

# Grand Rounds

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# Chief Complaint

- Melena
- Chronic diarrhea
- Weight loss

# History of Present Illness

- 64 y/o HF with PMH CAD s/p PCI, HLD, CHF, NSTEMI admitted with melena
- Black tarry stools x 2 weeks
- Watery diarrhea x 2 months with 6-8 BMs/day
- No h/o colonoscopy
- Unexplained weight loss of greater than 40 lbs over the last 8 months
- Diffuse abdominal pain associated with N/V/D

# History of Present Illness

- N/V x 2+ months
- EGD at outside GI center 3 days prior to admission for N/V/abdominal pain with findings of bile reflux, gastritis, and esophagitis with biopsy results pending
- After EGD, pt started on Omeprazole and Sucralfate
- Pt unable to tolerate sucralfate secondary to N/V

# History of Present Illness

- Pt presented to MHH ER with N/V/D/abdominal pain/melena and found to be hypotensive
- Hypotension responded to fluid boluses
- NGT lavage negative
- Pt reported being on Clopidogrel and ASA for recent NSTEMI s/p cardiac cath with PCI to LAD one month earlier

# Past Medical History

- CAD s/p PCI with stent placement to the LAD 8/09
- NSTEMI 8/09
- HLD
- CHF

# Past Surgical History

- Cholecystectomy
- Hiatal hernia repair

# Social History

- Married with 5 sons and 12 grandchildren
- Lives in Southeast Houston
- Retired from the catering business
- No tobacco use
- No alcohol use
- No IV drug abuse
- No transfusions
- No tattoos

# Family History

- No family history of colon cancer, liver disease, or IBD
- Father deceased at age 62 from CHF
- Mother deceased at age 83 from lung CA
- Brother and sister with DM-2 and HTN

# Allergies

- NKDA

# Medications

- ASA 325mg po daily
- Sucralfate 1g per 10mL 2 tsp po BID
- Clopidogrel 75mg po daily
- Hyoscyamine 0.125mg SL q6-8 hours
- Metoprolol 50mg po daily
- Lisinopril 5mg po daily
- Omeprazole 20mg po daily
- Simvastatin 40mg po qHS
- KCL 20meq po daily

# Review of Systems

- Gen: +fatigue, +weight loss
- HEENT: negative
- CV: negative
- Pulm: +DOE
- GI: +abdominal pain, +N/V, +diarrhea, +melena
- GU: negative
- MSK: +bilateral ankle swelling
- Neuro: +weakness
- Psych: negative
- Derm: negative

# Physical Exam

- BP: 91/52
- HR: 84
- R: 16
- T: 97.6
- O2sats: 93% on RA

# Physical Exam

- General: Normal
- HEENT: Normal
- Neck: Normal
- Heart: +II/VI SEJ murmur at LLSB
- Lungs: Normal
- Abd: soft, nontender, nondistended, +BS, no G/R/R, no palpable hepatosplenomegaly/masses
- Ext: trace bilateral LE edema
- Neuro: Normal
- Skin: Normal

# Labs

WBC	4.0
Hgb	9.2
Hct	28.1
Plt	156
MCV	84.2

# Labs

PT	15.5
INR	1.44
PTT	41.5

# Labs

Na	132
K	3.4
Cl	106
CO2	23
BUN	15
Cr	0.7
Glu	117
Ca	7.6

# Labs

Alb	1.8
Alk phos	45
ALT	9
AST	9
Tbili	0.7
Dbili	0.1
Ibili	0.6

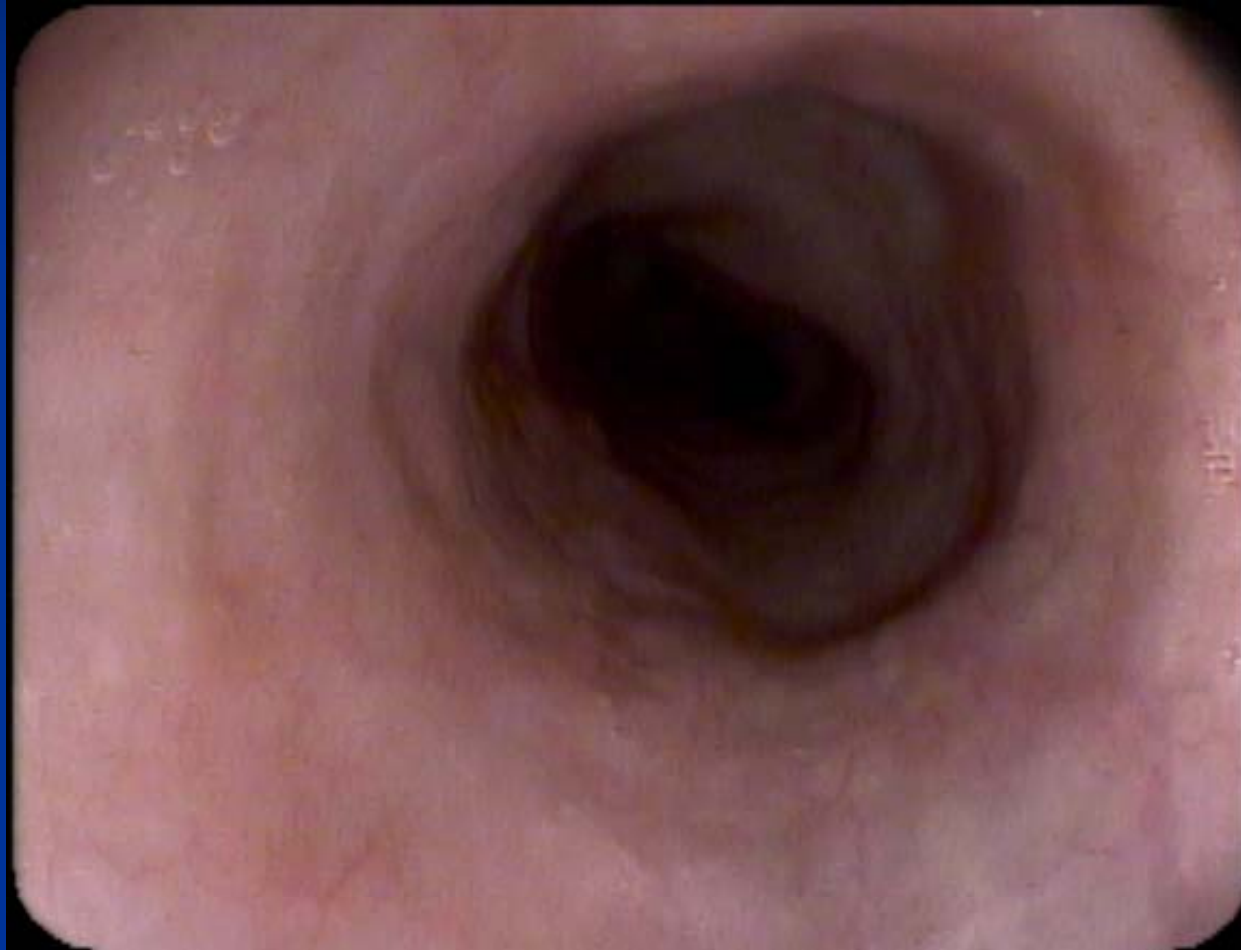
# Imaging

- CT Abd/Pel
  - Liver, pancreas, and spleen normal
  - CBD measures 11.4mm tapering to the level of the ampulla with no intra/extrahepatic ductal dilatation
  - Mild to moderate amount of ascites
  - Sigmoid colon demonstrates a long segment of circumferential wall thickening with associated scattered diverticula

# Questions

- What is the differential diagnosis?
- How would you further evaluate this patient?

