INSELSPITAL
Universitätsklinik für
Viszerale Chirurgie und Medizin

GI Manifestations of Vasculitis

Bible Class 17.07.2019

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Bauchzentrum
BERN

Goals of the presentation

- Beyond the basics: discuss pathophysiology of vasculitis on a molecular basis
- Learn the exact mechanism of action of medical treatments
- Analyze the literature for potential missed treatment targets
- Ultimately become rheumatologists ourselves

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- Discuss the classification, epidemiology and basic management of common vasculitides with GI manifestations.

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- Discuss the **classification**, epidemiology and basic management of common vasculitides with GI manifestations.

Definition of vasculitis – Classification

Large vessel vasculitis

-
-

Medium vessel vasculitis

-
-

Small vessel vasculitis

-

1.
2.
3.

-
-

Variable vessel vasculitis

-

Vasculitis with systemic diseases

-
-

Single-organ vasculitis

Definition of vasculitis – Classification

Large vessel vasculitis

- Takayasu arteritis
- Giant cell arteritis

Medium vessel vasculitis

- Polyarteritis nodosa
- Kawasaki disease

Small vessel vasculitis

- ANCA-associated vasculitis
  1. Granulomatosis with polyangiitis (Wegener's disease)
  2. Microscopic
  3. Eosinophilic granulomatosis with polyangiitis (Churg-Strauss disease)
- IgA vasculitis (Henoch– Schönlein purpura)
- Cryoglobulinemic vasculitis

Variable vessel vasculitis

- Behçet's disease

Vasculitis with systemic diseases

- Systemic lupus erythematosus
- Rheumatoid vasculitis

Single-organ vasculitis

Which GI patients raise suspicion?

Which GI patients raise suspicion?

- features of gastrointestinal ischemia
- absence of risk factors for atherosclerotic vascular disease.

- Absence of ischemia does not exclude vasculitis

- Easy in vasculitides with early onset…

The Five Factor Score?

The Five Factor Score?

1. Cardiomyopathy
2. CNS involvement
3. Severe GI Symptoms (?)
4. Renal failure (Cr > 140mmol/L)
5. Proteinuria (> 1g/d)

polyarteritis nodosa, microscopic polyangiitis and eosinophilic granulomatosis with polyangiitis (EGPA)

TABLE 4. Mortality associated with the five-factors score (FFS)*

FFS	Dead (%)	Alive (%)	Relative Risk	No. of Patients
0	11.9	88.1	0.62	218
1	25.9	74.1	1.35	81
2	45.95	54.05	2.40	37
Total	64	272		336†

* The 5 prognostic factors are cardiomyopathy, CNS involvement, severe GI tract symptoms, renal failure (i.e., Cr > 1.58 mg/dL), high proteinuria (>1 g/d). FFS = 0 when all 5 factors are absent; FFS = 1 when only 1 factor is present; FFS = 2 when 2 or more factors are present.

† Number of patients used to establish the score.

Guillevin, L. et al. Prognostic factors in polyarteritis nodosa and Churg–Strauss syndrome. A prospective study in 342 patients. Medicine (Baltimore) 75, 17–28 (1996).

Large vessel vasculitis : Takayasu arteritis

Epidemiology?

Large vessel vasculitis : Takayasu arteritis

Epidemiology

- ♀ 20-40yo
- Japan, Southeast Asia, India and Mexico
- Japan >40 cases per million vs NA 1-3

Takayasu arteritis: GI Manifestations?

Takayasu arteritis: GI Manifestations

Ischemia (Small intestine, Colon, Liver, Spleen)

- 25% stenosis of mesenteric or celiac arteries[1]
- 4% mesenteric ischemia[1]
- 73% ↑ ALP 73% (ischemic liver involvement?)[2]

Concomitant IBD

- 5% in a US cohort[3]
- IBD precedes Takayasu (median 4y)[3]
- No difference in IBD or Takayasu prognosis[3]

3: Sy, A. et al. Vasculitis in patients with inflammatory bowel diseases: a study of 32 patients and systematic review of the literature. Semin. Arthritis Rheum. 45, 475–482 (2016).

