Gastrointestinal and Mesenteric Amyloidosis – Review of CT and MRI Findings

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Disclosure of Commercial Interest:

- **Neither I nor my immediate family members have a financial relationship with a commercial organization that may have a direct or indirect interest in the content.**

Outline


Objectives


Introduction


Epidemiology


Pathological Findings


Management and Prognosis


Gastrointestinal System Amyloidosis


Organ-themed Clinical Cases, followed by a differential diagnosis

Objectives

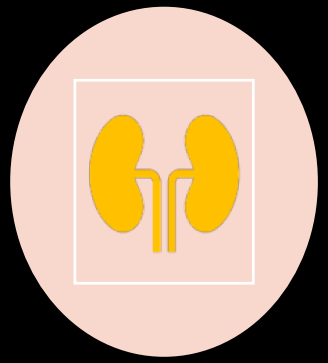
- Provide brief introduction on amyloidosis, classification, pathophysiology, and management.
- Review spectrum of findings of amyloidosis in the gastrointestinal system and the mesentery and highlight differentiating findings from other pathologies.
- Highlight cases of gastrointestinal amyloidosis and similar pathologies that it might mimic.

Target audience: Attending Radiologists, Body Specialists, Radiology Trainees, and Radiology Assistants.

Introduction

Amyloidosis is a rare medical condition characterized by extracellular deposition of abnormal fibrillar precursor proteins called amyloid, that accumulate in an insoluble form in organs or tissues.

Highly morbid disease with a median survival reported without treatment is only 13 months.



Amyloid deposits cause anatomic disruption of normal tissue function and organ blood supply.

Radiological findings can precede the clinical findings. Therefore, it's vital to know the diverse presentations and image findings of amyloidosis.

Classification

I. Anatomic: based on organ involvement:
- Localized: Single deposit in an organ
- Systemic: Deposition within multiple organs
  - Primary systematic: associated with plasma cell dyscrasias.
  - Secondary systematic: associated with chronic infection/inflammation.

II. Biochemical Classification: based on type of fibril protein in deposit (See Table).
- More than 30 proteins identified.
- AL: Most common type.

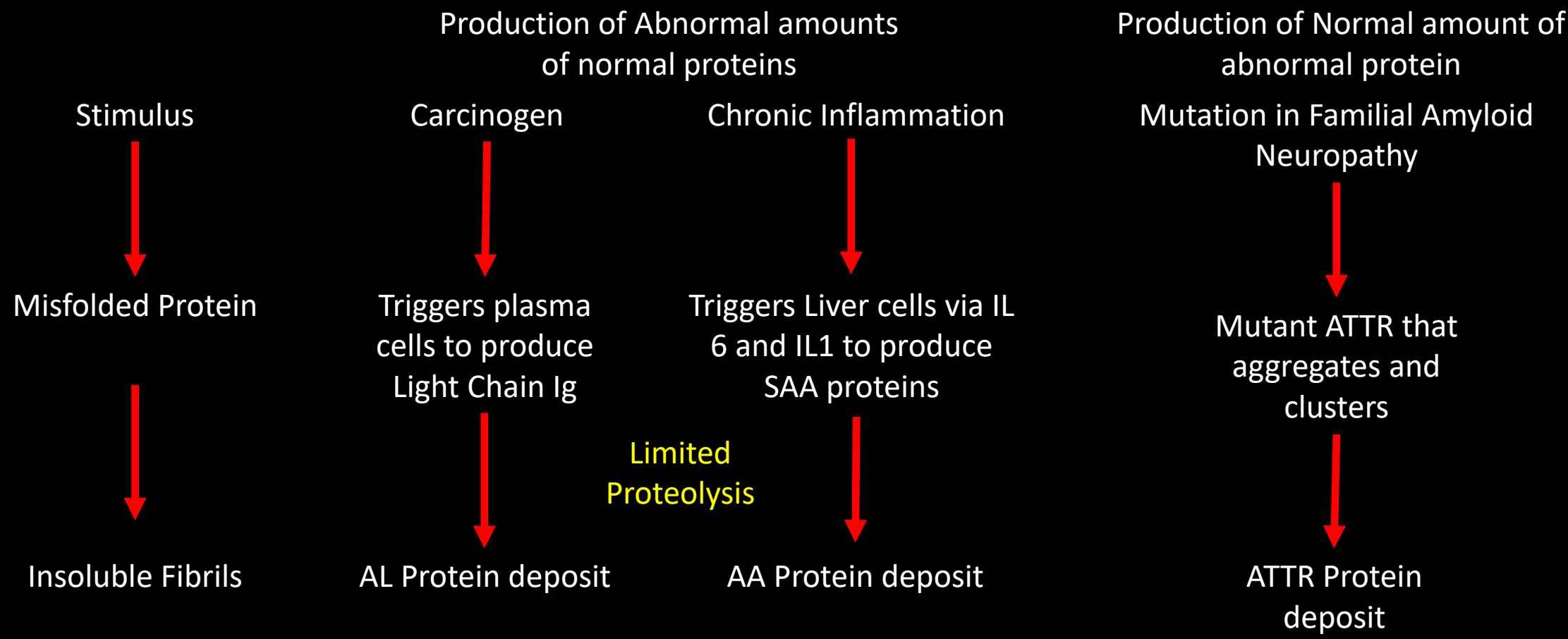
Main Common Categories of Systemic Amyloidosis (Biochemical Classification)

Name	Amyloid Protein	Syndrome	Comments
AL	Light chains Immunoglobulins (Kappa, Lambda)	Idiopathic Primary Amyloidosis / Monoclonal Gammopathy	Multiorgan involvement
AA	Serum amyloid A protein (apoSAA)	Reactive/Secondary Amyloidosis.	Chronic inflammation/malignancy
AB2M	Beta-2 Microglobulin	Dialysis-associated amyloidosis	
AIAPP	Islet Amyloid Polypeptide	Insulinoma, Type 2 Diabetes	
ATTR	Transthyretin	Familial Amyloid Neuropathy	Age-related systemic amyloidosis

Epidemiology

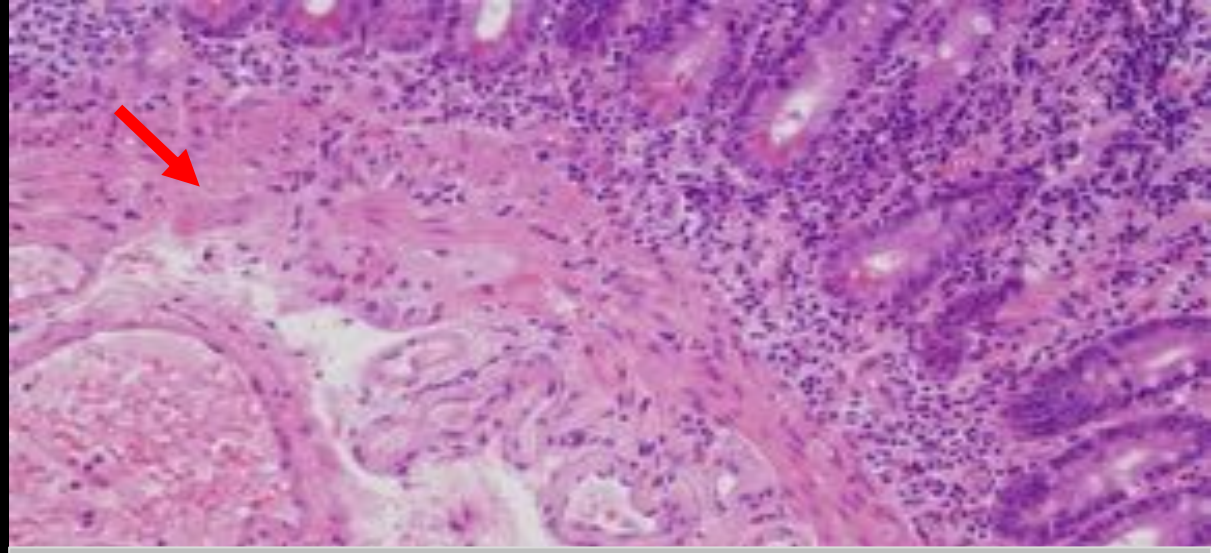
- Epidemiology
  - Systematic amyloidosis: 80-90%
  - Localized amyloidosis: 10-20%
  - Respiratory system commonly involved (50%) .
- More than 12,000 adults in the United States live with AL amyloidosis.
- Estimated incidence rate of 9.7 - 14.0 cases per million person-year.
- Age: 6th and 7th decades of life

Pathophysiology

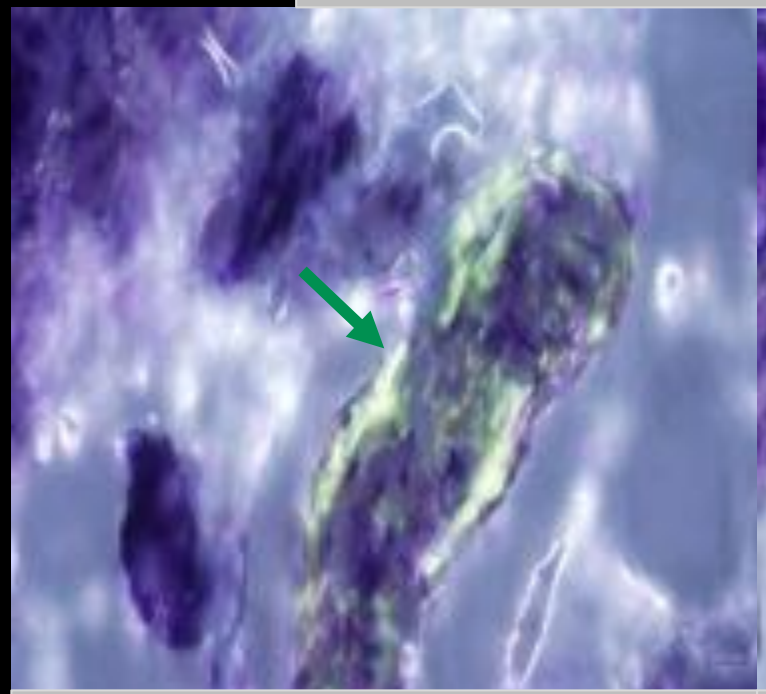


Pathological Findings and Diagnosis

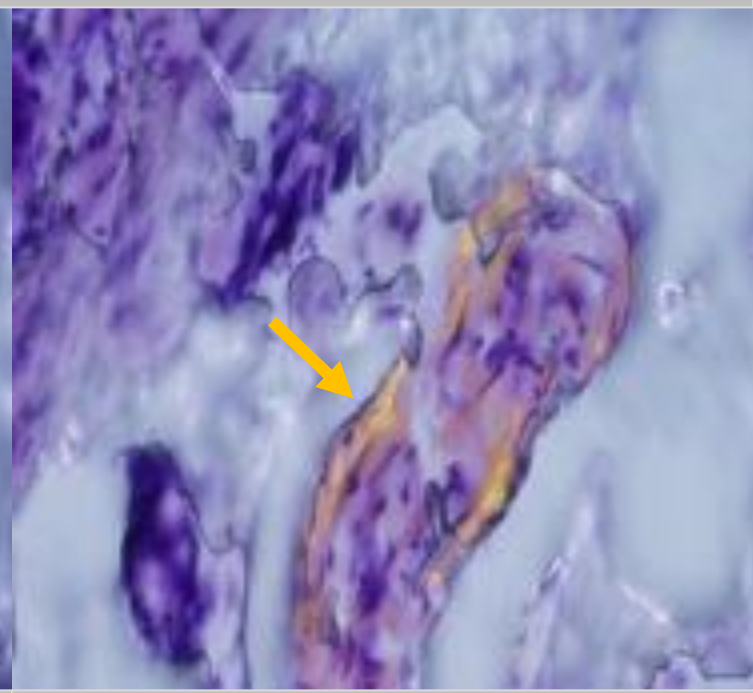
- Extracellular deposit of protein fibrils with a β-sheet fibrillar structure.
  - Combination of fibril proteins, glycosaminoglycans and amyloid P.
- Characteristically, the amyloid deposit shows apple-green birefringence when stained with Congo red and viewed under polarized light.
- May contain calcification and ossification.



Amorphous eosinophilic deposits along the interstitium is characteristic of amyloidosis (Specimen from small bowel).



Apple Green Birefringence under polarized light characteristic of amyloid deposition



Positive Congo Red Stain

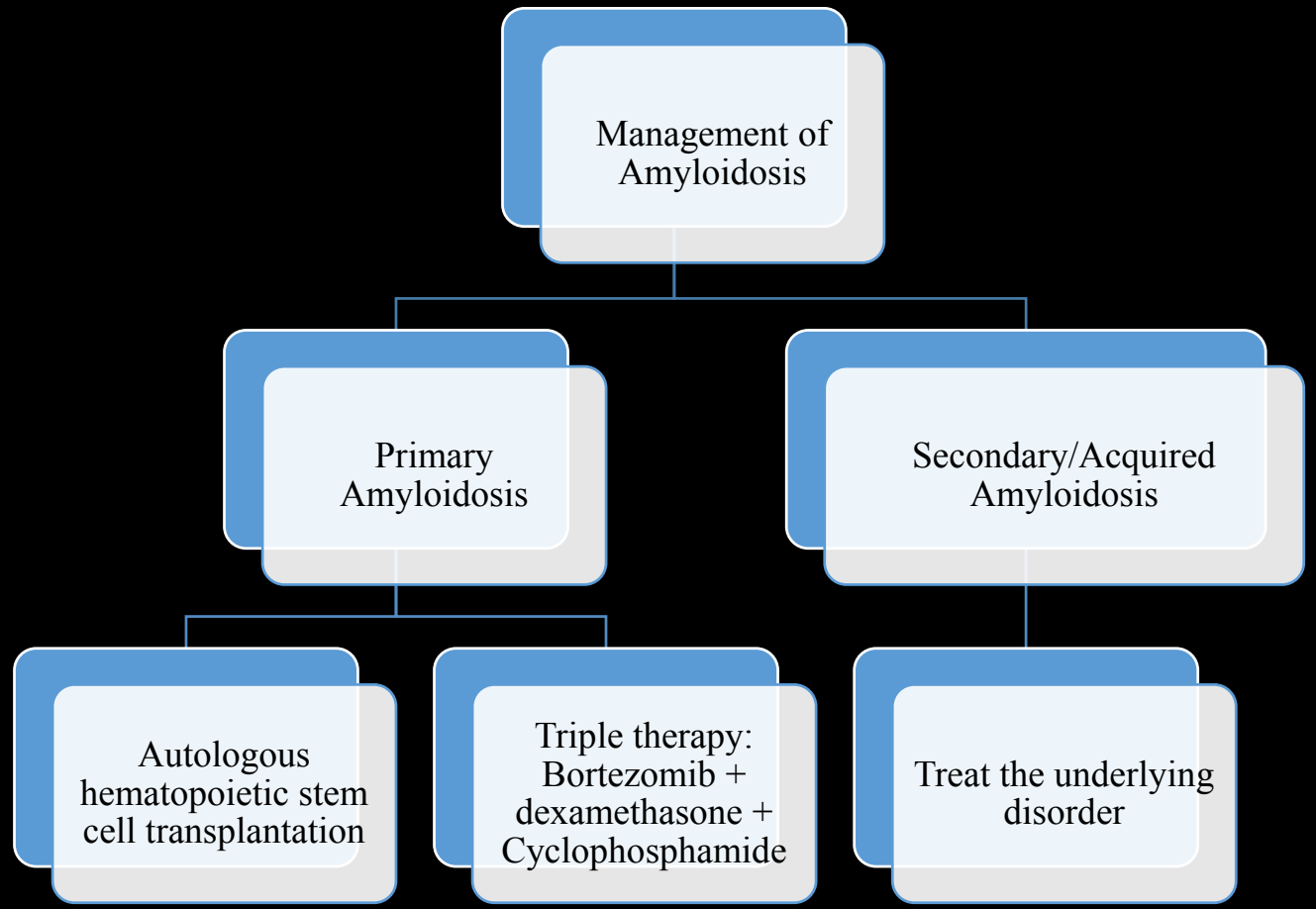
Management and Prognosis

Management:

- Goal of therapy is to improve mortality rates by reducing quantity of precursor proteins.

Prognosis:

- Varies depending on the nature, number, and extent of organ involvement.
- Median survival may be as short as 4-6 months, with cardiac or hepatic failure and infection being the major causes of death.



