IgG4 relatert sykdom

Øyvind Midtvedt

Rikshospitalet

Immunmediert fibroinflammatorisk sykdom :

- Ofte tumorliknende
- Ofte forhøyet s-IgG4
- Karakteristisk histologi
- Mono – multiorgan
- Sammensatt diagnose
- Indolent – svingende forløp

Kasus nr 1 « Hans « f. 64

- Innlagt nyremedisinsk avd
- Redusert allmenntilstand
- Smerter i mage og rygg i varierende grad over lengre tid
- Kreatinin 1288 , kalium 5,3
- Urin stix ;1+ protein ,2+ blod, ingen sylindre

Hydronefrose og retroperitoneal fibrose

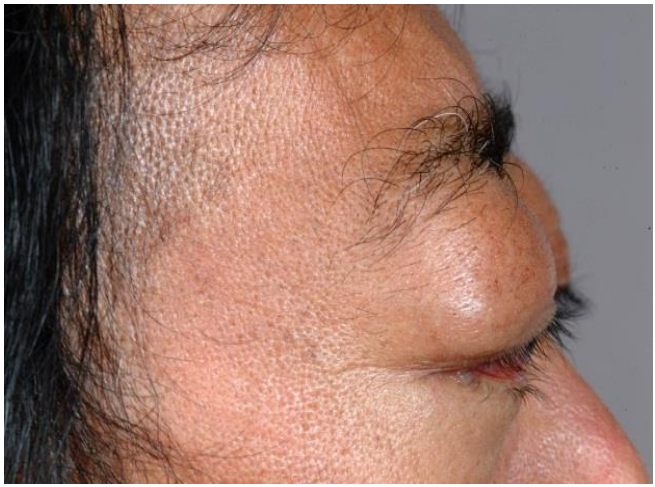
- Negativ ANA , negativ ANCA
- SR 52, CRP 45 , eosinofile 0,1(ref<0,4)
- IgG4 0,76 g/l (ref 0,03 -2,01 g/l)
- Plasmablaster 994 /ml (ref 276-4414)
- Nefrostomi og bilateral JJ stent

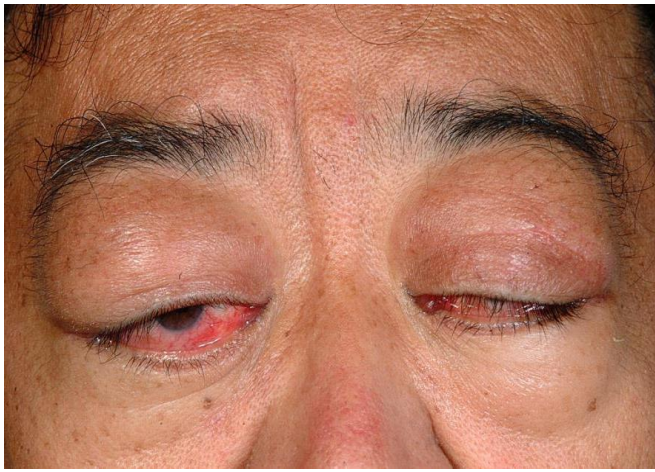
Kasus 2: «Lama» f-51

- Henvist revmatolog i 2005
- Eosinofil granulomatose med polyangitt ?
- Tidligere vurdert av: Øyelege, ØNH, nevrolog, hematolog, lungelege, infeksjonsmedisiner
- Exophthalmus, hevelse i gl.lacrimalis

SR 58,CRP 5, eosinofili 3,47 (ref<0,4),
IgE > 5000 (ref<120),
fT4 12,9, TSH 3,3 Negativ ANA,ANCA,TRAS, antiTPO,

- Histologi: Betennelsesinfiltrater med lymfocytter, eosinofile, plasmaceller, fibrose

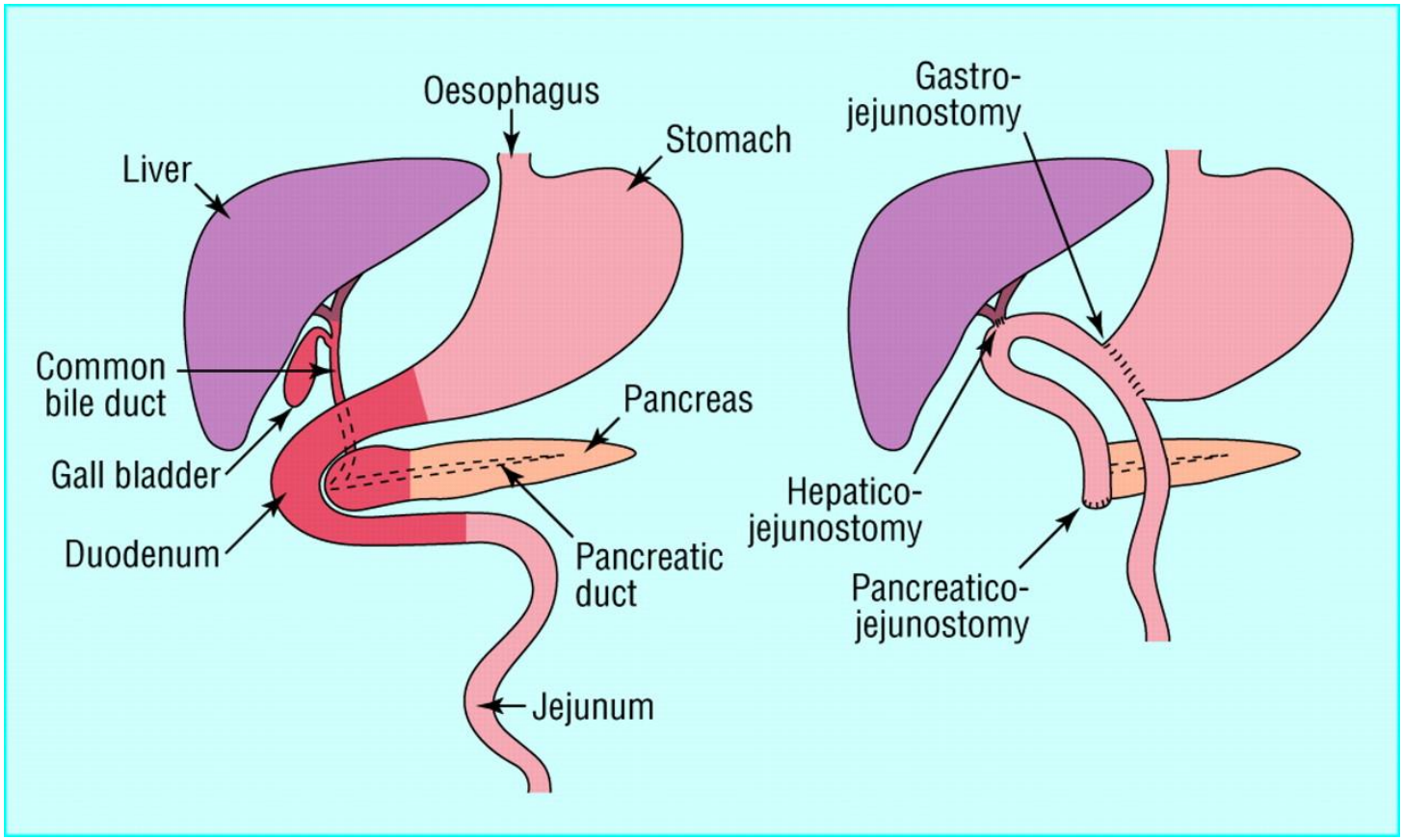




Kasus 3:»Svein» f-56

- Magesmerter, vekttap, icterus
- CT Abdomen/ERCP – suspekt pancreas canser
- Innlagt kirurgisk avd for Whipple operasjon

Whipples operasjon



«Det er store pancreatittforandringer i pancreas og pancreas palperes fibrotisk i hele sin lengde»
Operasjonsbeskrivelsen

«Hans»

Hydronefrose grunnet RPF
forhøyet SR/CRP, normal IgG4
nefrostomi / JJ stent

«Lama »

Eksoftalmus grunnet hevelse i gl lacrimalis og orbita tumor, eosinofili

«Svein»

Whipples operasjon for pancreas canser. Pancreas palperes fibrotisk i hele sin lengde.

Historikk

Mikulicz
1850-1905

1892

Ingela Sjøgren 1979

Høy IgG4 ved autoimmun pancreatitt 2001

«High serum IgG4 concentrations in patients with Sclerosing pancreatitis» NEJM -01,Hamano et al

IgG4 relatert sykdom 2003

«Autoimmune pancreatitis is a systemic autoimmune disease» Am J Gastro.-03,Kamisawa et al

Rituximab ved IgG4 Revma avd, OUS 2007

2010

«Rituximab therapy leads to Rapid decline of serum IgG4 levels and prompt clinical Improvement in IgG4 related Systemic disease» AR -10, Khosroshani et al

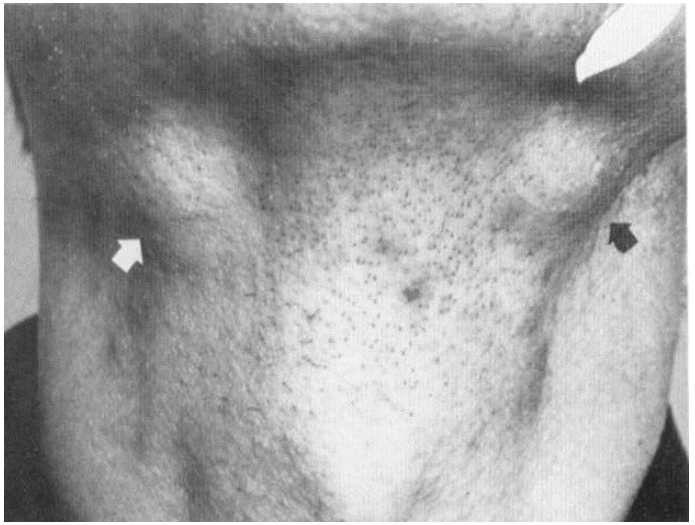
IgG4 relatert sykdom Vikse J. ,Tidsskr. 2017

Acta Med Scand 205: 139–141, 1979

Primary Sclerosing Cholangitis Associated with Fibrosis of the Submandibular Glands and the Pancreas

Ingela Sjögren, Bo Wengle and Magnus Korsgren

From the Department of Internal Medicine, University Hospital, Uppsala, and Falu Hospital, Falun, Sweden



- « A new syndrome of primary sclerosing cholangitis associated with fibrosis of the submandibular glands and the pancreas is described in a 43 year old male «

- » A few cases of primary cholangitis have been reported in wich an inflammatory reaction and fibrosis of other tissues co-existed, such as Riedel`s struma, retroperitoneal fibrosis, and inflammatory pseudotumour of the orbit»

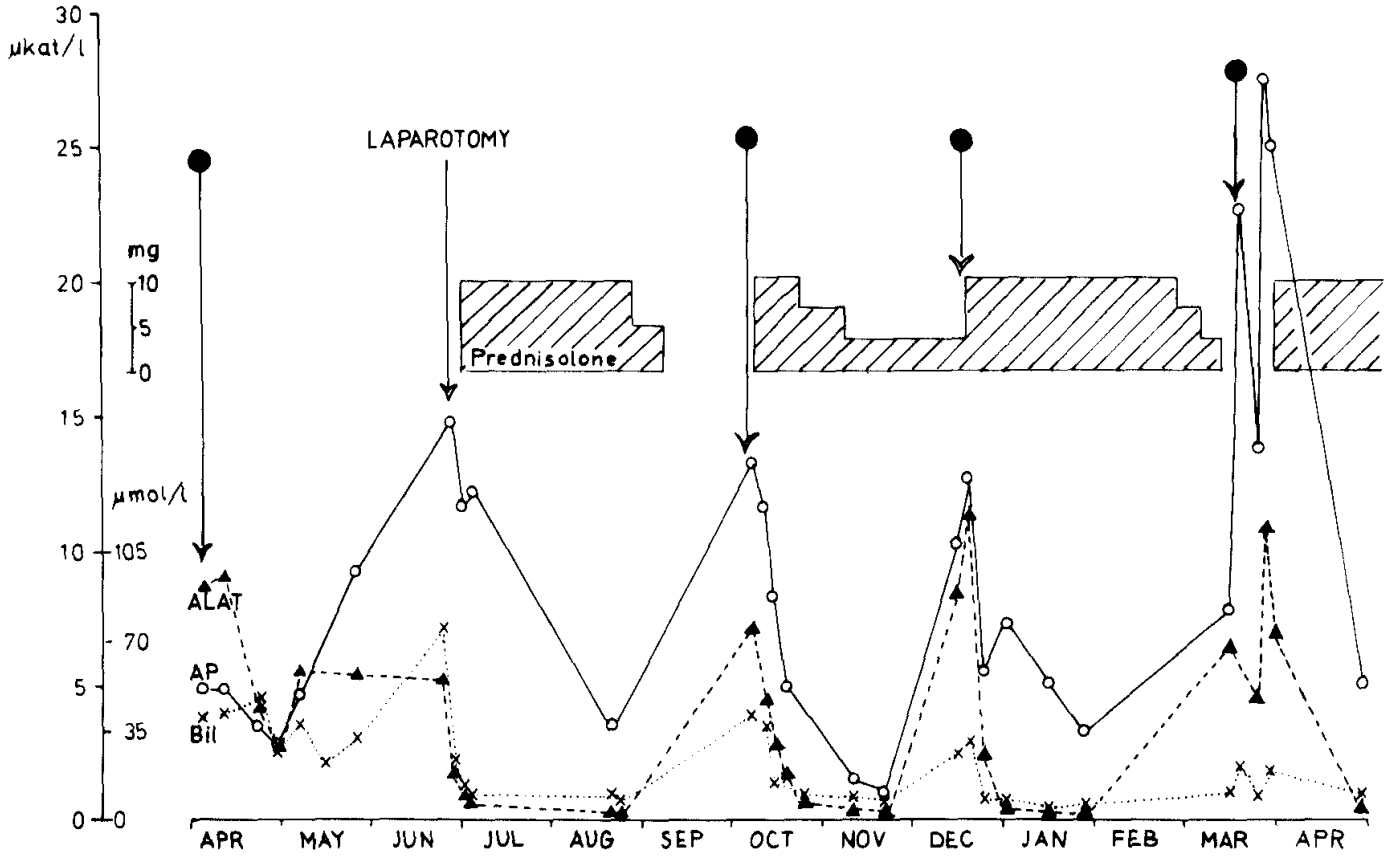


Fig. 1. Symptoms, including malaise, itching, clay-coloured stools, dark urine and frank icterus (🧍), recurred following reduction of the prednisolone dosage, together with an increase of serum alkaline phosphatase (○—○), serum alanine aminotransferase (▲---▲), and serum bilirubin (×···×).

