IgG4-RELATED DISEASE

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ESIM, RIGA 7.2.2017

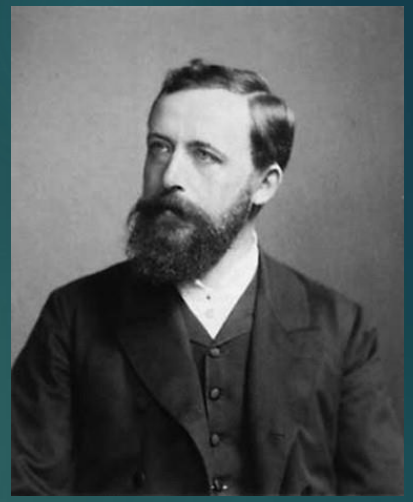
IgG4-related disease, IgG4-RD

- Inflammatory and fibromatous disease:
  - Dense lymphoplasmasytic infiltration where IgG4-positive plasmacells prevail
  - Vortical ,"storiform" fibrosis
  - Often elevated S-IgG4
  - Good response to corticosteroids

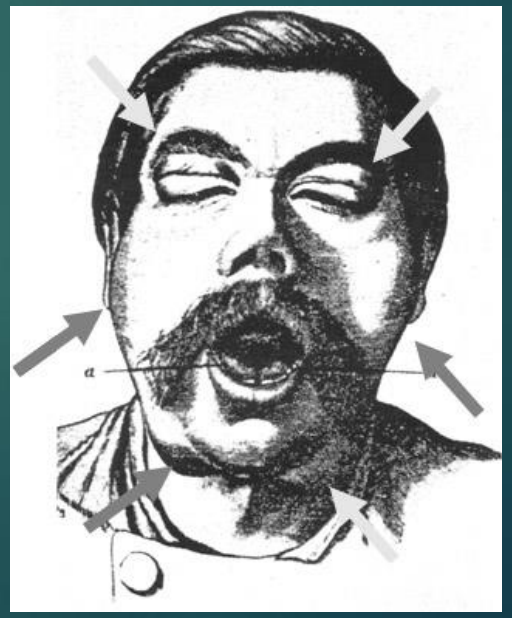
Once upon a time 124 years ago…

Mikulicz' disease (MD)

- 1892 bilateral, symmetrical and painless swelling of the lacrimal and salivary gland
- 1933 Henrik Sjögren: Keratoconjunctivitis sicca, xerostomy, arthritis (Sjögren´s syndrome, SS)
- 1953 Morgan & Castleman: "MD ja SS morphologically identical. MD is a subtype of SS:".



Johann von Mikulicz-Radecki 1850-1905

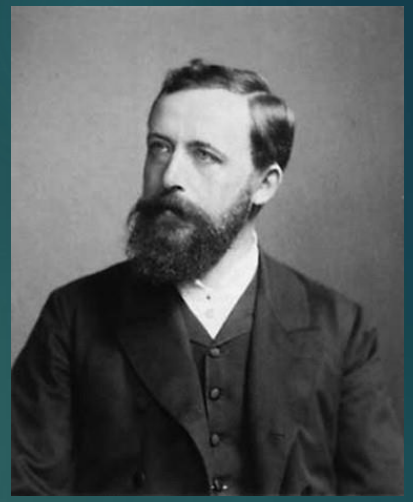


(Kamisawa T, Yamamoto M, Takahashi H, 2003, 2004, 2005 etc.)

- …and then there was silence…

Mikulicz' disease (MD)

- 1892 bilateral, symmetrical ja painless swelling of the lacrimal and salivary gland
- 1933 Henrik Sjögren: Keratoconjunctivitis sicca, xerostomy, arthritis (Sjögren´s syndrome, SS)
- 1953 Morgan & Castleman: "MD ja SS morphologically identical. MD is a subtype of SS:".
- 2003 in Japan: a connection between MD and type 1 autoimmune pancreatitis through histological and ja immunohistochemical studies
- → IgG4-RD systemic characteristics were identified



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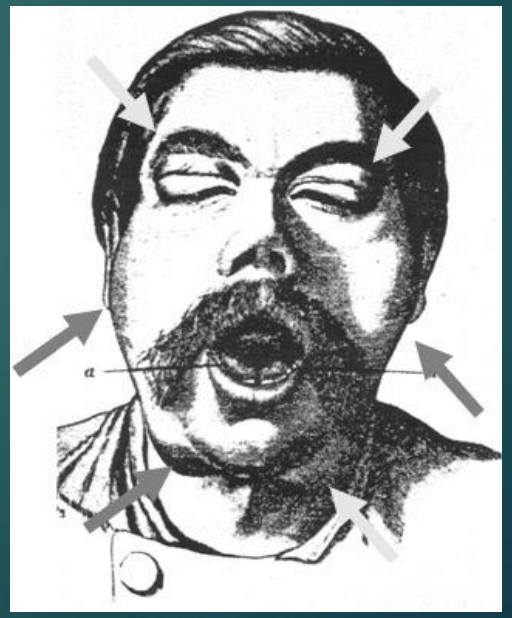


(Kamisawa T, Yamamoto M, Takahashi H, 2003, 2004, 2005 etc.)

Autoimmune pancreatitis (AIP)