Gastrointestinal System Amyloidosis - Introduction

- Gastrointestinal system is the most commonly involved organ system in primary and secondary amyloidosis

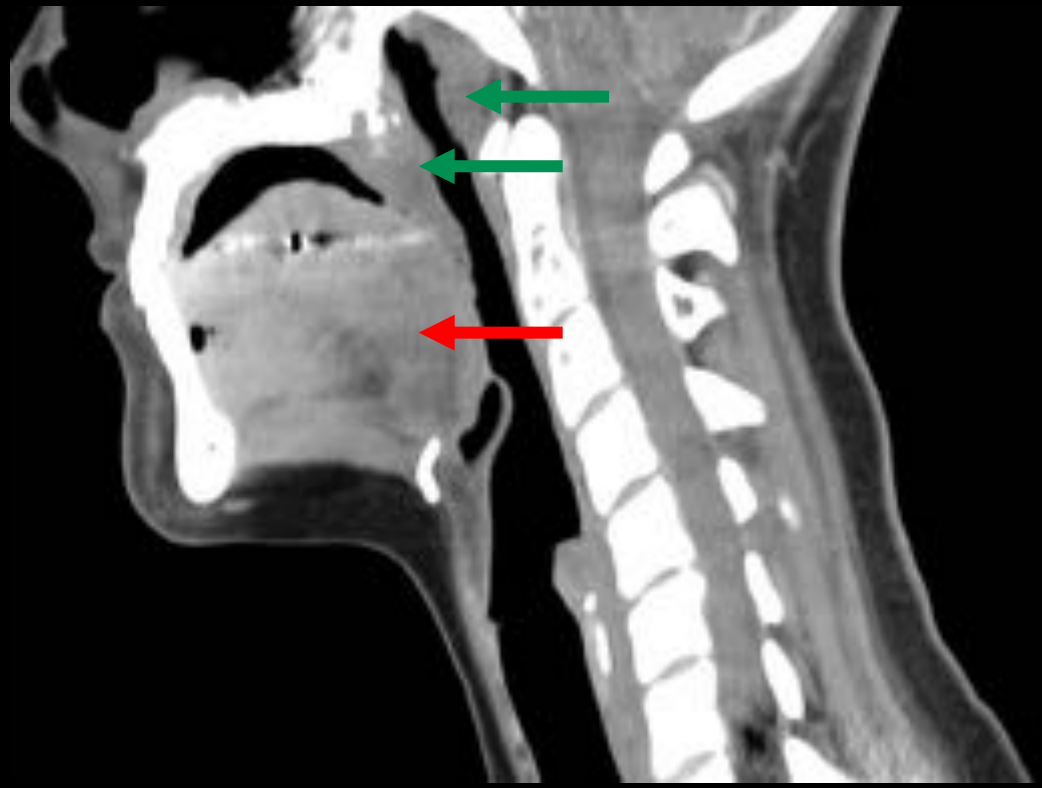
- Depending on the involved organ, symptoms can vary

- Common GI symptoms:
  - reflux, constipation, nausea, abdominal pain, diarrhea, weight loss, malabsorption, hemorrhage, and early satiety.

Gross pathology of amyloid infiltrated enlarged liver that shows pale and waxy areas – corresponding to amyloid deposits.

Oral/Pharyngeal Amyloidosis – Clinical Case

- **Case:** 26 year old female with recurrent upper respiratory symptoms including recurrent sinusitis, allergies, difficulty breathing and headaches.
- Pathology showed amyloid deposition secondary to plasma cell dyscrasia. Patient was treated with radiation therapy and steroids.



CT Neck with IV contrast
Diffuse non-enhanced enlargement of the tongue (Macroglossia)
Diffuse non-enhanced thickening of the nasopharynx / soft palate with macrocalcifications

Differentials of Amyloid-related-macroglossia:

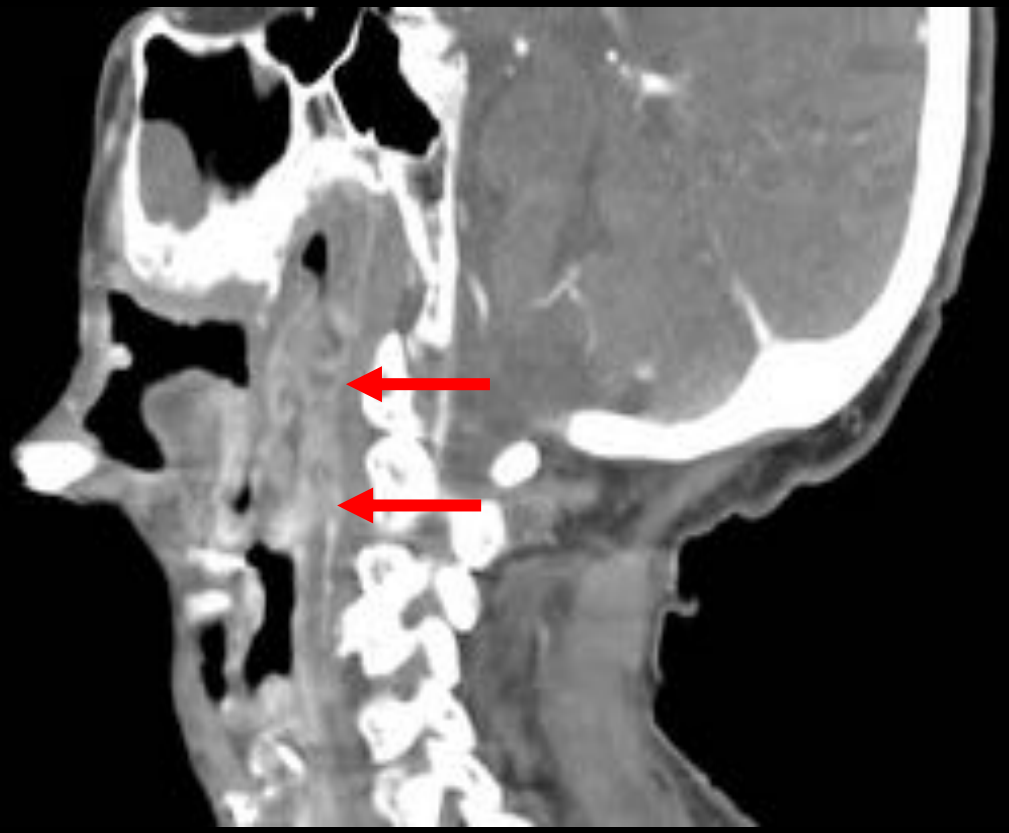
1. **Squamous Cell Carcinoma:**
   - CT Finding: **Invasive enhancing mass** arising from surface of oral tongue with exclusion of lingual tonsil
2. **Dermoid & Epidermoid:**
   - CT Finding: **Hypodense** single **mass** usually with thin, **imperceptible wall**
3. **Thyroglossal Duct Cyst:**
   - CT Finding: **Hypodense mass** with thin **rim** of peripheral **enhancement, typically midline**

Differential Diagnosis of Pharyngeal Thickening / Mass

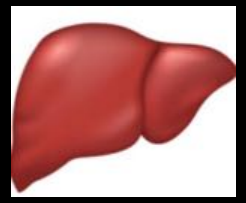
1. Squamous cell carcinoma:
   - Ill-defined, contrast-enhancing diffuse or asymmetric thickening of soft palate
2. Non-Hodgkins Lymphoma:
   - poorly circumscribed, iso-enhanced, diffusely infiltrative mass
3. Benign Mixed Tumor:
   - Well circumscribed enhancing-lesions
   - May contain calcifications, cysts, hemorrhage.

TAKE HOME POINT

Amyloid deposition will appear as diffused non-enhancing thickening of the pharynx and enlargement of the tongue

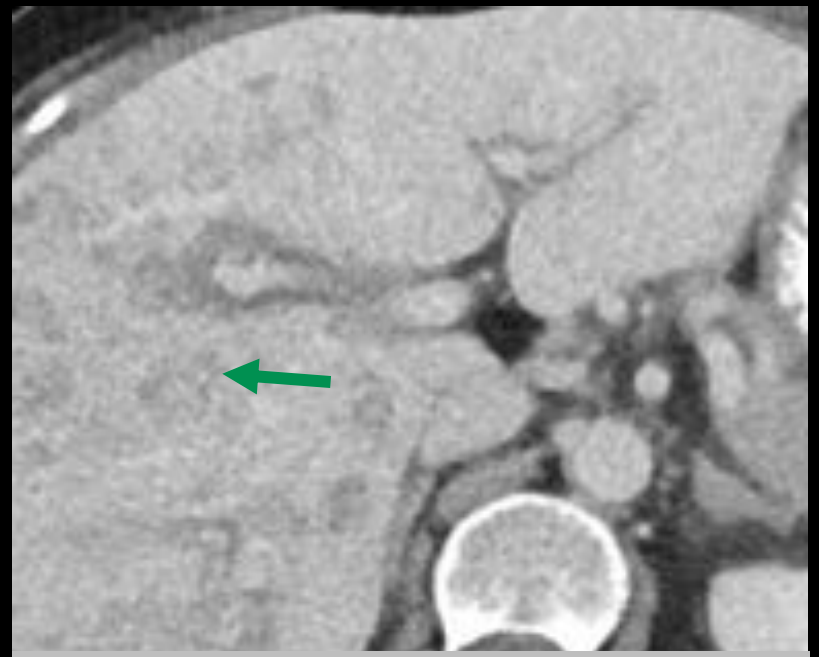


CECT neck shows heterogeneously enhancing mass along the aspect of the nasopharynx and oropharynx. The patient had prominent lymph nodes.
Pathology: Biopsy showed a nasopharyngeal squamous cell carcinoma.

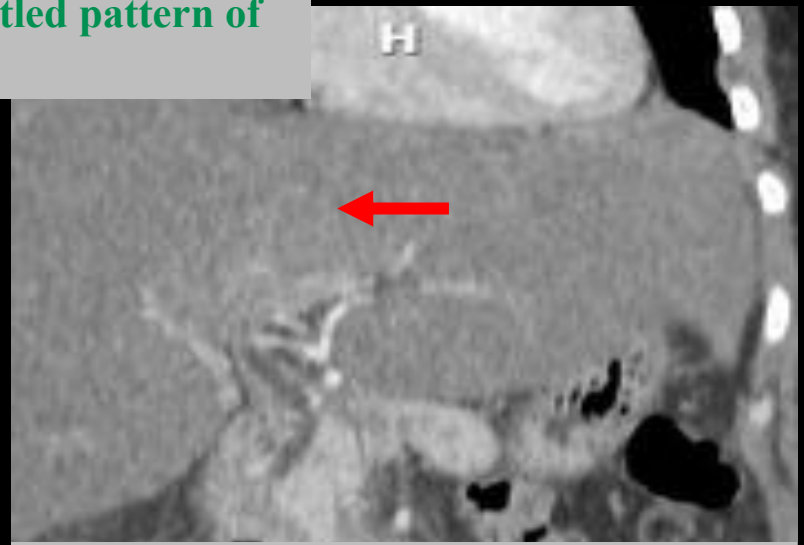


Hepatic Amyloidosis

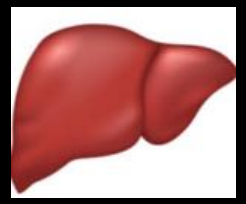
- Hepatic involvement can be seen in up to 90% of patients with AL amyloid and 60% of patients with AA amyloidosis.
- Clinically may manifest as elevated LFTs.
- Hepatic manifestations has a poor prognosis and reflects severe systemic disease.
  - Median survival in patients with hepatic amyloidosis is nine months.
- Radiological findings can include:
  - Mottled pattern of contrast enhancement
  - Heterogeneity of liver parenchyma with diffuse hypoattenuation



Contrast + CT shows mottled pattern of contrast enhancement.

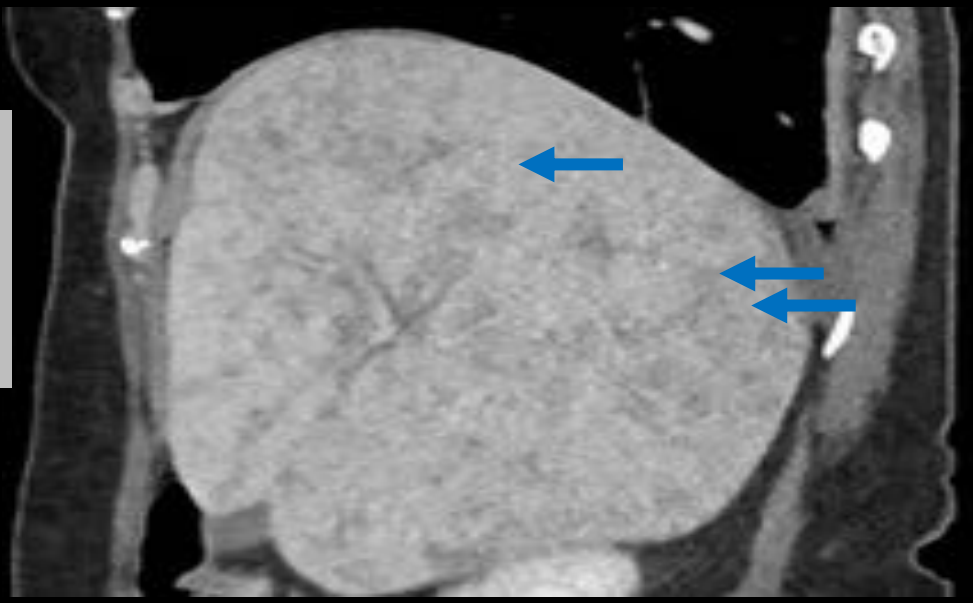


Diffuse hypoattenuation of the liver parenchyma, mimicking hepatic steatosis. Non-specific **parenchymal heterogeneity**

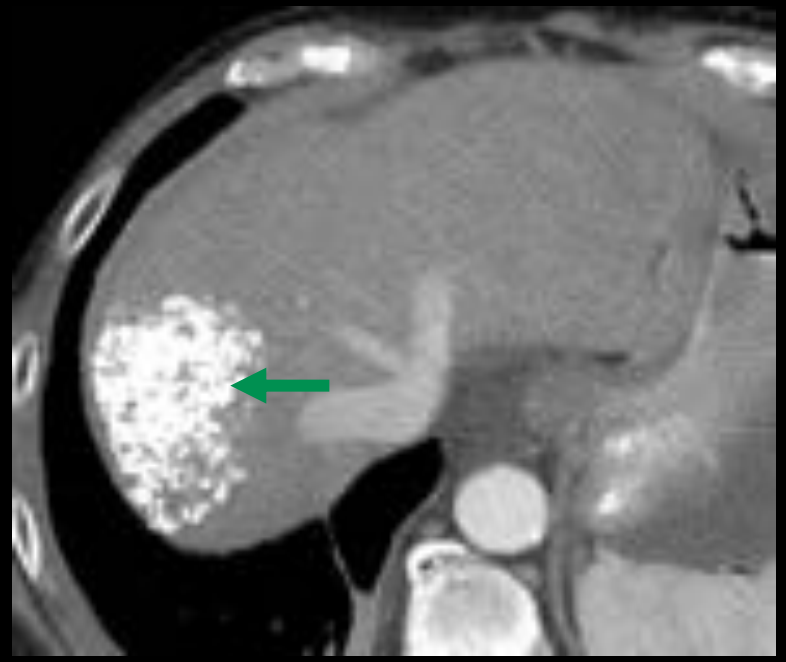


Hepatic Amyloidosis Patterns of Involvement

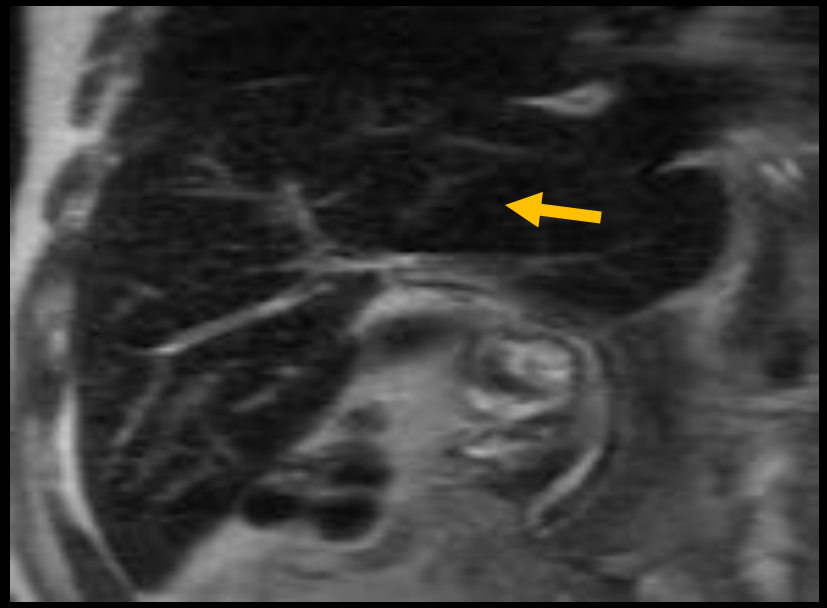
CT: Mottled pattern with deposition near the sinusoids and the vessels.