Takayasu arteritis: Management and outcomes

liaise with Rheumatologist / angiologist / vascular surgeon

Induction

- Prednisone 0.5-1 mg/Kg/d – taper (sustained remission 28–50%)
- Severe flare: Prednisone + IFX (analog IBD)

Maintenance

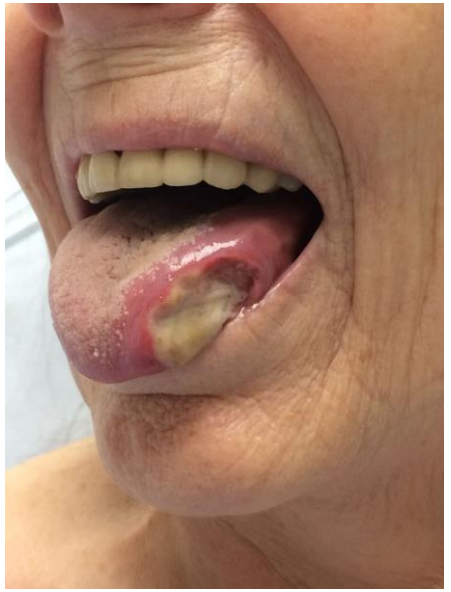
- MTX 15-25mg/w
- Alternatives: MMF, IFX, Tocilizumab (Actemra®), Cyclophospamide

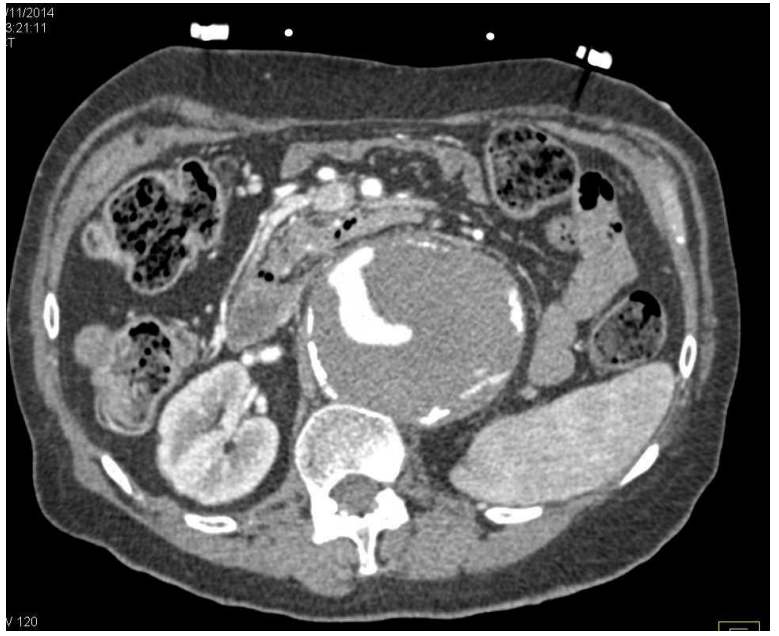
Endovascular / vascular surgery

- *Restenosis* 15–30% at 5–20 y for open surgery
- *Restenosis* 30–70% at 5–10 y for angioplasty

Case

- 76yo female presents with painful tongue ulcer, abdominal pain and headaches
- PE: periumbilical and epigastric bruit
- CT:





Soowamber M. et al . Gastrointestinal aspects of vasculitides Nat Rev Gastroenterol Hepatol. 2017 Mar;14(3):185-194.

Large vessel vasculitis : Giant cell arteritis

Epidemiology?

Large vessel vasculitis : Giant cell arteritis

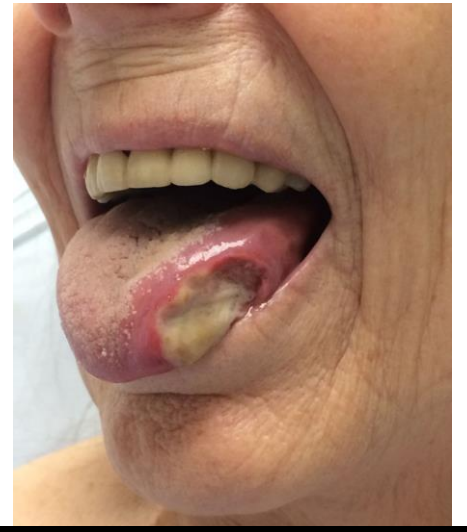
Epidemiology

- Western countries
- Mainly caucasian
- Incidence increases with age, never<50, peaks at 70–80 y

3: Kermani TA et al. Increase in age at onset of giant cell arteritis: a population-based study. Ann Rheum Dis. 2010 Apr;69(4):780-1. Epub 2009 Oct 22.

