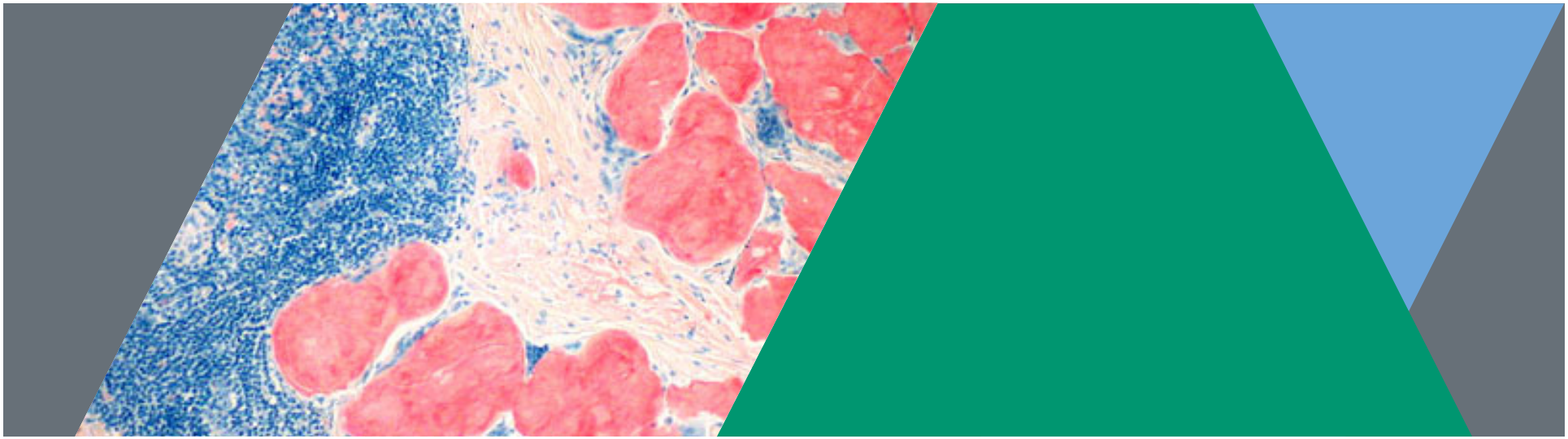
INSELGRUPPE

Gastrointestinal amyloidosis

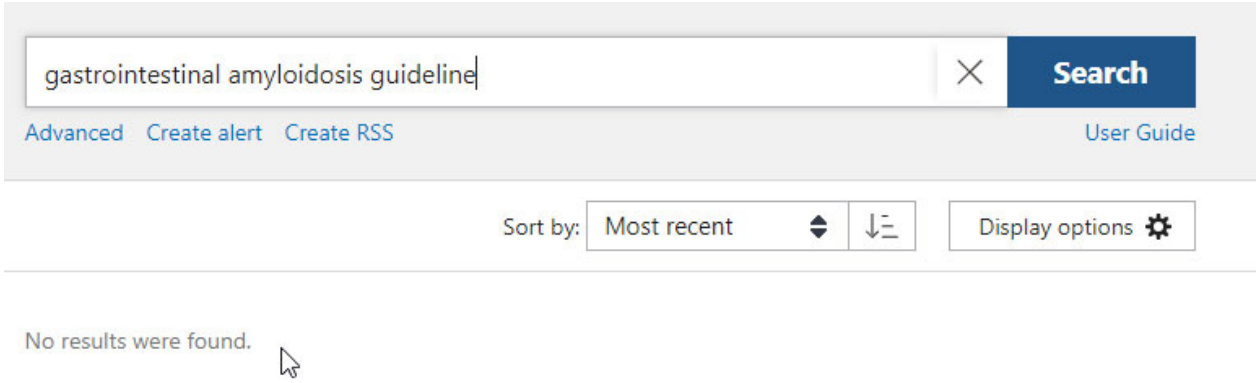
Wednesday Seminar 14.02.2024

Niklas Krupka



What will be covered?