- 1961 Sclerosing pancreatitis and hypergammaglobulinemy
- 1995: AIP

  Painless obstructive jaundice

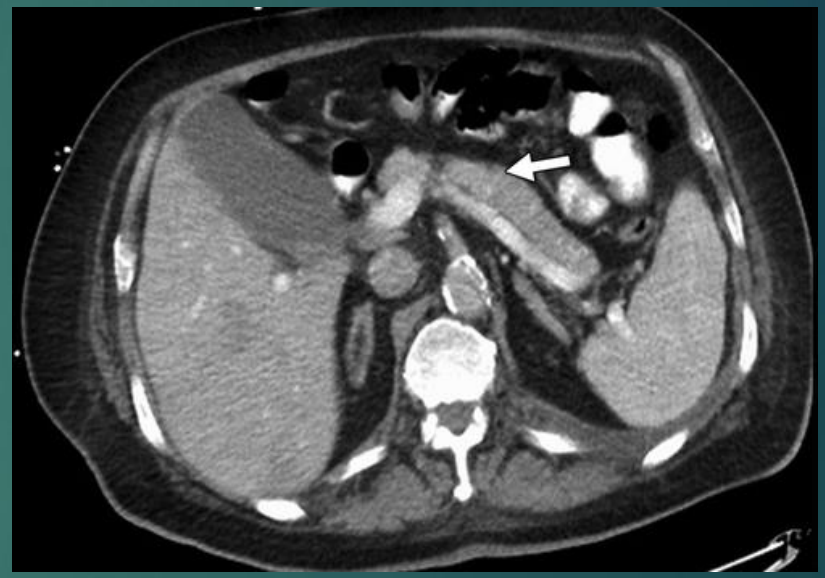
  - Swelling of the pancreas

  → Stenosis of the pancreatic duct

  Elevated S-IgG

  - Good response to corticosteroids
  - A link to other immune mediated diseases

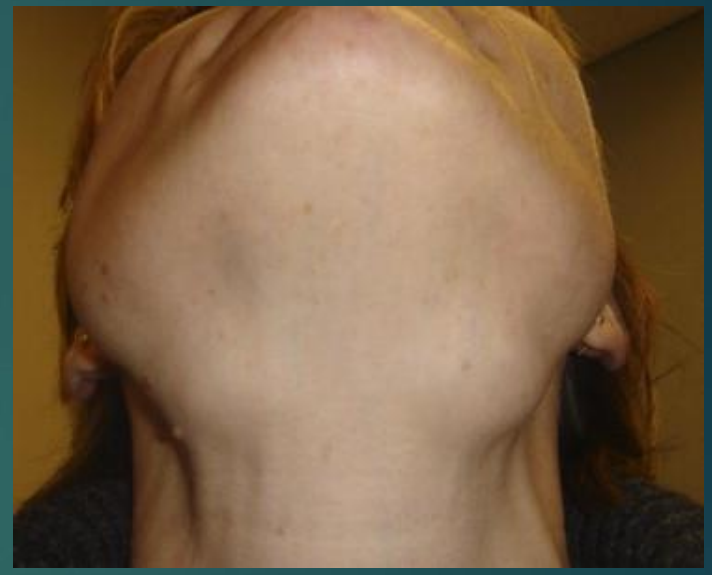
Abdominal CT: "Sausage" pancreas



Hedigre SS ym. Am J Roentgenol 2013;201:14-22

Küttner´s tumor

- Küttner 1896: sclerosis and swelling of the submandibular gland(s)
- Histology: sclerosing sialadenitis
- IgG4-RD manifestation in the submandibular gland(s)



Stone JH, Semin Diagn Pathol. 2012

IgG4-RD general characteristics

- Male preponderance >50-year-olds (M:F = 3:1)
- Comes creeping…
- Painless swelling of the organs, "tumefactive" lesions
- Inflammatory pseudo-tumor
- Described in almost every organ.
- General symptoms are scarce
- Occasionally acute: fever and acute phase reaction
- Patient history often shows allergy or atopy: chronic rhinitis/ sinuitis, asthma
  - Often eosinophilia, elevated S-IgE

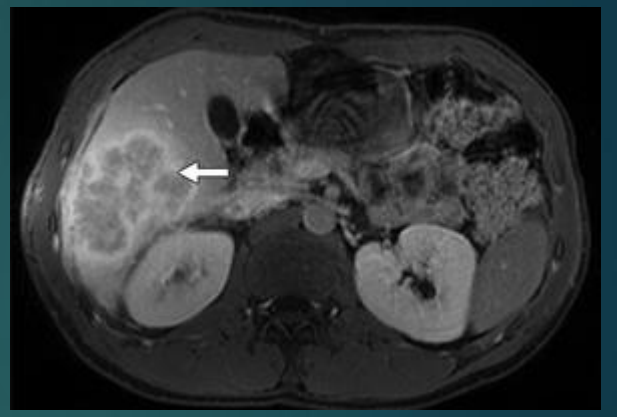
IgG4-cholangitis

- In IgG4-cholangitis: 80 %: has AIP as well
- In AIP: 40%: has IgG4-cholangitis as well
- Resemblance with primary sclerosing cholangitis (PSC) and cholangiocarcinoma.
- Differs from PSC:
  - In middle-aged and elderly men
  - Good response to corticosteroids
  - Association to inflammatory bowel disease is rare
  - No increased risk of cholangiocarcinoma

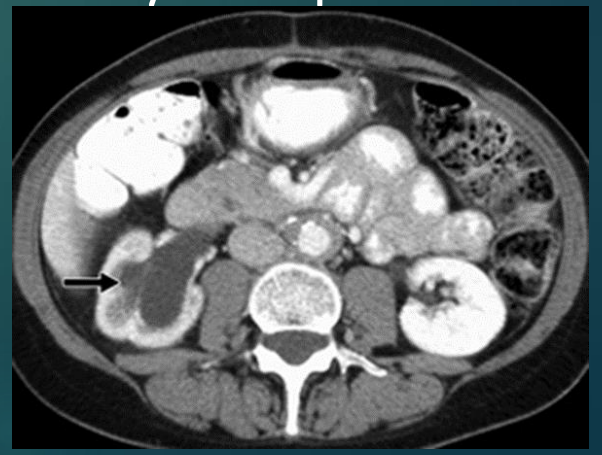
Other intra-abdominal manifestations

- **Cholecystitis** without gall stones
- Pseudotumor of the liver
- **Nephropathy**
- Chronic periaortitis – **retroperitoneal fibrosis**
- **Aortitis** and inflammatory aortic aneurysm
- Fibrosing mesenteritis

Liver pseudotumor



Retroperitoneal fibrosis and hydronephrosis



Hedigre SS et al. Am J Roentgenol 2013.

IgG4-RD in the lungs

- 4 major clinical syndromes
  1. Inflammatory pseudotumor
  2. Tracheobronchial stenosis
  3. Interstitial pneumonia
  4. Pleuritis

  Symptoms: cough, hemoptysis, shortness of breath, pleural effusion
- Radiological findings
  1. Nodular lesions
  2. Ovale ground-glass changes
  3. Interstitial lung disease, jossa honeycomb manifestation, bronchiectasy and diffuse ground glass changes

