (Paclitaxol protein bound).
- Patient after starting chemotherapy was admitted to her local hospital which her chemotherapy was discontinued and she later passed away.