«Primary Sclerosing Cholangitis Associated with Fibrosis of the Submandibular Glands and The Pancreas « Sjøgren I et al Acta Med Scand 1979

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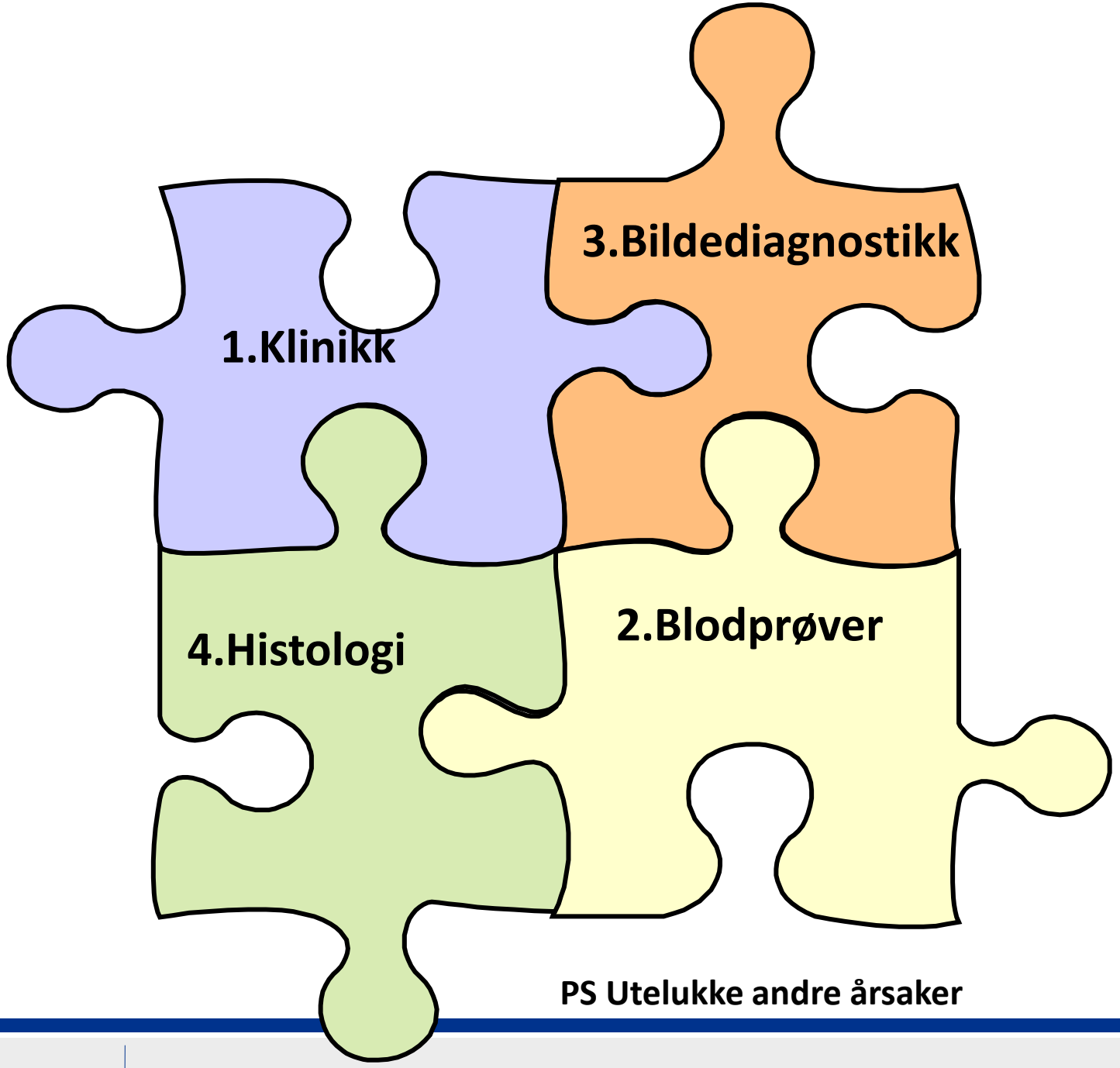
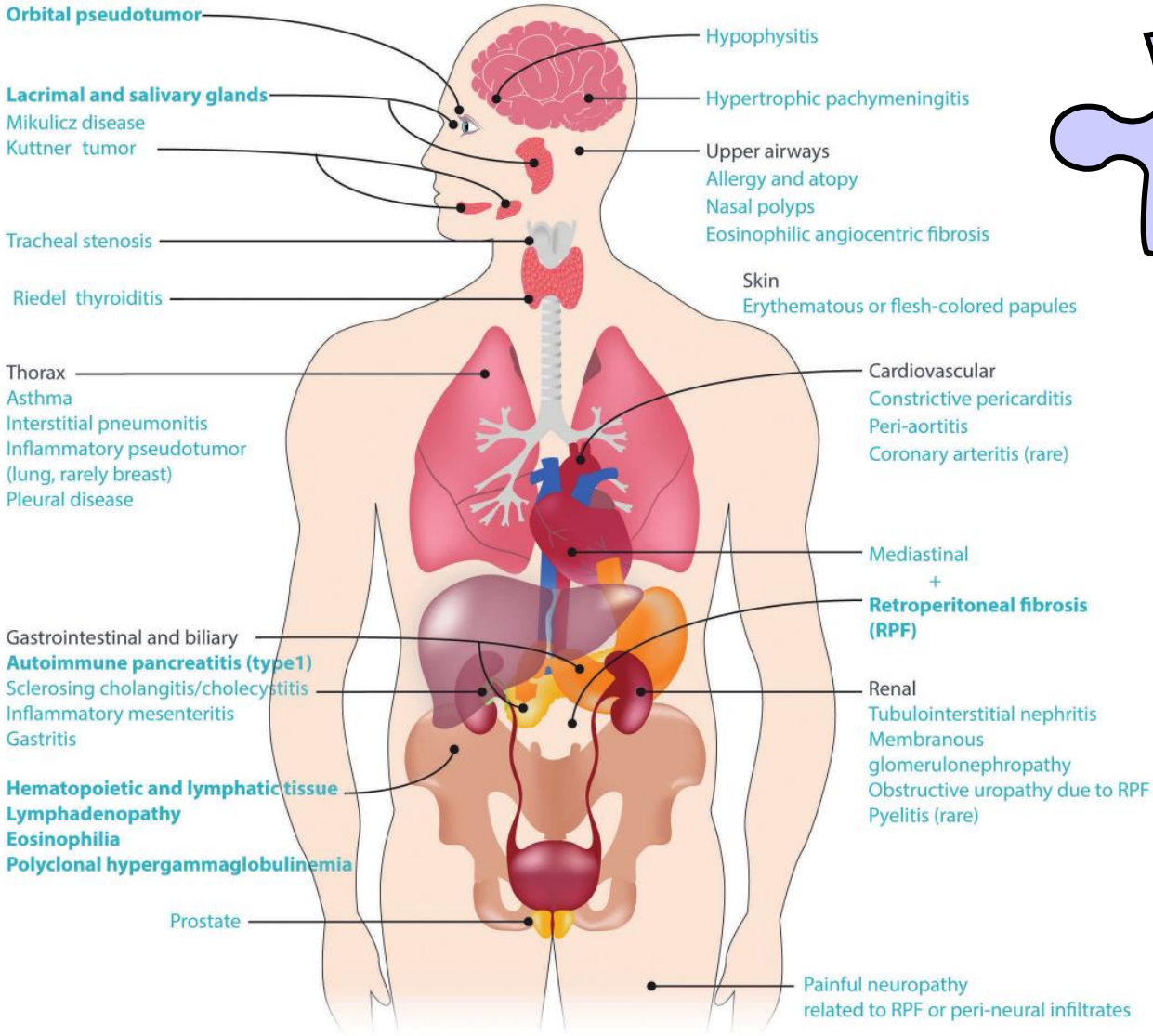
2017 IgG4 relatert sykdom Vikse J. ,Tidsskr.



PS Utelukke andre årsaker



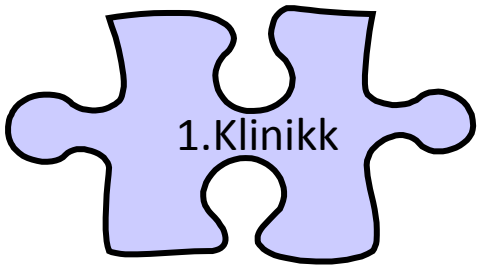


Figure 1. Manifestations of IgG4-related disease by organ system. The most common primary disease features are indicated in bold.

«IgG4 related disease: what a hematologist needs to know « Chen et al Haematologica 2019

Table 1. Clinical characteristics of patients from two large published cohorts.

	Japan (n=334)[17]	Boston (125)[16]
Mean age at diagnosis	63.8 years	55.2 years
Male sex	61.4%	60.8%
Ethnicity	100% Japanese	76% White
Elevated serum IgG4	>95%	51%
Mean number of organs involved (range)	3.2 (1-11)	2.3 (1-7)
Affected organs		
Salivary glands	72.3%	28% (submandibular) + 16.8% (parotid)
Lacrimal glands/orbit	57.1%	22.4%
Lymph nodes	56.5%	27.2%
Pancreas	25.5	19.2%
Retroperitoneal/ aorta	24.9	18.4% (retroperitoneal) + 11.2% (aorta)
Kidney	23.7%	12%
Lung	23.4%	17.6%

«IgG4 related disease: what a hematologist needs to know « Chen et al Haematologica 2019

Table 1: Comparisons of the two types of AIP.

Characteristics	Type 1	Type 2
Other nomenclatures [5]	LPSP AIP without GEL IgG4 related	IDCP AIP with GEL IgG4 unrelated
Ethnic [5]	Asia > United States, Europe	Europe > United States > Asian
Age [2, 5, 18]	60 years or older	A decade younger
Sex [5]	Usually male	Equal
Symptom [5]	Obstructive jaundice often Abdominal pain rare Pancreas swelling common	Obstructive jaundice often Abdominal pain common Pancreas swelling common
Serology [2, 5]	High serum IgG4, auto-Ab+	Normal serum IgG4, auto-Ab−
Histopathology [5]	Lymphocyte and plasmacyte infiltration and fibrosis Infiltration of IgG4 plasma cells	Granulocyte epithelial lesion often with destruction and obliteration of the pancreatic duct
Extrapancreatic lesion [5, 15, 17]	Sclerosing cholangitis Sclerosing sialadenitis Retroperitoneal fibrosis, etc.	Unrelated with OOI
Ulcerative colitis [2, 5]	Rare	Often
Histology needed for diagnosis [5]	No	Yes
Respond to steroid [2, 5]	Responsive	Responsive
Relapse rate [5]	High	Low

Review article
«From Pathogenesis,Cinical Manifestation, And Diagnosis to Treatment: An overview on Autoimmune Pancreatitis» Ou Cai et al Gastroenterology Research and Practice 2017

Lunge

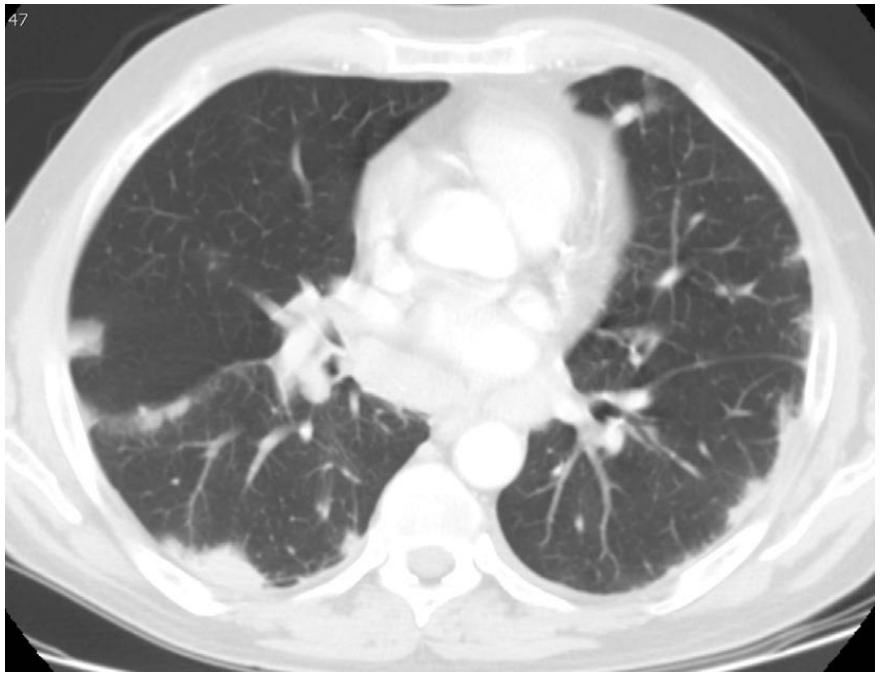


Fig. 6. Peripheral nodules and consolidation in 69-year-old man with IgG4-RD. Chest CT axial scan at the level of the aortic root on lung windows. There are multiple, bilateral peripheral lung nodules and consolidative opacities that also extend along the right major and minor fissures, in a perilymphatic distribution that is characteristic of IgG4-RD. The patient denied pulmonary symptoms.