Giant cell arteritis: GI Manifestations

Giant cell arteritis: GI Manifestations

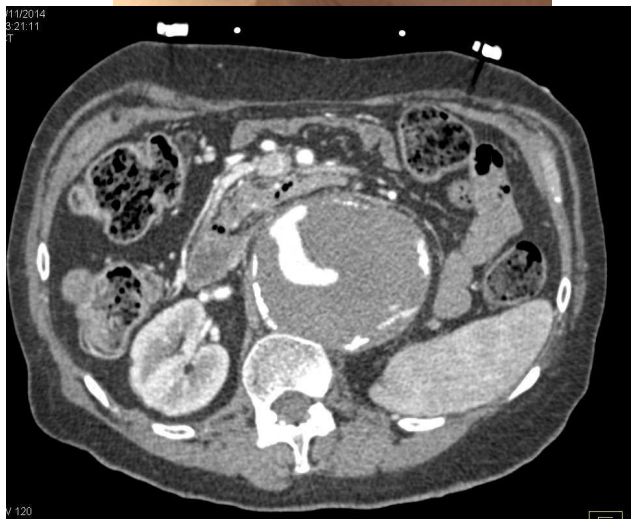


Mesenteric vessel involvement very rare

- 12 cases in the literature[4]

More often:

- Tongue necrosis (dysphagia, pain, edema / gangrene)
- Abdominal aortic aneurysm (dt 6-7y)
- NS Liver enzyme abnormalities (10-50%)



4: Scola, C. J., Li, C. & Upchurch, K. S. Mesenteric involvement in giant cell arteritis. An underrecognized complication? Analysis of a case series with clinicoanatomic correlation. Medicine (Baltimore) 87, 45–51 (2008).

Giant cell arteritis: Management

Giant cell arteritis: Management

Screening

- US for aortic aneurysm at diagnosis yearly for ≥5y

Medical treatment (Similar to Takayasu)

Induction

- Prednisone
- Severe flare: Prednisone + MTX or Tocilizumab[6] (Actemra®)

Maintenance

- MTX or Tocilizumab iv or sc (Actemra®)

6: Villiger PM et al. Tocilizumab for induction and maintenance of remission in giant cell arteritis: a phase 2, randomised, double-blind, placebo-controlled trial. Lancet. 2016 May 7;387(10031):1921-7.

Case

- 55 yo mail with abdominal and right flank pain, fever, malaise and weight loss
- Routine lab non specific
- CT Scan: focal renal infarction
- Angiography:

Case courtesy of A.Prof Frank Gaillard, Radiopaedia.org, rID: 12791

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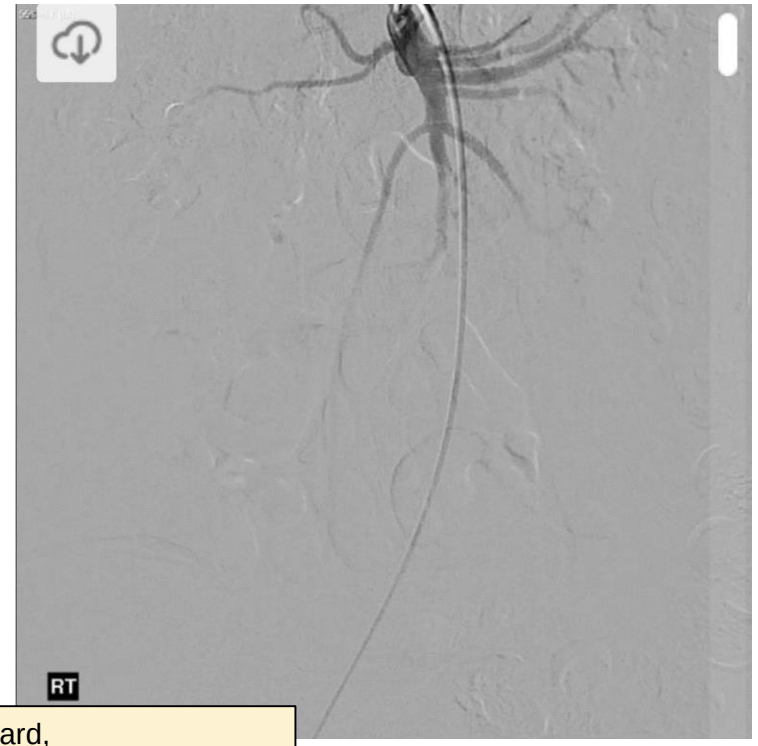