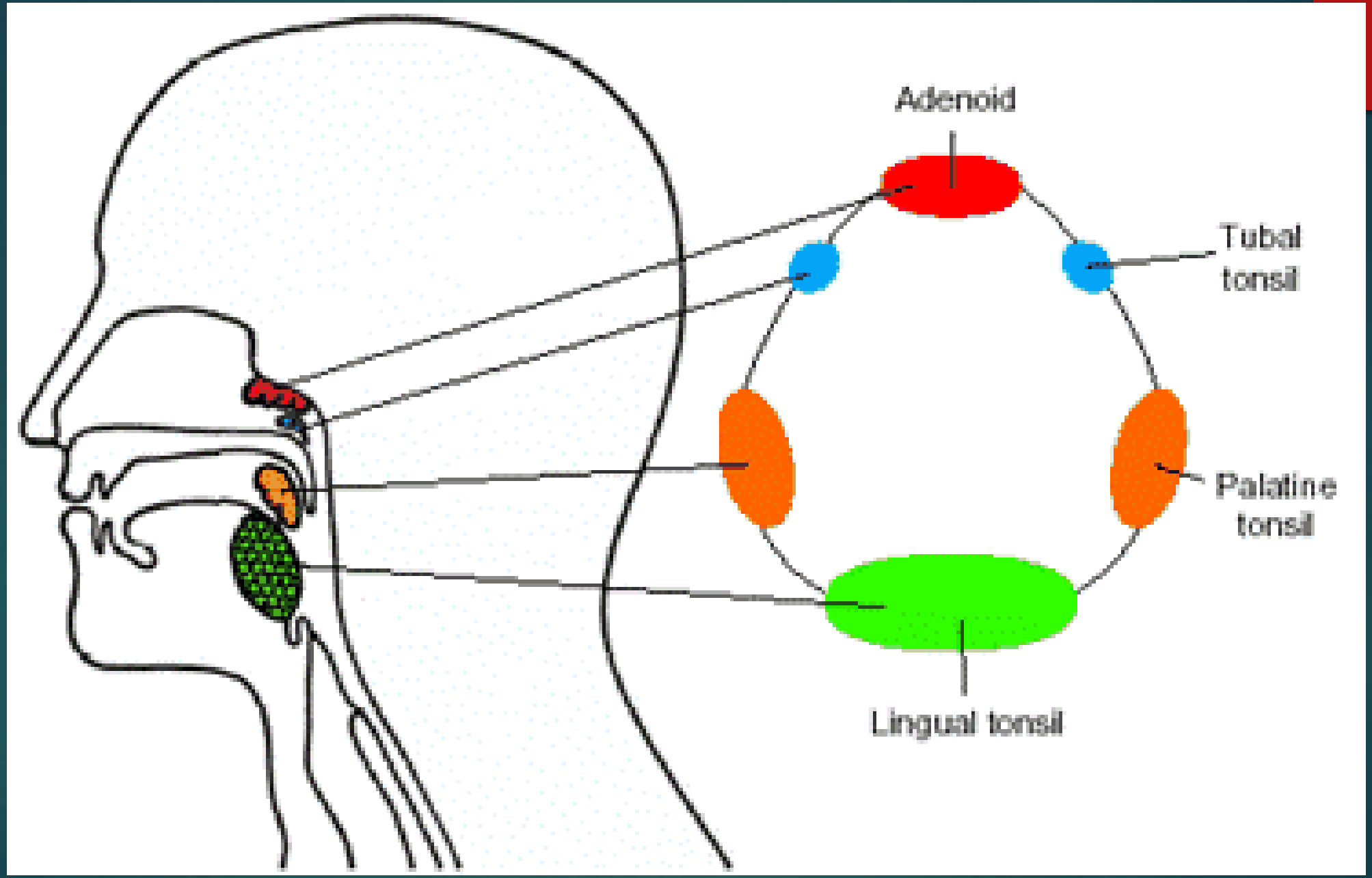
Other intrathoracic manifestations

- Pleura and pericardium
  - Nodular thickening of the visceral or parietal pleura
  - Pleural or pericardial effusions
  - Constrictive pericarditis
- Inflammation of the thoracal aorta
- Fibrosing mediastinitis
- Lymfadenopathy

Manifestations in the ears, nose and throat

- 40 % allergy; asthma, chronic sinusitis, nose polyps, allergic rhinitis
- Crusted lesions in the nose, anosmia, otitis media, lacrimal gland effected, acute hypacusis, laryngitis, mastoiditis
- Destructive lesions in bone during sinuitis and otitis
- Lesions in Waldeyer´s ring... oooooops, what´s that???

Ikeda R ym. Otorhinolaryngology-Nead and Neck Surgery 2010.


Adenoid
Tubal tonsil
Palatine tonsil
Lingual tonsil

Manifestations in the ears, nose and throat

- 40 % allergy; asthma, chronic sinusitis, nose polyps, allergic rhinitis
- Crusted lesions in the nose, anosmia, otitis media, lacrimal gland effected, acute hypacusis, laryngitis, mastoiditis
- Destructive lesions in bone during sinuitis and otitis
- **Lesions in Waldeyer´s ring: pharynx, hypofarynx, larynx, vocal cords and trachea**

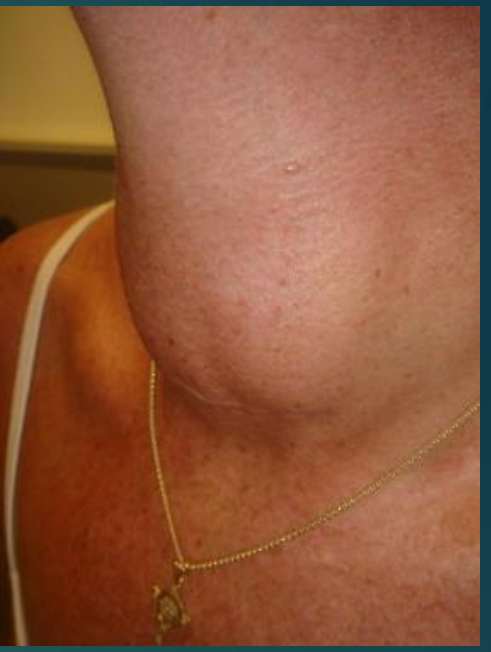
Ikeda R ym. Otorhinolaryngology-Nead and Neck Surgery 2010.

IgG4-RD in the orbita

- Dacryoadenitis
- Myositis in the orbita
- Perineuritis in the optical and trigeminal nerve
- Inflammatory pseudotumor of the orbita
- Symptoms
  - Swelling of the lacrimal gland and eylids
  - Motor skill disorders of the eyes
  - Blurred vision
  - Proptosis of the eye
  - Sicca symptom in the eyes

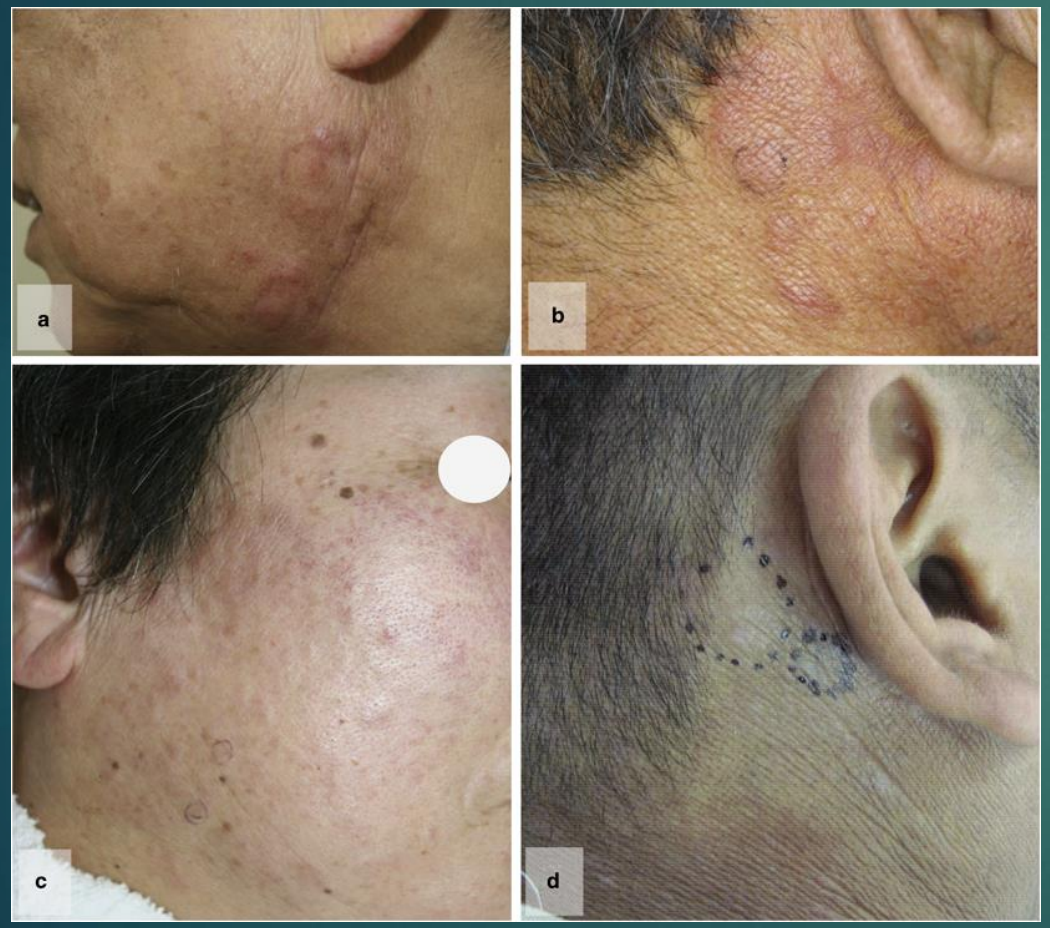
IgG4-RD in the thyroidea

- 1894 BM Riedel: "Iron hard, fixed and mostly painless struma"
  - Symptoms: Dyspnea, dysphagia, hoarseness, aphony
  - Hypothyroidism in 25-80%
- A fibrosing type of Hashimoto´s thyroiditis is included in IgG4-RD