Lymfadenopati

Interstitielle fortetninger

Pleura

«Immunglobulin G4- related disease»
Wallace et al Clin Chest Med 2019

Retroperitoneal fibrose (RPF)

- RPF and IgG4 :

  ”The same thing , but different” , J. Stone
- RPF:
- Få organer involvert
- Lavere sIgG4 (ofte normal)
- Presenteres i fibrotisk stadium

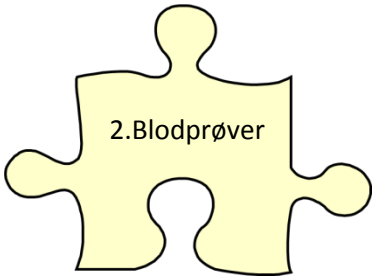
	Proliferative subtype	Fibrotic subtype
Origin of disease	Glandular tissues, epithelial tissues	Extraglandular tissues, sometimes body regions (eg, retroperitoneum, mediastinum) rather than distinct organs
History of atopy	High frequency	Low frequency
Number of organs affected	Commonly multiorgan	Commonly single organ or single-body region
Organs affected	Lymph nodes, lacrimal gland, major salivary glands, pancreas, bile ducts, kidney, lung, pituitary, paranasal sinus	Retroperitoneum, aorta and periaortic tissue, mesentery, mediastinum, pachymeninges, thyroid (Riedel's)
Laboratory parameters		
IgG4 level	High	Normal or slightly elevated
IgG1 level	High	Normal or slightly elevated
IgE level	High	Normal or slightly elevated
Eosinophilia	Common	Unusual
Hypocomplementemia	Common	Unusual
Potential autoantigens	Laminin-511, galectin-3, annexin A11, prohibitin	Undefined
Pathology		
Lymphoplasmacytic infiltrate IgG4-positive cells per HPF	Dense: >50, often >100; IgG4/IgG ratio >40%	Can be sparse; fewer than in proliferative subtype, but IgG4/IgG ratio >40%
Germinal centre	Common	Unusual
Storiform fibrosis	Common	Common
Obliterative phlebitis	Occasional	Common
Responsiveness to treatment	Excellent	Less robust than in proliferative subtype, but good if initiated early

HPF=high-power field.

Table: **Characteristics of the proliferative and fibrotic IgG4-related disease subtypes**

«Management of IgG4 related disease « W. Zhang, J. Stone, Lancet 2019

2.Blodprøver



- IgG4 > 1,35 g/l (IgG4 ref.0,03-2,01g/l)
- IgG4/IgG ratio > 8-10%
- Høy IgG
- Høy SR og normal CRP
- Høy IgE
- Eosinofili
- Lav komplement (spesielt ved nyreaffeksjon)
- +ANA ,RF faktor og ANCA kan forekomme

IgG4

- IgG4 kan være normal (opptil 40%)
- Redusert hvis påbegynt med steroider
- Som regel høyere ved inflammatorisk vs fibrotisk manifestasjon
- Svært høy verdi – økt risiko for multiorgan

IgG4-related disease: clinical and laboratory features in one hundred twenty-five patients.
Wallace ZS et al Arthritis Rheumatol -2015

IgG4

- Kan variere med sykdomsaktiviteten
- Kan få residiv selv med normal IgG4
- Høy IgG4 kan forekomme ved revmatisk sykdom, autoimmune sykdommer, malignitet, og hos friske (5%)

Cutoff values of serum IgG4and histopathological IgG4+ plasma cells for diagnosis of patients with IgG4-related disease. Masaki ,Y. et al Int. J.Rheumatol. 2012:580814
The diagnostic utility of serum IgG4 concentrations in IgG4 related disease ,Carruthers et al ARD 2015

TABLE 3. Differential Diagnosis in Patients With Suspected IgG4-Related Disease Associated With Elevated Serum IgG4 Levels[66-71]

Disease	No. of patients tested	No. of patients with serum IgG4 levels >135 mg/dL	Percentage of patients with IgG4 levels >135 mg/dL
Sjögren syndrome	284	22	7.7
Pancreatic cancer	153	8	5.2
Systemic lupus erythematosus	122	17	13.9
Rheumatoid arthritis	83	12	14.5
Biliary tract cancer	64	4	6.2
Chronic pancreatitis	45	2	4.4
Systemic sclerosis	44	3	6.8
Liver cirrhosis	22	2	9.1
Chronic hepatitis	21	1	4.8
Castleman disease	16	7	43.7
Hypereosinophilic syndrome	16	2	12.5
Interstitial lung disease	12	4	33.3
Behçet disease	10	1	10
Eosinophilic granulomatosis with polyangiitis	7	5	71.4
Asthma	7	1	14.3
Inflammatory myopathies	6	1	16.7
Antiphospholipid syndrome	5	1	20
Mixed connective tissue disease	5	0	0
Microscopic polyangiitis	5	1	20
Healthy controls	77	1	1.3

”Diagnostic approach to the complexity of IgG4 –Related disease”, Stone et al 2015 Mayo clin

Plasmablast ved IgG4

- Presenterer antigen
- Differensieres til IgG4 + plasmaceller

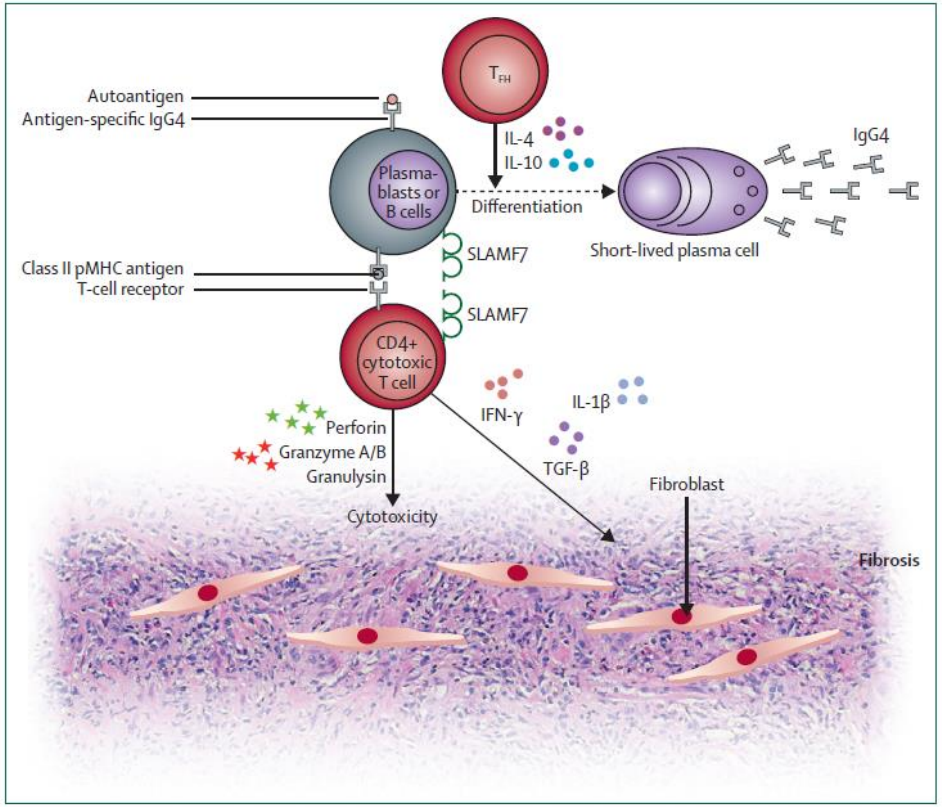


Figure 2: Pathophysiology of IgG4-realted disease

«Management of IgG4-related disease» W. Zang et al, Lancet 2019

Plasmablast pr ml ved IgG4

Median : 4698 (610-7952) 592 (19-4294) 94 (1- 653) p< 0,001

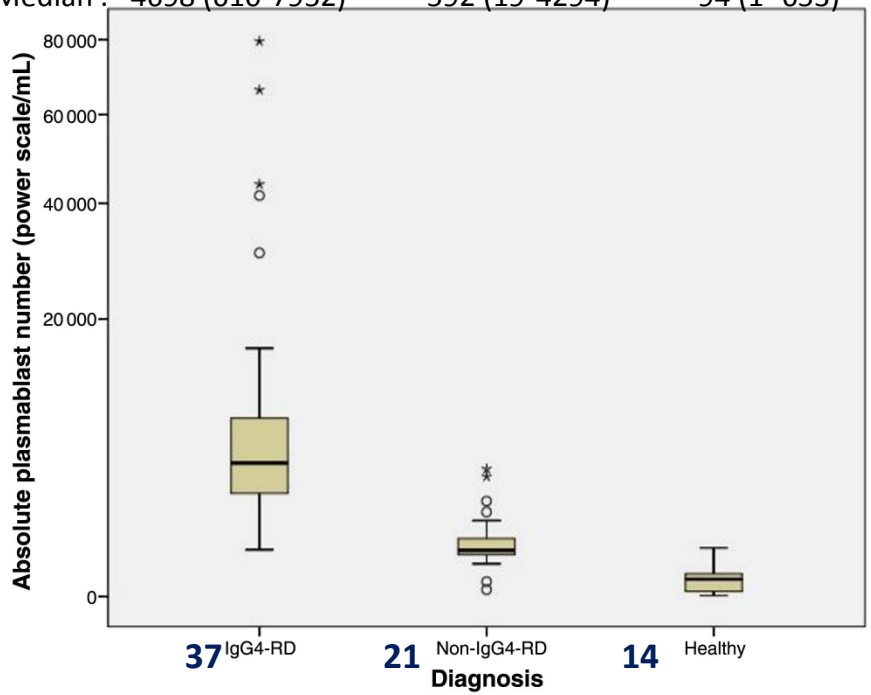


Figure 1 Box plot of median plasmablast count (power scale /mL) by diagnosis. Open circles represent outliers and asterisks represent extreme outliers.

13 IgG4 pas med normal
S-IgG4 – likevel høy plasmablast

>2 organ høyere enn 1 organ
(7370 vs 3435, P=0,01)

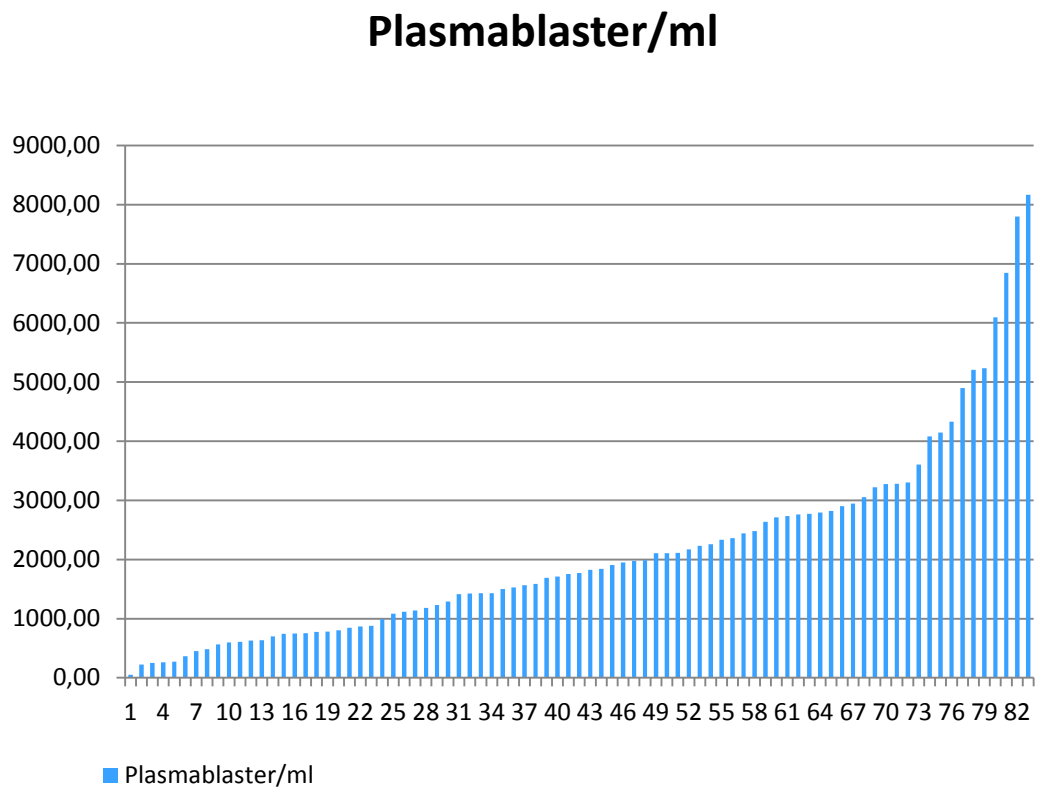
Plasmablasts as a biomarker for IgG4-related disease, independent of serum IgG4 concentrations.
Wallace ZS, J Stone et al Ann Rheum Dis 2015

Plasmablast

- Antall plasmablast pr ml
- Kan reflektere sykdomsaktivitet
- Påvirkes av behandling
- Kan vær nyttig hvis biopsi ikke er mulig (eks aorta)
- Ikke spesifikt for IgG4 relatert sykdom

Plasmablasts as a biomarker for IgG4-related disease, independent of serum IgG4 concentrations.
Wallace ZS, et al Ann Rheum Dis 2015

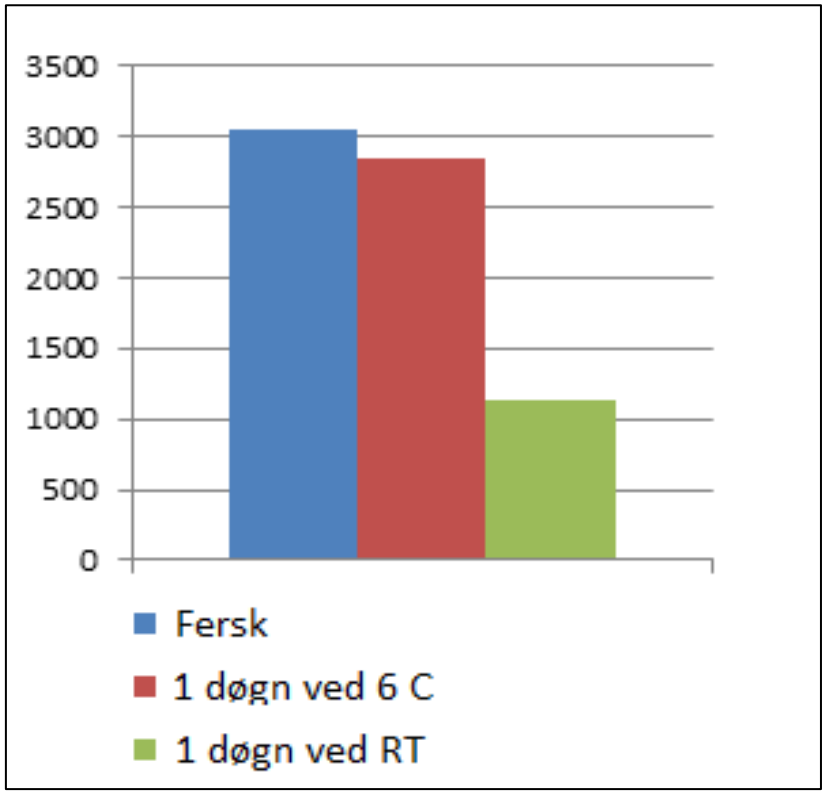
Plasmablaster per ml hos friske



5 og 95 prosent persentil: 276 – 4414 /ml

Liv Osnes, Seksjon for cellulær immunologi

Plasmablaster per ml målt i fersk prøve og et døgn gammel prøve

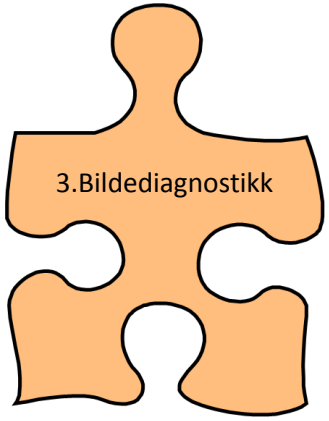


Plasmablast bør analyseres samme dag ev. stå i kjøleromstemperatur (6 grader)