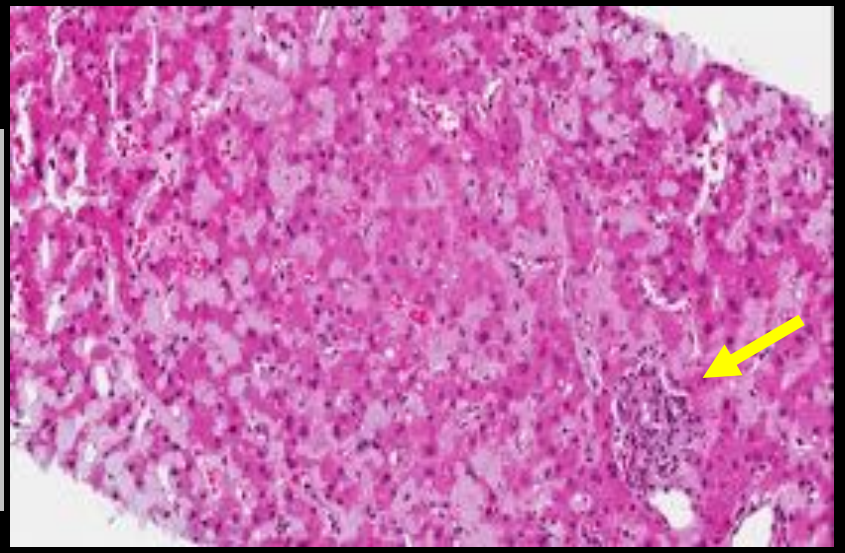
CT: Hetatic calcifications du to Amyloid deposits



MRI : no altered signal intensity on a T2 HASTE sequence

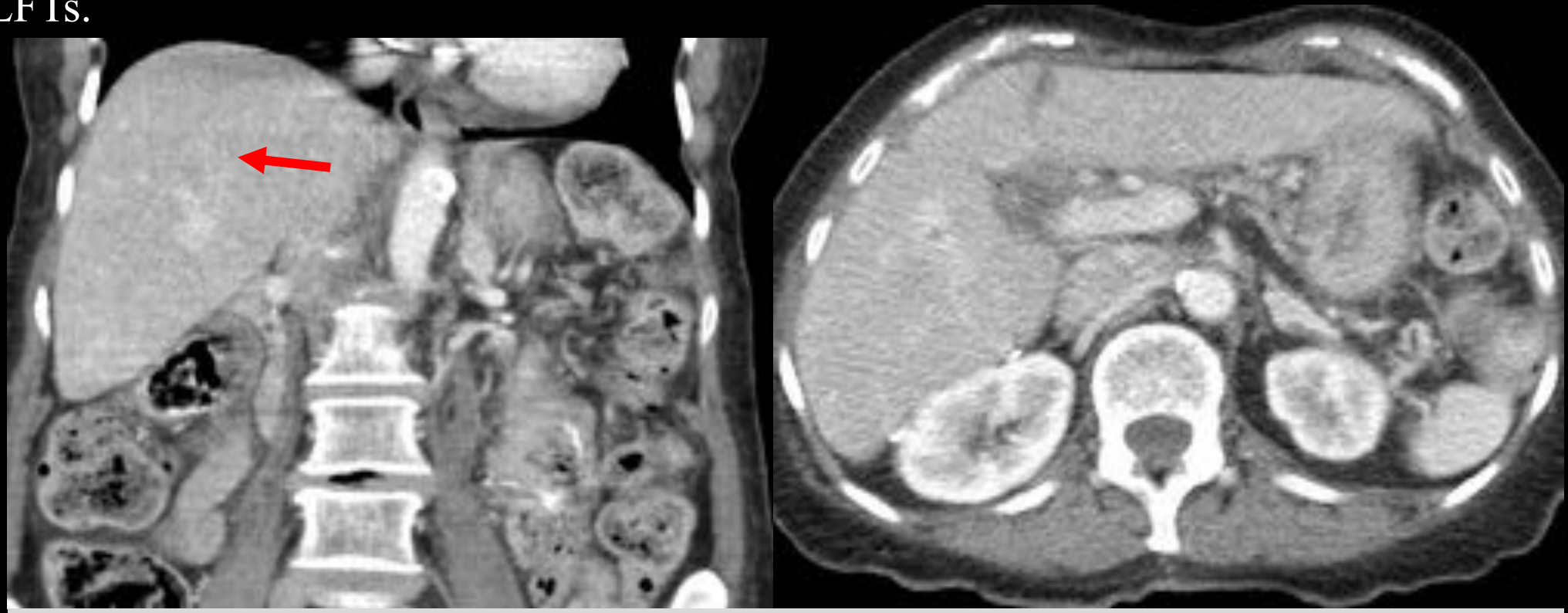


Path: Diffuse involvement of hepatic sinusoids by amyloid deposition (sinusoidal pattern)



Hepatic Amyloidosis – Clinical Case #1

- History: 84 year old female with history of diabetes, hypertension with elevated LFTs.

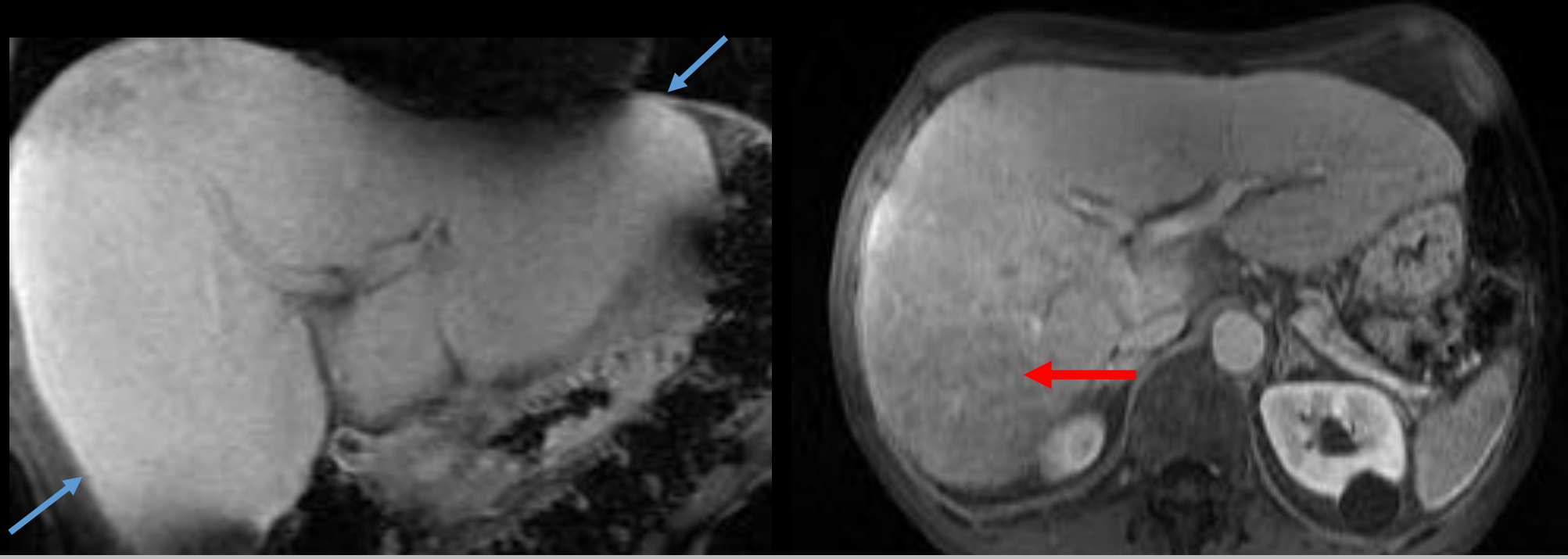


Coronal and axial CECT shows mild hypoattenuation of liver parenchyma, non-specific heterogeneity of the liver.

- Pathology: Biopsy of the liver showed amyloidosis. The Congo red stain was positive and showed apple green birefringence.

Hepatic Amyloidosis – Clinical Case #2

- History: 80 y/o M with history of anorexia, weight loss, and elevated LFTs.



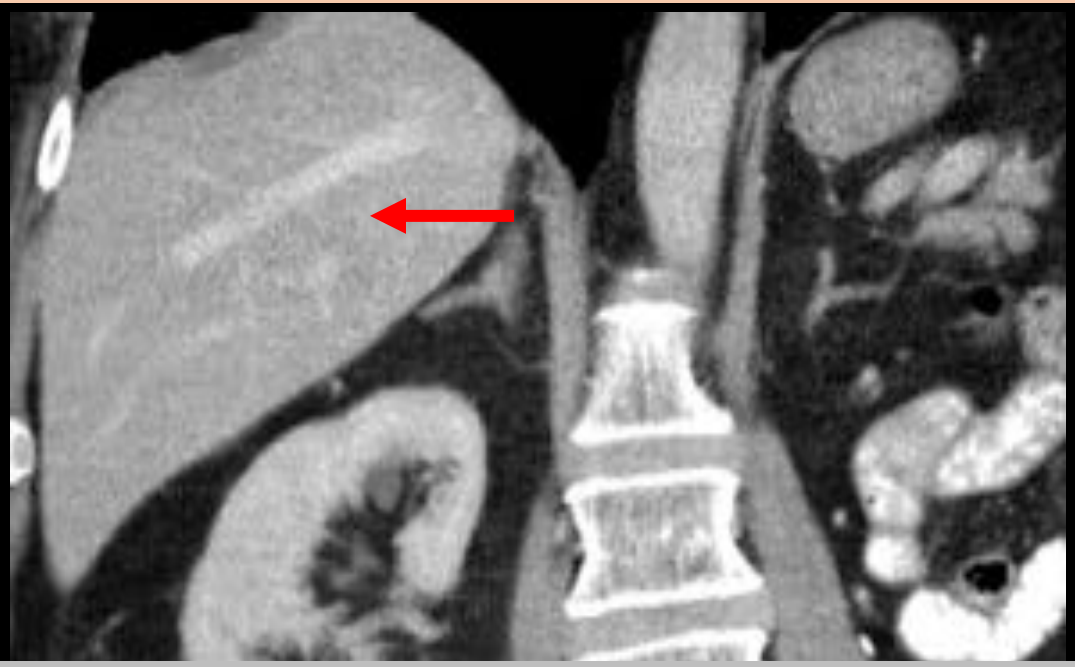
Coronal and axial T1 FS post gad images demonstrate **hepatomegaly** with **heterogenous enhancement** most pronounced in the right hepatic lobe.

- Pathology: Biopsy of the liver showed extensive amyloidosis involving the sinusoids and vessels. The Congo-red stain for amyloid was positive and showed apple green birefringence under polarized light.

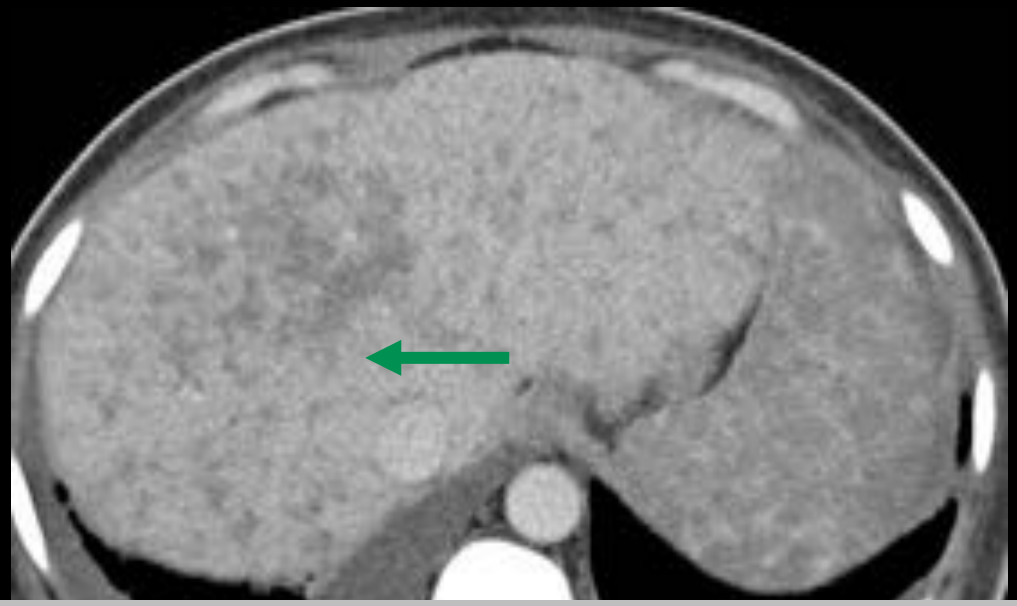
Differential Diagnosis of Hepatic Amyloidosis

Differentials of Liver Amyloidosis:

1. Hepatic Steatosis:
   - Can be differentiated on MRI: Signal dropout on opposed-phase vs. in-phase T1
2. Budd–Chiari syndrome:
   - Decreased peripheral enhancement caused by portal sinusoidal venous stasis and enhancement of the central portion of the liver parenchyma.
3. Primary hepatic neoplasms including HCC, Hepatic adenoma, FNH
4. Infectious/Inflammatory: Tuberculosis, Sarcoidosis



Coronal CECT shows diffuse **decreased liver attenuation** **consistent with hepatic steatosis.**



Axial CECT shows multiple non-enhanced lesions in the liver in a patient with history of abdominal tuberculosis.

TAKE HOME POINT

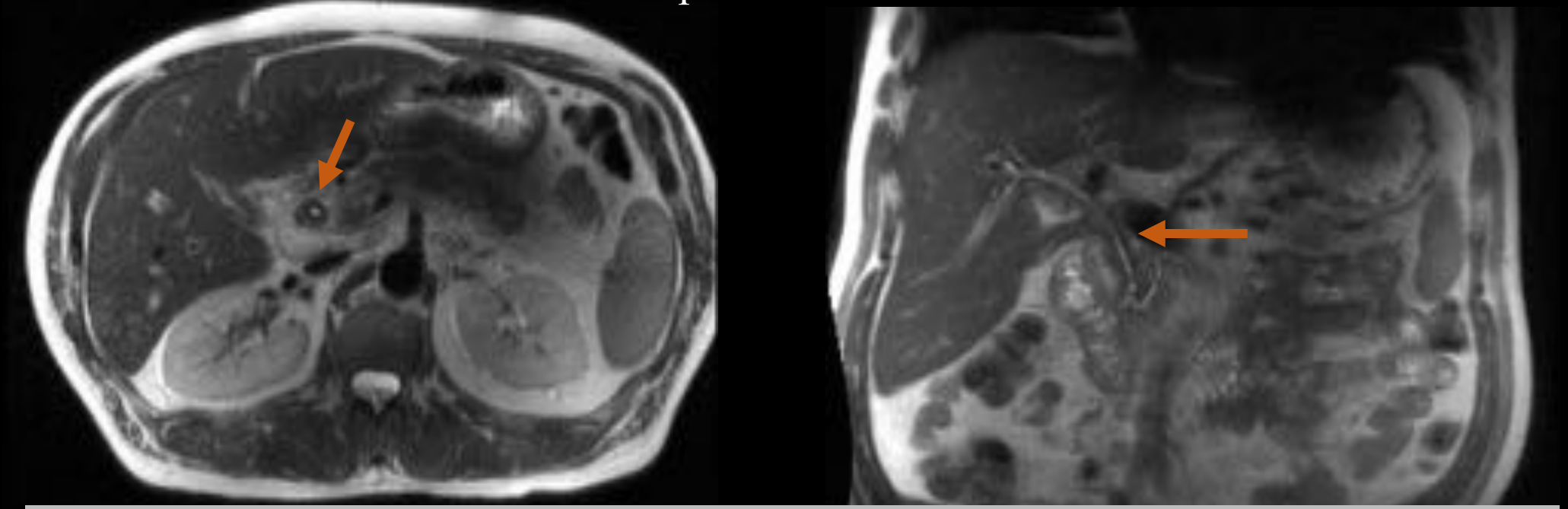
Amyloid liver deposition will appear as:

1. **CT: mild hypoattenuation with non-specific heterogeneity.**
2. **MRI: Heterogenous enhancement on T1 fat-saturated image**

Biopsy: Essential for diagnosis

Biliary Amyloidosis – Clinical Case #1

- **History:** 54 y/o M with known history of amyloidosis that presents with recurrent biliary strictures that were treated with stent placements.

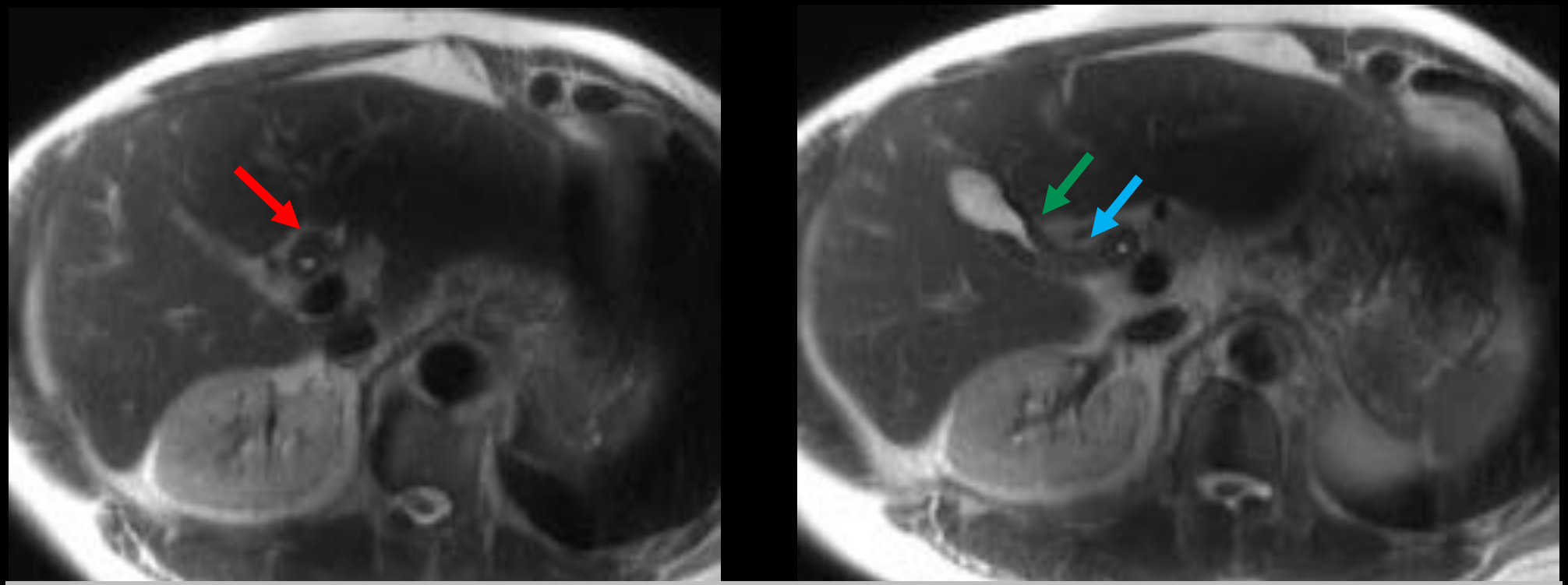


Axial and coronal T2 HASTE images show marked concentric T2 hypointense thickening of the CBD.

- Pathology: Biopsy of the common bile duct stricture showed amyloidosis. The Congo red stain was positive and showed apple green birefringence.

Biliary Amyloidosis – Clinical Case #2

- History: 54 year old male with history of hypertension, hyperlipdemia, and ETOH abuse was admitted with painless jaundice. He underwent a EGD, sphincterotomy, and biopsy.