# EGD



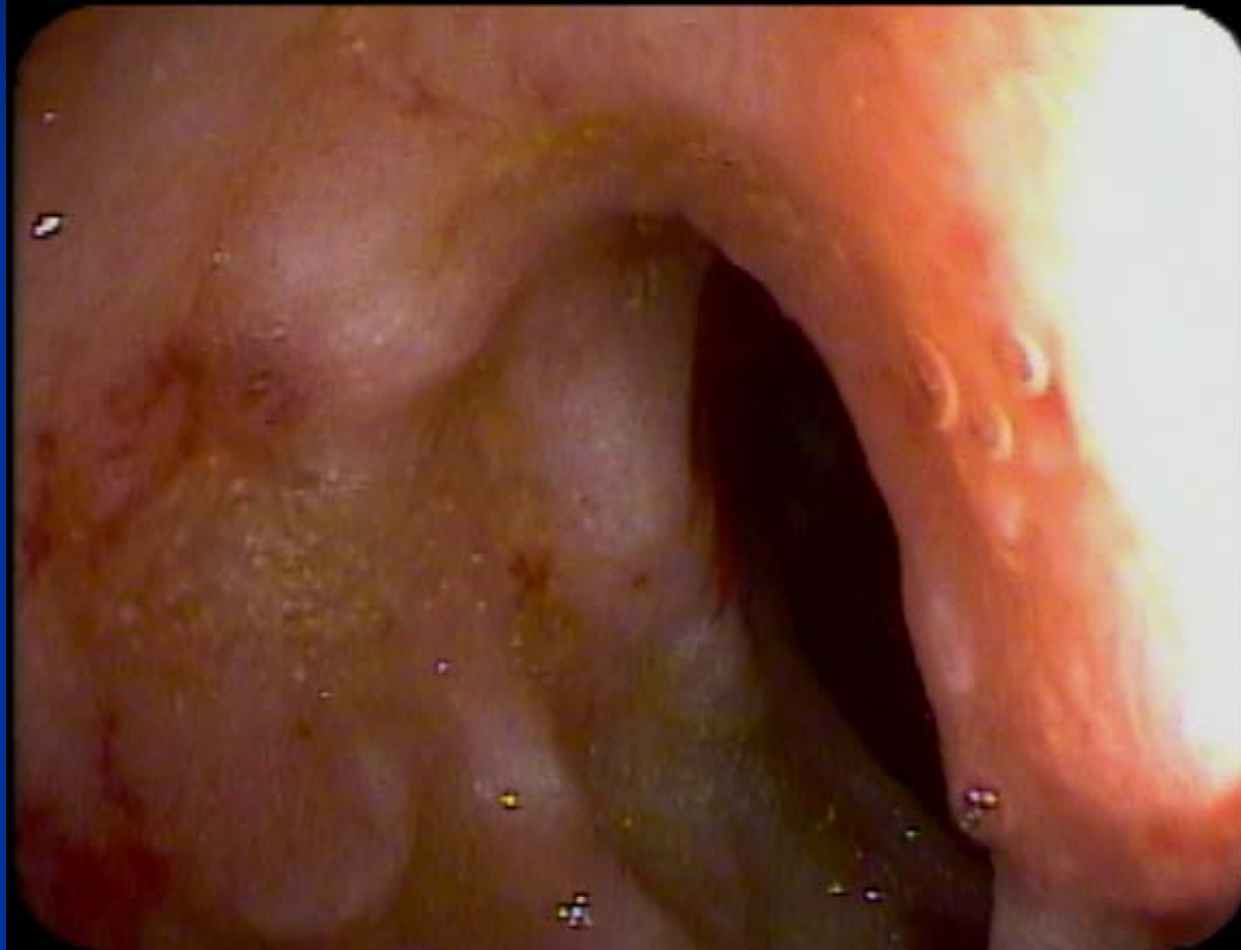
# EGD



# EGD



# EGD



# Colonoscopy



# Colonoscopy



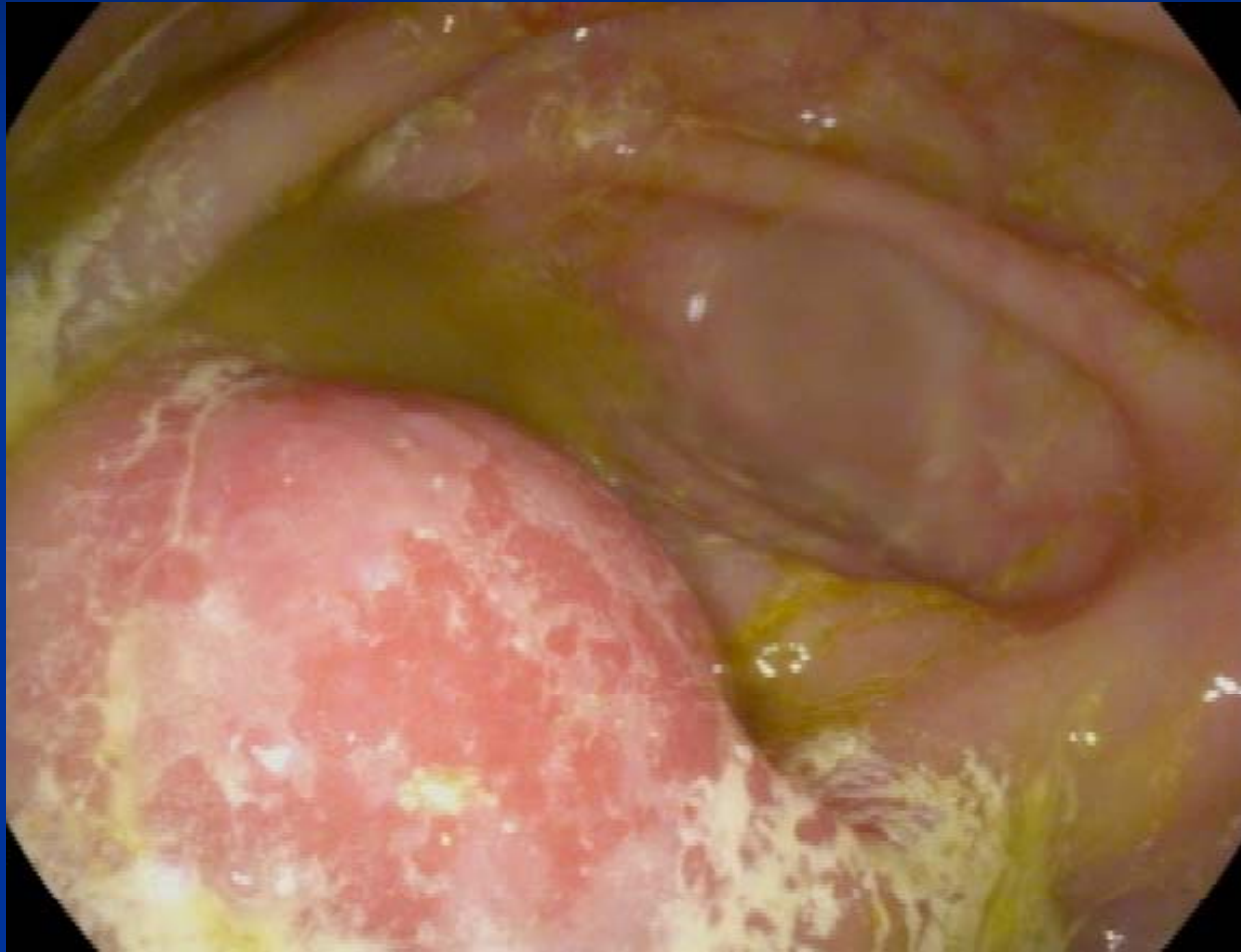