Nytteverdien av analysen er ikke kjent

Liv Osnes , Seksjon for cellulær immunologi

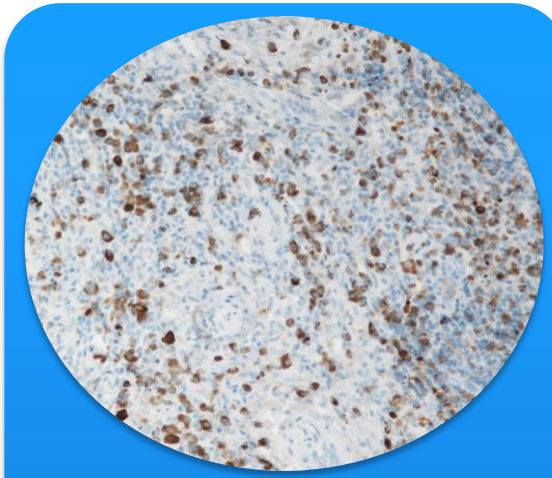
3.Bildediagnostikk



- Ofte tumor eller infiltrat på CT eller MR
- Malignitet?
- PET-CT: Organutbredelse, vurdere sykdomsaktivitet, lokalisere biopsisted, differensialdiagnose

Utility of FDG PET/CT for differential diagnosis of patients clinically suspected of IgG4-related disease, Lee J et al Clin Nucl Med -16

4.Histologi

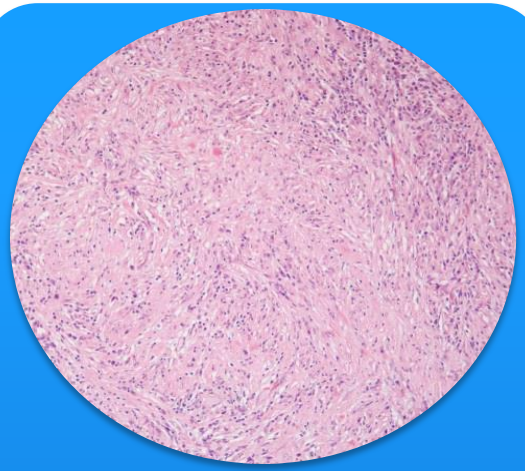


Lymfoplasmacytær infiltrat

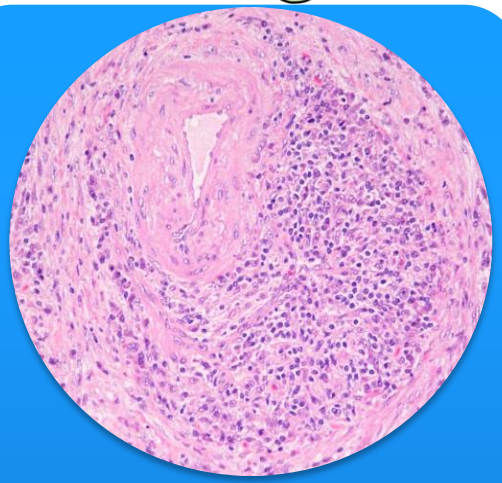
Ofte eosinofili

IgG4 + >10/HPF

Andel IgG4+/IgG >40%



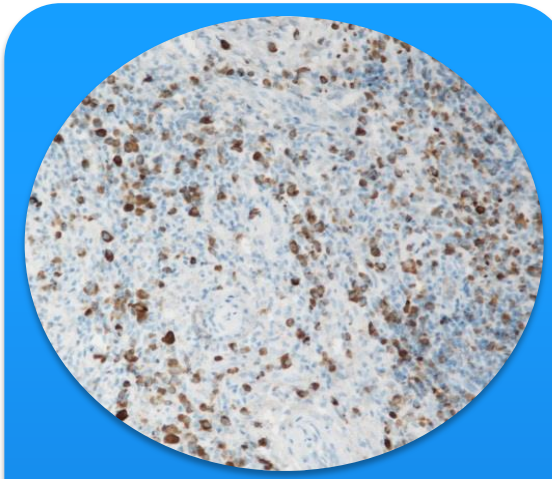
Storiform fibrose



Obliterativ flebitt

Granulomer, nekrose, kjempeceller ser en vanligvis ikke

4.Histologi



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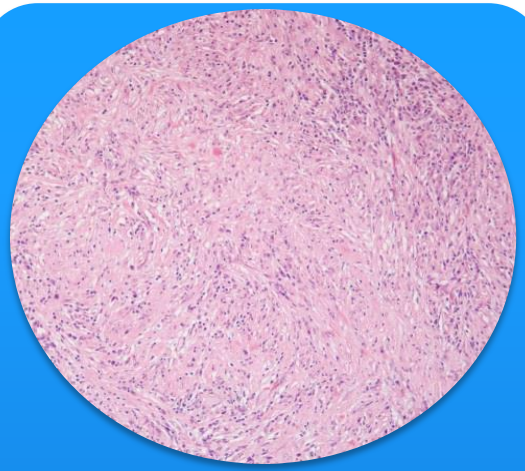

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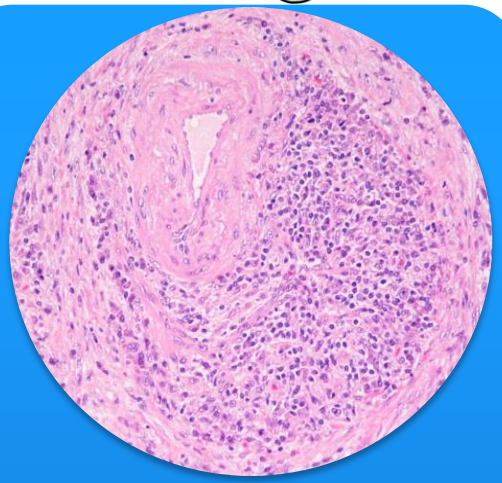

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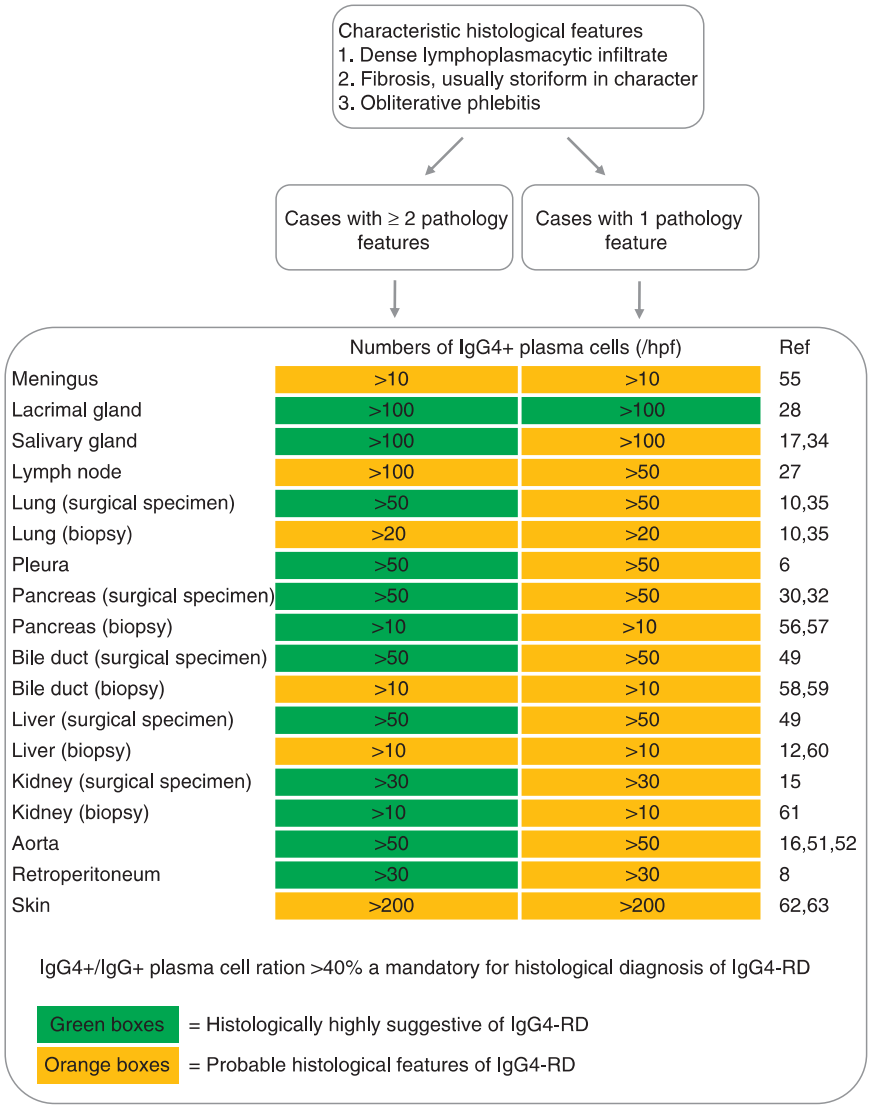

Figure 3 Histological diagnostic scheme of IgG4-related disease.[6,8,10,12,15–17,27,28,30,32,34,35,49,51,52,55–63]

«Consensus statement on the pathology of IgG4- related disease» Deshpande et al 2012

Diagnostiske kriterier

1. Klinikk: sykehistorie, kliniske funn, bildediagnostikk
2. Blodprøver: IgG4>1,35g/l eller elevert IgG4/IgG ratio
3. Histopatologiske funn: lymfoplasmacytær infiltrasjon, storiform fibrose, obliterativ flebitt, IgG4 + plasmaceller (IgG4+>10/HPF,IgG4+/IgG>40%)

1+2= mulig IgG4 relatert sykdom

1+3= sannsynlig IgG4 relatert sykdom

1+2+3= sikker IgG4 relatert sykdom

Utelukke andre årsaker

” Are classification criteria for IgG4-RD now possible?
The concept of IgG4-related disease and proposal of comprehensive diagnostic criteria in Japan”
Okazaki et al Int. J.Rheum-12

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ACR- EULAR klassifikasjons kriterier er under utarbeidelse

Utelukke andre årsaker

” Are classification criteria for IgG4-RD now possible?
The concept of IgG4-related disease and proposal of comprehensive diagnostic criteria in Japan”
Okazaki et al Int. J.Rheum-12

Epidemiologi

- Sjelden: Prevalens 62 pr mill i Japan
- Kjønn: Menn > kvinner (3:1 ved IgG4 pancreatitt)
- Alder: 50-70 år (beskrevet hos barn)
- Risikofaktor: HLA-DRB1, FCGR2B, røyking , løsningsmidler ?
- Spesialitet: Gastroenterolog/kirurg, ØNH, øye, urolog, endokrinolog, lunge, nevrolog, nefrolog, hud, hematolog, infeksjonsmedisiner…

- REVMATOLOG – behersker ”system sykdom”
- NOSVAR: 45 pasienter med IgG4 relatert sykdom

“Prevalence of IgG4-related disease in Japan based on Nationwide Survey in 2009.” Uchida et al .Int J Rheumatol 2012

Patofysiologi

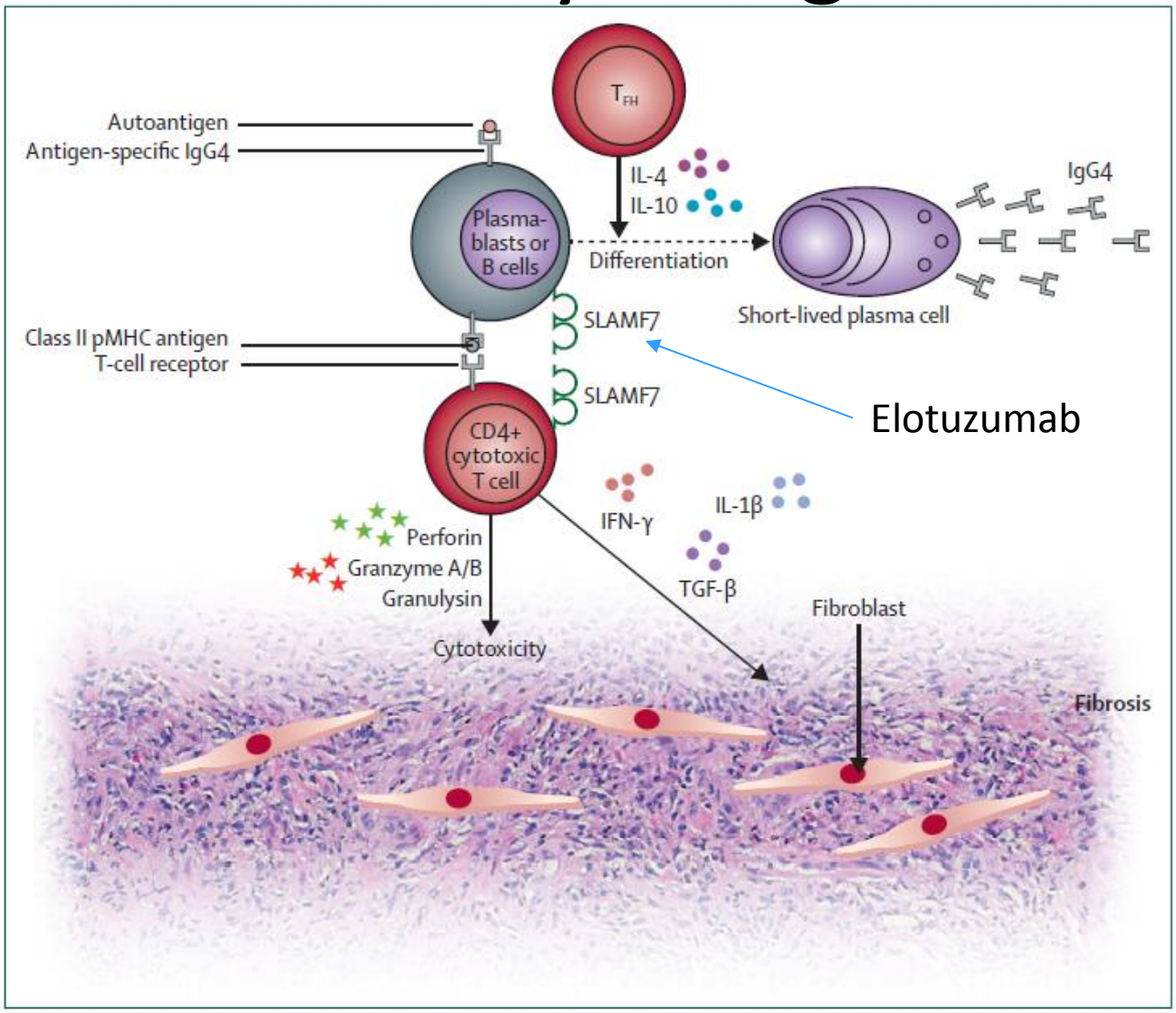


Figure 2: Pathophysiology of IgG4-realted disease

«Management of IgG4-related disease» W. Zang et al, Lancet 2019

Hva slags antigen ?