- What is amlyoid(osis)?
- Why should I care about this as a GI doctor?
- How is amyloidosis diagnosed?

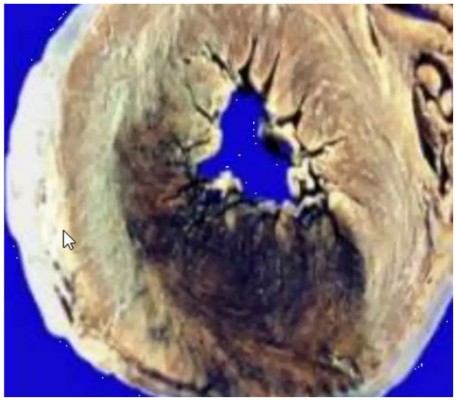


Amyloidosis is a rare disease

1000–3000 cases/y in the US

Amyloid: Deposits which showed close similarity to starch after they were dyed with iodine and sulphuric acid

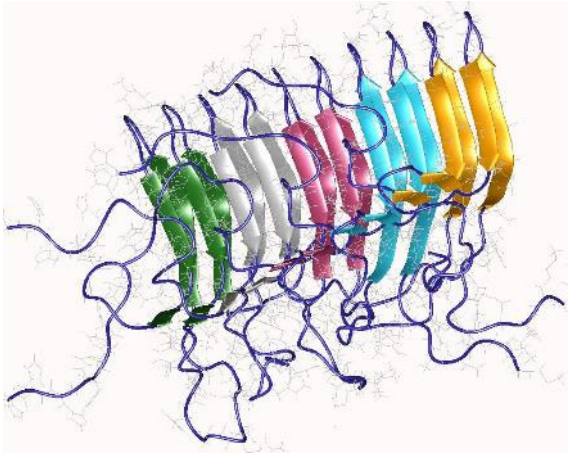
Rudolf Virchow 1853



Amyloid

High concentrations of proteins that have the tendency to fold improperly

Mutant proteins that are prone to misfolding



Protein deposits with a fibrillar morphology and a β-sheet secondary structure

Amyloid-opedia

Table 1 The classification of amyloidosis suggested by the International Symposium on Amyloidosis

Types of amyloid deposition	Name of clinical classification	Site of amyloid deposition	Precursor protein	Pathology and clinical feature
AL	Systemic AL amyloidosis	Systemic	Immunoglobulin light-chain	It deposits on all but the central nervous system. Prognosis is poor with heart failure.
	Localized AL amyloidosis	Localized		It only deposits on local organs. There is no transition to a systemic type, and the prognosis is good.
AA	AA amyloidosis	Systemic	Serum amyloid A	It easily deposits in the kidney and GI tract with a background of chronic inflammatory diseases.
Aβ2M	Dialysis amyloidosis	Systemic	β2-microglobulin	It develops in long-term dialysis patients. It mainly deposits in osteoarthritis and may deposit in the GI tract.
ATTR	Hereditary amyloidosis	Systemic	Mutated TTR	It occurs in familial amyloid polyneuropathy patients.
	Senile systemic amyloidosis	Systemic	Wild-type TTR	It is easy to develop carpal tunnel syndrome.

AA, amyloid A; AL, amyloid light-chain; ATTR, amyloid transthyretin; Aβ2M, amyloid β2-microglobulin; GI, gastrointestinal.

← Including IBD!

...and many more (rare)

Iida T et al. Journal of Gastroenterology and Hepatology 33(2018) 583–590

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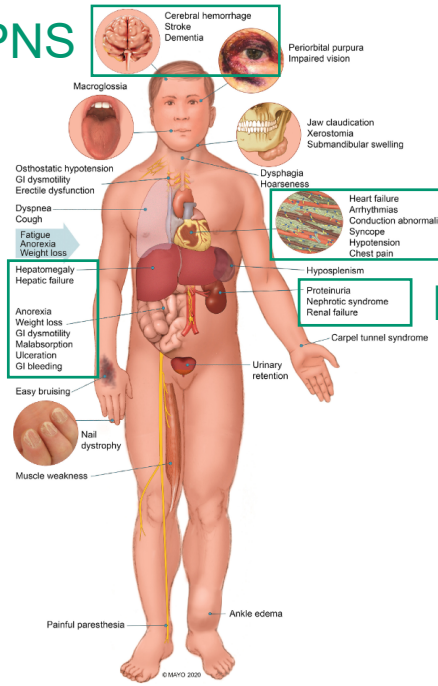
Which organs are most commonly affected in amyloidosis?