# Colonoscopy



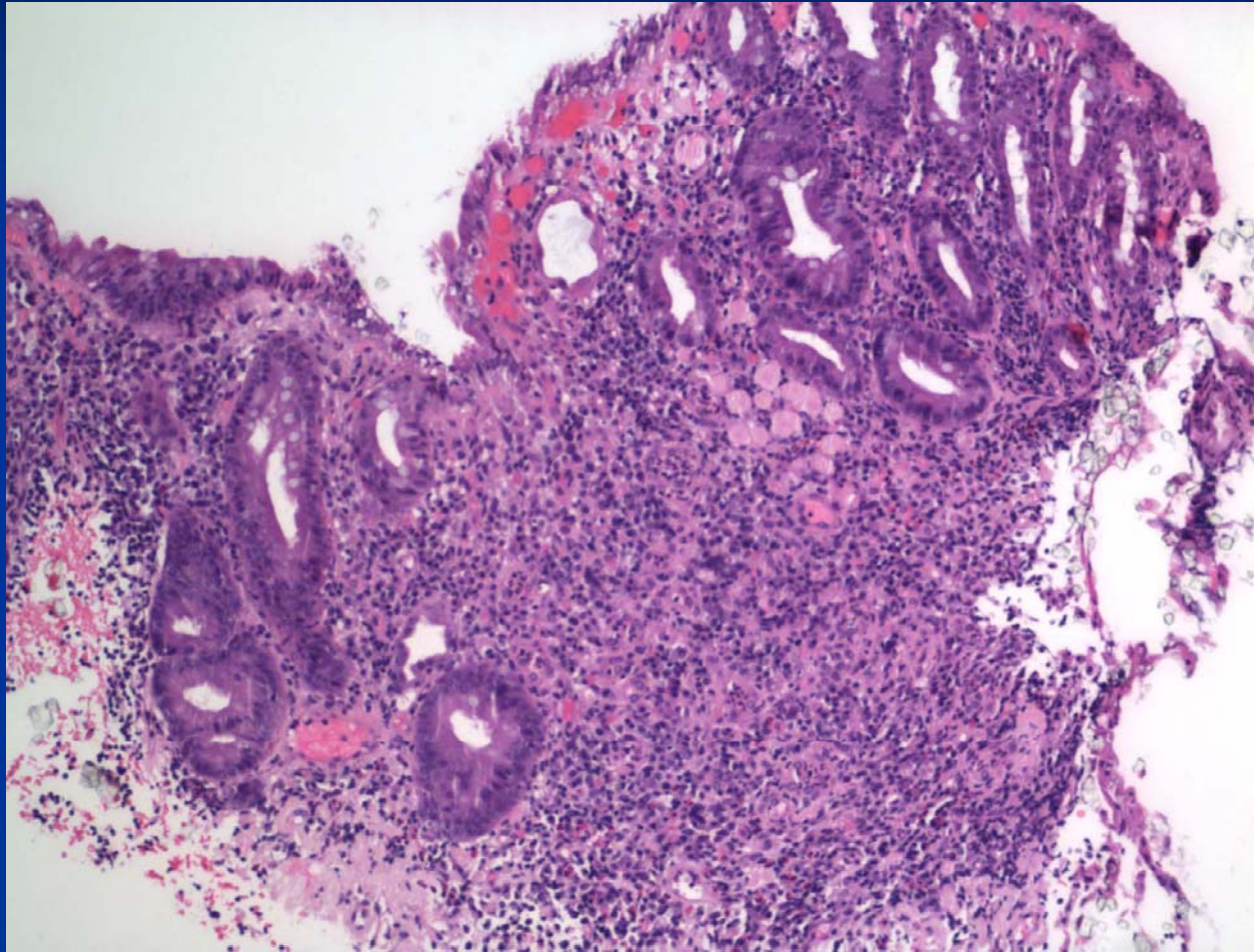
# Colonoscopy



# Colonoscopy

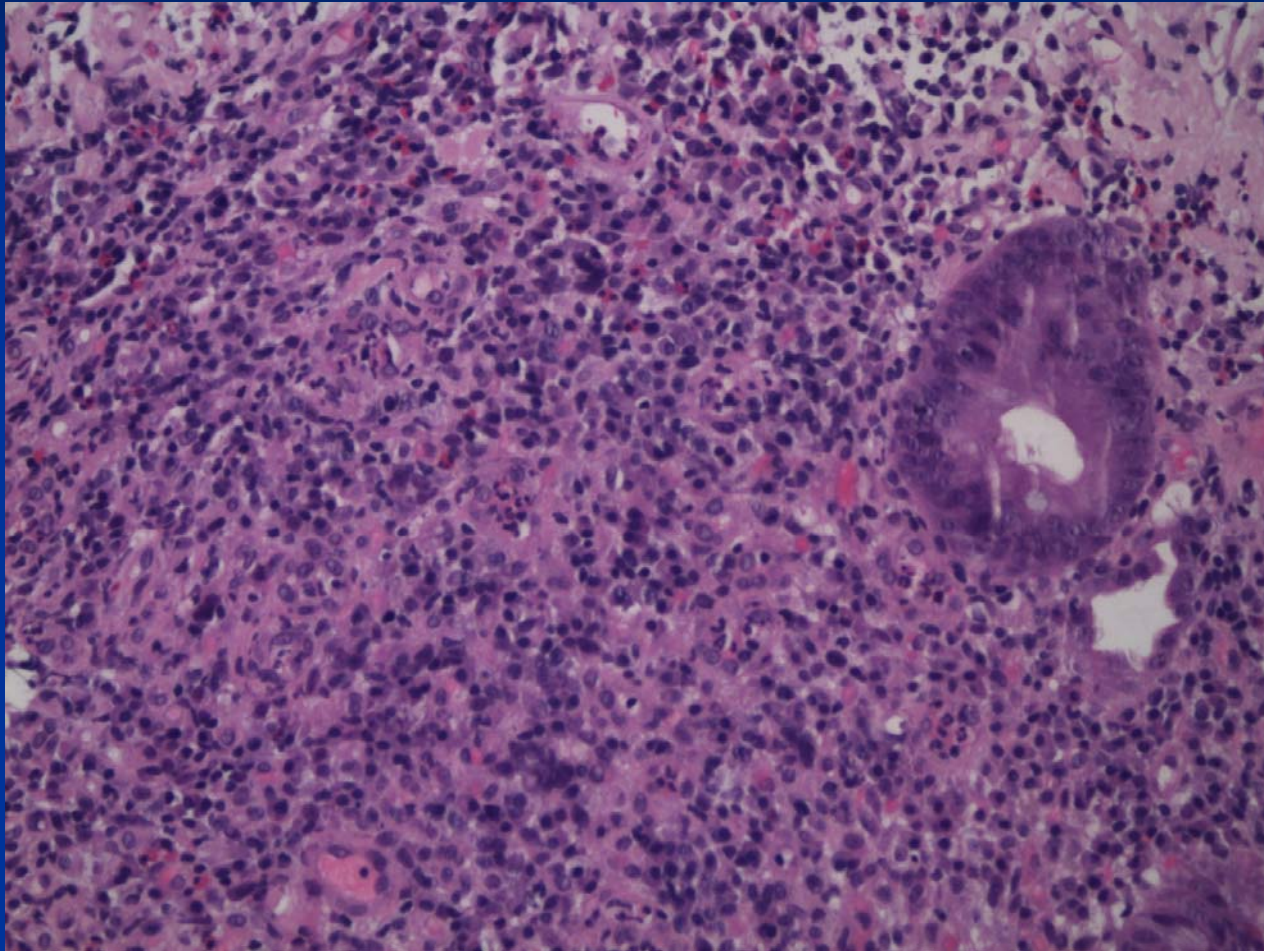