- Galectin-3 (Perugino et al JACI 2019;143)
- Annexin A-11 (Hubers et al Gut 2018)
- Laminin 511 (Shiokawa et al Sci Trans med 2018)
- Prohibin (Du et al Plos One 2015)

Tarm Mikrobiota ?

Tohoku J. Exp. Med., 2018, **244**, 113-117

Differences in Gut Microbiota Profiles between Autoimmune Pancreatitis and Chronic Pancreatitis

Shin Hamada,[1] Atsushi Masamune,[1] Tatsuhide Nabeshima[1] and Tooru Shimosegawa[1]

[1]Division of Gastroenterology, Tohoku University Graduate School of Medicine, Sendai, Miyagi, Japan

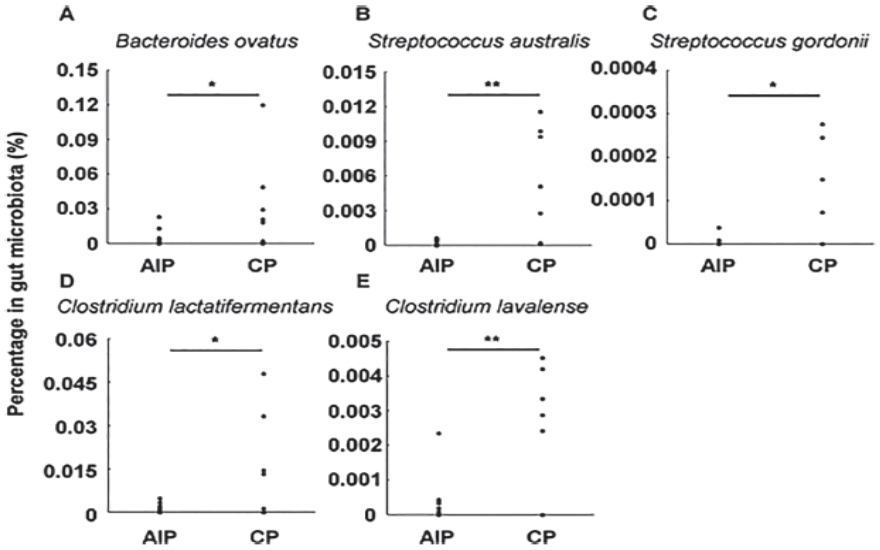
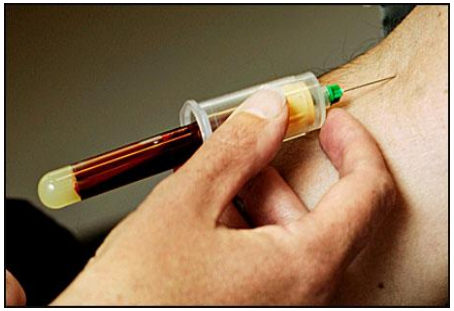


Fig. 2. Identification of increased bacterial species in CP.
Proportions of bacterial species in gut microbiota were determined in patients with AIP before the steroid treatment (N = 12) and CP (N = 8). A, *Bacteroides ovatus*; B, *Streptococcus australis*; C, *Streptococcus gordonii*; D, *Clostridium lactatifermentans*; E, *Clostridium lavalense*. $^{*}P < 0.05$, $^{**}P < 0.01$.

AIP= Autoimmun panceratitt type I (IgG4 relatert)

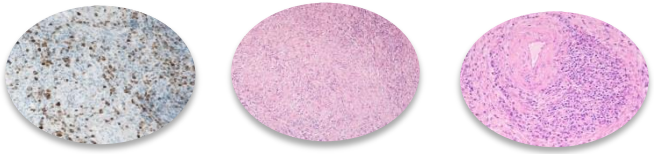
CP= Kronisk pankreatitt

Utredning ved klinisk mistanke om IgG4 sykdom



IgG subklasser,s-elfo,IgE,C3,C4
Hb, hvite med diff, trombocytter,
SR, CRP, lever inkl amylase, bilirubin,
Kreatinin, fT4, TSH, ANA, ANCA, ACE, U-stix

CT /MR/Ultralyd
Ev PETCT



Histologi
Be om IgG4 farging

Viktig !
Utelukke andre sykdommer!

Panel 2: Differential diagnosis of IgG4-related disease, by organ system

Orbits and periorbital tissues
- Lymphoma
- Graves' orbitopathy
- Granulomatosis with polyangiitis
- Sarcoidosis

Ears, nose, and sinuses
- Allergic disease
- Churg-Strauss syndrome
- Granulomatosis with polyangiitis
- Sarcoma
- Chronic infection

Salivary glands
- Lymphoma
- Sjögren's syndrome
- Sarcoidosis
- Sialodocholithiasis

Meninges
- Idiopathic hypertrophic pachymeningitis
- Inflammatory myofibroblastic tumour
- Lymphoma
- Granulomatosis with polyangiitis
- Giant-cell arteritis
- Langerhans-cell histiocytosis
- Sarcoidosis

Pituitary
- Neoplasms
- Histiocytosis
- Primary hypophysitis
- Secondary hypophysitis (sarcoidosis, ipilimumab-induced)

Lymph nodes
- Multicentric Castleman's disease
- Lymphoma
- Sarcoidosis
- Systemic lupus erythematosus

Thyroid gland
- Thyroid lymphoma
- Differentiated thyroid carcinoma (papillary variant)
- Other malignant disease

Lungs
- Malignancy (adenocarcinoma or bronchioloalveolar carcinoma)
- Inflammatory myofibroblastic tumour
- Sarcoidosis
- Granulomatosis with polyangiitis
- Castleman's disease
- Lymphomatoid granulomatosis
- Idiopathic interstitial pneumonitis
- Erdheim-Chester disease

Aorta
- Primary large-vessel vasculitis (giant-cell or Takayasu's arteritis)
- Sarcoidosis
- Erdheim-Chester disease
- Histiocytosis
- Lymphoma
- Infectious aortitis

Retroperitoneum
- Lymphoma
- Sarcoma
- Methysergide-induced retroperitoneal fibrosis
- Idiopathic retroperitoneal fibrosis

Kidney
- Lymphoma
- Renal-cell carcinoma
- Drug-induced tubulointerstitial nephritis
- Idiopathic membranous glomerulonephritis
- Pauci-immune, necrotising glomerulonephritis
- Sarcoidosis
- Sjögren's syndrome
- Systemic lupus erythematosus (membranous nephropathy)

Pancreas
- Pancreatic cancer

Biliary tree
- Pancreatic cancer
- Cholangiocarcinoma
- Primary sclerosing cholangitis

Liver
- Cholangiocarcinoma
- Hepatocellular carcinoma
- Primary sclerosing cholangitis

Prostate
- Benign prostatic hypertrophy

Skin
- Cutaneous lymphoma

Differensialdiagnose:

Avhenger av manifestasjoner

- Lymfom
- Graves
- Malignitet
- Sarkoidose
- Histiocytose
- Annen revmatisk sykdom;
- Sjøgren, EGPA, GPA, SLE

«IgG4 related disease» Stone et al Lancet 2015

«Hans»

Hydronefrose grunnet RPF
forhøyet SR/CRP, normal IgG4
nefrostomi +JJ stent

«Lama »

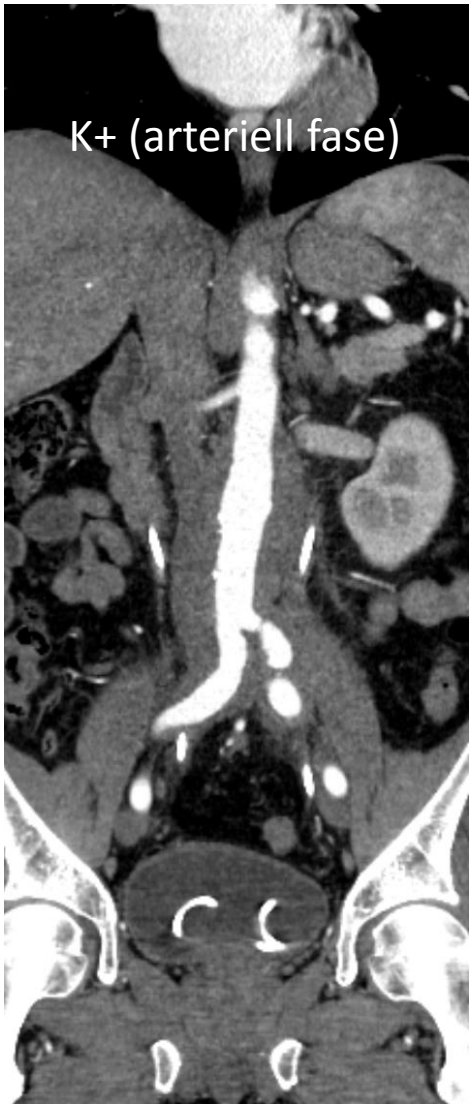
Eksoftalmus grunnet hevelse i gl lacrimalis og orbita tumor, eosinofili

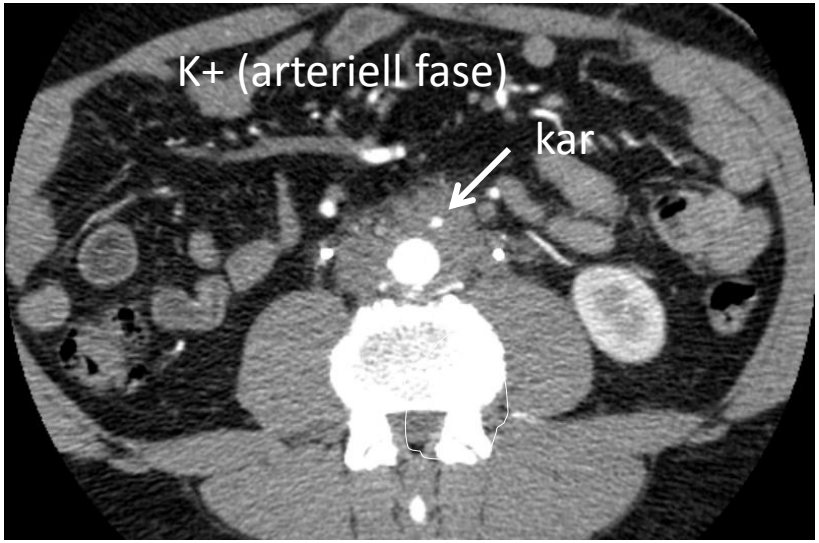
«Svein»

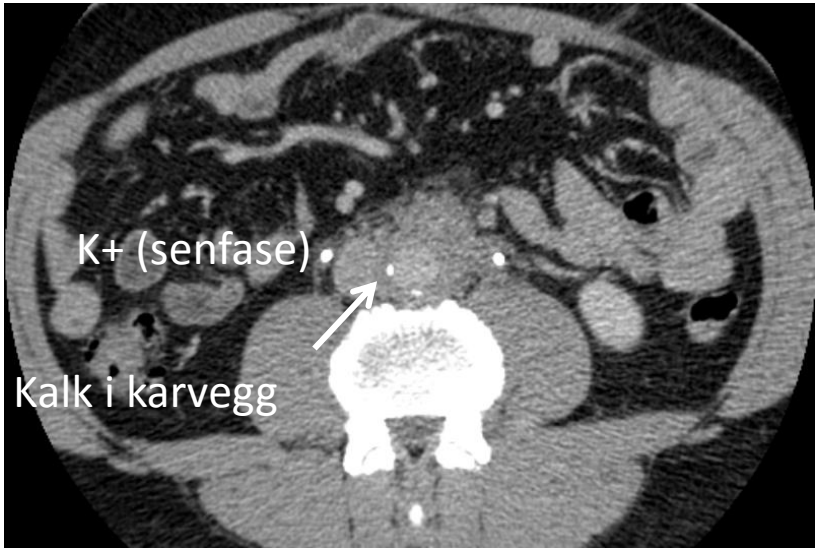
Whipples operasjon for pancreas canser. Pancreas palperes fibrotisk i hele sin lengde.