Stone JH. Semin Diagn Pathol 2012:29:177-190

IgG4-RD in the skin



Ear region, cheek and mandibular skin:

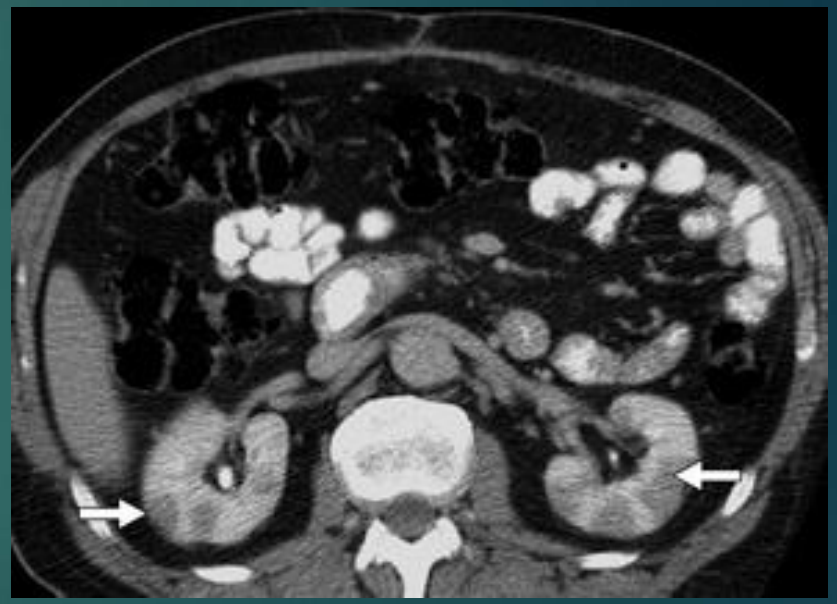
-erythematosis and itching plaques of subcutaneous nodules

Sato Y ym. Mod Pathol 2013;26:523-32.

IgG4-nephropathy
IgG4-related kidney disease, IgG4-RKD

- Modest symptoms
- Mild proteinuria, hematuria, kidney failure
- Pseudotumors
- Histology: tubulointerstitial nephritis and fibrosis
- Occasionally membranous glomerulonephritis

CT: cortical lesions



Hedigre SS et al. Am J Roentgenol 2013

IgG4-RKD
Clinical features

- 75-85% men
- Median age 65 years
- Often symptomless, incidental finding
- Occasionally hydronefrosis due to retroperitoneal fibrosis
- Most common extrarenal manifestations
  - 1. Pancreas
  - 2. Salivary gland
  - 3. Lacrimal gland
  - 4. Lymphatic nodules

Saeki T et al. Kidney Int 2010

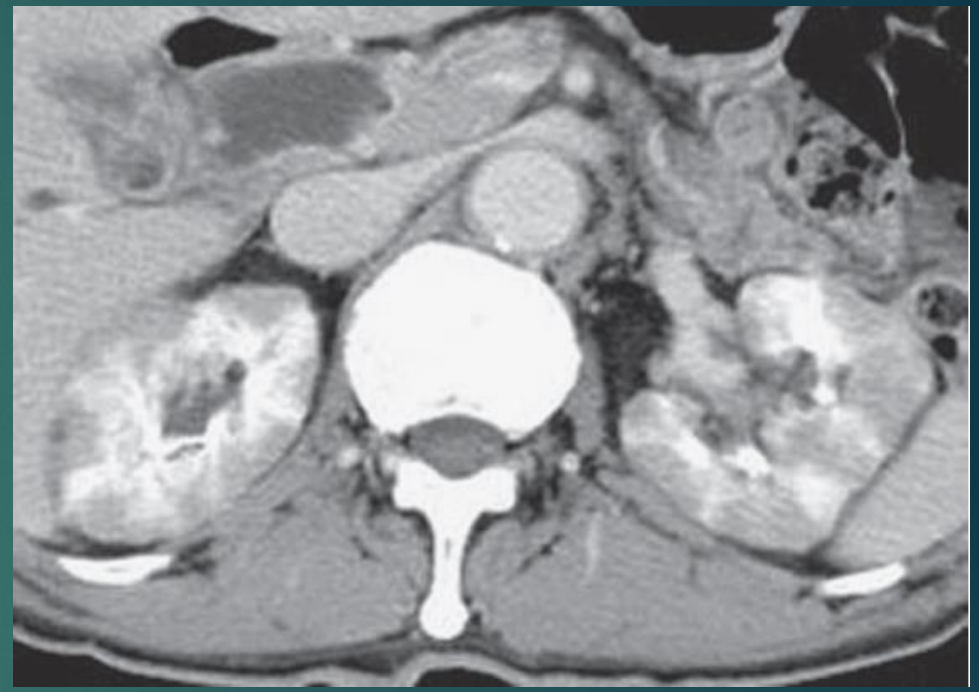
IgG4-RKD
Laboratory findings

- 90% clearly elevated S-IgG4
  - often X 10-30
- 60% hypocomplementemia
- 50% mild proteinuria
- 40% elevated B-Eosinophiles
- RF, nuclear antibodies sometimes elevated
- anti-DNA, anti-SS-A, anti-SS-B, anti-Sm anti-RNP normal
- CRP, IgA, IgM, cryoglobulin, M-component, ANCA normal

Saeki T et al. Kidney Int 2010

IgG4-RKD
Radiologic findings

- Contrast-CT scan
- 65% multiple hypodense regions
- 30% diffuse swelling of the kidneys
- 10-20 % mass lesions
  - resemblance to malignant tumors



Kawano M et al. Clin Exp Nephrol 2011

Table 2 Histopathologic hallmarks of IgG4-RD

Major
Lymphoplasmacytic infiltrate
High percentage of IgG4-positive plasma cells
Storiform fibrosis
Obliterative phlebitis
Mild to moderate tissue eosinophilia
Minor
Germinal centers
Lymphoid follicles
Nonobliterative phlebitis
Obliterative arteritis (usually found in lung)