# Pathology



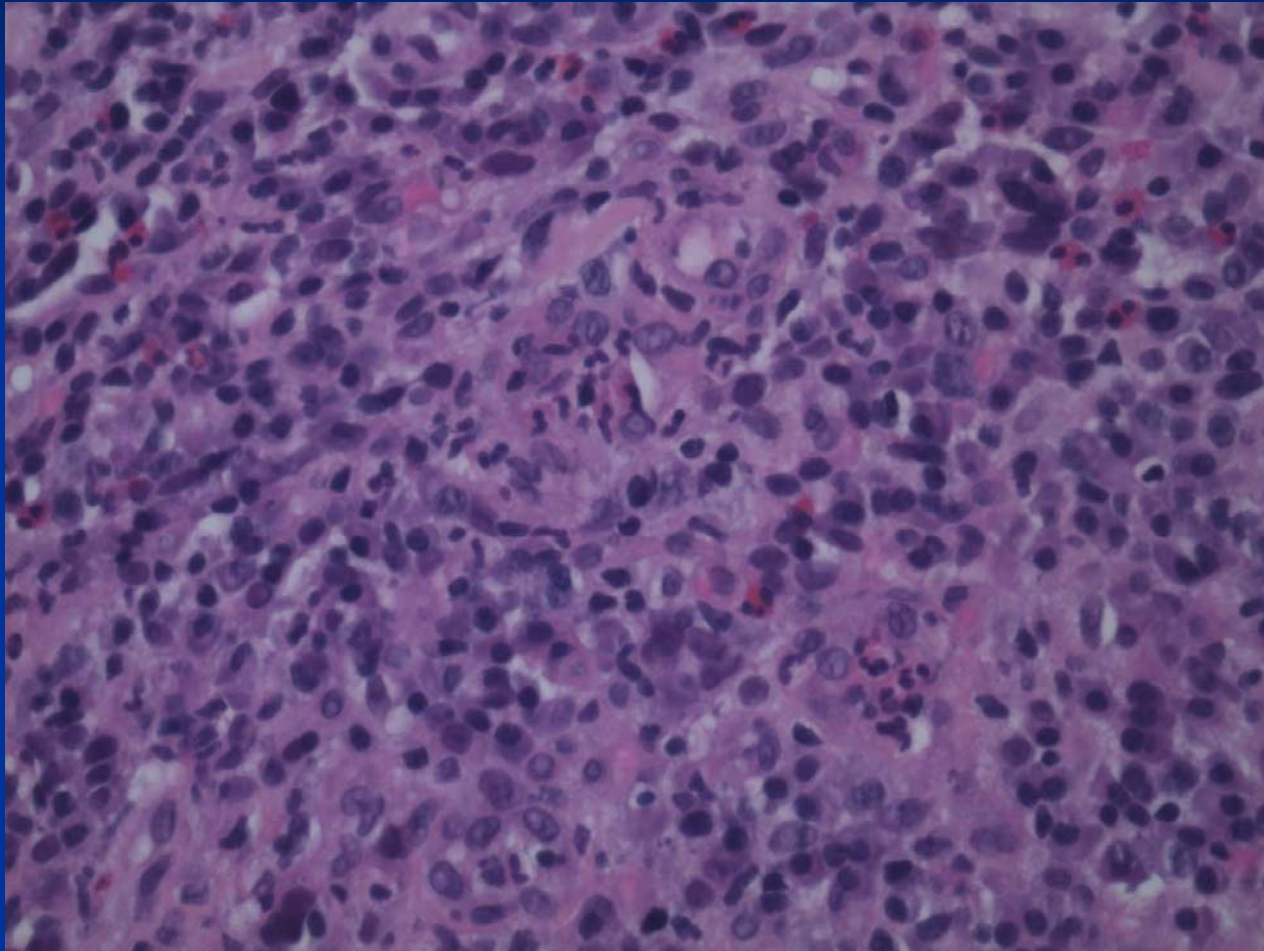
IC valve - moderate chronic inflammatory cells in the lamina propria with reactive changes in the gland