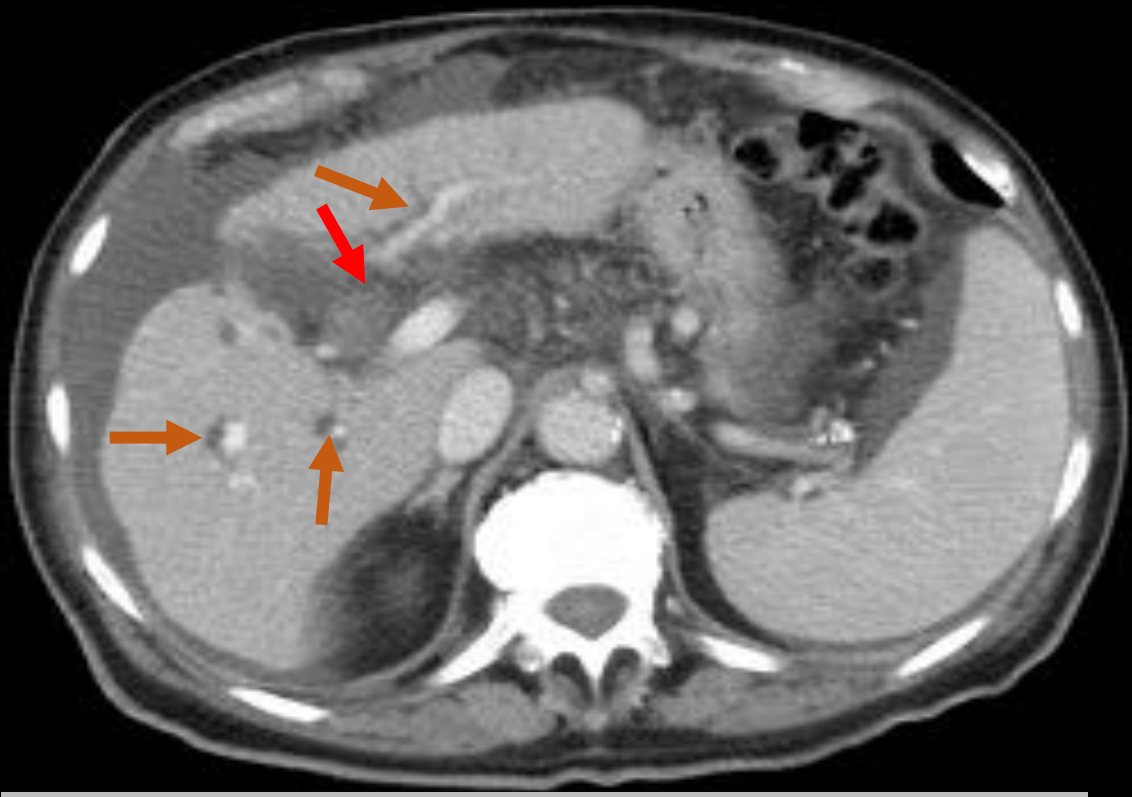
Axial T2WI images show **thickening of the common bile duct**; **cystic duct stricture**; **gallbladder wall thickening**

- Pathology: Biopsy of the CBD showed amyloidosis.

Differential Diagnosis of Biliary Stricture

Differentials of Biliary Strictures secondary to Amyloidosis:

1. **Cholangiocarcinoma:** Biliary mass
   - CT: hypodense solitary or satellite lesions and biliary dilatation.
   - MRI: Iso/Hypo-intense on T1WI ; Hyperintense peripherally and hypointense centrally on T2WI
2. **Autoimmune pancreatitis/cholangitis:**
   - CT: Circumferential bile duct thickening with hyperenhancement.
   - MRI: smooth concentric ductal wall thickening with hyperenhancement on T1WI C+
3. **Primary sclerosing cholangitis:**
   - CT: Hyperenhancement and thickening of the bile ducts that represent inflammation.
   - MRI: Hyperintense on T2WI



Axial CECT shows a **3 cm non-enhancing mass** at the confluence of the confluence of the hepatic ducts with **biliary ductal dilatation**. Biopsy was consistent with **cholangiocarcinoma**

TAKE HOME POINT

Amyloid Biliary Disease will appear as:

1. **CT: non-enhanced thickening of the CBD**
2. **MRI: Concentric T2 hypointense thickening of the CBD**

Biopsy: Essential for diagnosis

Gastrointestinal Amyloidosis

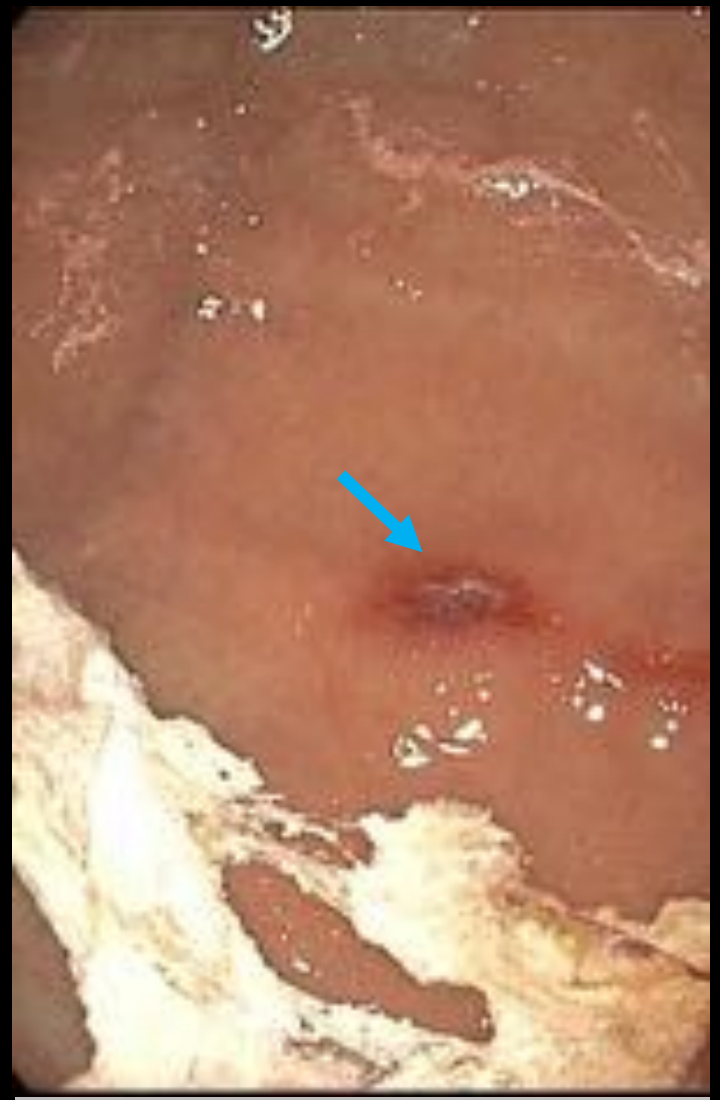
Amyloid deposition can occur anywhere in the GI tract from mouth to anus, similar to Crohn's disease.

Manifestations vary with amyloid fibril type:

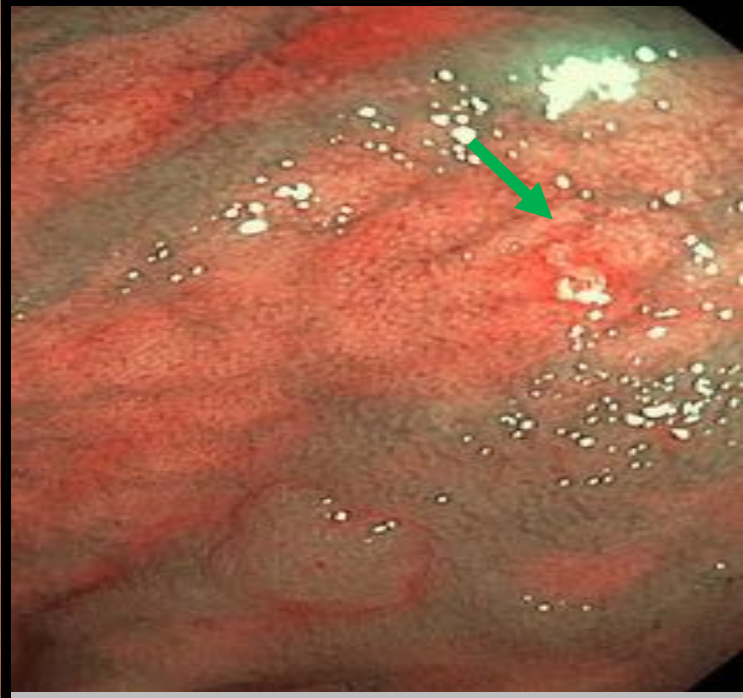
- AL amyloid deposition in submucosa and muscularis propria may manifest as nodular, polypoid masses
- AA amyloid mucosal deposition leads to ulceration, diarrhea, and malabsorption.

Imaging Findings:

- Mucosal nodularity
- Ulceration
- Diffuse thickening
- Polypoid protrusions
- Thickening of folds
- Luminal narrowing
- Bowel Dilatation

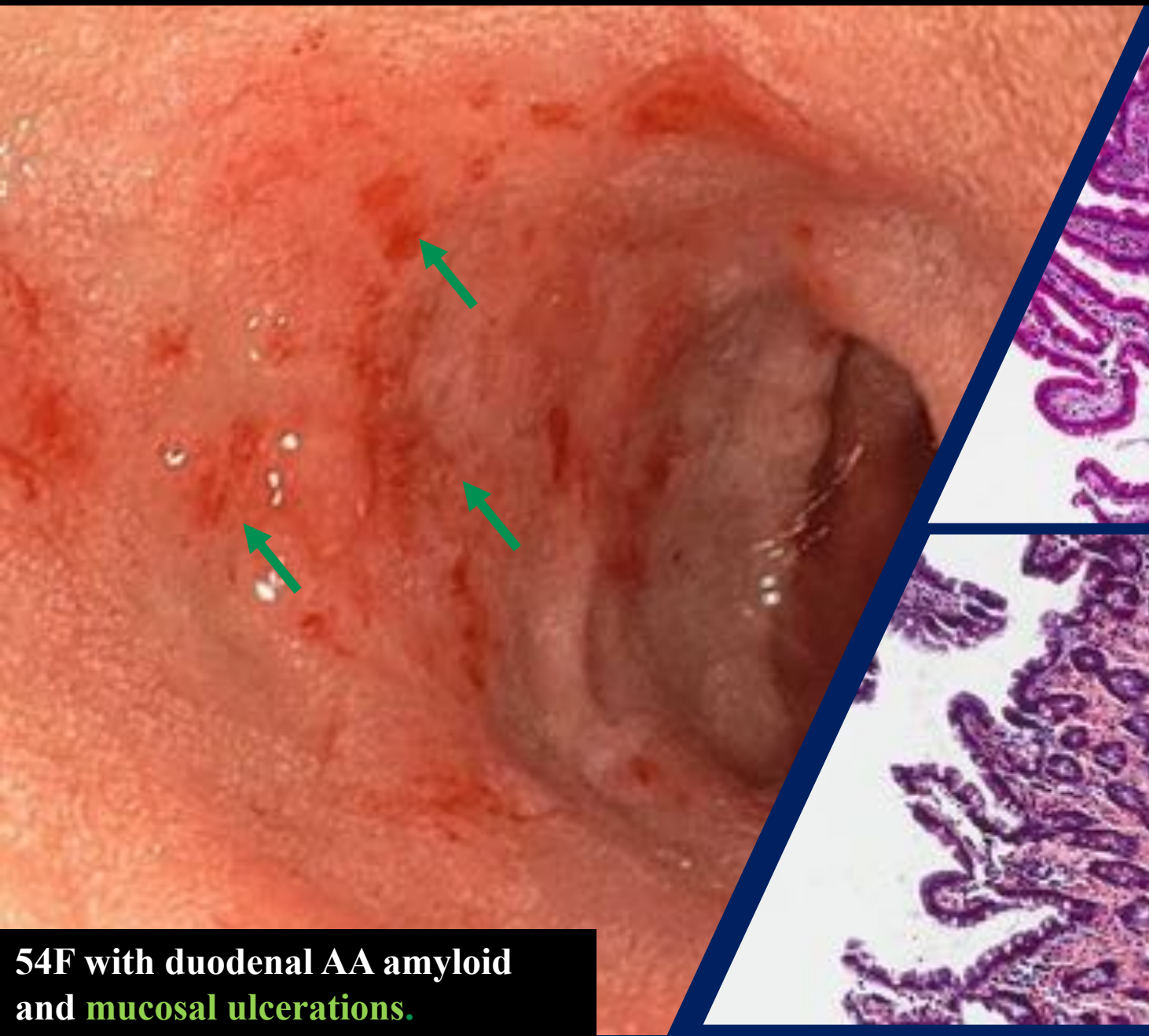


Gastric amyloid ulcer

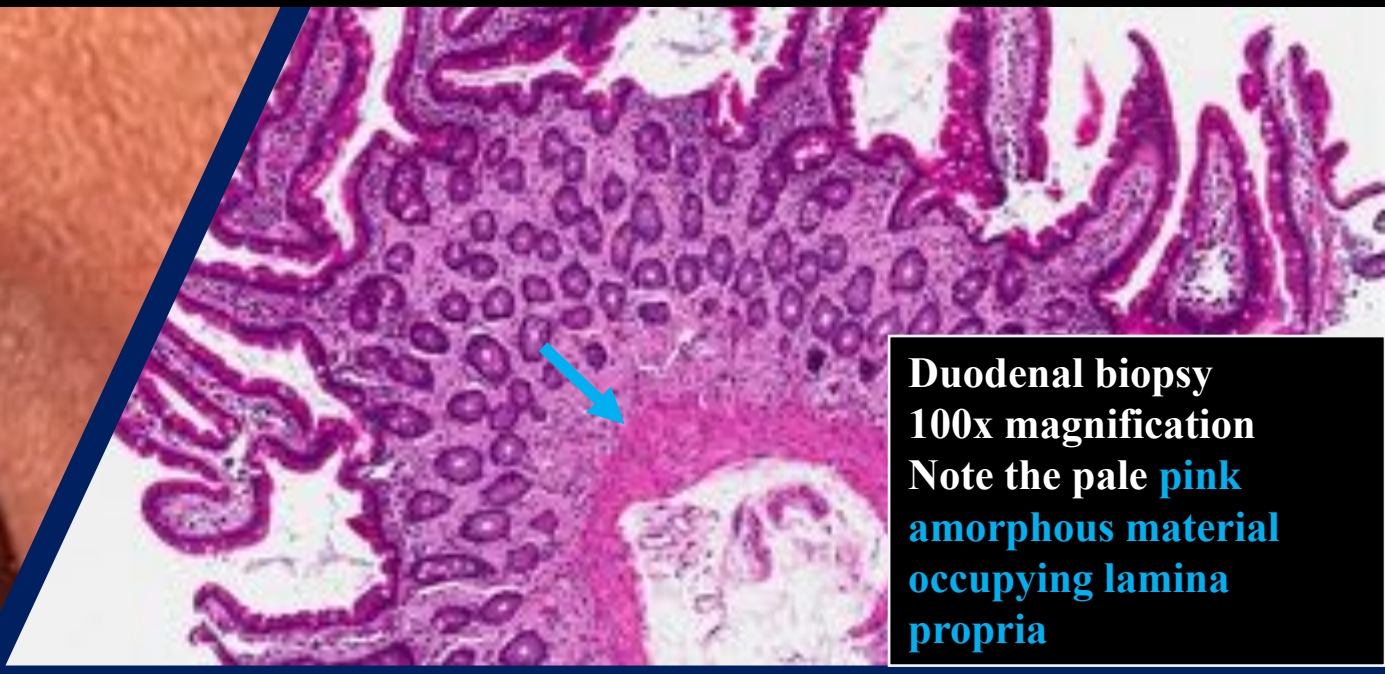


Colonic amyloid polyp

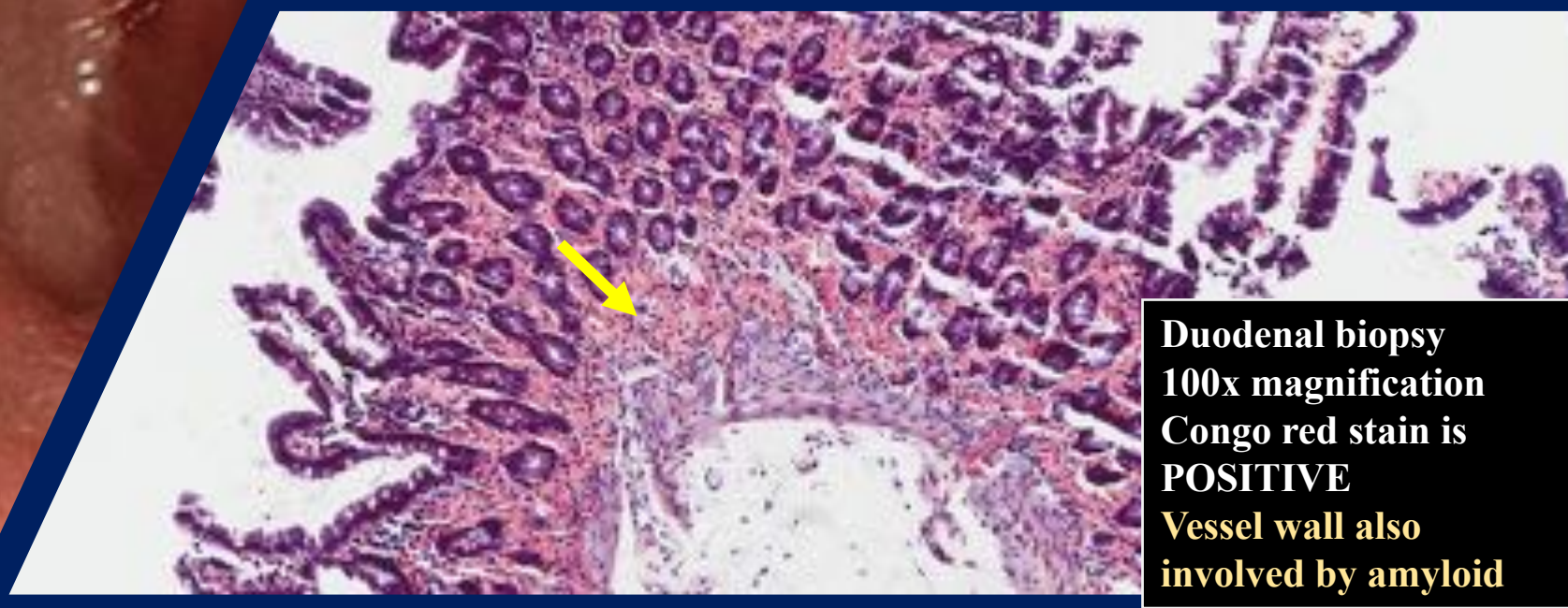
Gastrointestinal Amyloidosis



54F with duodenal AA amyloid and mucosal ulcerations.