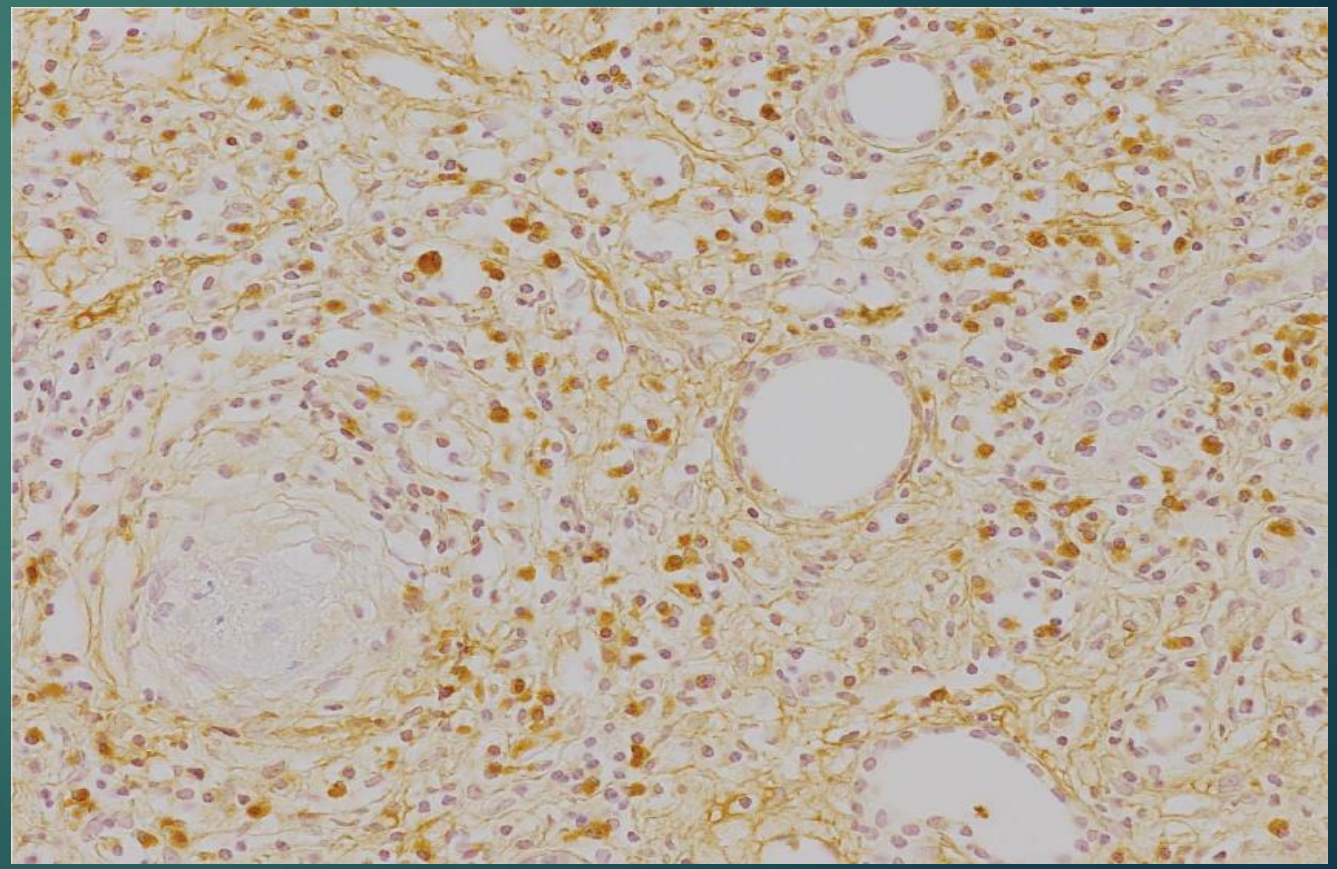
Abbreviation: IgG4-RD, immunoglobulin G4–related disease.

Mahajan VS, et al. Annu Rev Pathol. 2014.

IgG4-RKD
Histopathologic findings

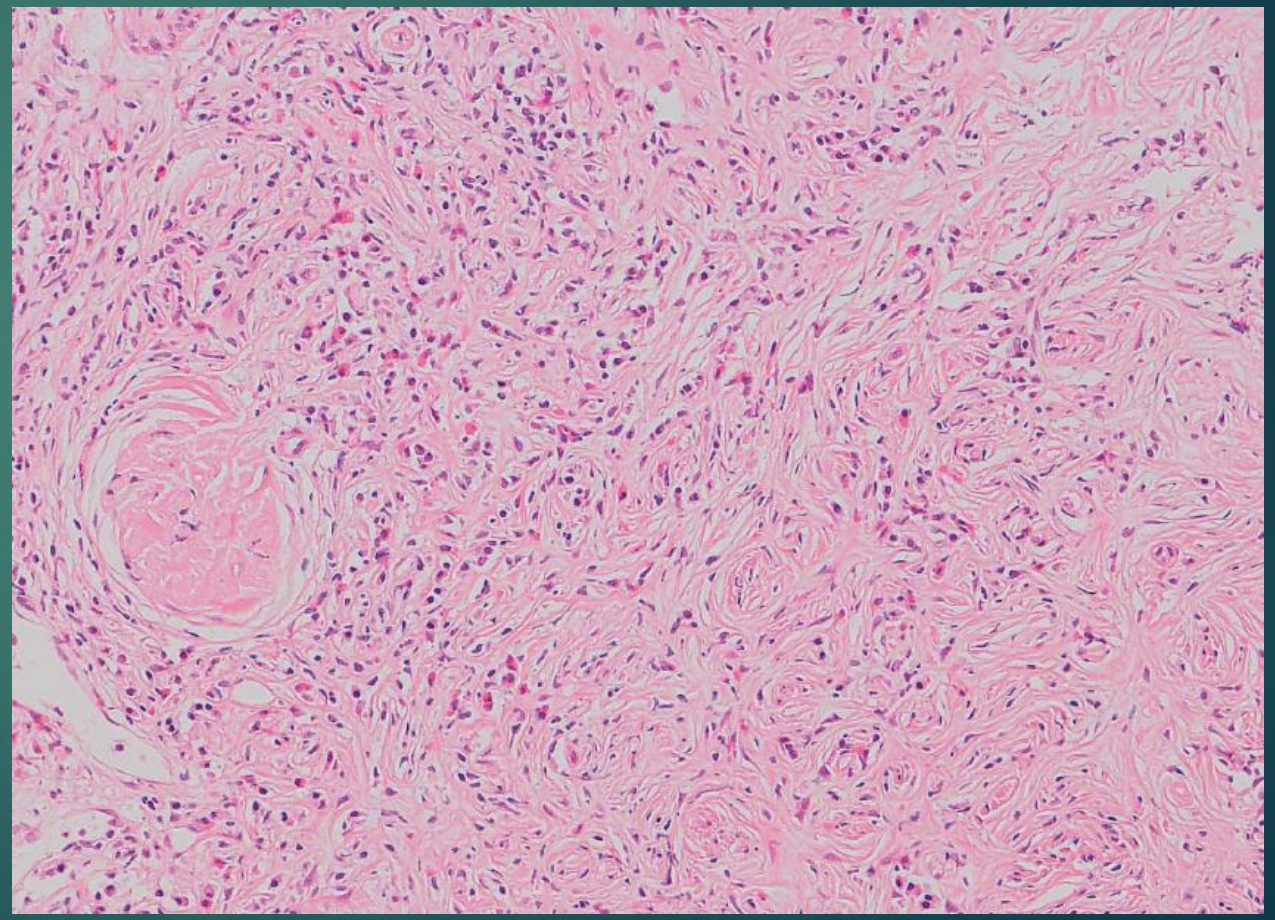
- IgG4 positive

tubulointerstitial nephritis (TIN)