# Pathology



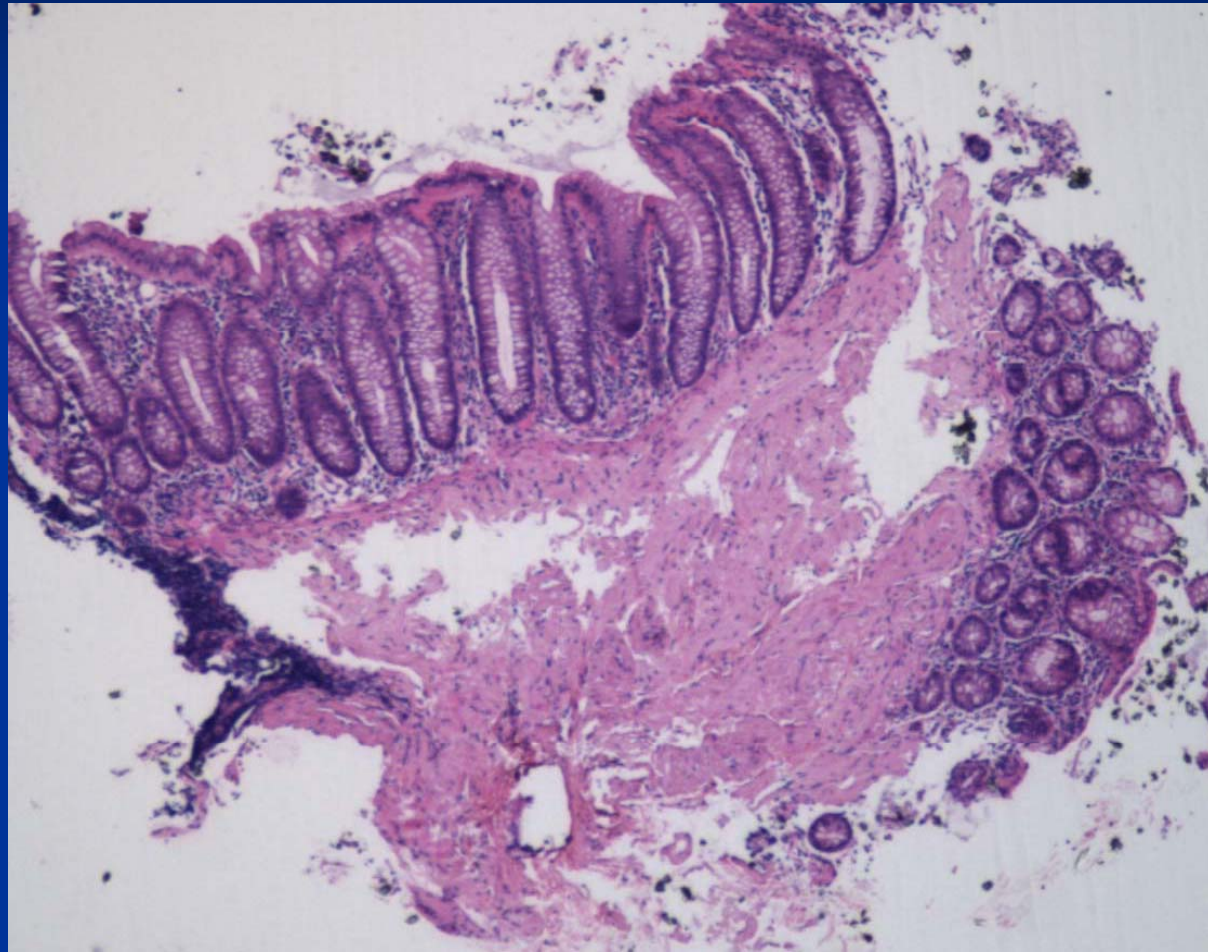
IC valve - higher magnification with mixed inflammatory infiltrate

# Pathology



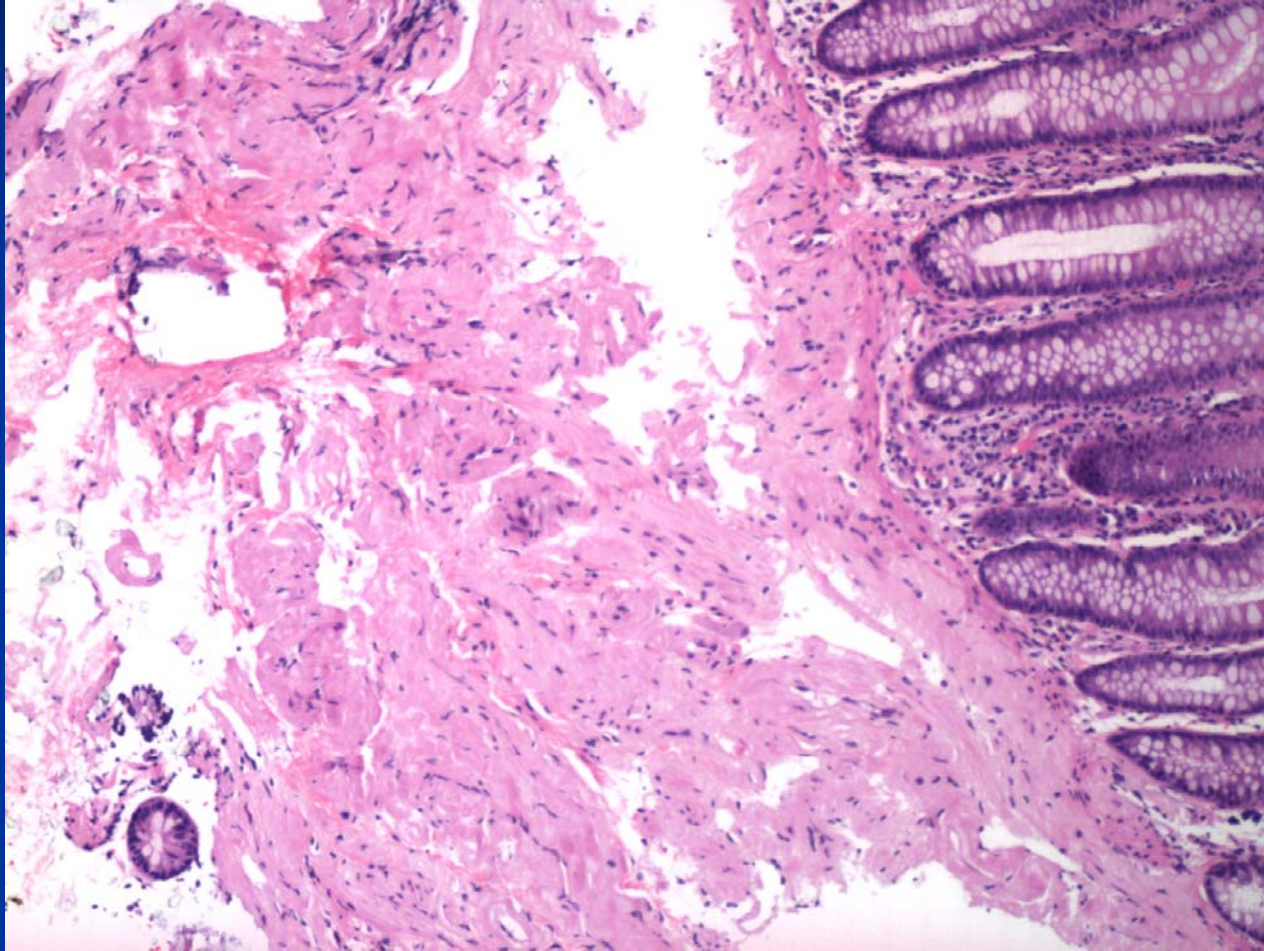
IC valve - 100x magnification with mixed inflammatory infiltrate including lymphocytes, neutrophils and eosinophils