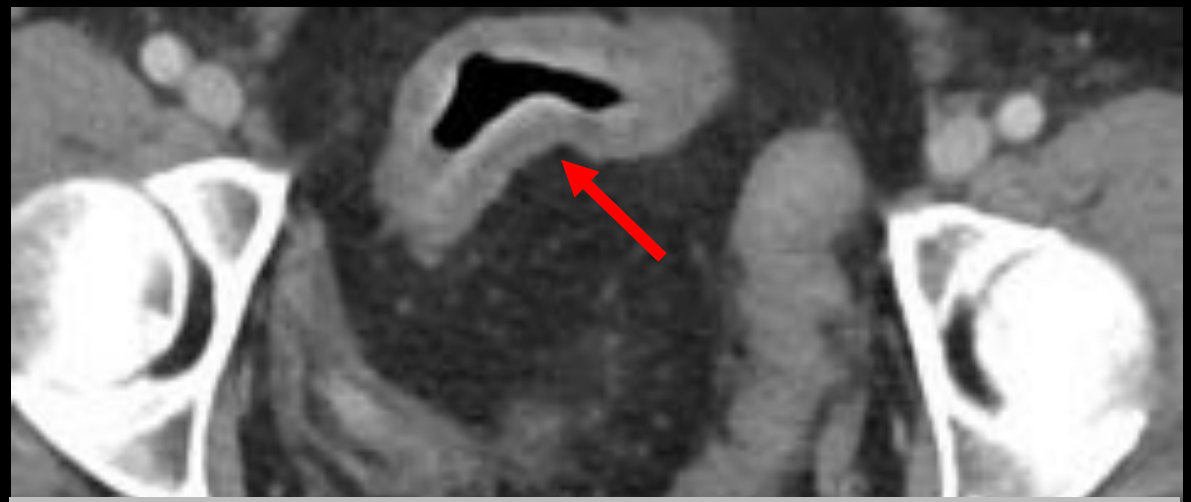


Duodenal biopsy
100x magnification
Note the pale pink amorphous material occupying lamina propria

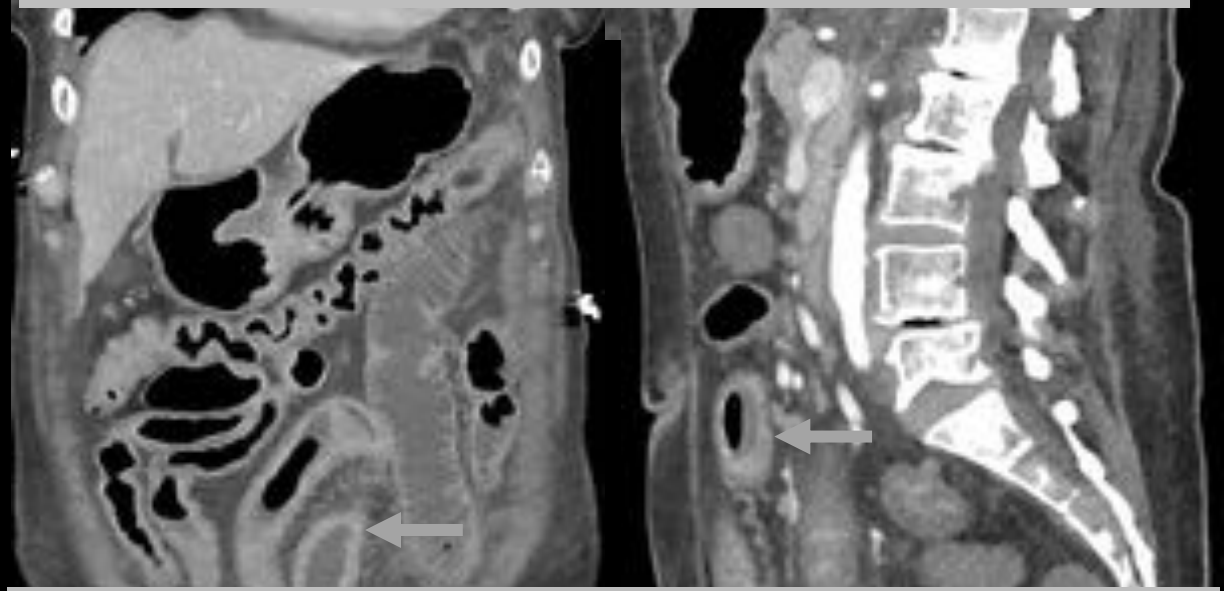


Duodenal biopsy
100x magnification
Congo red stain is POSITIVE
Vessel wall also involved by amyloid

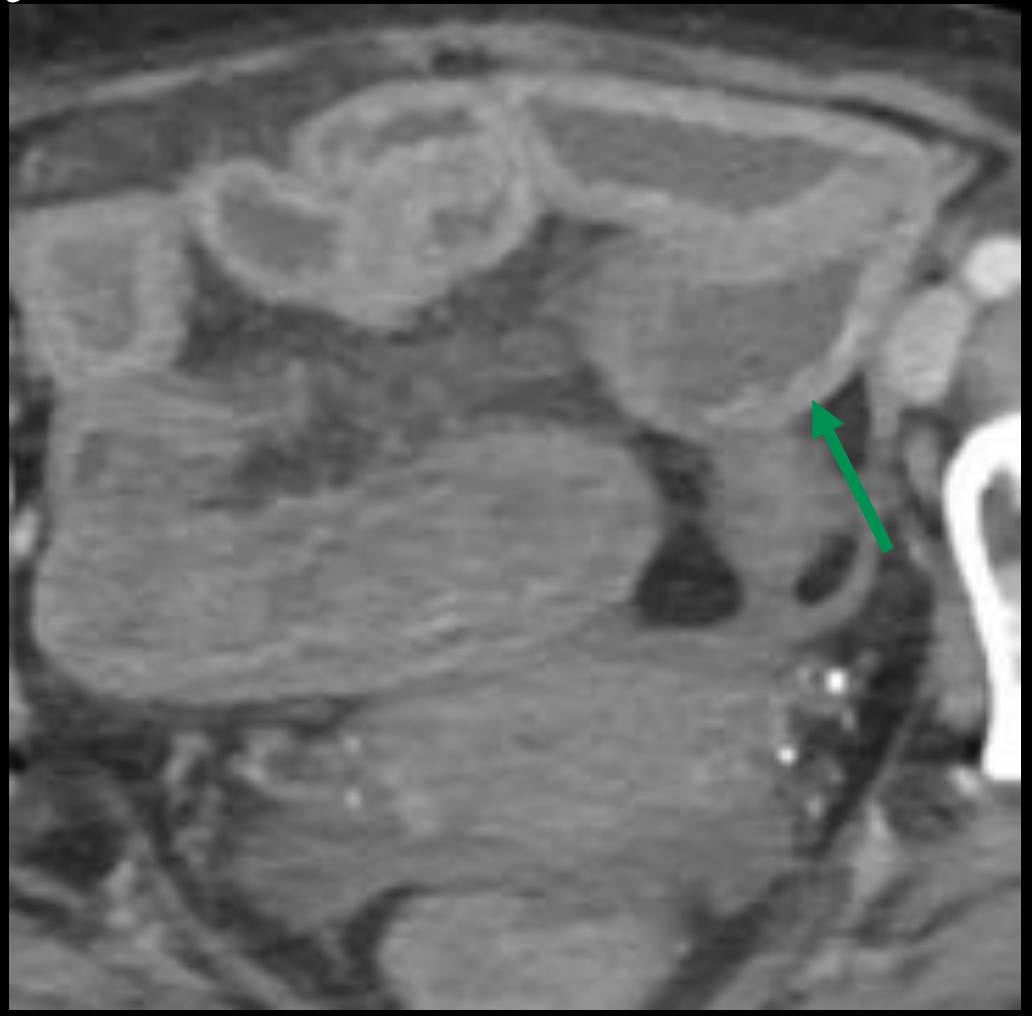
Gastrointestinal Amyloidosis



Diffuse thickening of the sigmoid colon in a patient with amyloidosis



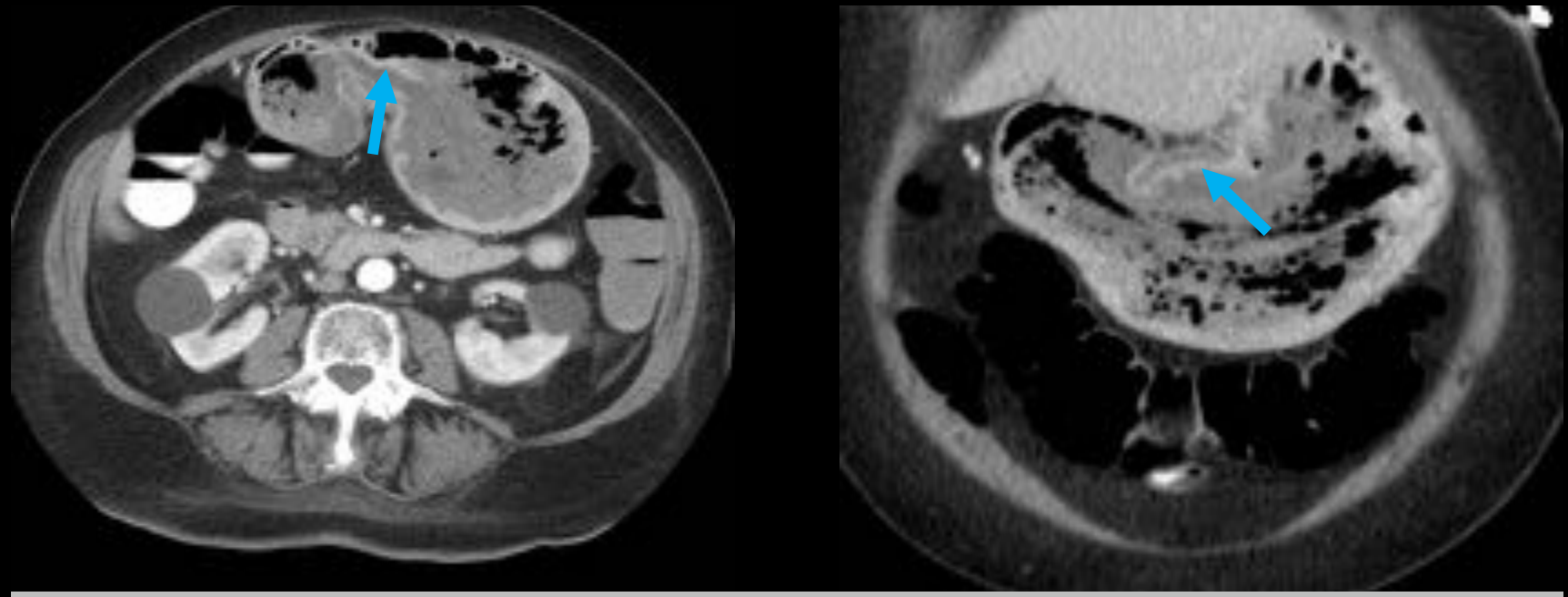
Diffuse thickening of the small bowel in patients with intestinal amyloidosis.



C+CT in a 61 yo f with h/o amyloid "Target Sign"- mucosal hyperemia and submucosal edema, in this case representing **acute enteritis superimposed on chronic mural thickening secondary to amyloidosis** in a 61 year old female.

Gastric Amyloidosis – Clinical Case #1

History: 85 year old female that presented with an upper gastrointestinal bleed secondary to an ulcer.

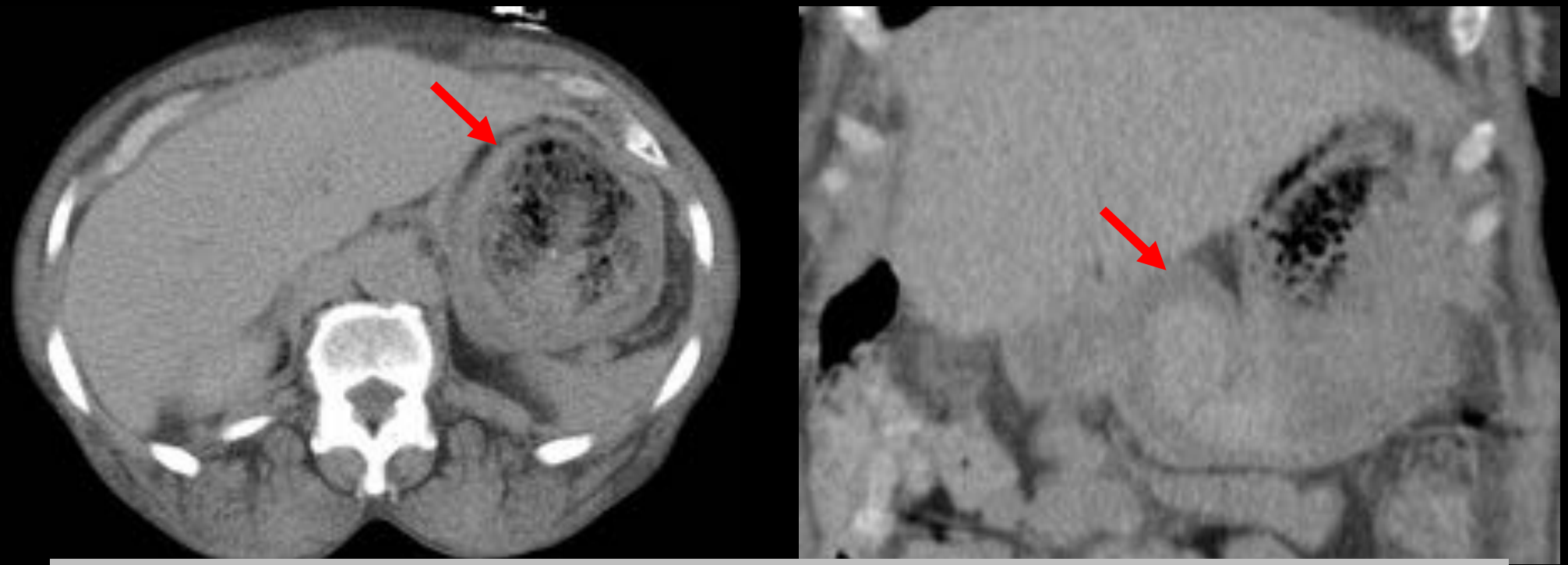


Axial and coronal CECT images show tubular hyperdense regions within the gastric antrum which reflected active contrast extravasation from gastric bleed.

- The patient underwent an upper endoscopy and bleeding was controlled with epinephrine. Pathology: Biopsy showed amyloid deposition with no evidence of malignancy.
- Management: Patient was managed non-operatively and was placed on medical therapy.

Gastric Amyloidosis – Clinical Case #2

History: 66 year old female with AL Lambda Amyloidosis with cardiac involvement (on treatment) that presented with epigastric pain and back pain – was found to have pancreatic cyst few years ago.



Axial and coronal noncontrast CT images demonstrates thickening of the gastric wall.

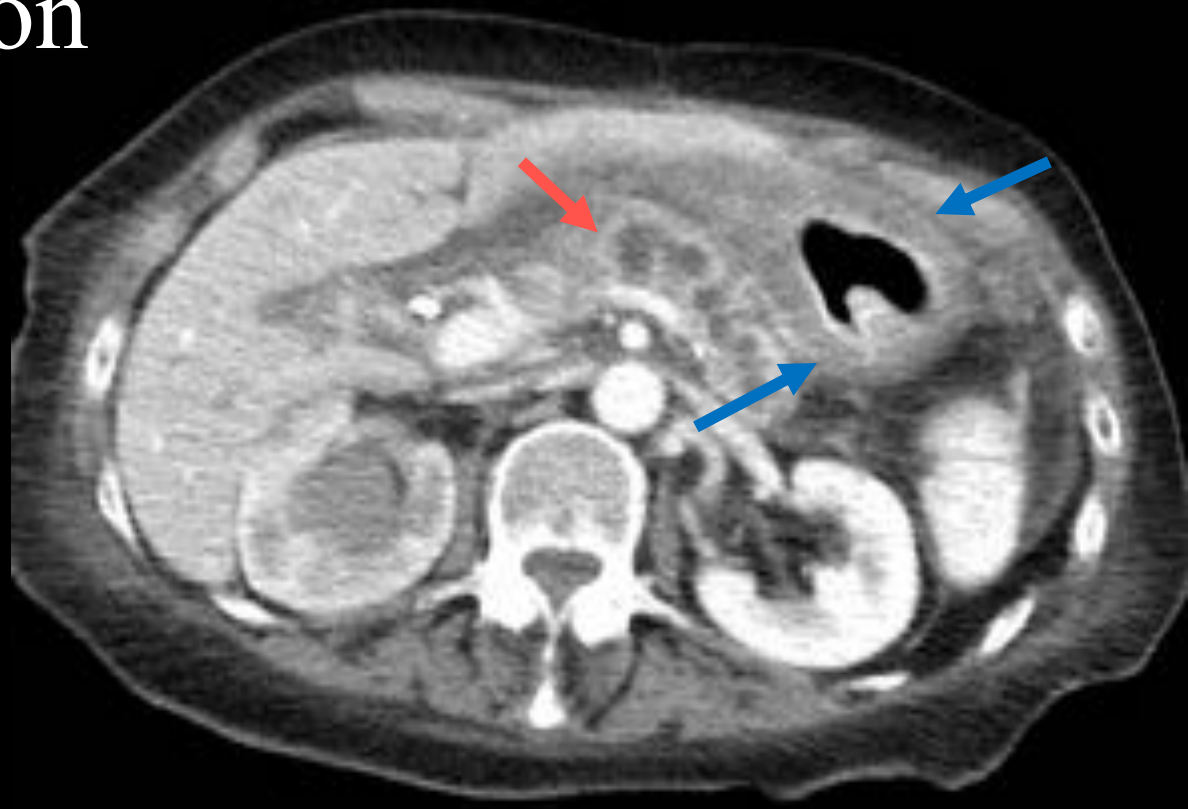
Follow up EGD showed a mass – biopsies were positive for adenocarcinoma. She underwent a partial gastrectomy with Roux-en-y reconstruction.