IgG4-RKD
Histopathologic findings

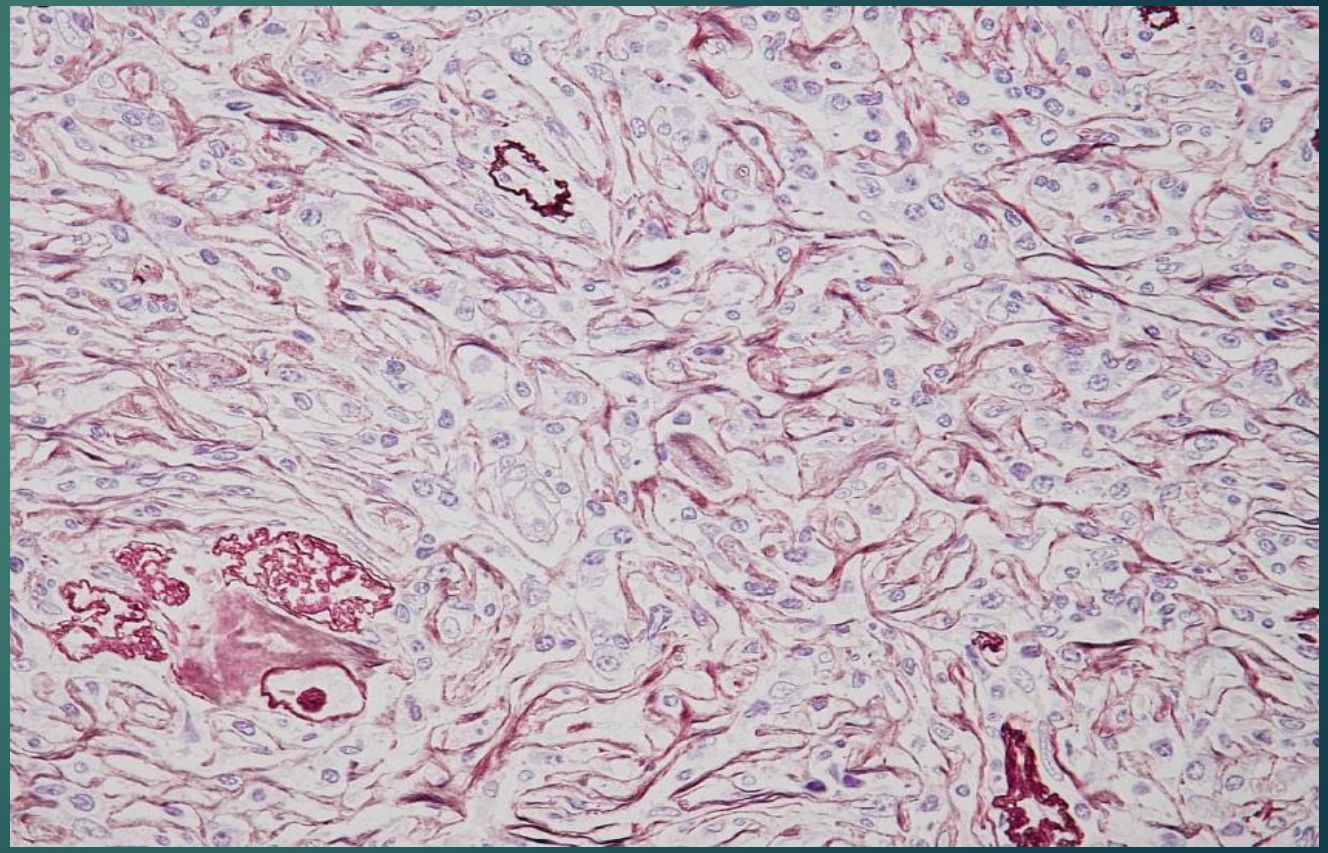
- "Storiform" or vortex fibrosis



IgG4-RKD
Histopathologic findings

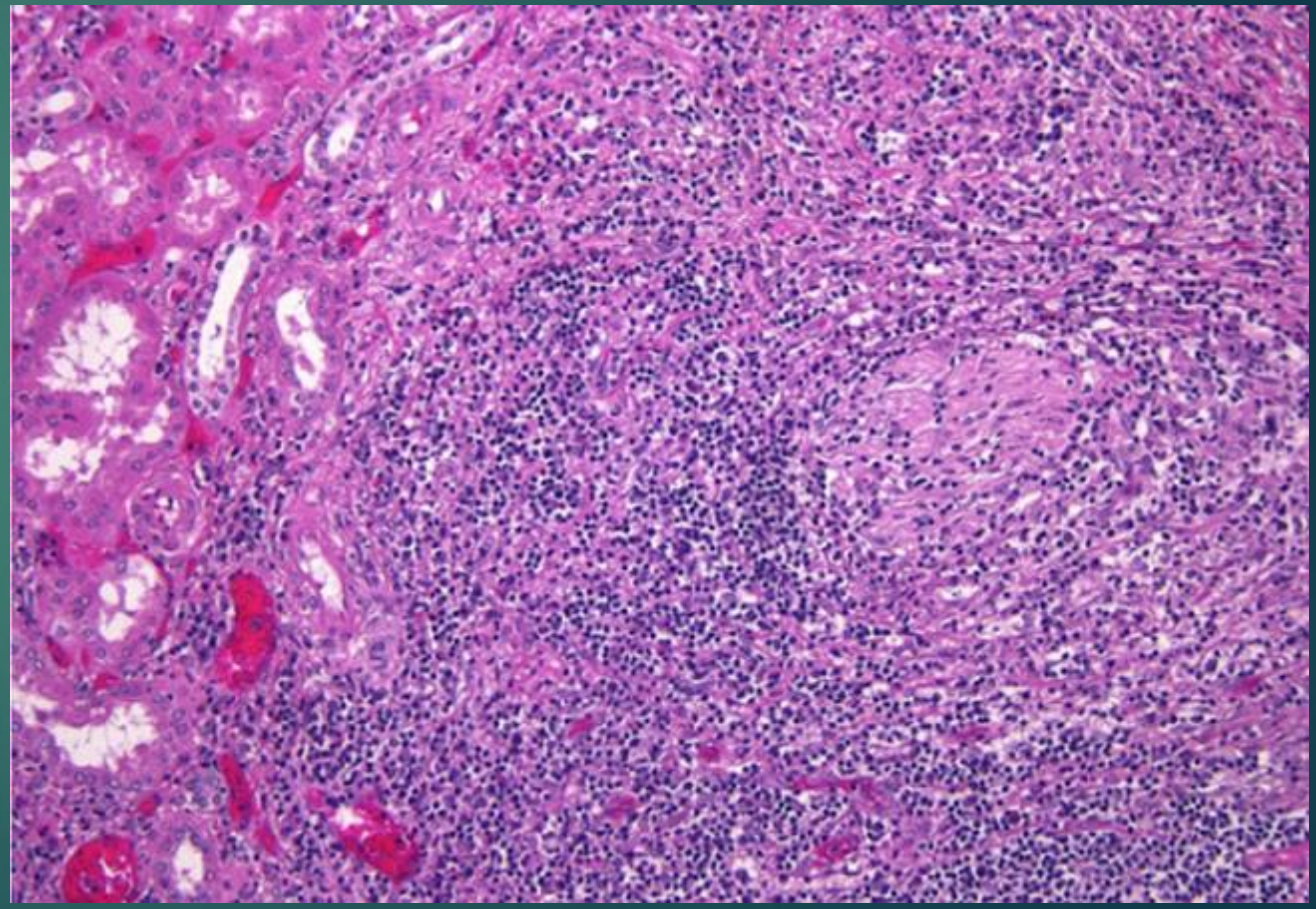
- "Bird's eye fibrosis"