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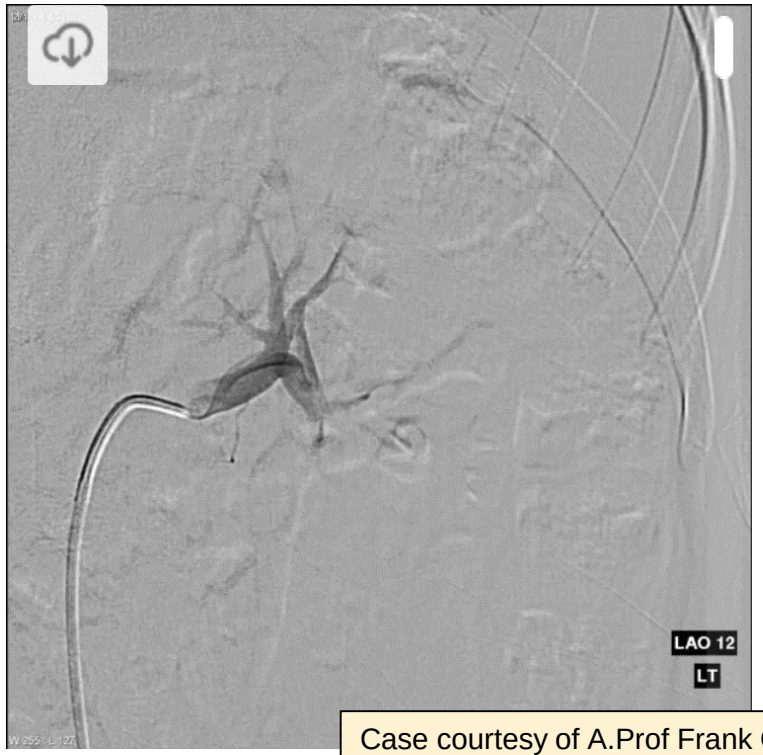

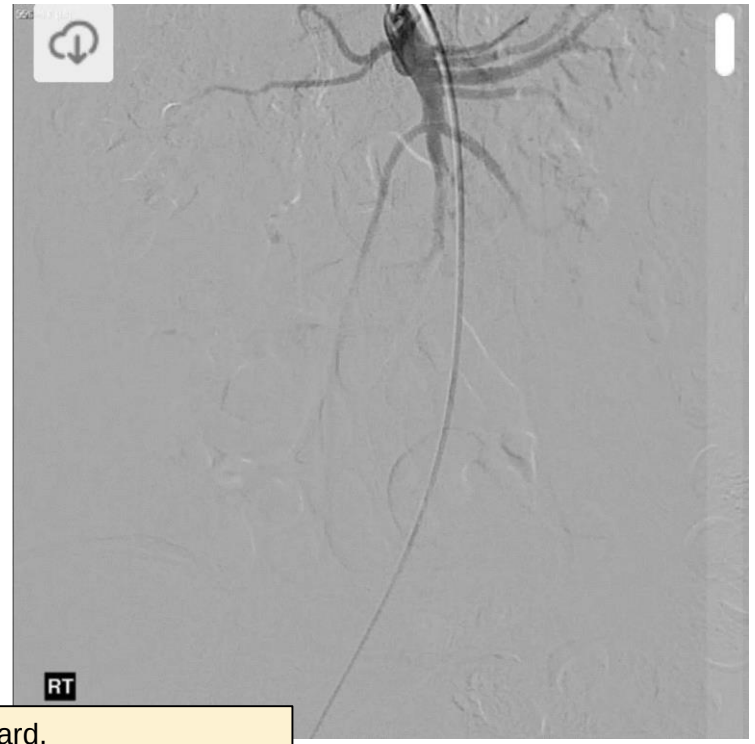

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Medium vessel vasculitis : Polyarteritis nodosa

Epidemiology?

Medium vessel vasculitis : Polyarteritis nodosa

Epidemiology

- ♂ mid-50s
- Annual incidence 0-8 per million[7,8]
- Massive incidence decline after HBV control[9]

7: Forbess, L. et al. Polyarteritis nodosa. Rheum. Dis. Clin. North Am. 41, 33–46 (2015).
8: Mahr, A. et al. Prevalences of polyarteritis nodosa, microscopic polyangiitis, Wegener's granulomatosis, and Churg–Strauss syndrome in a French urban multiethnic population in 2000: a capture–recapture estimate. Arthritis Rheum. 51, 92–99 (2004)
9: Guillevin, L. et al. Hepatitis B virus-associated polyarteritis nodosa: clinical characteristics, outcome, and impact of treatment in 115 patients. Medicine (Baltimore) 84, 313–322 (2005).