Pathology: showed three foci of extensive amyloid deposition with co-existent adenocarcinoma in the submucosa.

Differential Diagnosis of Gastric Thickening / Ulceration

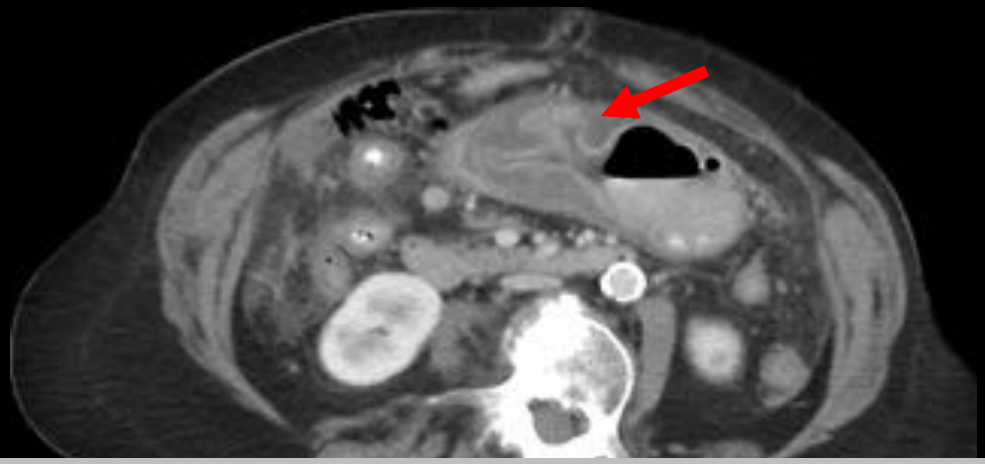
Differentials of Gastric Thickening/Ulceration:

1. **Gastritis:**
   - Erosions along rugal folds; edema secondary to inflammation
2. **Portal Hypertension, Varices:**
   - CT: Thickened stomach with enhancement of varices on PV phase.
3. **Gastric Carcinoma:**
   - Soft tissue density – nodular thickening of the gastric wall with potential local infiltration. Nodular, peritoneal, and nearby organ involvement is common.
4. **Gastric Metastases and Lymphoma:**
   - Massive nodular thickening of folds but usually normal distensibility in the case of lymphoma
5. **Zollinger-Ellison Syndrome:**
   - CT: Hypervascular pancreatic mass with thickened gastric folds

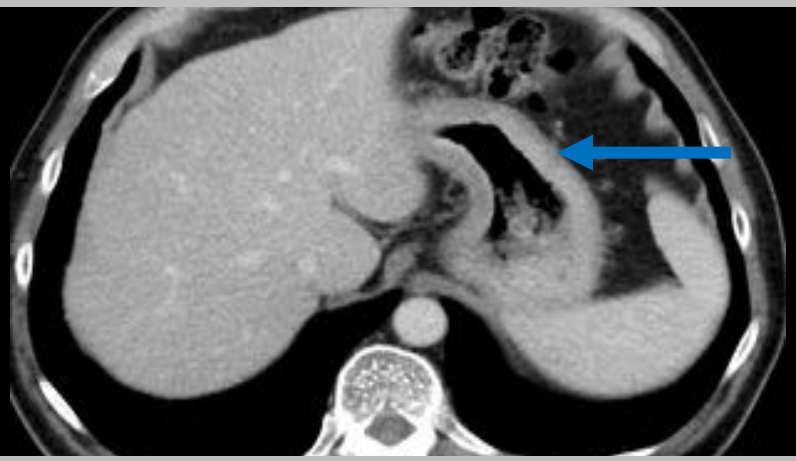


Axial CECT image shows diffused circumferential gastric wall thickening, with biopsy consistent with adenocarcinoma. Atrophic pancreas and pancreatic duct dilatation are also noted

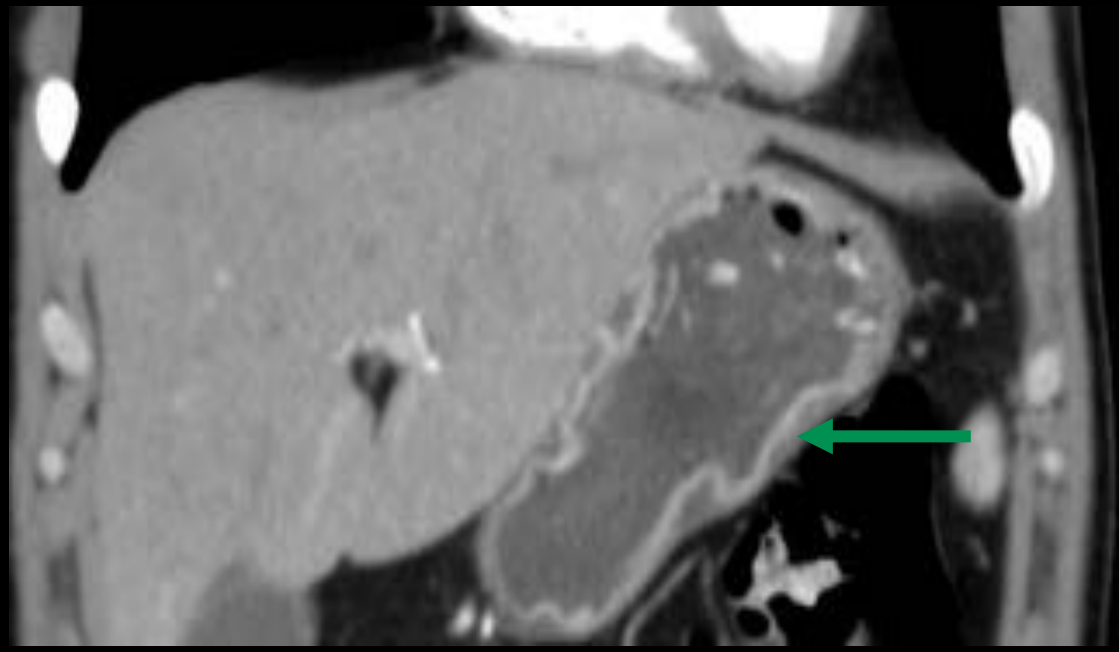
Differential Diagnosis of Gastric Thickening / Ulceration



Axial CECT of the abdomen that shows marked wall thickening/edema involving the gastric antrum associated with focal contour abnormality of the wall consistent with perforated gastric ulcer



Axial CECT of the abdomen showing diffuse gastric wall thickening without a discrete mass and nonvisualization of normal gastric rugae folds, similar to prior and consistent with known history of gastric cancer with linitis plastica. Pathology showed poorly differentiated signet call carcinoma.



Coronal CECT image of the abdomen showing nonspecific gastric mucosal hyperenhancement in patient with gastritis

TAKE HOME POINT

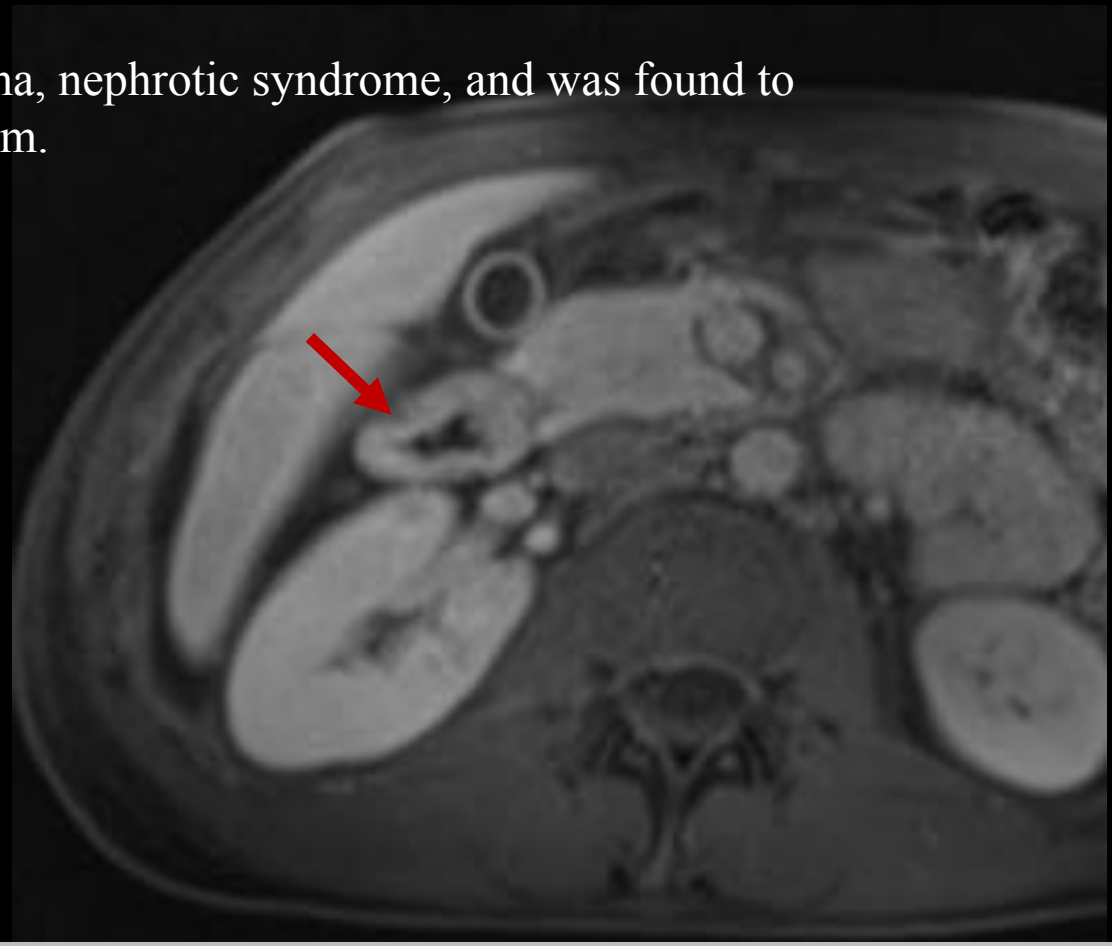
Amyloid can present as gastric wall thickening, or ulceration (usually the antrum). Inflammatory / Neoplastic processes should be considered. Biopsy is essential for diagnosis.

Duodenal Amyloidosis – Clinical Case #1

- **History:** 40 year old male presented with lower extremity edema, nephrotic syndrome, and was found to have a elevated IgG lambda concerning for plasma cell neoplasm.

- The patient was further worked up and was found to have cardiac amyloidosis. Patient had symptoms of early satiety, and abdominal cramping.

- Endoscopy was preformed, and biopsies showed amyloid deposits in the duodenum.

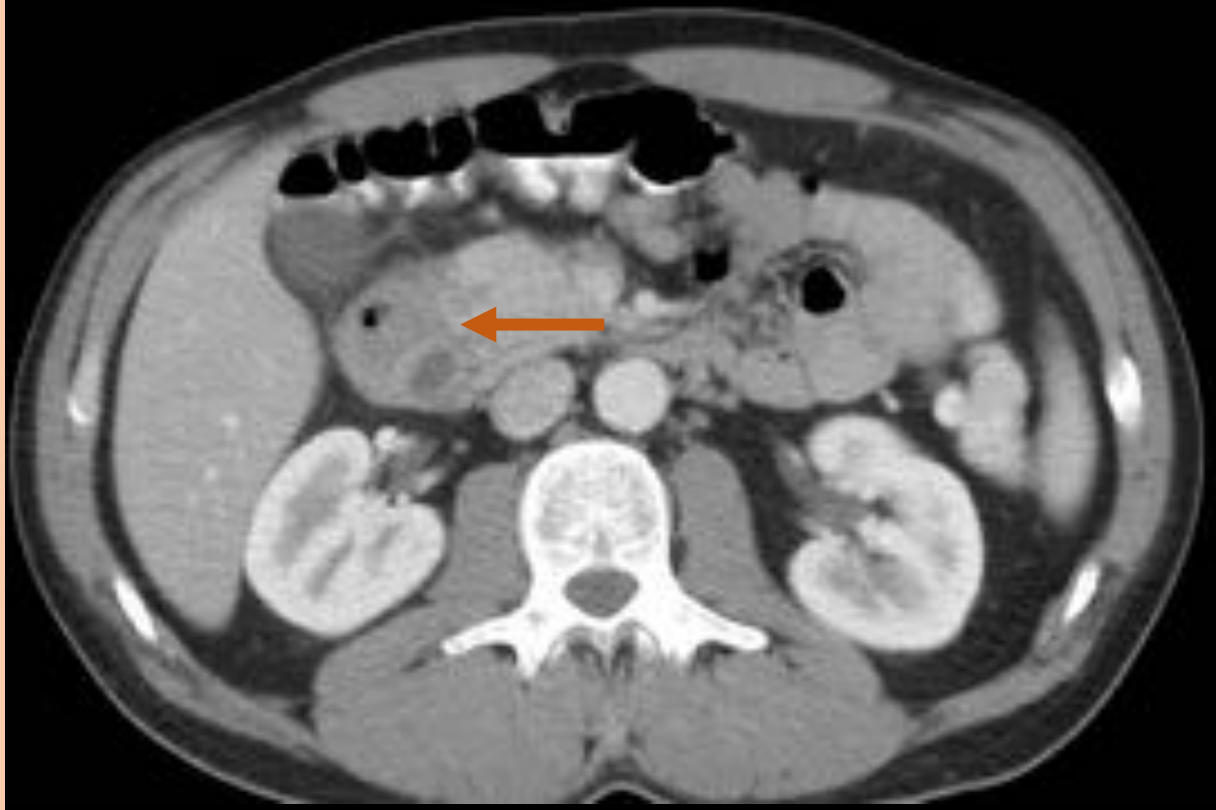


Axial T1 FS MRI of the abdomen showed circumferential thickening of the duodenum and hepatomegaly with no cirrhotic morphology.

Differential Diagnosis of Duodenal Thickening

Differentials of Duodenal Thickening/Mass:

1. Duodenitis/Pancreatitis:
   - CT: Thickened Duodenal wall with surrounding inflammation.
2. **Duodenal Polyps:**
   - CT signs of intraluminal / extraluminal mass.
3. **Duodenal Diverticulum:**
   - CT: Air-fluid level / fluid filled diverticulum – may mimic pancreatic cyst/mass too.
4. **Bruner Gland Hyperplasia**
   - CT: Heterogenous, slightly enhancing lesion
5. **Lymphoma:**
   - CT: Bulky hypovascular soft tissue mass
   - MRI: Low signal on T1WI, variable enhacement with contrast.



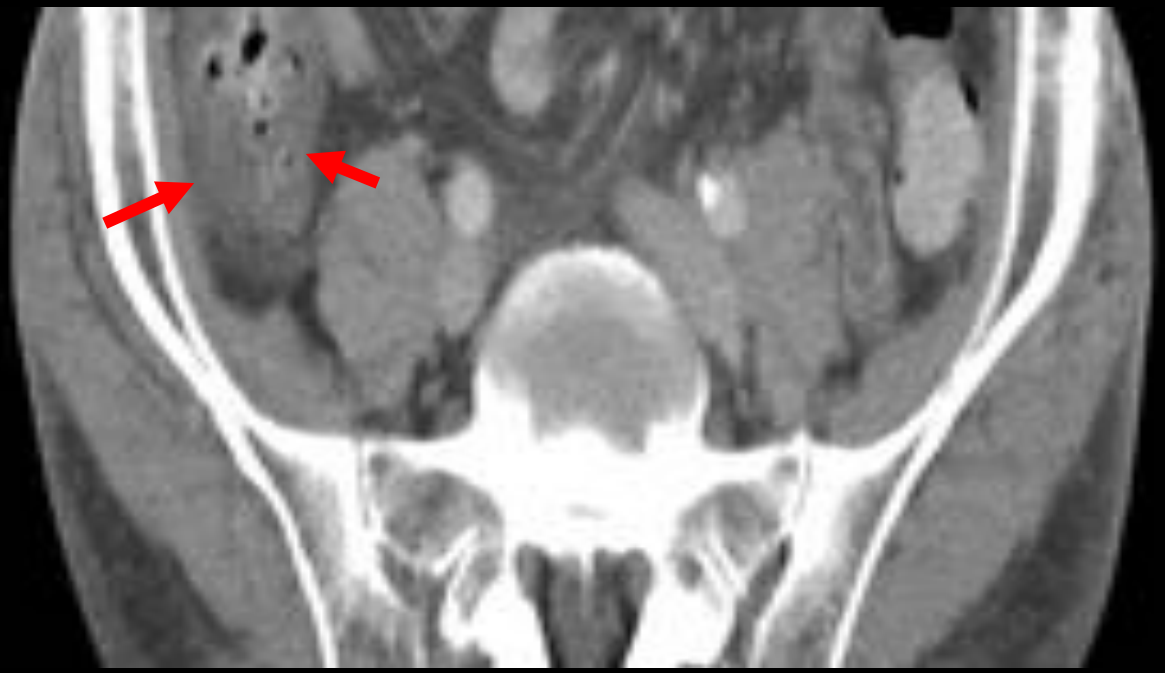
CECT image of the abdomen shows duodenal diverticulum with surrounding inflammation consistent with duodenal diverticulitis.