# Pathology



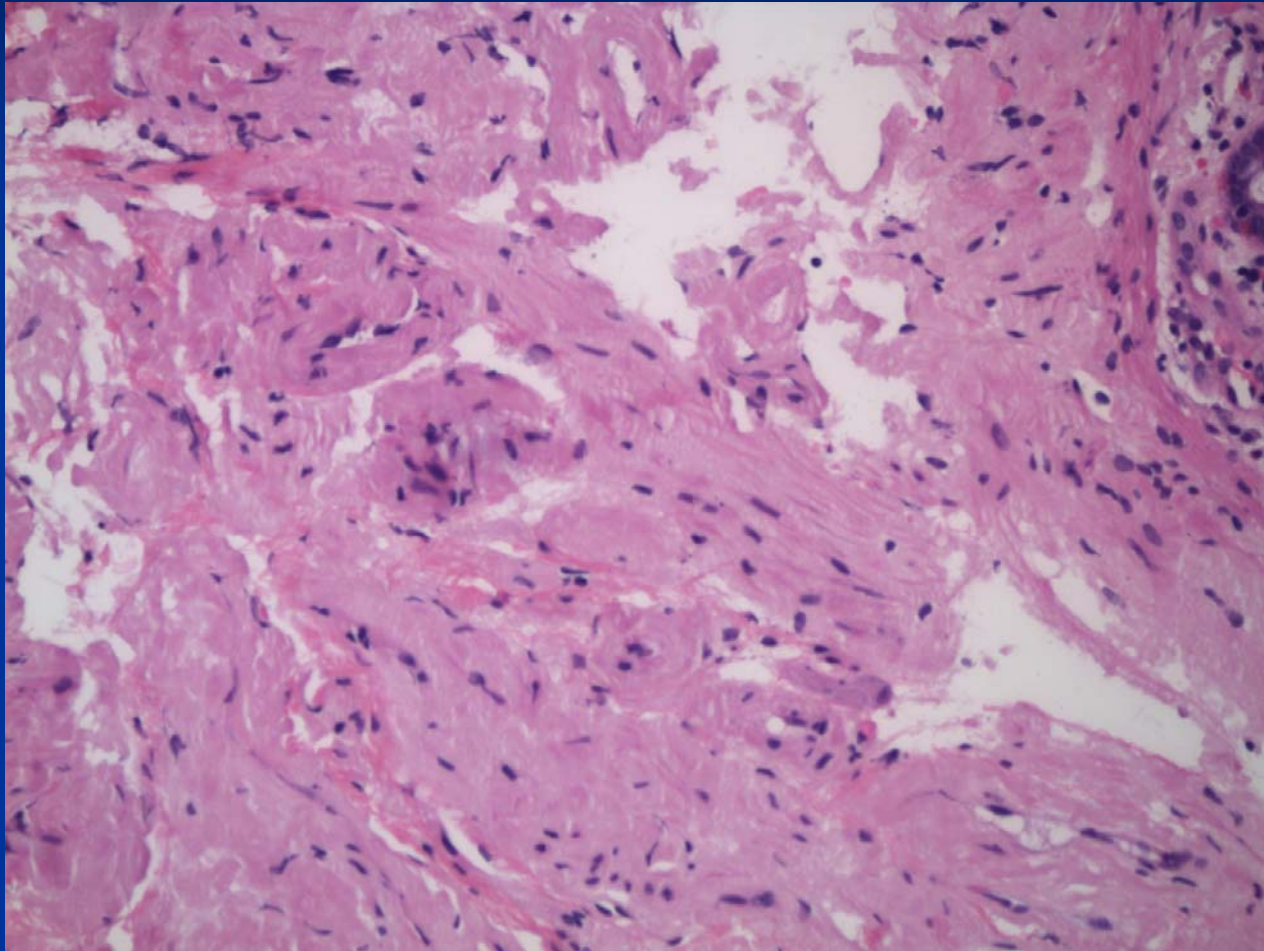
IC valve - crushed lymphoid aggregate with a large submucosal area with amorphous, fibrillary material

# Pathology



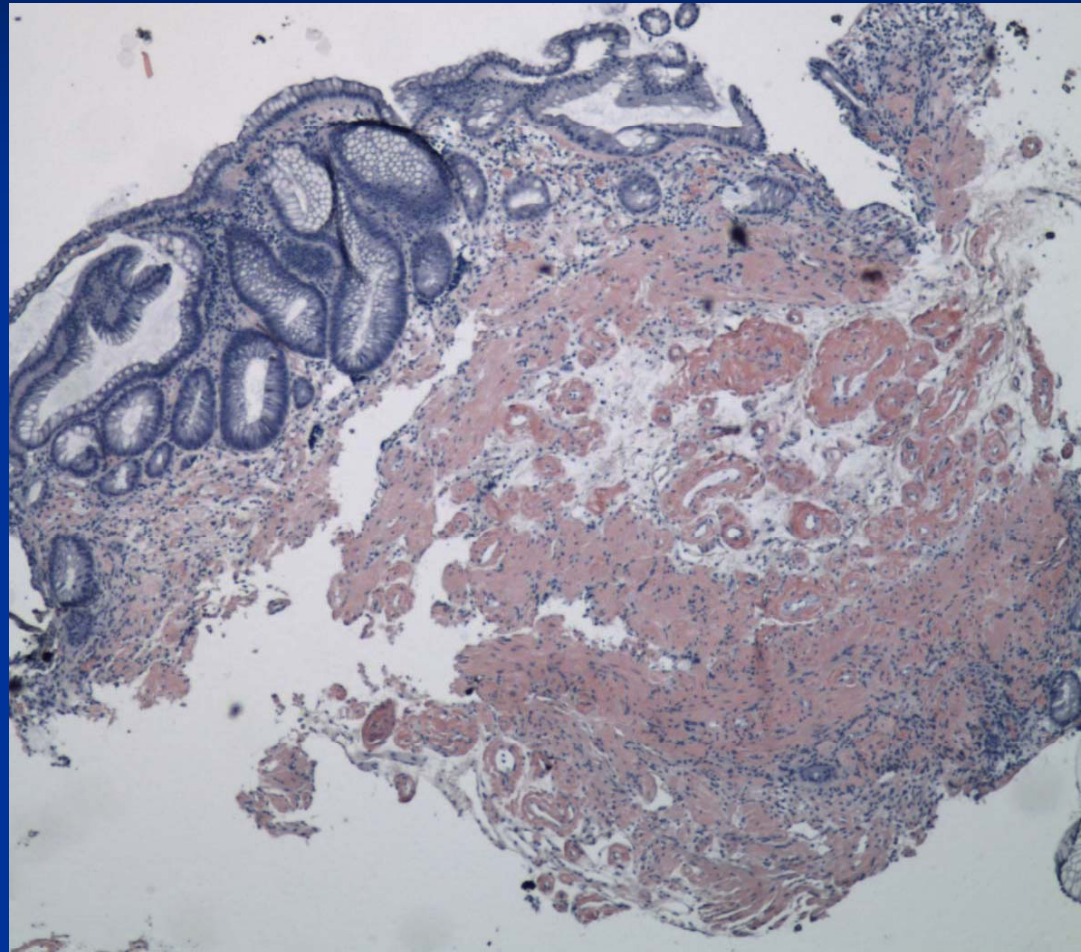
Medium power view of the amorphous, pink material suspected to be amyloid