Polyarteritis nodosa: Gastrointestinal manifestations

Polyarteritis nodosa: Gastrointestinal manifestations

Abdominal pain (mesenteric ischemia)

- Nausea / vomiting
- diarrhea
- Hematochezia / melaena / hematemesis
- intra-abdominal bleeding.
- Jejunal ulcers

Polyarteritis nodosa: Management

Polyarteritis nodosa: Management

Induction in severe flares incl. GI-Manifestations (FFS≥1)

- Methylprednisolon 7-15mg/Kg days 1-3 and…
- Prednisolon 1mg/kg iv and…
- Cyclophosphamide 2 mg/kg/d po or 7-15mg/Kg every 2-3weeks

Induction in non severe cases (FFS=0)

- Prednisolon 1mg/kg iv

Maintenance

- AZA 2mg/Kg/d
- MTX 20-25mg/w

Case

19yo Japanese informatics student

- History of 川崎病 (some kind of vasculitis…. medical reports in Japanese)
- inpatient due to acute abdominal pain and vomiting
- On day 2 develops acute chest pain
- CTCA:

Case courtesy of Dr Craig Hacking, Radiopaedia.org, rID: 35218

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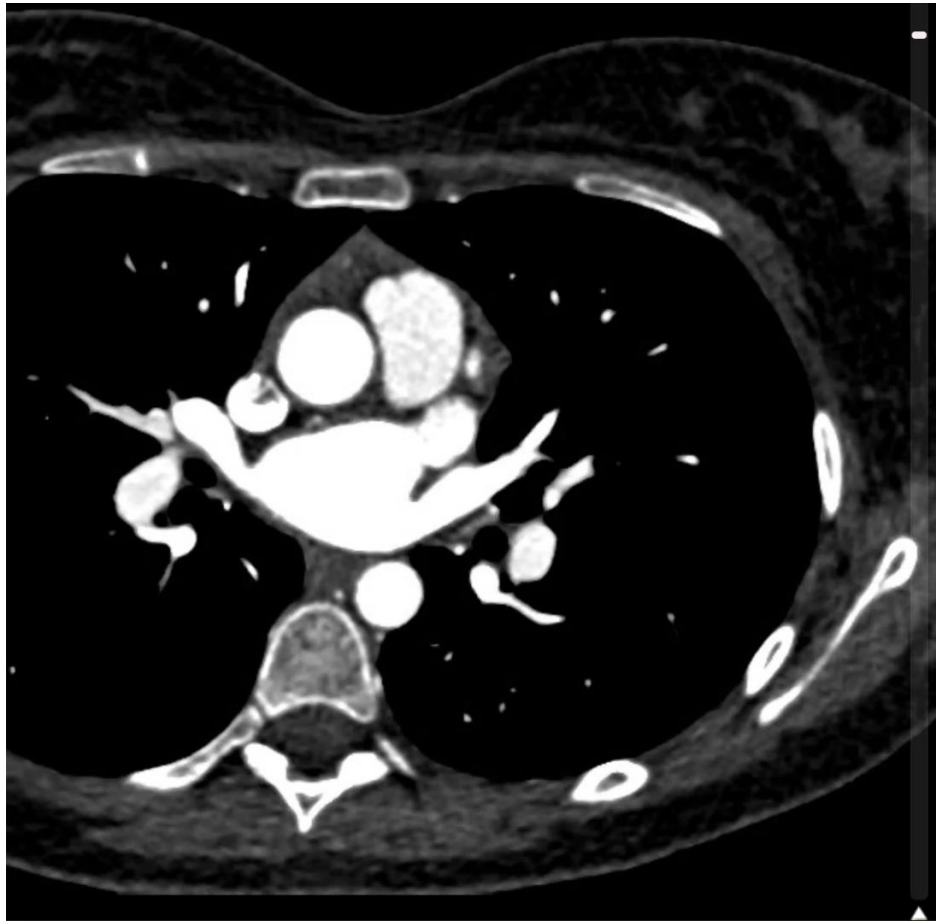


Case courtesy of Dr Craig Hacking, Radiopaedia.org, rID: 35218

Medium vessel vasculitis : Kawasaki disease

Epidemiology?

Medium vessel vasculitis : Kawasaki disease

- Age 6-48 months in >80% of cases
- more prevalent in Asian populations
- Japan: annual incidence 265/100,000 children <5 yo
- North America, Australia and Europe, 4–25/100,000 children <5 years

Kawasaki disease : Gastrointestinal manifestations

Kawasaki disease: Gastrointestinal manifestations

Children

- 60% abdominal symptoms preceding diagnosis
- abdominal pain, nausea and vomiting
- acute abdomen
- 5-20% Gallbladder mucocele within the first 2 weeks (GB wall vasculitis?)