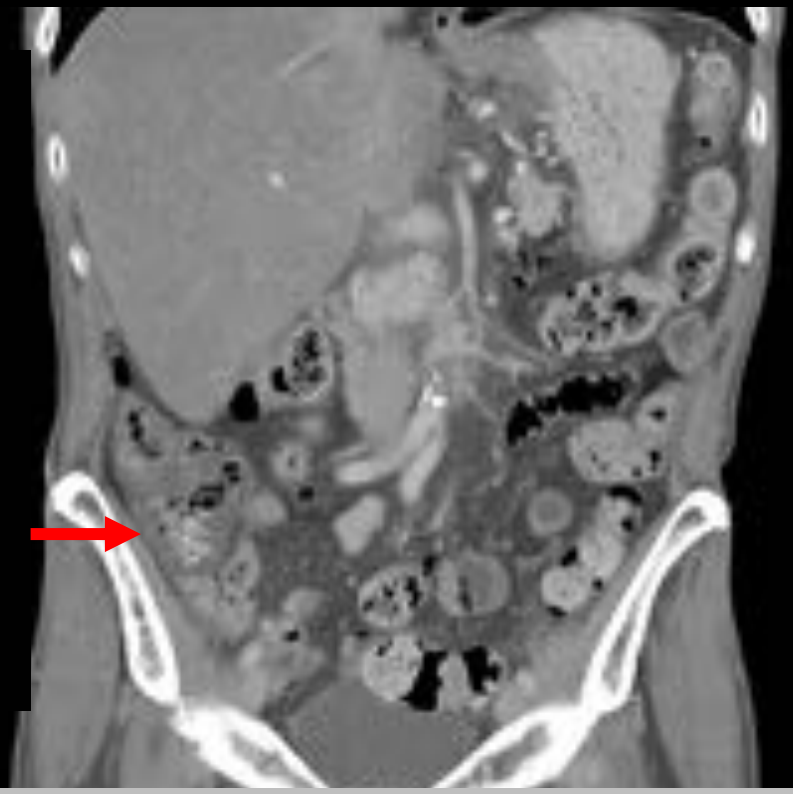
TAKE HOME POINT

Amyloid can present as duodenal wall thickening, or ulceration (usually the antrum). CT/MR Findings show smooth thickening without enhancement. Biopsy essential for diagnosis.

Cecal Amyloidosis – Clinical Case #1

- History: 80 year old male with history of weight loss, abdominal pain and anemia. On colonoscopy, no evidence of colitis was found





Axial and coronal CECT images show mild concentric wall thickening and soft tissue infiltration of the cecum.

- **Pathology:** Biopsy of the cecum showed amyloid deposition within the submucosal vessels that were positive on Congo red stain and showed apple green birefringence on polarization.

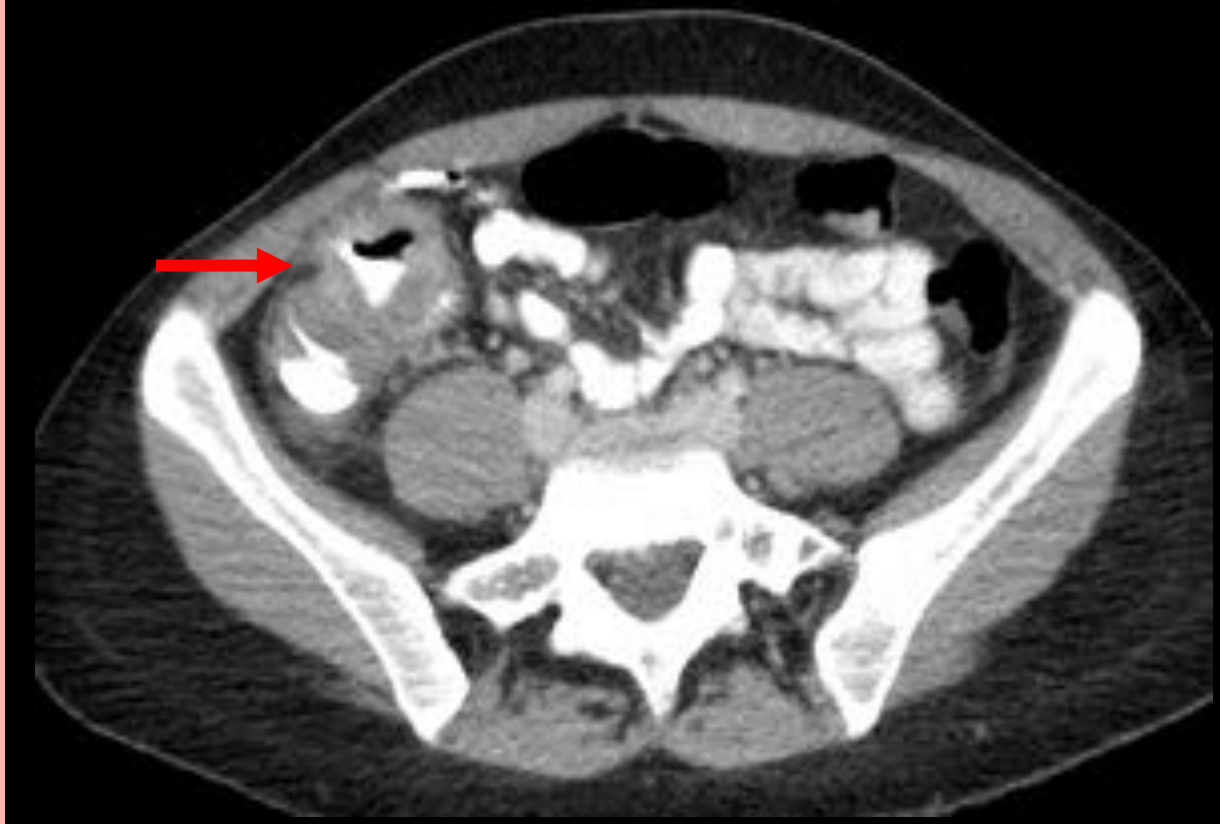
Differential Diagnosis of Cecal Thickening

Differentials of Cecal Thickening/Mass:

1. **Infections:** Colitis, Diverticulitis
   - CT: Thickened wall with surrounding edema / inflammation.
2. **Ischemic colitis:**
   - CT: Thickened hypo-enhanced wall.
   - CT signs of intraluminal / extraluminal mass.
3. **Chron's Disease**: Skip lesions!
   - CT: Thickened edematous wall, pericolonic infiltration, fistulas, strictures.
4. **Colon Cancer:**
   - Short segment
   - Soft tissue attenuation
   - Regional lymphadenopathy and metastatic disease

TAKE HOME POINT

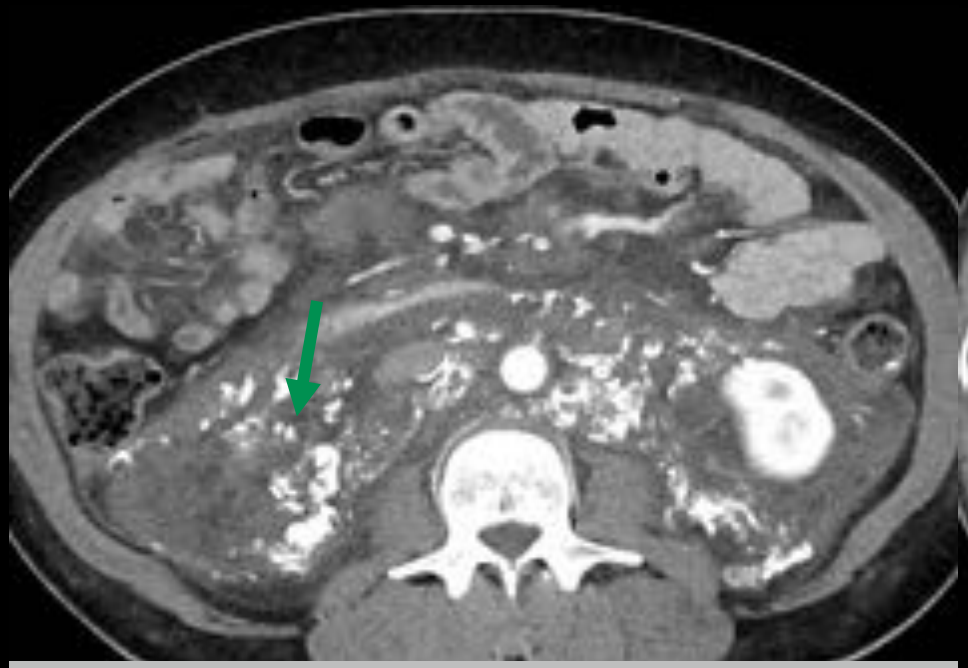
Amyloid should be considered for the differential diagnosis of a long segment circumferential mural thickening of the colon.



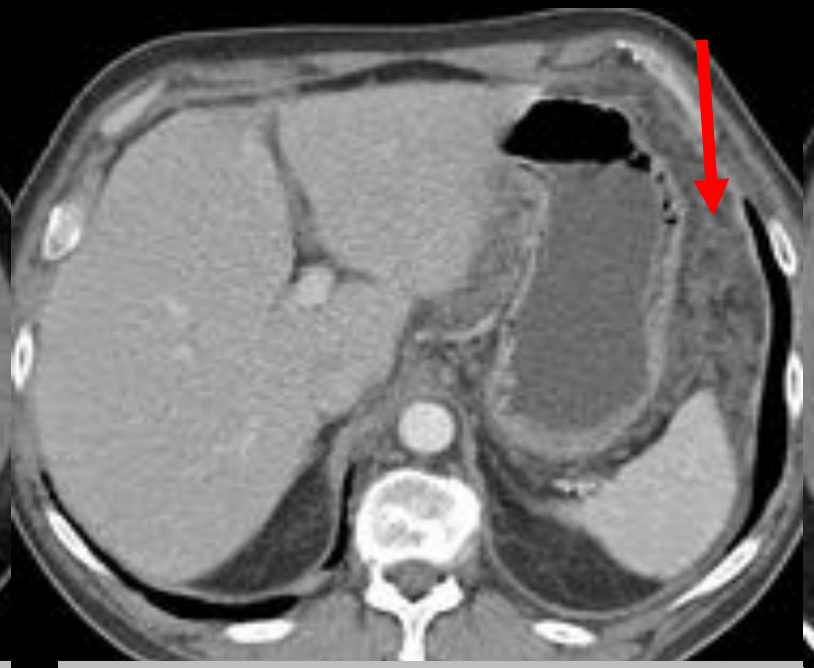
Axial CECT image of the abdomen shows diffused thickening of the cecum with soft tissue density, adjacent regional lymphadenopathy was apparent (not shown). pathology of the mass showed adenocarcinoma of the colon.

Amyloidosis of the Abdominal Cavity and Mesentery

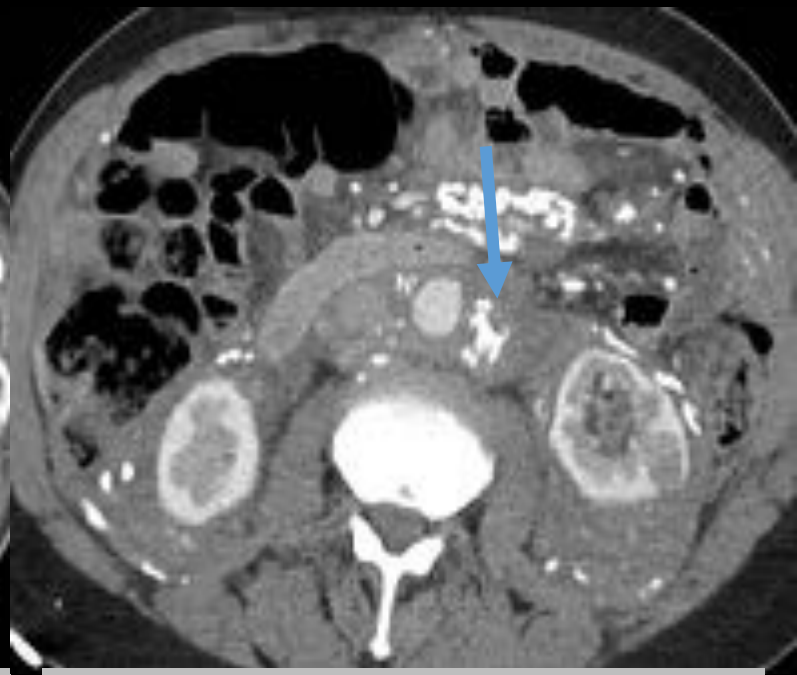
- Amyloid can rarely deposit in the abdominal wall, retroperitoneum or mesentery. It usually presents as:
  1. Infiltrative process.
  2. Amyloidoma, or localized deposit of amyloid, is a soft-tissue density lesion that may contain calcifications or focal areas of necrosis. Can present with cavitations



Amyloid retroperitoneal deposits with calcifications



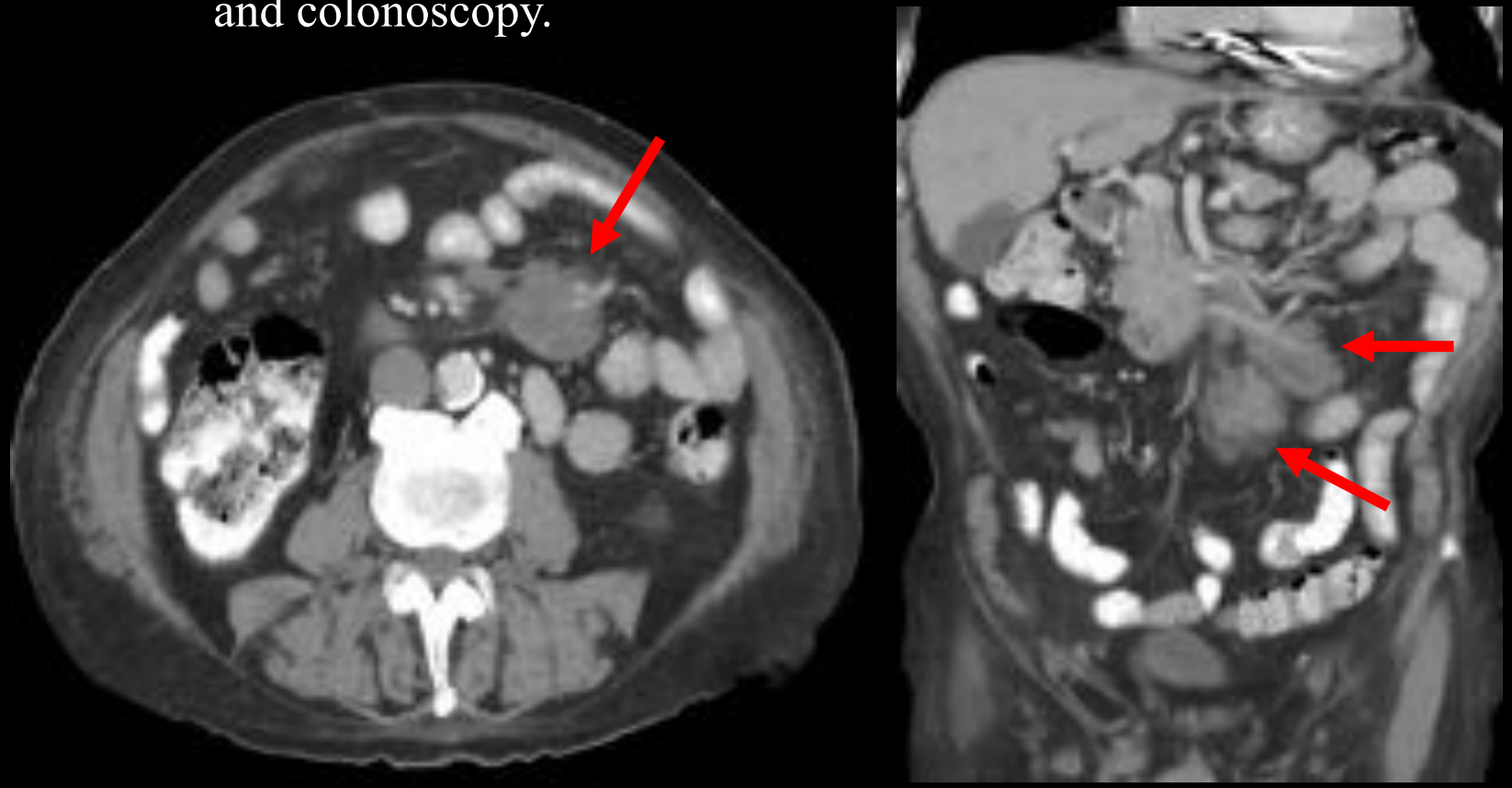
Amyloid Omental Deposits



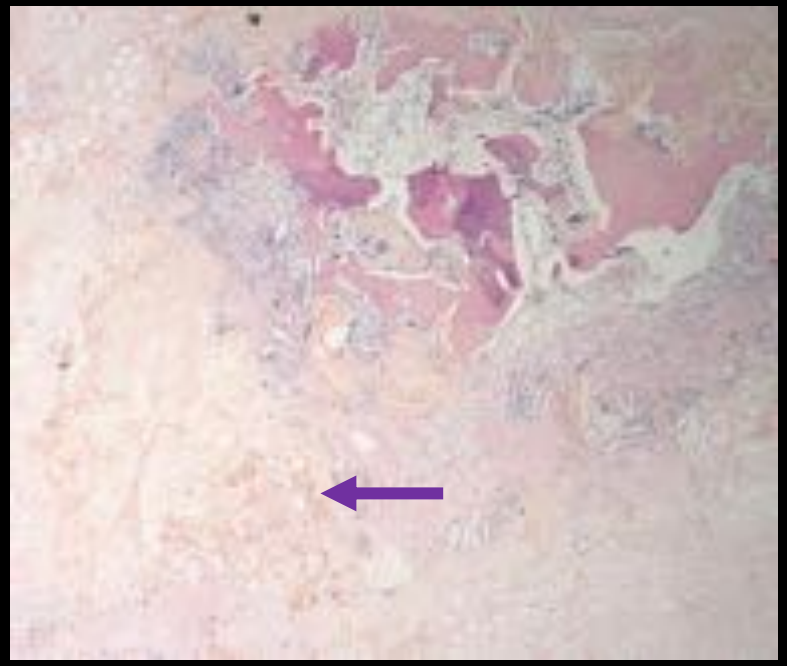
Mesenteric deposits with calcifications

Mesenteric Amyloidosis – Clinical Case #1

- History: 80 y/o M with history of 3 months of diarrhea and weight loss, with a negative endoscopy and colonoscopy.