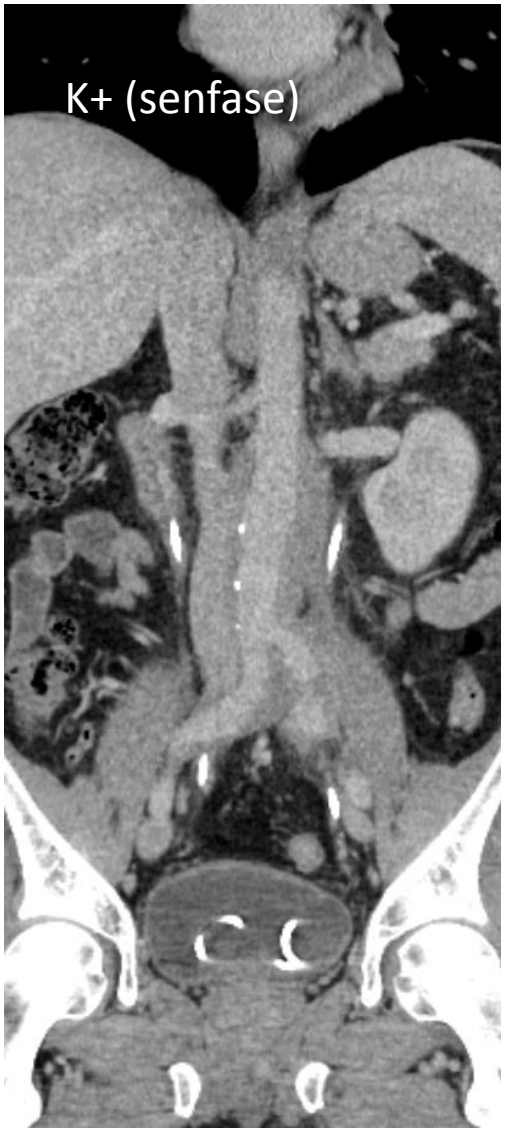
Kasus nr 1 « Hans « f. 64

- Innlagt nyremedisinsk avd
- Kreatinin 1288 og postrenal nyresvikt
- IgG4 0,76g/l (ref < 1,35)
- Plasmablaster 994 /ml (ref 276-4414)

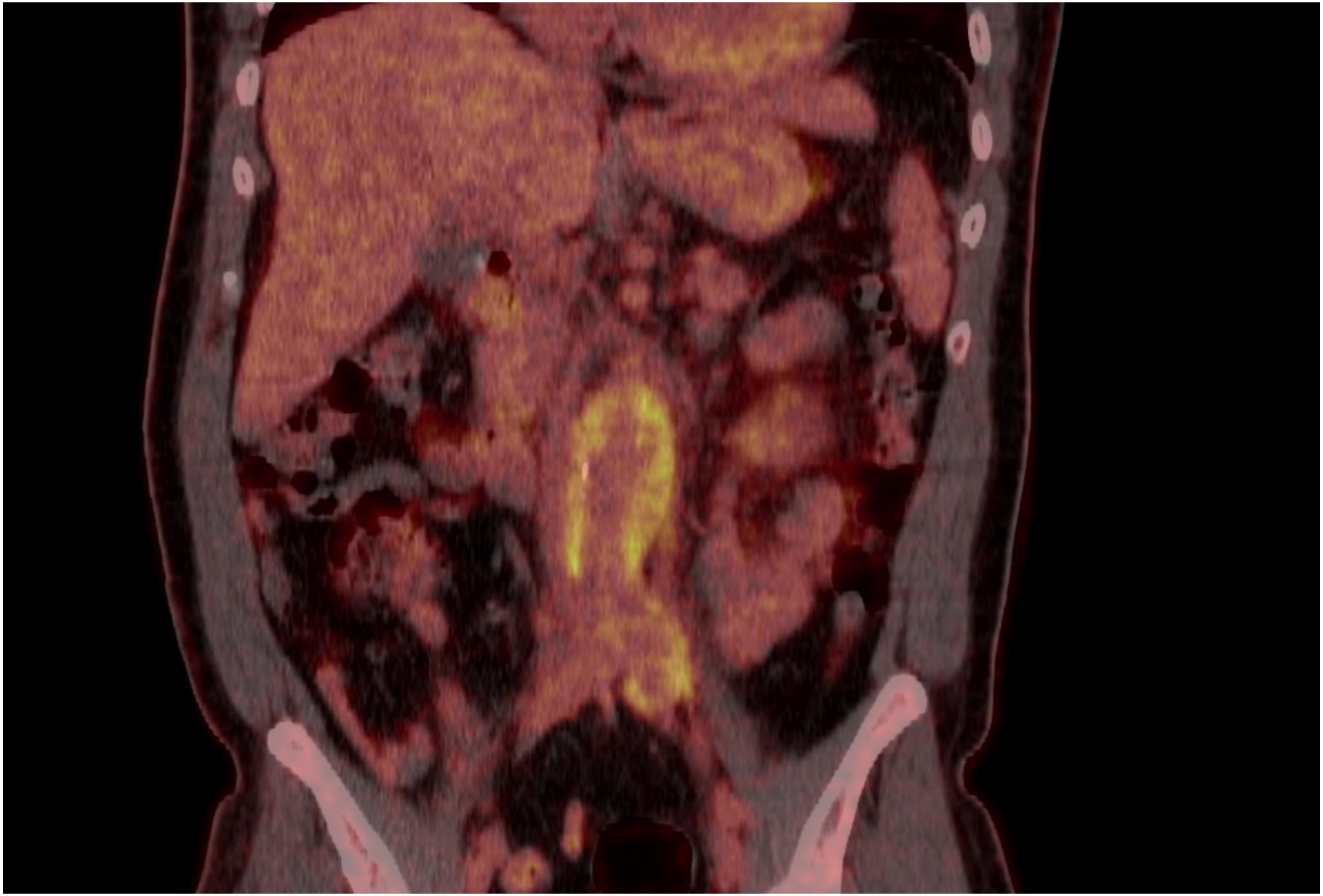




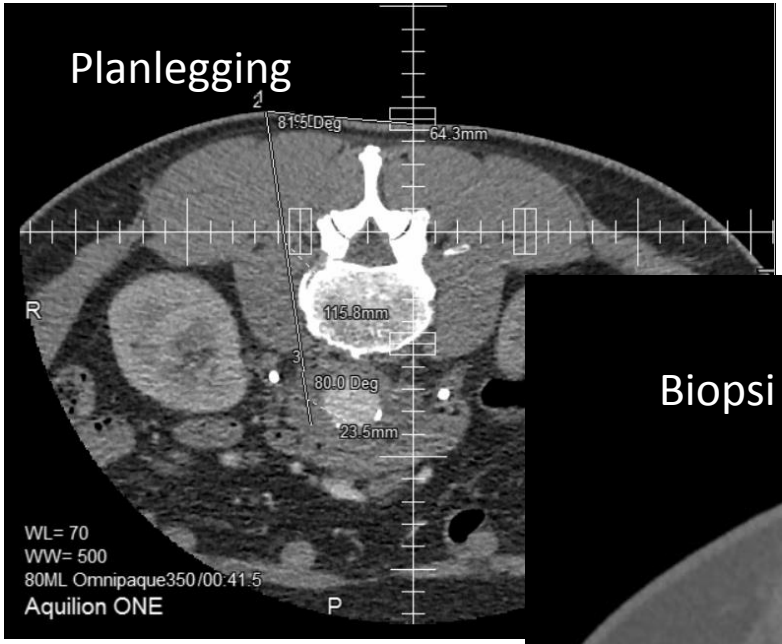


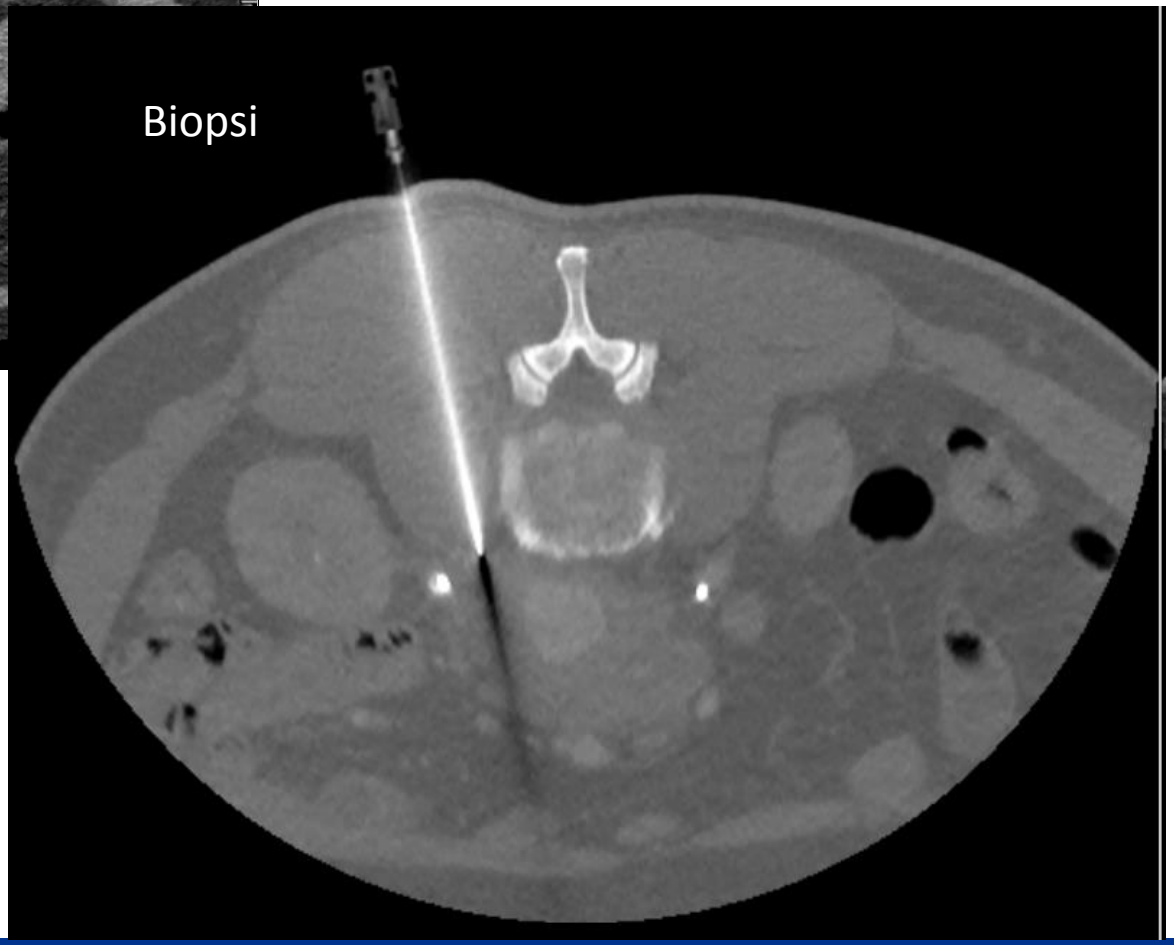


Bilder fra radiolog Eva Kirkhus



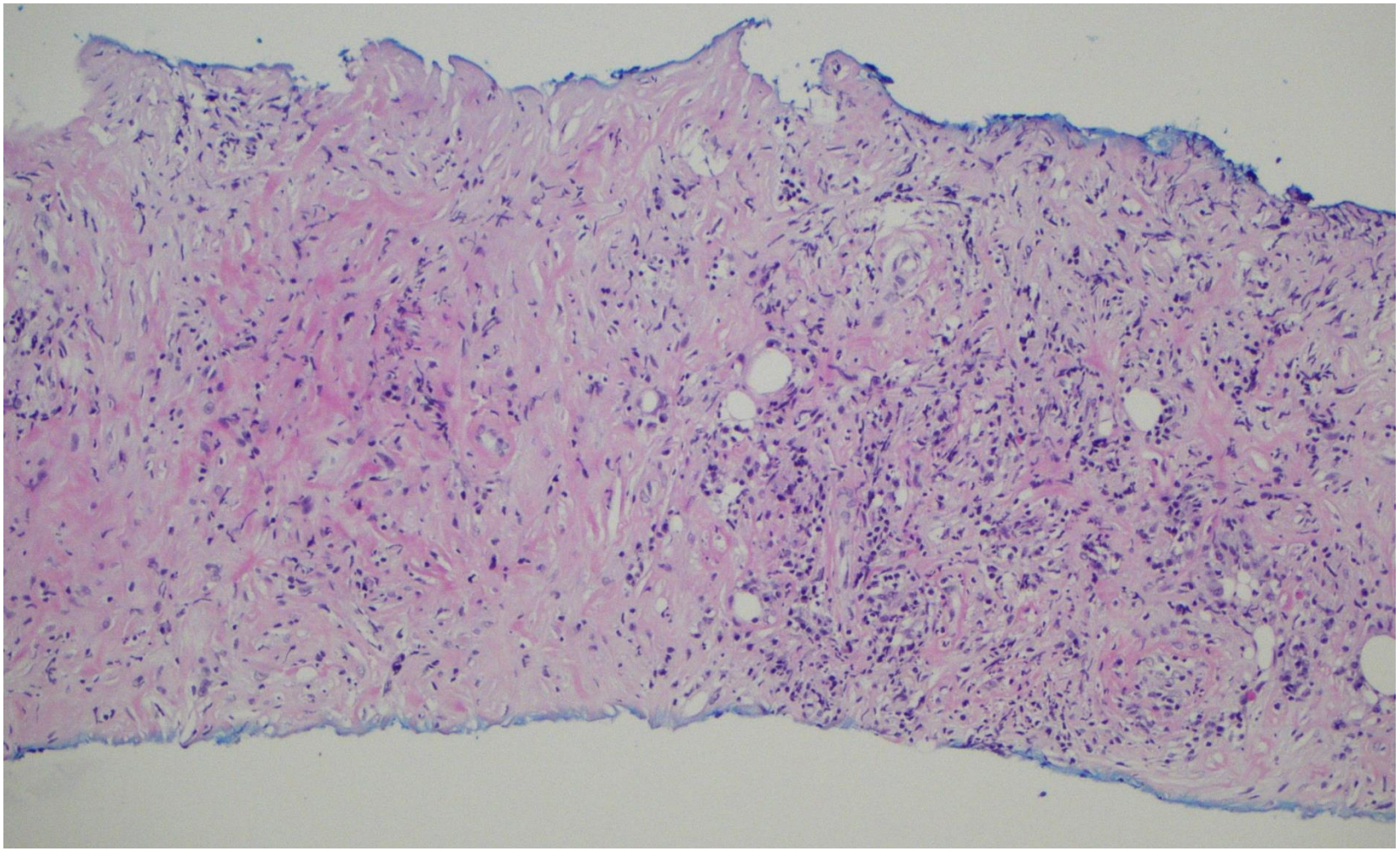
PETCT bilde fra nukleærmedisiner James Patrick Connelly