Adults

- 56% abdominal symptoms:
- abdominal pain
- jaundice

Kawasaki disease : Management

Kawasaki disease: Manangement

Initial management:

- ASS
- IVIG 2mg/Kg

- coronary artery aneurysms from 20–25% to 2–4%

Non responders (10%)

- Repeat IVIG

Weak evidence for refractory cases

- Glucocorticoids

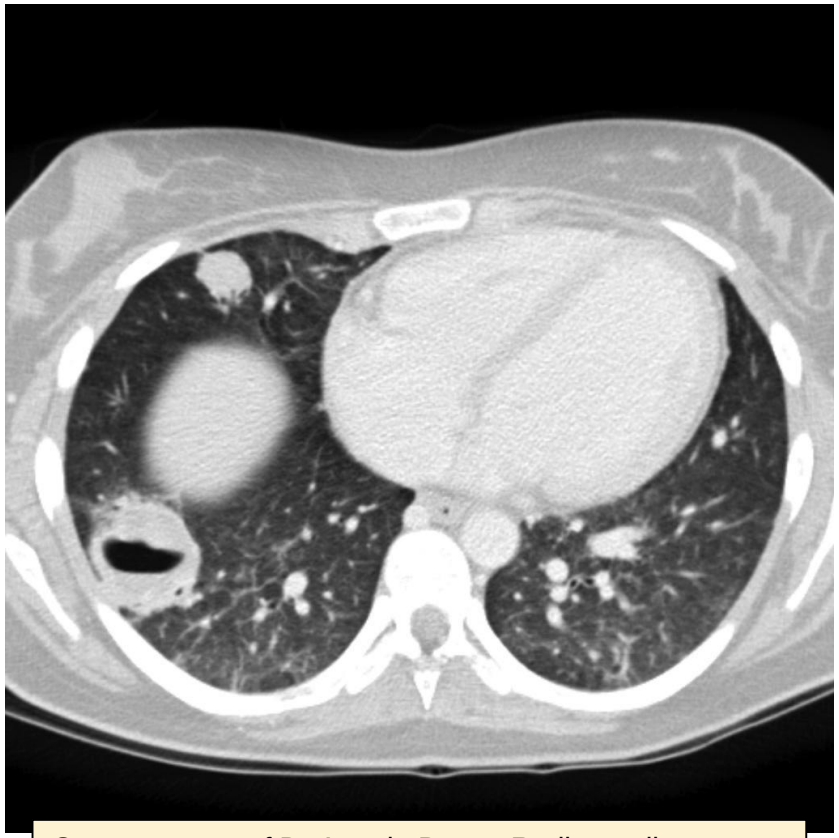
Very weak evidence (case reports)

- IFX, IL-1 antagonists (anakinra), plasma exchange, cyclophosphamide.

Granulomatosis with polyangiitis: typically affected organs - Serology

Granulomatosis with polyangiitis: Affected organs

- upper and lower respiratory tracts
- Kidneys
- anti-proteinase 3 ANCA (c-ANCA)
- Granulomatous necrotizing inflammation



Case courtesy of Dr Angela Byrne, Radiopaedia.org, rID: 8123

Granulomatosis with polyangiitis: Epidemiology

Granulomatosis with polyangiitis : Epidemiology

- global annual incidence 2–15 /million,
- lowest incidence reported in Japan
- global prevalence 23–160 / million
- rare in non-white
- peaks at 55–65 years

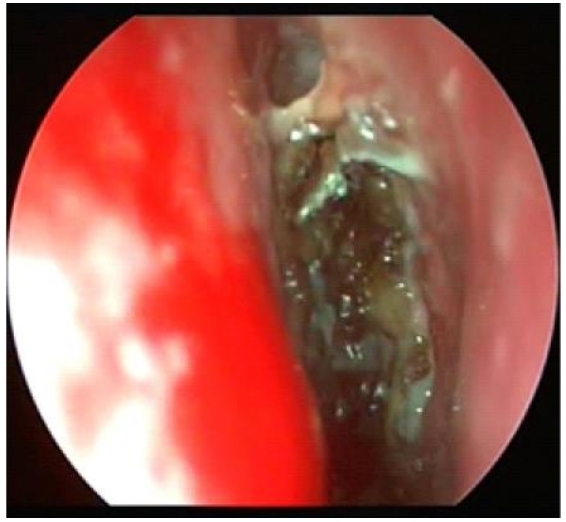
Granulomatosis with polyangiitis : GI manifestations

Granulomatosis with polyangiitis : GI manifestations

Symptoms in 5-11% of patients

Involvement: small intestine and colon

- transient abdominal pain
- bloody diarrhea and
- intestinal perforations



** Rare: granulomatous cholecystitis, hepatic granulomas, pancreatic mass*

Imaging: nonspecific

Endoscopy: ischemic changes, superficial granulomatous ulcers

Histology: esophageal ulcer biopsies usually non diagnostic

Colonic 30-40% sensitivity, if deep

AVA: Microscopic polyangiitis

- Non granulomatous necrotizing inflammation
- Anti-MPO ANCA (p-ANCA)
- Incidence 1–10 /million
- In contrast to GPA more common in Asian populations