Axial and coronal CECT images demonstrate infiltrative poorly enhancing masses surrounding the mesenteric root. There were no calcification seen or enlarged lymph nodes appreciated.

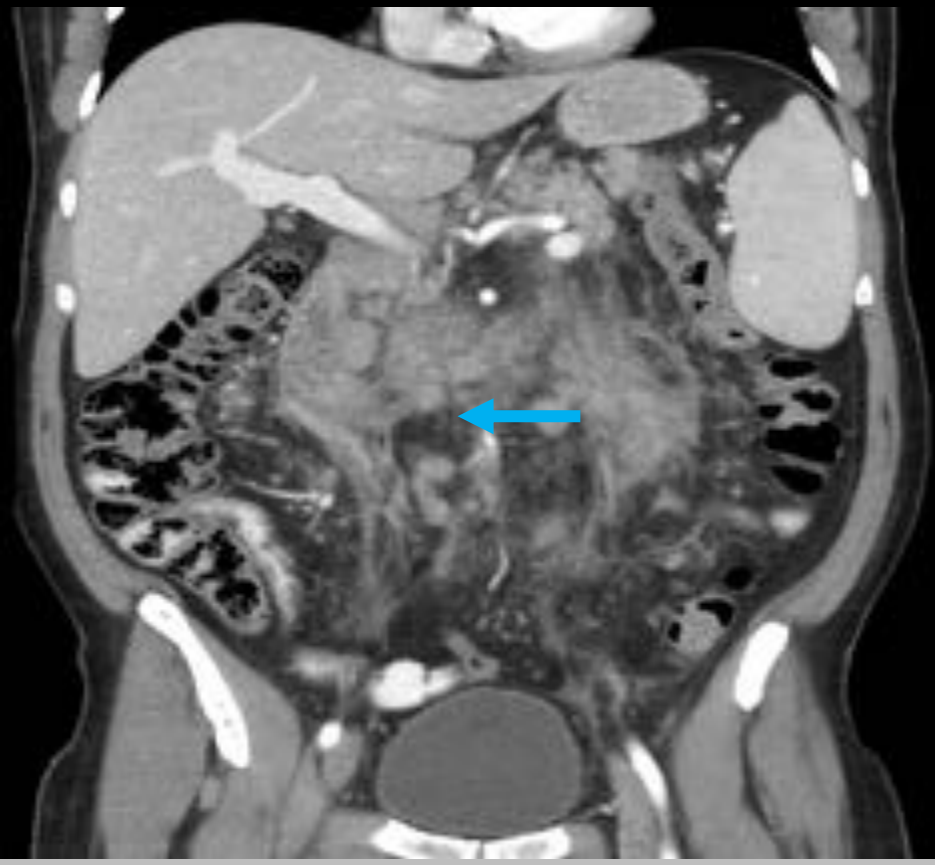


Pathology: Amyloid deposition in the mesentery, consistent with a diagnosis of a mesenteric amyloidoma. The Congo red stain was positive and showed apple green birefringence.

Differential Diagnosis of Abdominal wall, Retroperitoneum, and Mesenteric Infiltrative Process

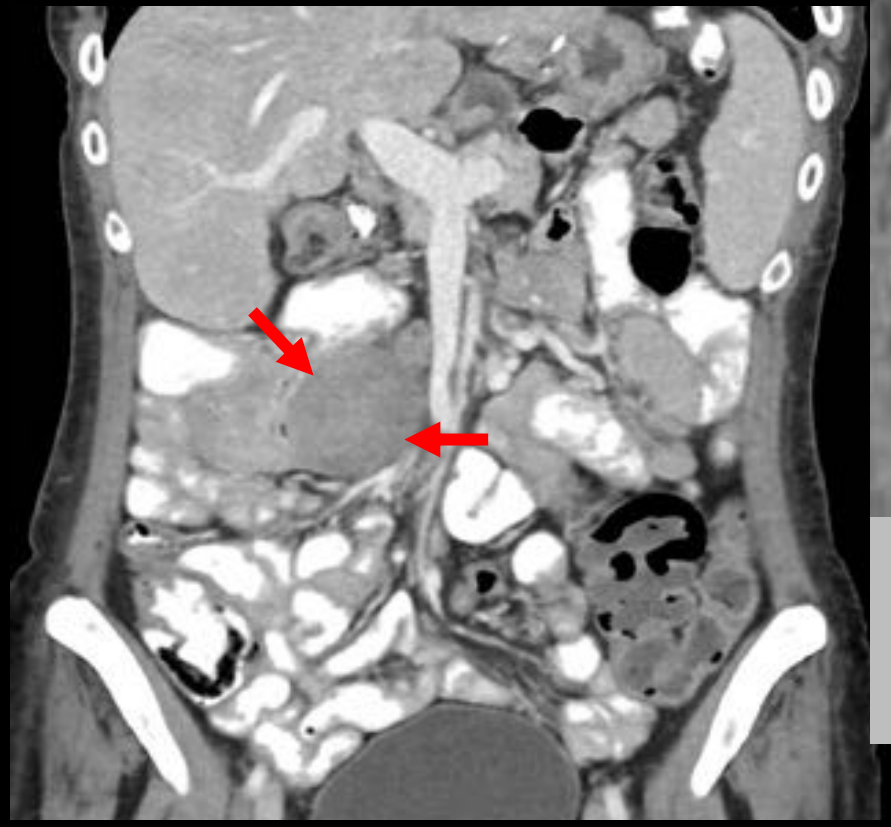
Differential Diagnosis:

1. **Lymphoma:**
   - CT: Enlarged lymph nodes with muscular attenuation
   - MRI: Low attenuation on T1, High attenuation on T2, Heterogenous enhancement with contrast on T1
   - PET: Most sensitive! Highly avid and hypermetabolic
2. Infectious:
   - Tuberculosis
     - Lymph involvement: enlarged, centrally necrotic lymph nodes with hyper-attenuated rims.
     - Tuberculosis Peritonitis: Omental deposits and ascites
3. **Sarcoidosis:**
   - CT: smooth enlarged non-necrotic lymph nodes +/- Calcifications
   - CT: Acute: contrast e**Retroperitoneal Fibrosis**
   - nhanced lesions, Chronic: non-enhancing
   - MRI: Low T1, High T2 (acute); Low T2 (Chronic)

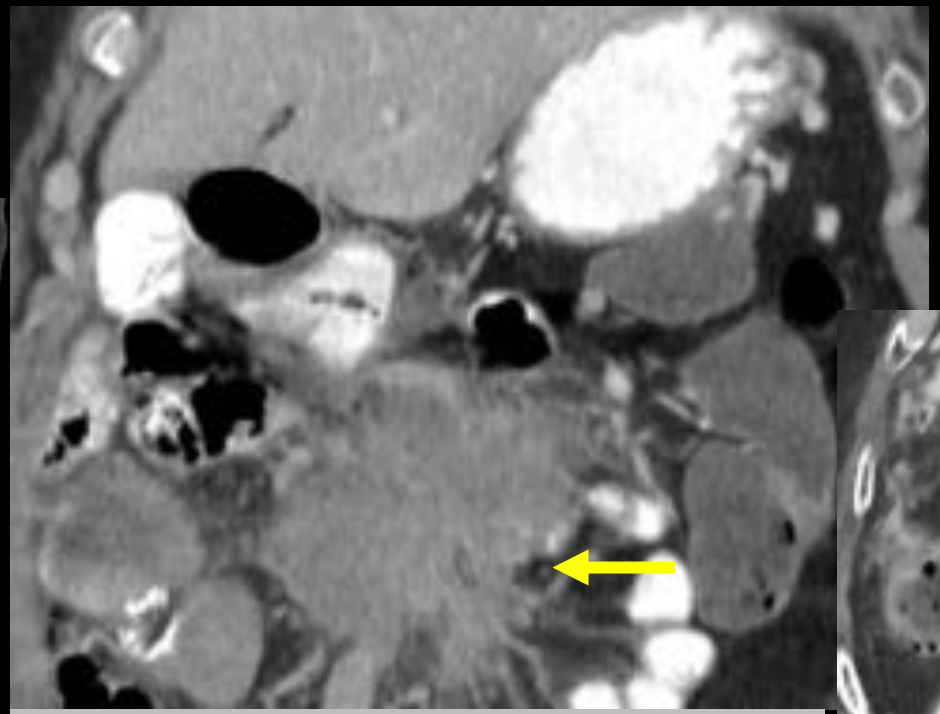


Coronal CECT image of the abdomen demonstrates multiple enlarged near confluent mesenteric lymph nodes and infiltrative changes along the mesentery. Pathology showed to be a Lymphoma.

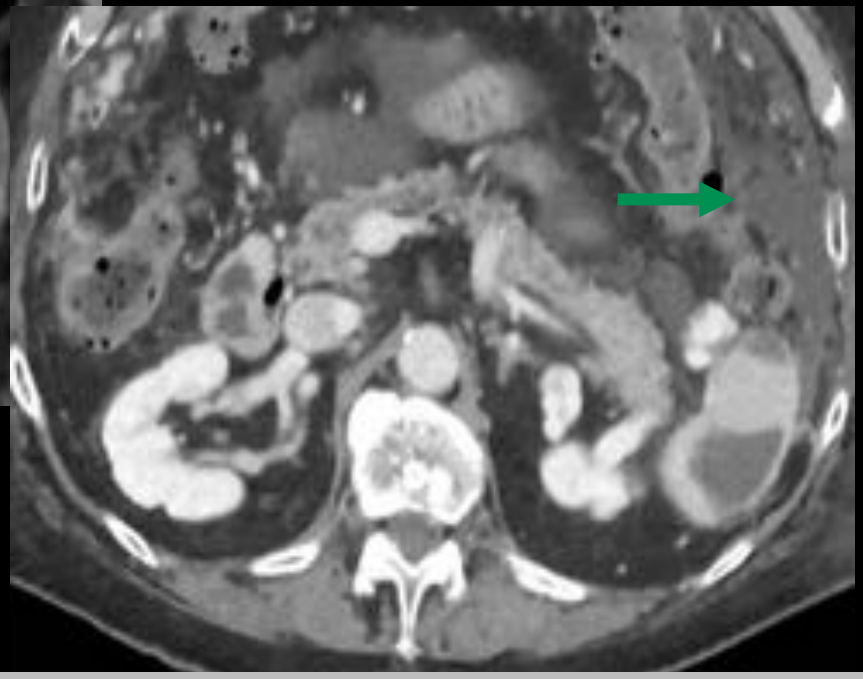
Differential Diagnosis of Abdominal wall, Retroperitoneum, and Mesenteric Infiltrative Process



Coronal CECT image shows a solid hypoattenuating mass in the mesentery. Pathology revealed Mesenteric Desmoid

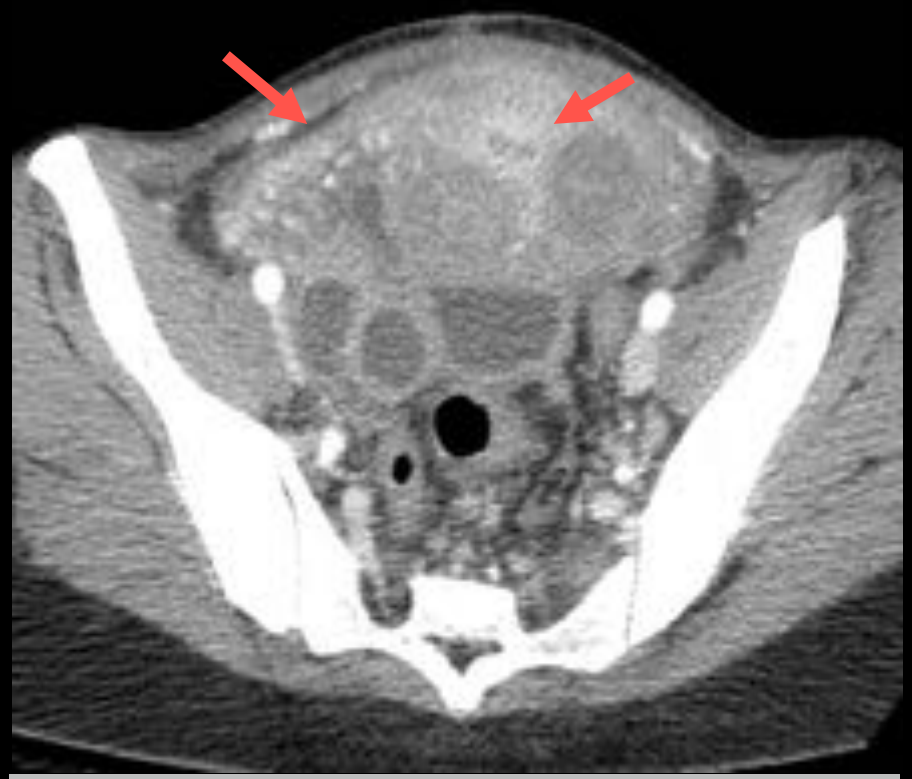


Coronal CECT image shows confluent infiltrating mass that on pathology showed IgG4 related sclerosing mesenteritis

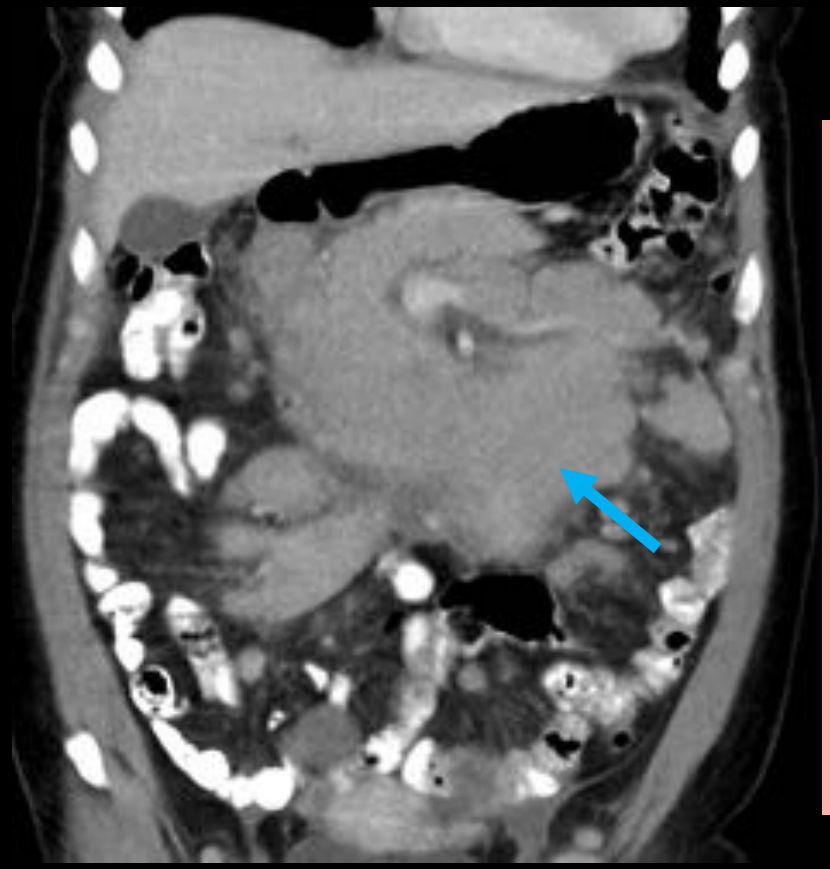


Axial CECT that shows irregular thickening of the peritoneal folds and omental implants that in a patient with malignancy was compatible with Peritoneal Carcinomatosis

Differential Diagnosis of Abdominal Wall, Retroperitoneum, and Mesenteric Infiltrative Process



Axial CECT image of the abdomen and pelvis shows thickening of the peritoneal folds and bowel wall thickening as well as peritoneal calcifications with cytology consistent with Tuberculosis



Coronal CECT image of the abdomen and pelvis that shows a confluent retroperitoneal lymphadenopathy. Pathology consistent with Lymphoma.

TAKE HOME POINT

Amyloid deposition in the retroperitoneum, mesentery and abdominal wall can mimic other processes (localized / diffused) such as lymphoma, dermoid tumors, IgG Sclerosing Mesenteritis, peritoneal carcinomatosis and infectious processes. Biopsy is essential for patient management.

Summary

- Amyloidosis is a rare medical condition, with a high morbidity if not treated. Thus, early diagnosis is essential to improve patient's survival.
- Amyloidosis presentation in the gastrointestinal tract can vary depending on the organ involved.
- Common presentations in the gastrointestinal system includes hepatomegaly, biliary strictures, thickened stomach and intestines, perforation, and rarely obstruction as well as mesenteric infiltration.
- Recognition of amyloidosis related imaging findings and its differential counterparts is important to correct diagnosis.

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