# Pathology



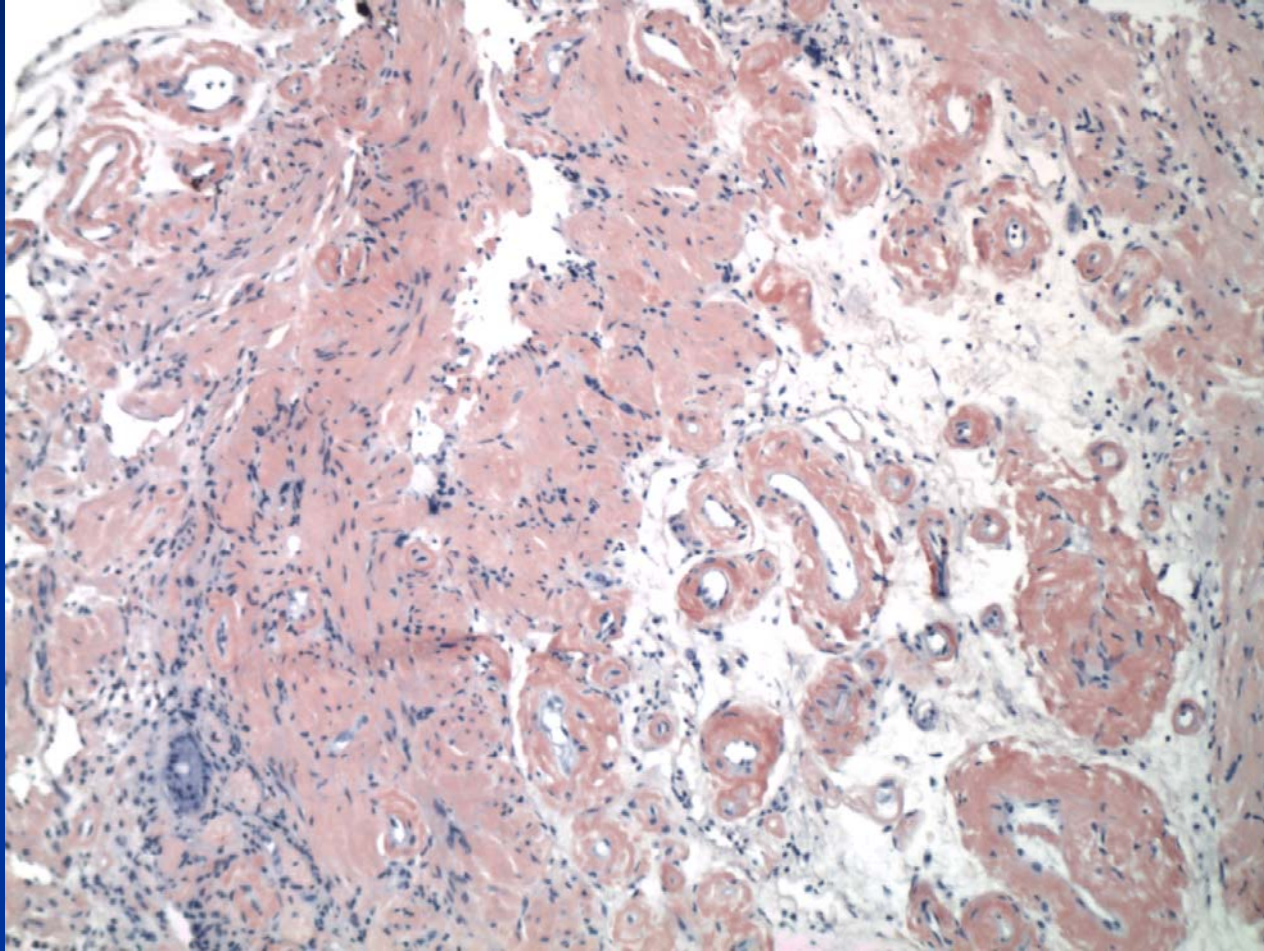
100x view of the amorphous, pink material suspected to be amyloid

# Pathology



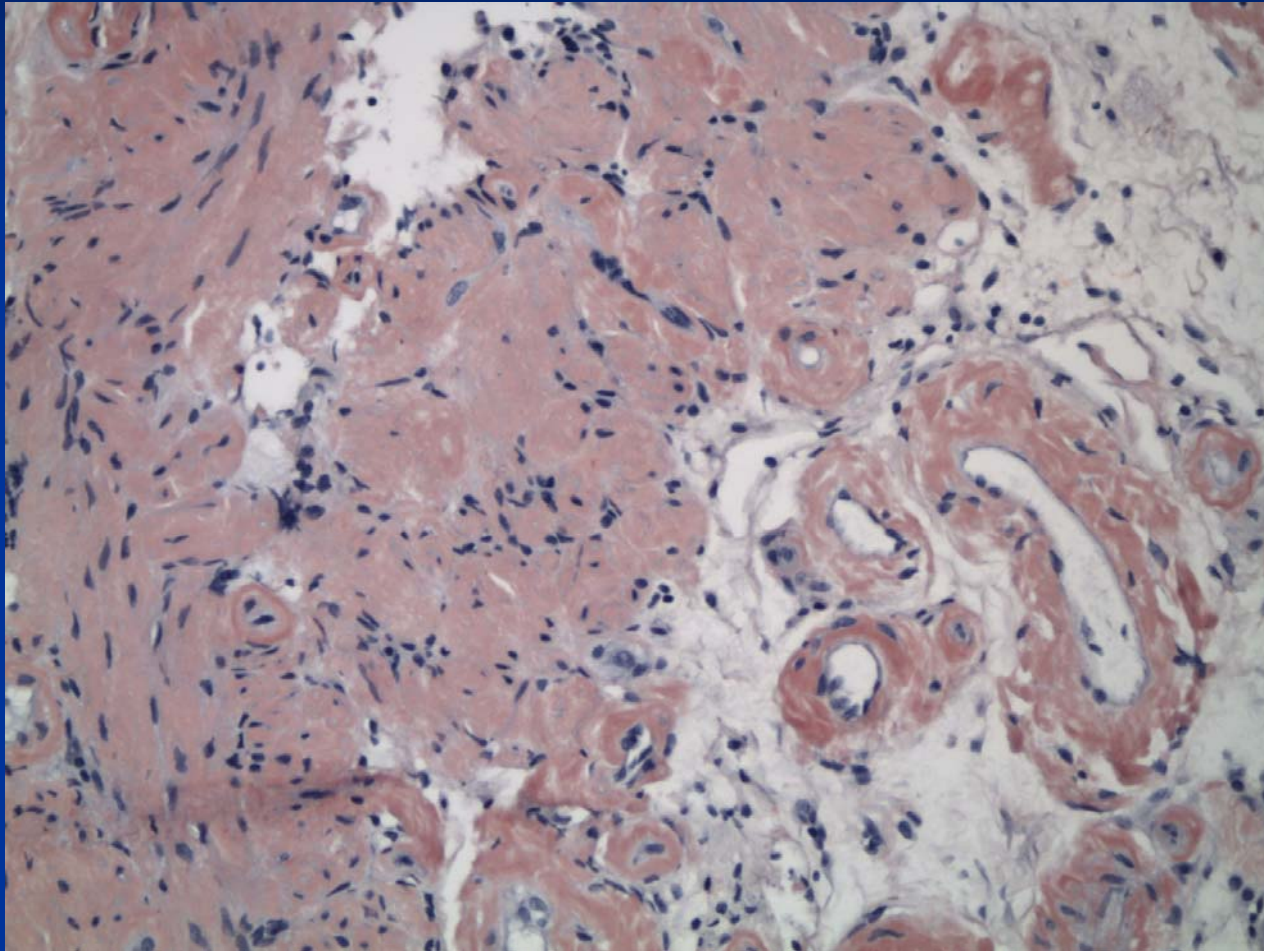
Amyloid stain - the pink amorphous, fibrillary material stains salmon pink and is consistent with amyloid

# Pathology



Higher power view of amyloid stain with amyloid deposits in the submucosa and in the surrounding vessel walls

# Pathology



Higher power view of amyloid stain with amyloid in the submucosa and around the vessel walls