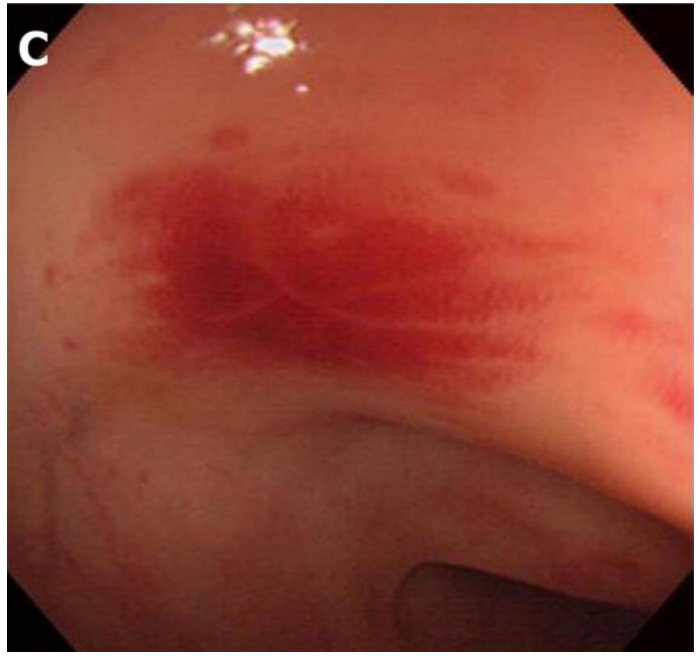
GI Manifestations 5–30% of patients

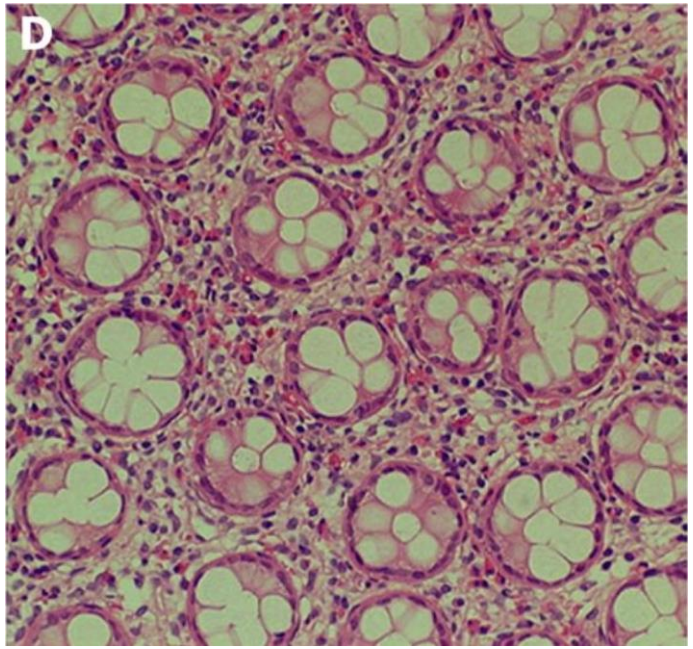
- Abdominal pain,
- Nausea / vomiting
- Diarrhea
- Rarely: colonic ischemic ulcers, peritonitis and perforations

Case

52 yo male presents with worsening abdominal pain

- History of new onset worsening episodic Dyspnea
- CT Scan: bowel wall thickening
- Colonoscopy: patchy mucosal erythema sigmoid colon to the splenic flexure





Hokama A. et al. Endoscopic and radiographic features of gastrointestinal involvement in vasculitis. World J Gastrointest Endosc 2012 March 16; 4(3): 50-56

AVA: Eosinophilic granulomatosis with polyangiitis

- Late-onset asthma + eosinophilia
- Vasculitic manifestations skin purpura or mononeuritis multiplex
- 30–40% anti MPO (p-)ANCA
- Cardiac involvement main cause for mortality (esp. in ANCA-negative)

GI Involvement in 30–50%

- Abdominal pain (91%)
- Overt bleeding (19–36%),
- Eosinophilic gastroenteritis: nausea and vomiting (18%) - diarrhea (45%)
- Acute abdomen (6–36%)
- Motility disorders

Management of AVA

Severe microscopic polyangiitis and all cases granulomatosis with polyangiitis

- Steroids
- Cyclophosphamide (2mg/kg/d po or 7.5-15mg/kg iv every 2-3 weeks)
- In ANCA+ Rituximab is an alternative to cyclophosphamide

Eosinophilic granulomatosis with polyangiitis

- Steroids
- Mepolizumab (anti IL-5)

Case

32yo with new diagnosis Hepatitis C presents with

Pain and rash in the upper and lower extremities

- **Lab tests?**
- **Treatment?**

Small vessel vasculitis: Cryoglobulinaemic v.