CNS/PNS

Liver/GI tract (~30%)

Heart

Kidney



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How does amyloid damage the GI tract?

Mucosal infiltration

- Duodenum > colon > esophagus
- Wall thickening, ulceration, inflammation
- Loss of absorptive function

Neuromuscular infiltration

- Stasis syndromes / prolonged transit

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How do patients with GI amyloidosis present?

Diarrhea

- 10-50%
- Chronic, watery
- DD: infectious
- Fcal may be elevated

Dysmotility

- Chronic constipation
- Gastroparesis
- Distension & pain
- Often SIBO

GI bleeding

- 5-30%
- Sometimes ulcerations
- Coagulation abnormalities
- Vascular involvement

Malabsorption

- Unintentional weight loss very common in amyloidosis
- Mechanism multifactorial
- Sometimes protein loss

Perforation

- Rare
- Probably due to ischemia

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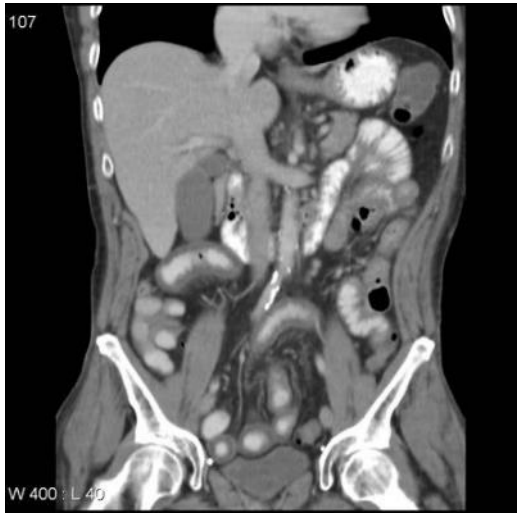
Diagnosis of amyloidosis



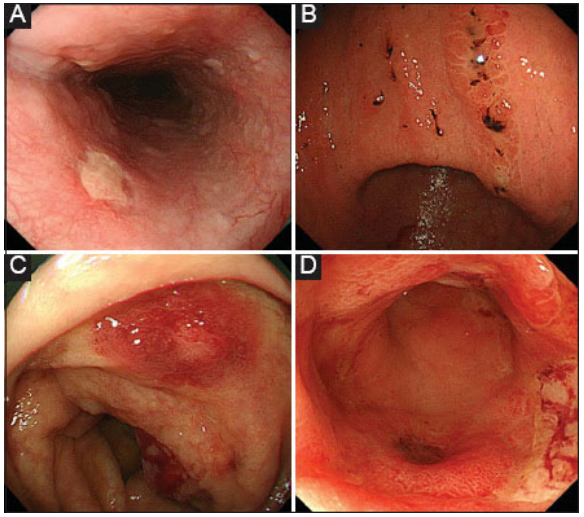


Table 3 Endoscopic findings of 36 cases with GI amyloidosis in our facility

Stomach	Depressed lesion: 45%, redness: 32%
(EGD: 31)	Edema: 29%, mucosal friability: 26%
	Elevated lesion like submucosal tumor: 26%
	Normal: 45%
Duodenum	Redness: 13%, edema: 13%
(EGD: 31)	White granular appearance: 13%
	Normal: 77%
Ileum	Redness: 16%, edema: 16%, stricture: 16%
(CS: 19)	Elevated lesion like submucosal tumor: 16%
	Normal: 68%
Colon, Rectum	Indistinct vascular pattern: 37%, redness: 32%
(CS: 19)	Edema: 32%, submucosal hematoma: 21%
	Normal: 47%