irregular fibrosis around the inflammatory cells



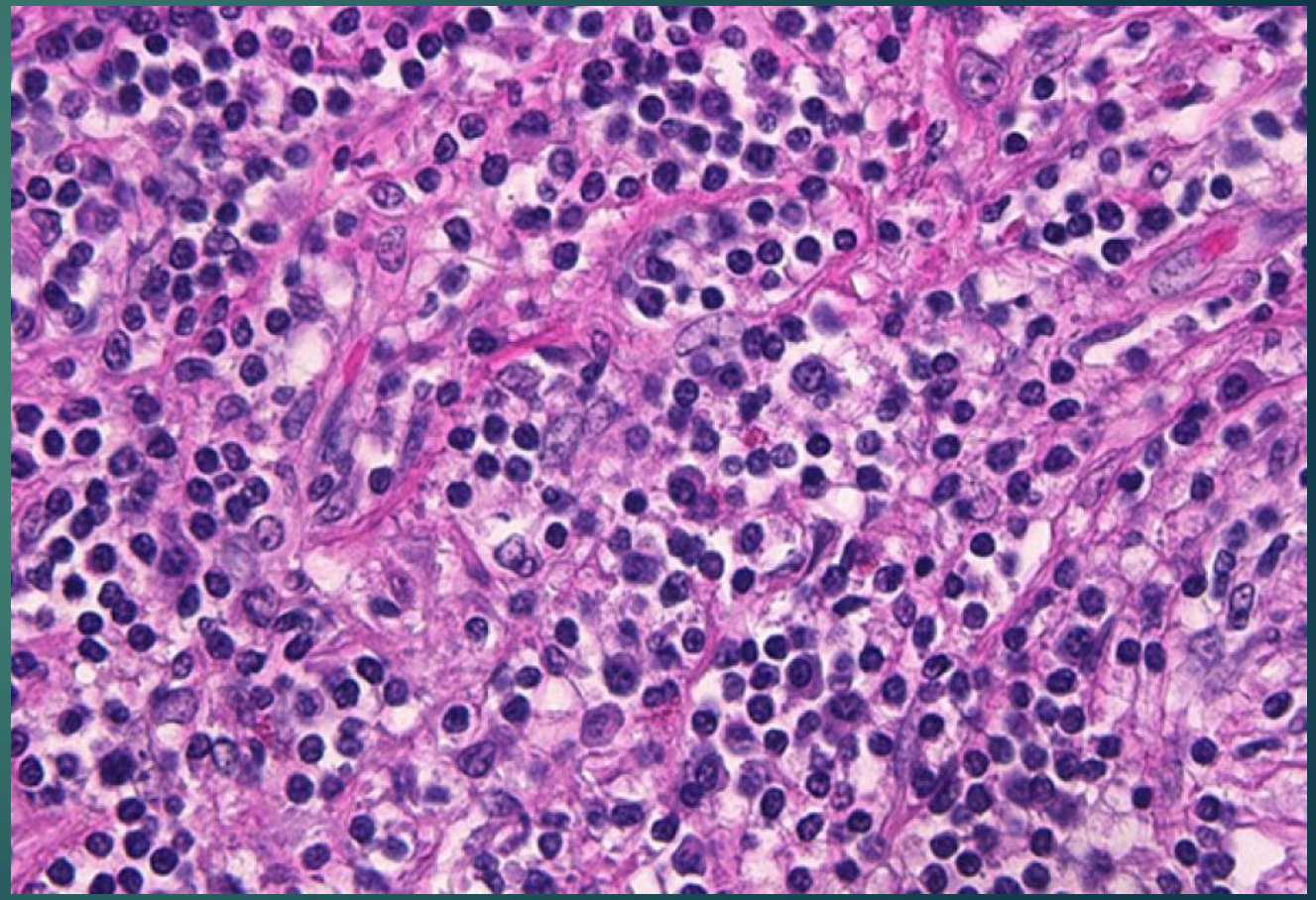
IgG4-RKD
Histopathologic findings

- **Border** between the TIN-region and normal region is **clear**



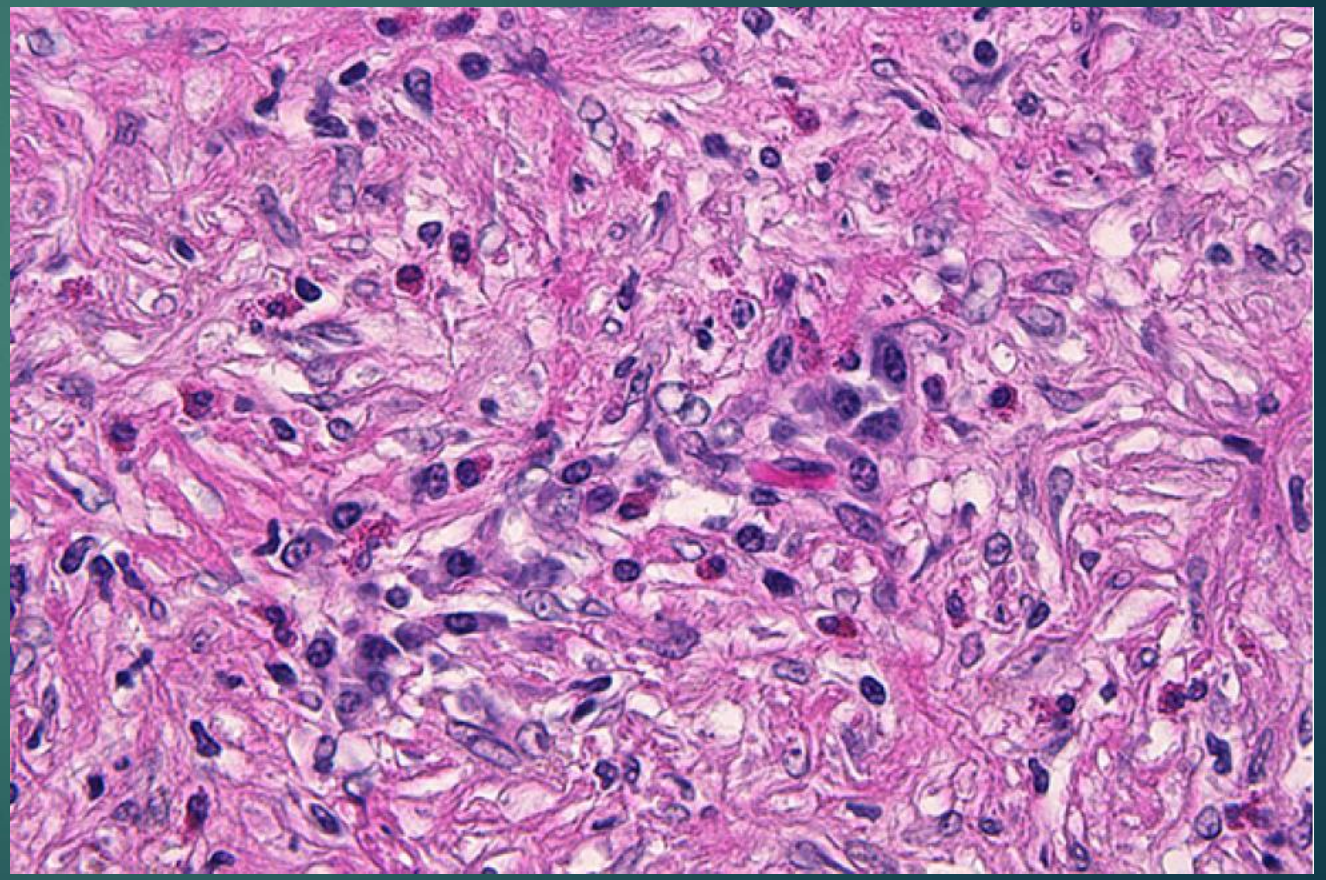
IgG4-RKD
Histopathologic findings