Cryoglobulins

- ABs that precipitate in < 37˚ C

Lab tests

- Low complement C4 with normal C3
- positive RF
- Cryoglobulins themselves difficult to detect. Repeat test if negative

Main involvement

- skin, kidneys and/or peripheral nerves

Small vessel vasculitis: Cryoglobulinaemic v.

Epidemiology

- mid-50s, ♂:♀ ratio 3:1
- HCV > 98%, rare: HIV, HBV, Sjögren, lymphoma

GI involvement rare (pain, bleeding, pancreatitis)

Liver involvement in 60% of HCV-patients with cryoglobulinemic vasculitis

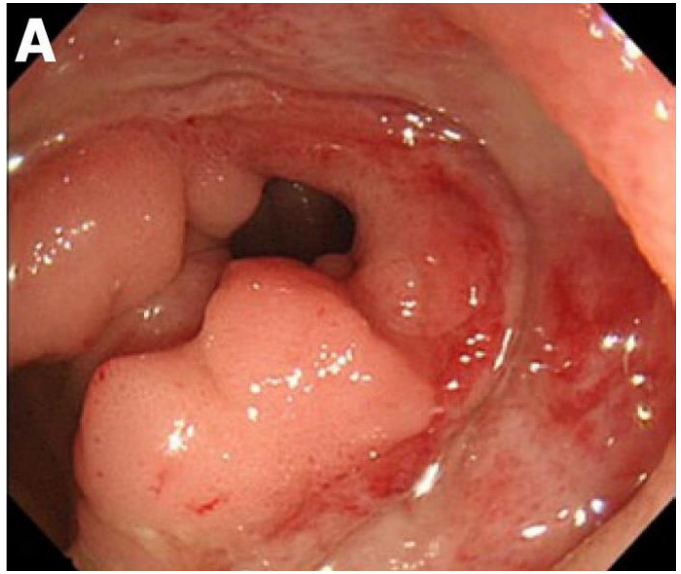
- Accelerated progression to cirrhosis
- *HCC less frequent…*

Treatment of the underlying virus

- Steroids or Rituximab in non viral cases

Case

- 53 yo Greek man
- Recurrent abdominal pain, diarrhea and oral aphthous lesions
- ER visit, suspicion of CD, calprotectin 982 mg/Kg
- Scheduled for colonoscopy in a week, presents with new ocular inflammation
- Colonoscopy showed a large ulcer with elevated margins in the terminal ileum
- **Could be CD or ?**



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variable vessel vasculitis: Behçet’s disease

Epidemiology and involvement?

Behçet's disease : Prevalence

Mediterranean

- 80–420 /100,000 ♂>♀

Asia

- 13.5–85 /100,000 ♂>♀

Western countries

- 0.12–0.64 / 100,000 ♀> ♂

Behçet's disease : Involvement

- oral / genital aphthous ulcers
- cutaneous, ocular, articular, gastrointestinal, thrombotic and/or CNS lesions

GI Involvement:

- Type I: mucosal ulcers from neutrophilic infiltrates - can mimic IBD
- Type II ischemia and infarction due to large-vessel vasculitis

GI Distribution

- Any part – T. ileum

Behçet's disease : Treatment

Cutaneous disease

- Colchicine

GI-Disease

- Analog IBD (Sulphasalazin, AZA, IFX, ADA)
- Cyclophosphamide

GI-Complications

- Surgery

Thrombosis

- Immunosuppression > Anticoagulation

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GI Distribution

- Any part – T. ileum

Bonus MC question

SLE patient complains of persistent diarrhea and mild abdominal pain. What is the most probable cause?

- SLE Enteritis
- SLE-related SMA vasculitis
- Adverse reaction to medications
- Concomitant IBD

MC question

SLE patient complains of persistent diarrhea and mild abdominal pain. What is the most probable cause?

- SLE Enteritis
- SLE-related SMA vasculitis
- **Adverse reaction to medications**
- Concomitant IBD

SLE Vasculitis

- **1.3 – 27% cutaneous vasculitis**
- **0.2-9% SMA Vasculitis**
  - ischemia of the ileum and jejunum

Treatment

- high-dose steroids
- complete bowel rest
- Cyclophosphamide if refractory or if other major organs involved (CNS / kidneys).
- Remission is achieved in 85%
- Relapse rate is 23% at 1 year

Questions?

Thanks for your attention!