High degree of clinical suspicion necessary

Iida T et al. Journal of Gastroenterology and Hepatology 33(2018) 583–590
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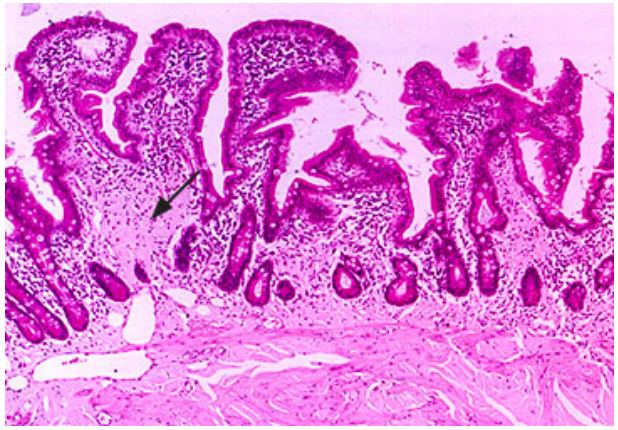
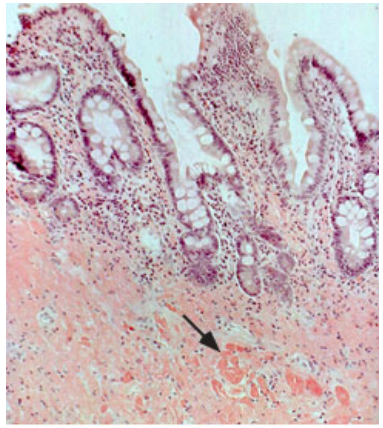
Amyloidosis – Histology

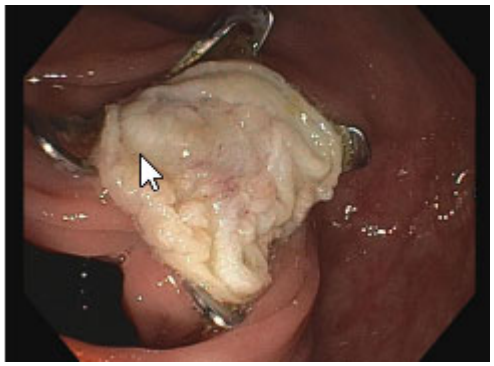
H&E



Congo red



Consider FTRD



Highest diagnostic yield: duodenum & rectum

Treatment (very briefly)

Table 3 Management of gastrointestinal amyloidosis based on the amyloid protein

Gastrointestinal amyloidosis	AL amyloidosis	AA amyloidosis	Hereditary amyloidosis	Dialysis-related amyloidosis
Treatment strategy	Systemic: Eligible: Autologous stem cell transplantation (ASCT) for plasma cell dyscrasias. Non-eligible: No standard protocol; combination of Bortezomib, Melphalan and Dexamethasone has shown improved survival. Localized: Observation or localized surgical excision	Chronic inflammatory conditions: Biologics (anti-TNF antibodies, humanized anti-IL6 receptor antibody) and immunosuppressants. Familial mediterranean fever: Colchicine.	Liver production of transthyretin: Orthotopic liver transplantation (OLT). Disease modifying therapy: Transthyretin stabilizers (Tafamidis and Diflunisal), Doxycycline, Patisiran and Inotersen may be used on case-to-case basis	Prevention: Removal of plasmatic β2-microglobulin ($A\beta_2M$) through hemodialysis or peritoneal dialysis. Early renal transplant

+ symptomatic treatment
(nutrition, prokinetics, laxatives antibiotics, surgery)

Dahiya DS et al. World J Gastrointest Endosc 2021 January 16; 13(1): 1-12

Summary

- GI amyloid disease is rare and can easily be missed
- Think of it in patients with unxplained: bleeding, malabsorption, diarrhea, dysmotility
- Think of it when there is proteinuria, hepatomegaly, cardiomyopathy, neuropathy
- Biopsy (D2 / rectum) → Congo red
- Prognosis determined by renal and cardiac function