# Pathology - EGD

- Duodenum – Chronic inflammation with amyloid deposition and reactive changes
- Antrum – Chronic active gastritis with amyloid deposition and reactive changes; H. pylori negative

# Pathology - Colonoscopy

- Ileocecal valve – Moderate chronic inflammation with amyloid deposition and reactive changes
- Right colon – Mildly increased plasmacytic infiltration in lamina propria and submucosal amyloid deposition
- Left colon – Severe focal chronic active inflammation with prominent amyloid deposition
- Rectum/sigmoid colon – Mild chronic inflammation and mild amyloid deposition

# Final Diagnosis

- Secondary Amyloidosis

# Discussion

- Gastrointestinal Manifestations of Amyloidosis
  - Amyloidosis – extracellular deposition of abnormal protein fibrils with a beta-sheet fibrillar structure

# Discussion

## ■ Types

### ■ Primary

- Most common form
- Generalized deposition of excess light chains
- Maximum GI involvement
- 15% of patients have multiple myeloma

### ■ Secondary

- Acute-phase reactant serum amyloid A protein
- Infectious, inflammatory, neoplastic disorders
- 48% of patients have rheumatoid arthritis

# Discussion

## ■ Types

### ■ Hemodialysis-related

- Long-term hemodialysis deposits beta-2 microglobulin
- Occurs after 14-15 years of dialysis

### ■ Hereditary

- Autosomal dominant inheritance of amyloidogenic proteins
- Rare

# Discussion

## ■ Types

### ■ Senile

- Found in 10-36% of patients over 80 years old
- Mainly involves the heart and GI tract

### ■ Localized

- Found in the esophagus, stomach, small bowel, and colon

# Discussion

## ■ Symptoms

- Weakness
- Weight loss
- Diarrhea
- Joint pain
- Peripheral neuropathy
- Shortness of breath

# Discussion

## ■ Clinical Manifestations

### ■ Mouth and Esophagus

- Macroglossia – found in 10-20% of patients with primary amyloidosis
  - Sleep apnea, difficulty chewing, airway obstruction
- Papules, vesicles, and ulcers
- Loss of facial expression and difficulty opening the mouth
- Prevalence of esophageal disease ranging from 13-22% of patients
- Dysphagia, heartburn, and hematemesis
- Dilated, atonic esophagus

# Discussion

## ■ Clinical Manifestations

### ■ Stomach and duodenum

- Gastric involvement 8-12% of cases with 1% symptomatic
- Nausea, vomiting, hematemesis, and epigastric pain
- Gastric outlet obstruction
- Gastric ulcers, hematomas, AVMs, and gastroparesis
- Duodenitis, polyps, erosions, ulcerations, and mucosal friability

# Discussion

## ■ Clinical Manifestations

### ■ Small intestine

- Degree of amyloid deposition greatest in small intestine
- 31% of patients affected at autopsy
- Vasculature frequently involved – vessel wall thickens, lumen narrows then occludes, resulting in ischemia and infarction
- Diarrhea, steatorrhea, protein loss, hemorrhage (25-45%), obstruction, mesenteric ischemia
- Malabsorption in 8.5% of primary amyloidosis

# Discussion

## ■ Clinical Manifestations

### ■ Malabsorption

- Presents with diarrhea, anorexia, and weight loss
- Median weight loss of 30 lbs
- PT prolonged in 24% of these patients
- Proteinuria in 95% of these patients
- Abnormal creatinine in 58% of these patients

# Discussion

## ■ Clinical Manifestations

### ■ Colon

- Polypoid lesions, ulcerations, and nodules
- Colonic dilatation, pseudoobstruction, strictures, submucosal hemorrhage, infarction, and perforation
- Diarrhea, weight loss, and steatorrhea are common symptoms in the advanced stage

# Discussion

## ■ Clinical Manifestations

### ■ IBD

- Study of 25 patients with amyloidosis out of 3050 with IBD, incidence of secondary amyloidosis in CD was 0.9% while only 0.07% in UC
- Of the patients mentioned above, 21 out of 25 with amyloidosis and IBD developed renal amyloidosis with proteinuria from which 10 died

# Discussion

## ■ Clinical Manifestations

### ■ Liver disease

- 56-95% of autopsied patients with amyloidosis had hepatic involvement
  - 62-90% with primary amyloidosis
  - 22-43% with multiple myeloma associated amyloidosis
  - 59-60% with secondary amyloidosis
- Most common findings are hepatomegaly, elevated alkaline phosphatase
- Stigmata of chronic liver disease and portal hypertension are rare
- Splenomegaly in 15-31% of patients

# Discussion

## ■ Systemic manifestations

- Most common presentation – weakness, fatigue, purpura (face/neck), and weight loss
- Joint involvement, peripheral neuropathy
- Autonomic dysfunction - orthostatic hypotension, diarrhea, and impotence
- Congestive heart failure and arrhythmias
- Renal insufficiency and nephrotic syndrome

# Discussion

## ■ Systemic manifestations

- Primary – tongue, nerves, heart, muscle, kidneys, skin, and GI tract
- Secondary – kidneys
- Hemodialysis-related – musculoskeletal
- Hereditary – peripheral/autonomic neuropathy

# Discussion

## ■ Diagnosis

- Serum and urine for the presence of monoclonal light chains – found in 89% of patients by immunoelectrophoresis with immunofixation
- Radiographic skeletal survey and bone marrow biopsy to search for multiple myeloma
- Carotene levels – low in 6% of patients mostly with malabsorption
- Renal insufficiency in almost 50% of patients at time of diagnosis
- Serum aspartate aminotransferase abnormal in 34% of patients
- Alkaline phosphatase elevated in 26-50% of patients

# Discussion

## ■ Diagnosis

- Amyloid stains pink with hematoxylin and eosin and displays metachromasia with methyl violet
- Most specific stain, Congo Red, produces red appearance in normal light and apple-green birefringence in polarized light
- CT scans may show small bowel thickening/dilatation and hepatomegaly
- Angiography may show luminal irregularities
- Endoscopically findings may include polypoid protrusions, fine granular appearance, and submucosal hemorrhage

# Discussion

## ■ Treatment

- Goal of treatment – suppress the synthesis of immunoglobulin light chains by controlling the underlying plasma cell disorder with chemotherapy
- Primary – high dose chemotherapy with hematopoietic stem cell transplantation
- Secondary – treatment of underlying disease

# Discussion

## ■ Prognosis

### ■ Primary

- Median survival less than 2 years with Melphalan and Prednisone
- 5 year survival rate about 60% with hematopoietic stem cell transplant
- Survival correlates with serum amyloid A protein concentration

# Discussion

## ■ Patient Update

- Patient evaluated by Cardiology, Rheumatology, and Hematology
- Patient underwent bone marrow biopsy indicating Multiple Myeloma with no evidence of amyloid in the bone marrow by Congo red stain but increased iron stores
- Outside GI clinic EGD pathology indicated amyloid deposits
- Patient was started on chemotherapy for Multiple Myeloma as well as TPN. Patient developed sepsis during her hospital course and died.

# References

- Ebert, E. et. Al. Gastrointestinal Manifestations of Amyloidosis. American Journal of Gastroenterology 2008; 103:776-787.