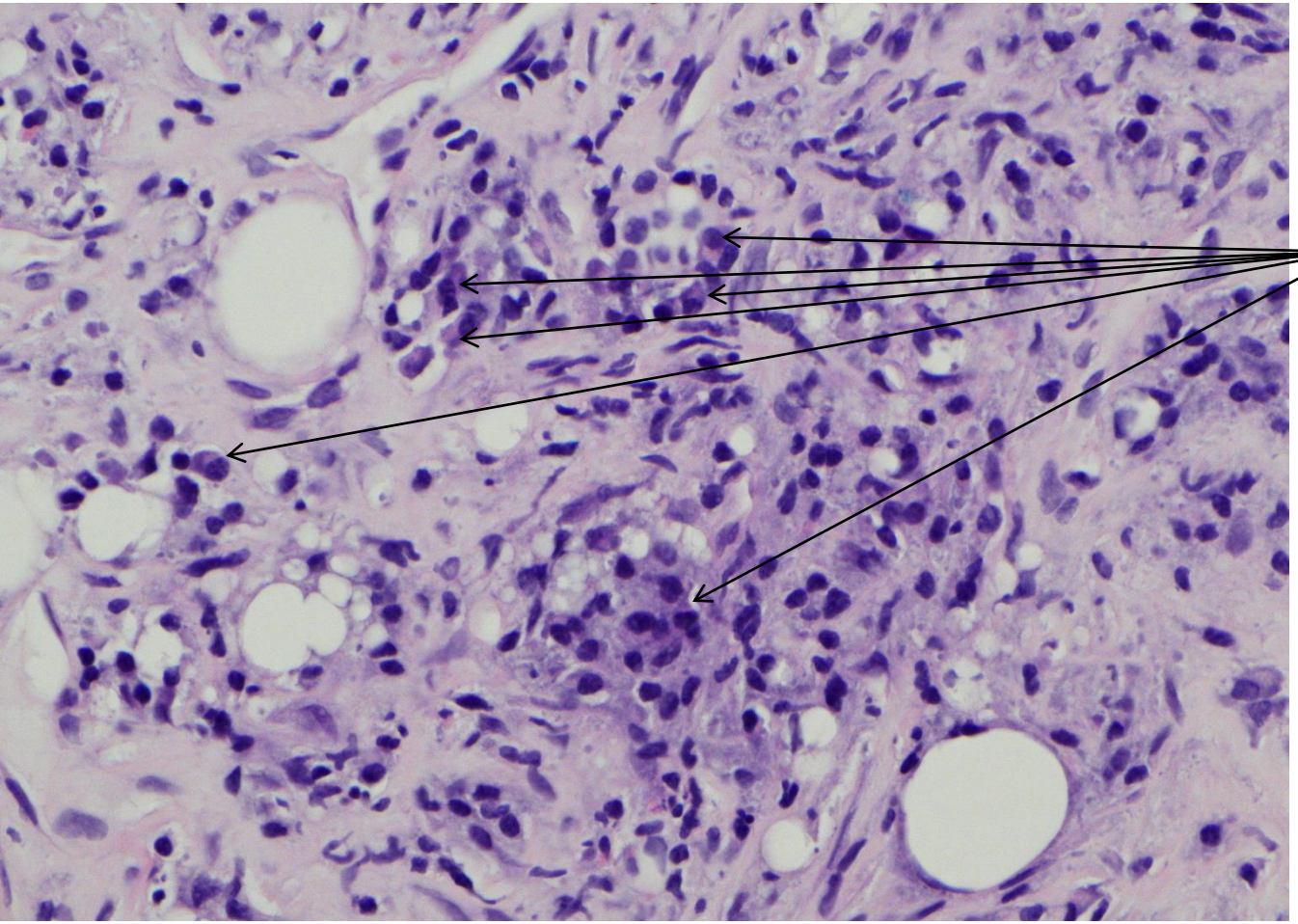
CT bilder fra Eva Kirkhus

Nålebiopsi med fibrose og betennelse



Bilde fra Melinda Raki, patolog

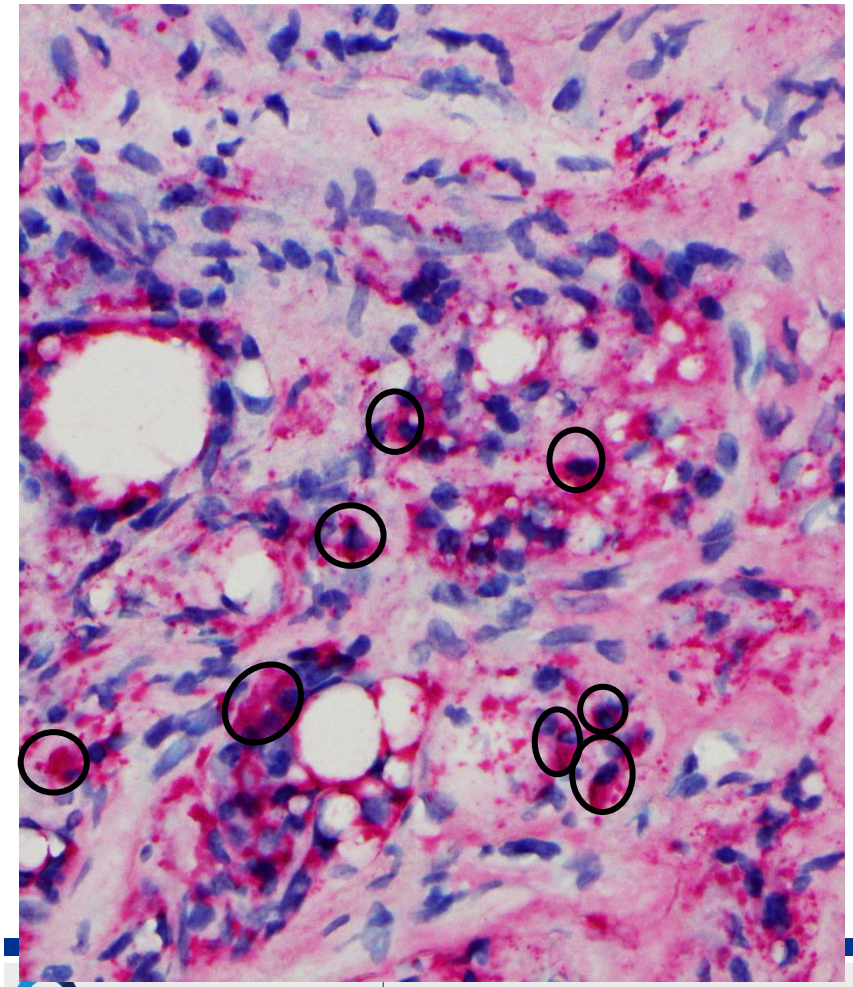
Lymfoplasmocyttært infiltrat



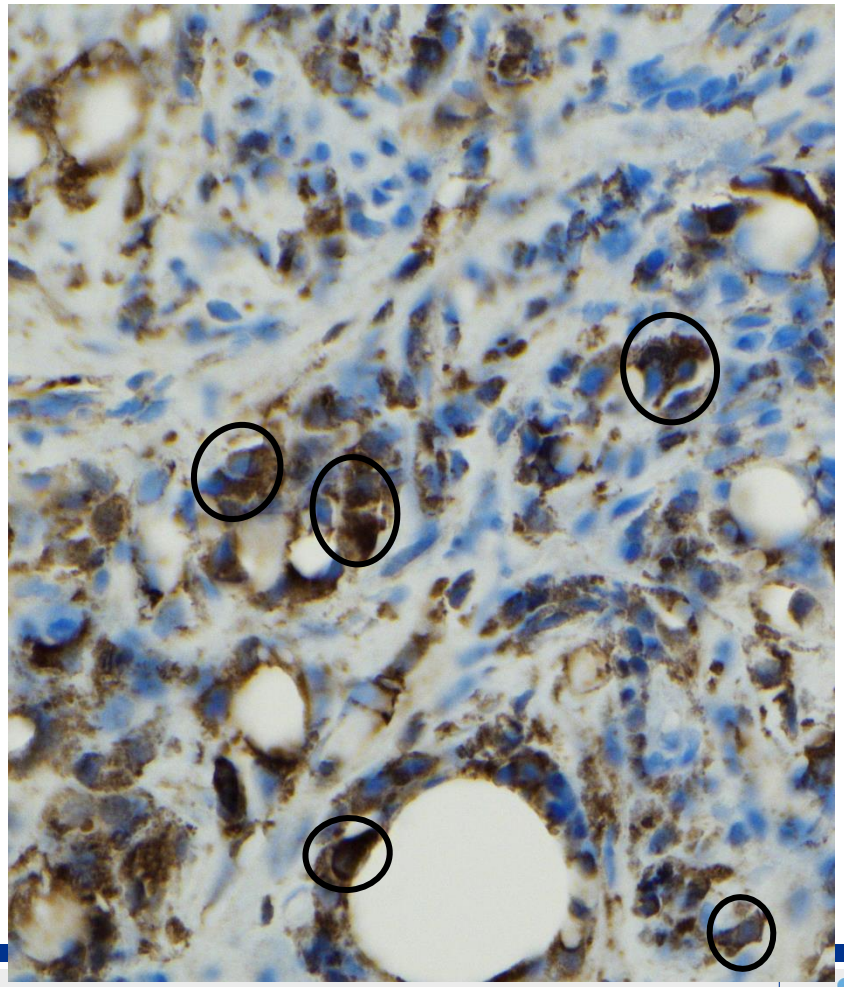
Plasmaceller
(eksentriske kjerner)

De fleste IgG+ plasmacellene er av IgG4 subklasse

IgG4 (rød)

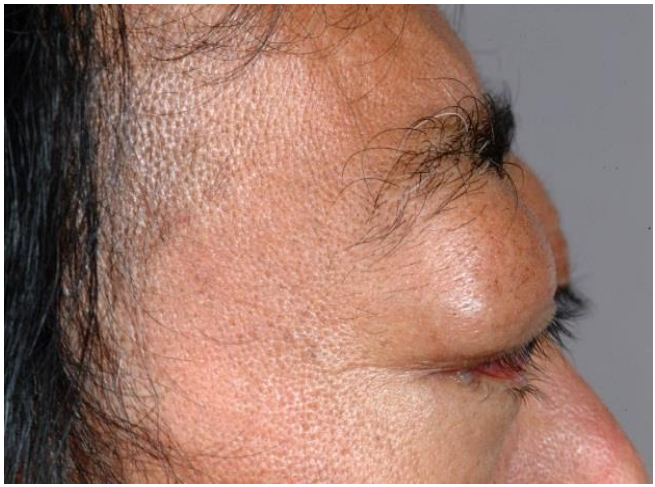


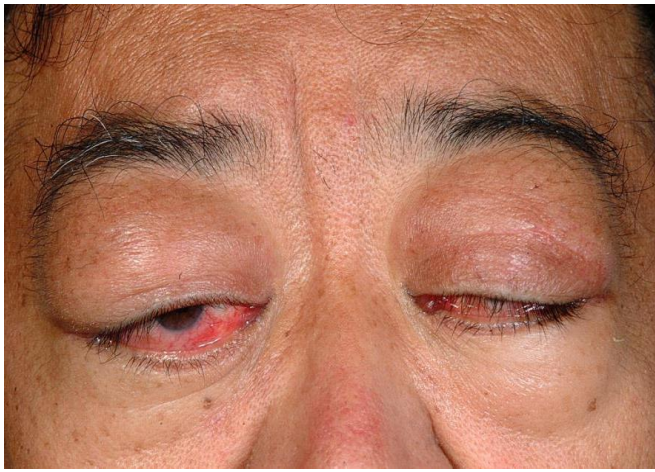
IgG (brun)



Kasus 2: «Lama» f-51

- Henvist revmatolog i 2005
- Eosinofil granulomatose med polyangitt ?
- Tidligere vurdert av: Øyelege, ØNH, nevrolog, hematolog, lungelege, infeksjonsmedisiner
- Exophthalmus, hevelse i gl.lacrimalis
  - SR 58,CRP 5, eosinofili 3,47 (ref<0,4)
  - IgE > 5000 , fT4 12,9,TSH 3,3
  - Negativ ANA,ANCA,TRAS, antiTPO,
- Histologi: Betennelsesinfiltrater med lymfocytter, eosinofile, plasmaceller, fibrose



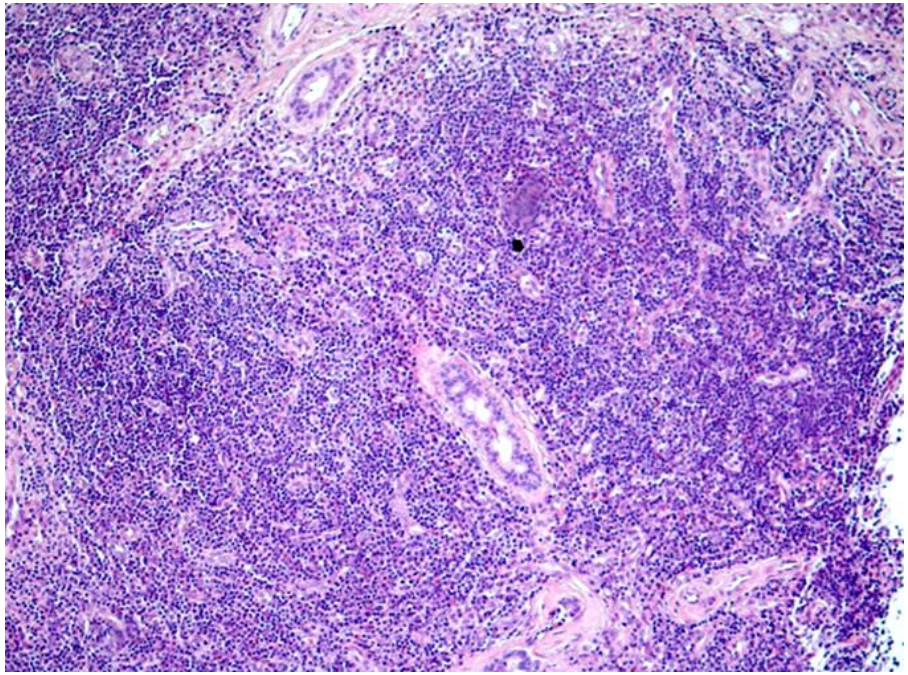


IgG4 relatert sykdom:

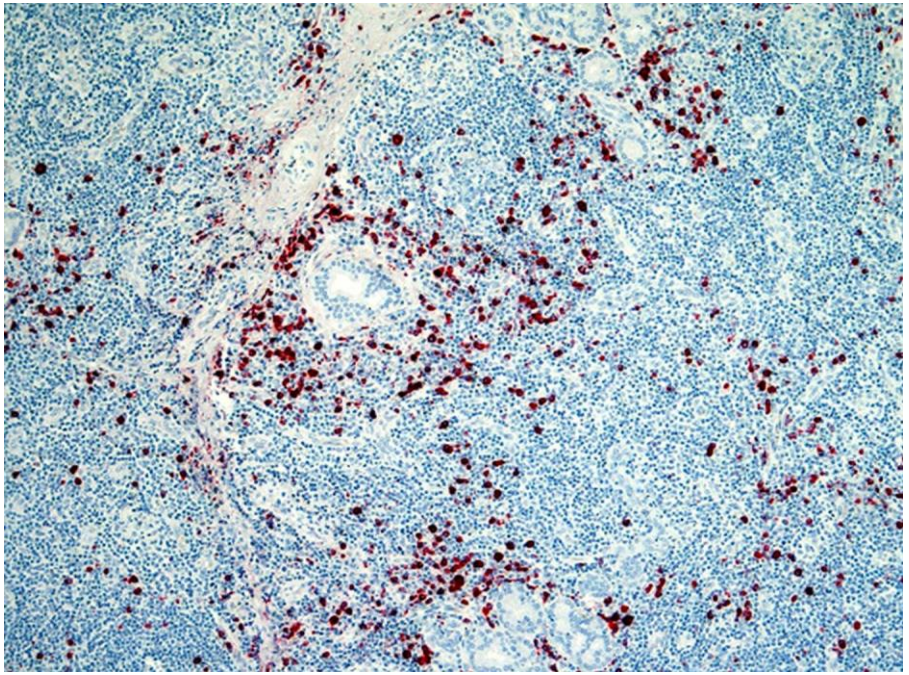
2008: s-IgG4: 11,6g/l (total IgG 33g/l)

2010: Biopsi fra gl. lacrimalis: IgG4 farging (tilgjengelig 2010)

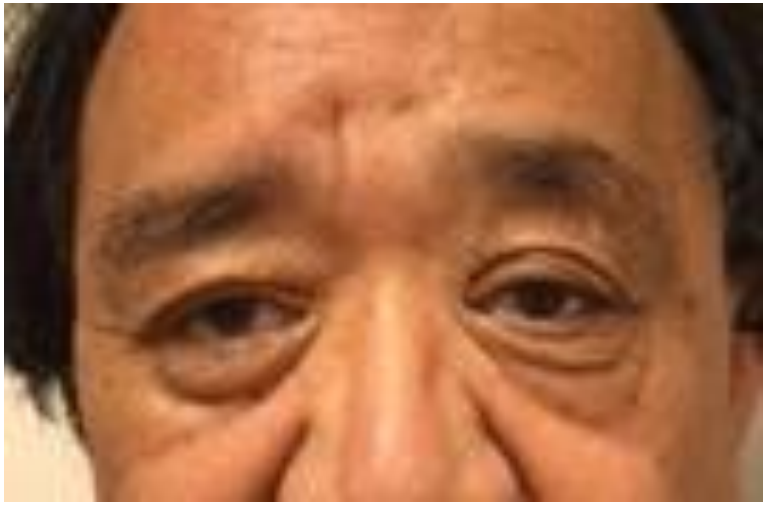
Kronisk betennelse med lymfoid hyperplasi



IgG4+ plasmaceller



Mai 2016



S-IgG4 0,45 g/l

Med tillatelse fra pasienten

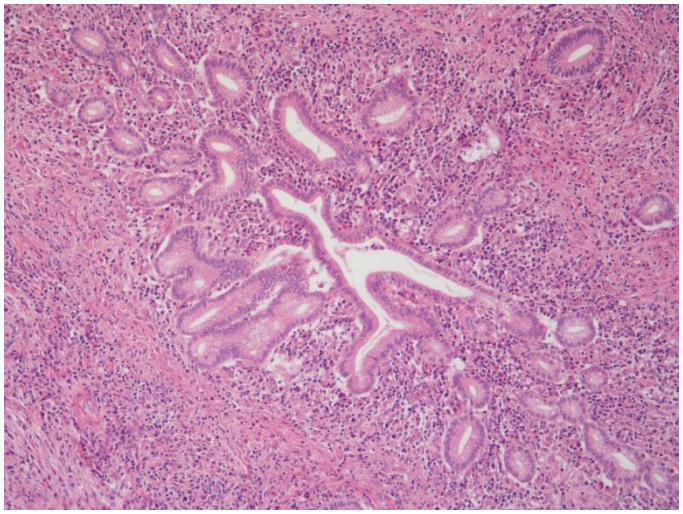
Kasus 3: «Svein» f-56

- Magesmerter, vekttap, icterus
- CT Abdomen/ERCP – suspekt ca.pancreatis
- Whipples operasjon (OUS)

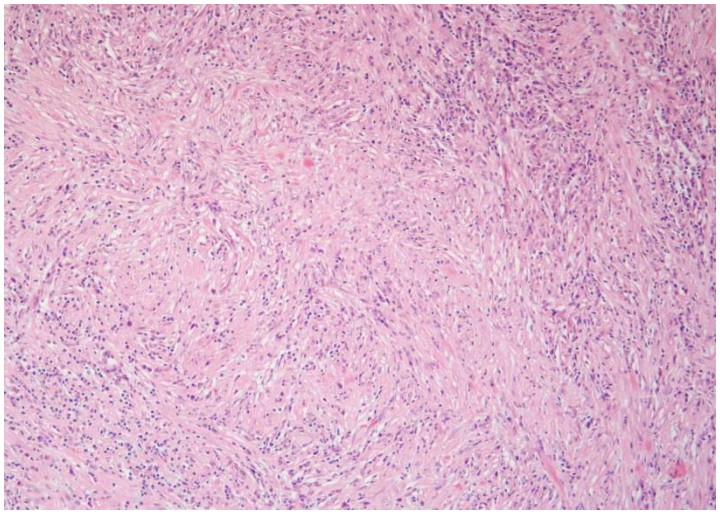
Histologi: Ingen malignitet

Pancreas biopsi

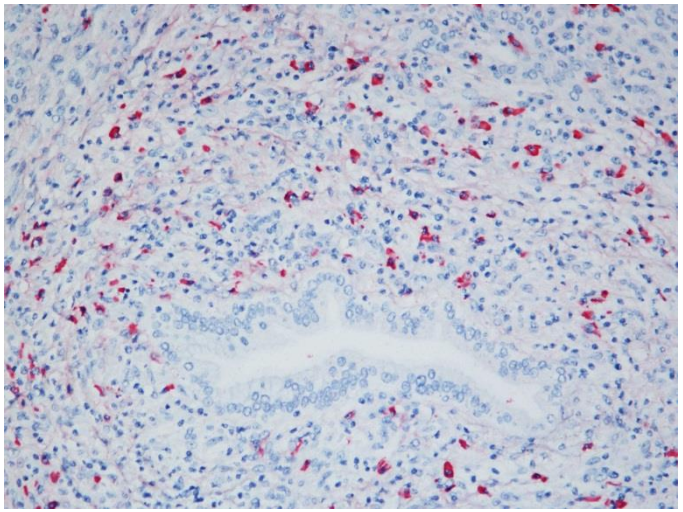
Periductal betennelse



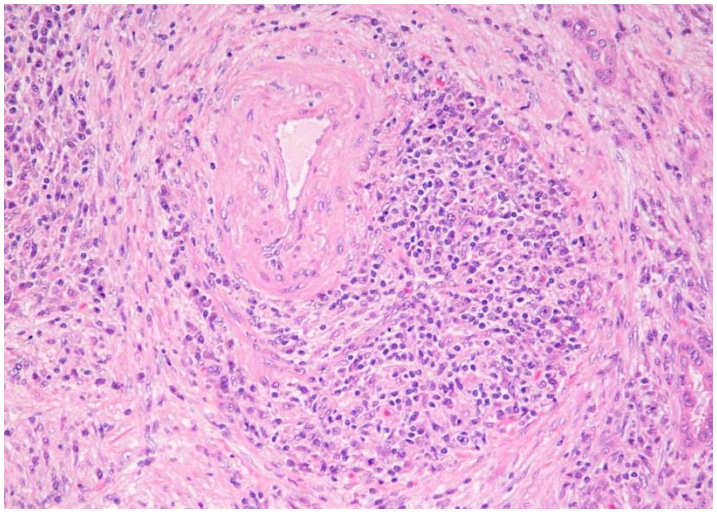
Storiform fibrose



IgG4 + plasmaceller

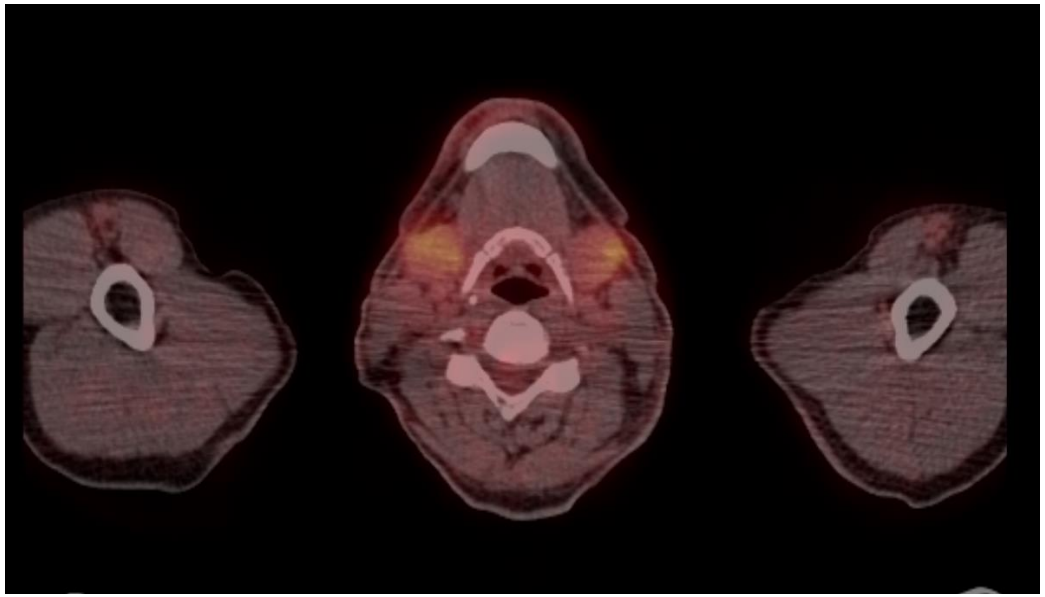


Obliterativ flebitt



IgG4 relatert sykdom:

Klinikk, IgG4 13,2g/l , histologi, bildediagnostikk



PET-CT: Opptak gl submandibularis

Lever og pancreas

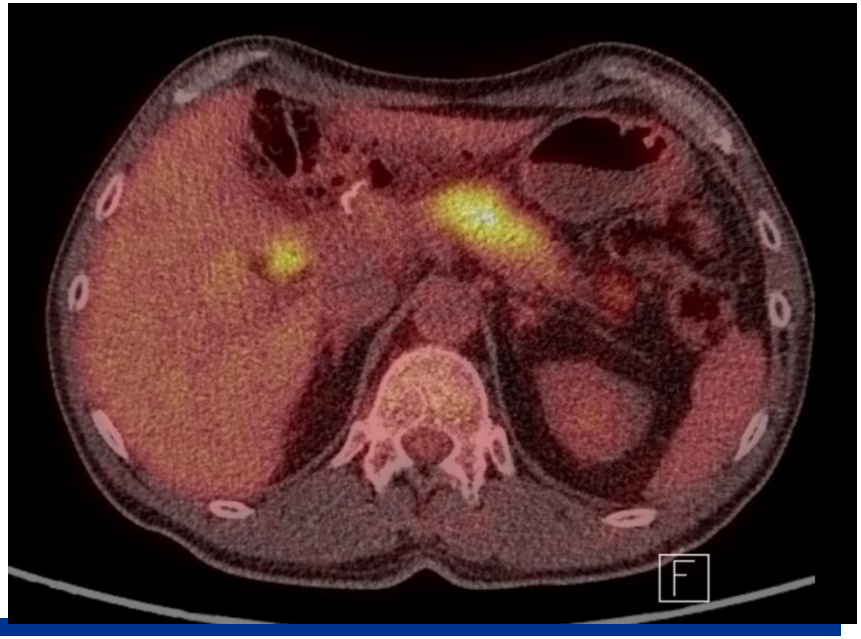


Table 1. Clinical characteristics of patients from two large published cohorts.

	Japan (n=334)[17]	Boston (125)[16]	OUS (45) NOSVAR
Mean age at diagnosis	63.8 years	55.2 years	59,2 år
Male sex	61.4%	60.8%	66,7 %
Ethnicity	100% Japanese	76% White	84 % Caucasere
Elevated serum IgG4	>95%	51%	82% (Kvinner 5,9g/l ,Menn: 6,7g/l)
Mean number of organs involved (range)	3.2 (1-11)	2.3 (1-7)	2,8 (1-6)
Affected organs			
Salivary glands	72.3%	28% (submandibular) + 16.8% (parotid)	42%
Lacrimal glands/orbit	57.1%	22.4%	38%
Lymph nodes	56.5%	27.2%	
Pancreas	25.5	19.2%	47% Pancreas , 9 Whipple
Retroperitoneal/ aorta	24.9	18.4% (retroperitoneal) + 11.2% (aorta)	18%
Kidney	23.7%	12%	16 %
Lung	23.4%	17.6%	

«IgG4 related disease: what a hematologist needs to know « Chen et al Haematologica 2019

Behandling

- Mål: Symptomlindring + forhindre fibrose/organskade

- ”Watchful waiting” – hvis lite symptomer og ingen truende organskade
- Prednisolon: Induksjon og vedlikehold
- Dose avhenger av sykdomsaktivitet og organaffeksjon
- Ofte residiv - ”relapsing-remitting condition”
- Syntetisk DMARD (Imurel, MTX, MMF)
- Rituximab (RA protokoll) – ingen konsensus om vedlikehold

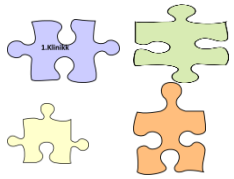
«Rituximab for IgG4 related disease: a prospective, open label trial» Carruthers et al ARD 2015

Behandling ved OUS

- Steroider: 42 av 45
- Rituximab: 36 av 45 (7 av 9 Whipples operert)
- Abatacept (Orencia): 1
- Ingen: 3

Oppsummering –IgG4

- Immunmediert fibroinflammatorisk
- Diagnose: klinikk-blodprøver-bildediagnostikk og histolog



- Behandling: Steroider + Rituximab
- ”Relapsing-remitting” – krever oppfølging

Takk !

- Torhild Garen (NOSVAR)
- Henrik Mikael Reims og Melinda Raki (Patolog)
- Charlotte Eldjarn og James Patrick Connelly (Nukleærmedisin)
- Eva Kirkhus (Radiolog)
- Liv Osnes (Seksjon for cellulær immunologi)
- Eli Taraldsrud (Enhet for cellulær immunologi og flowcytometri)