- Plasma cells and lymphocytes



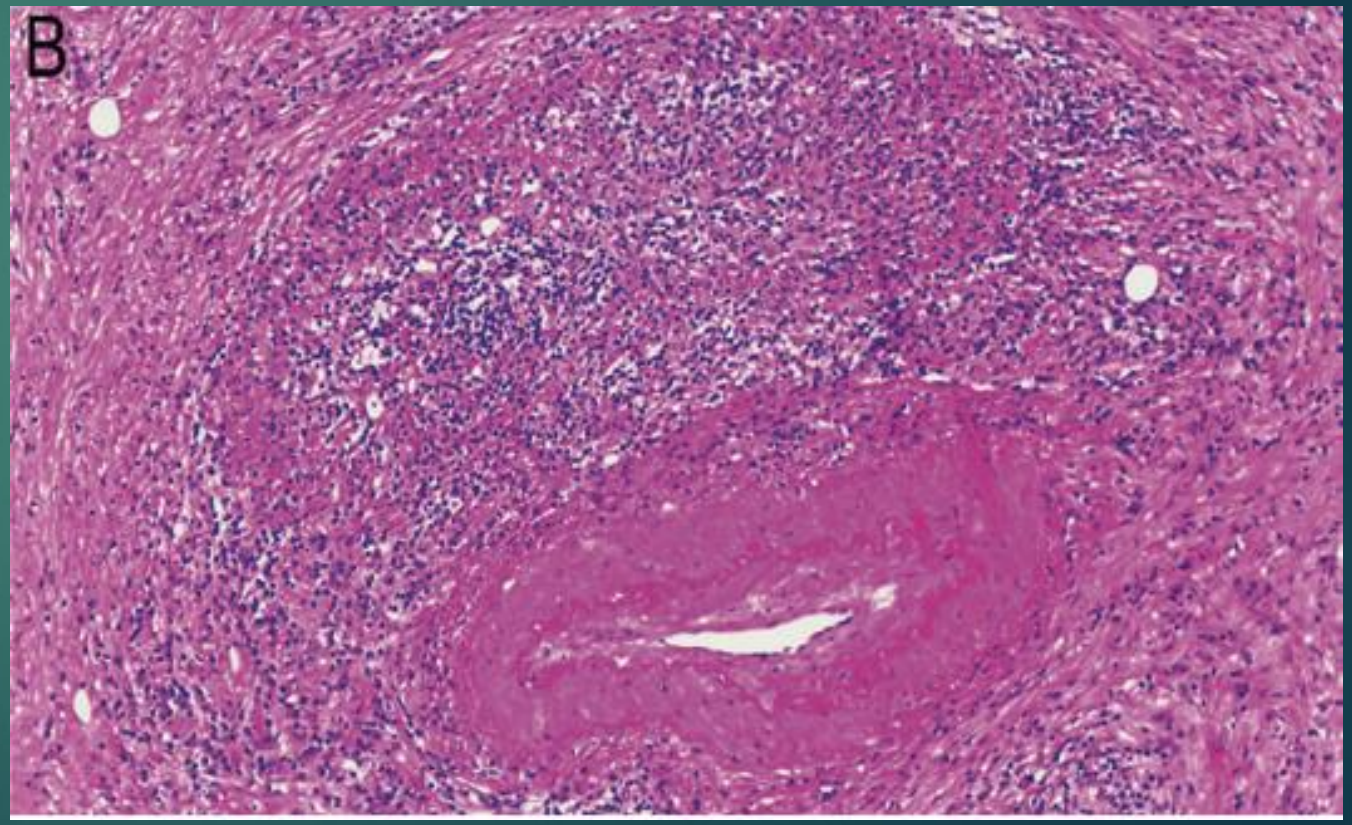
IgG4-RKD
Histopathologic findings

- Eosinophilic infiltration



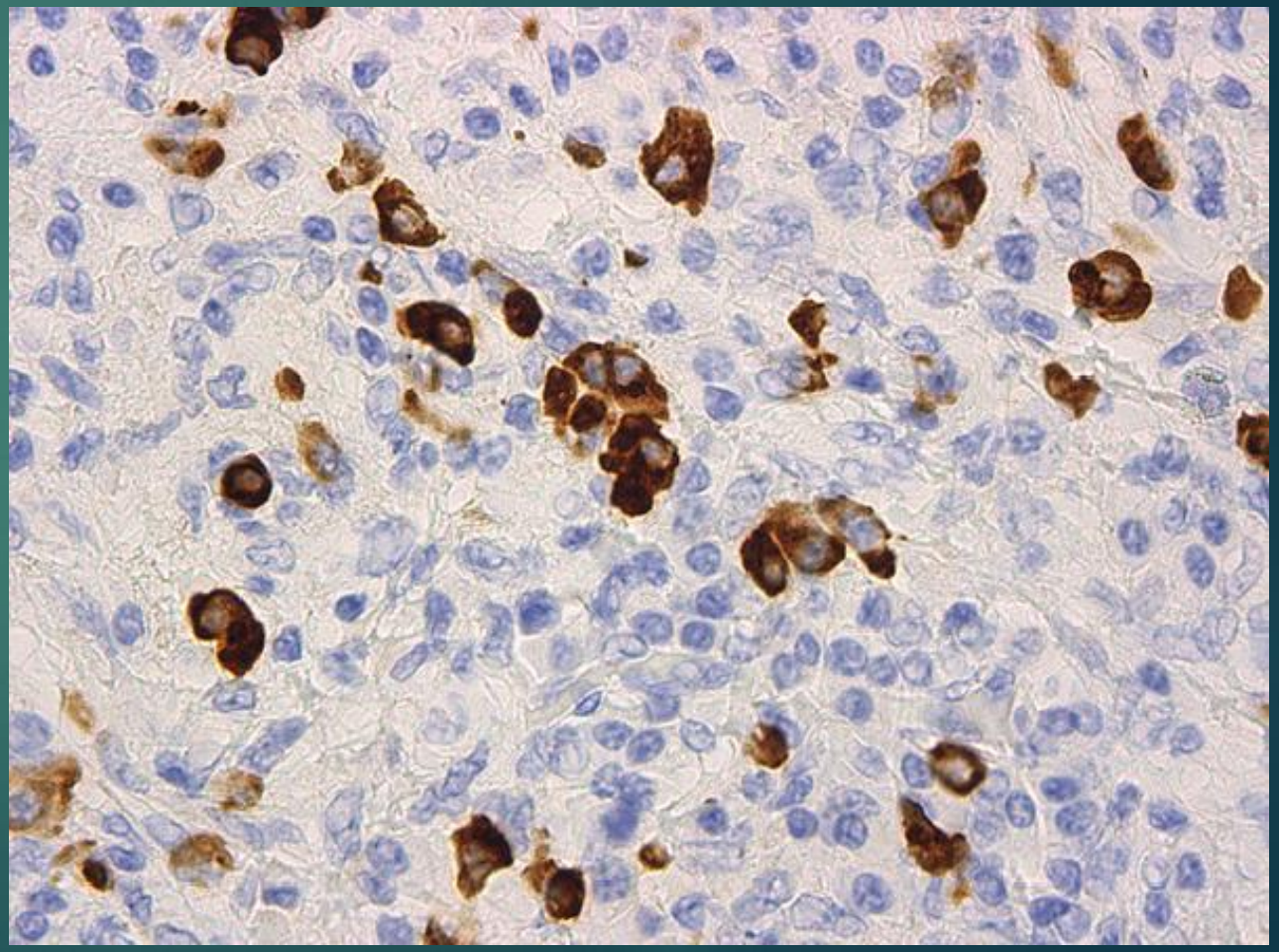
IgG4-RKD
Histopathologic findings

- Obliterative phlebitis
- Rarely in kidney biopsy!



IgG4-RKD
Histopathologic findings

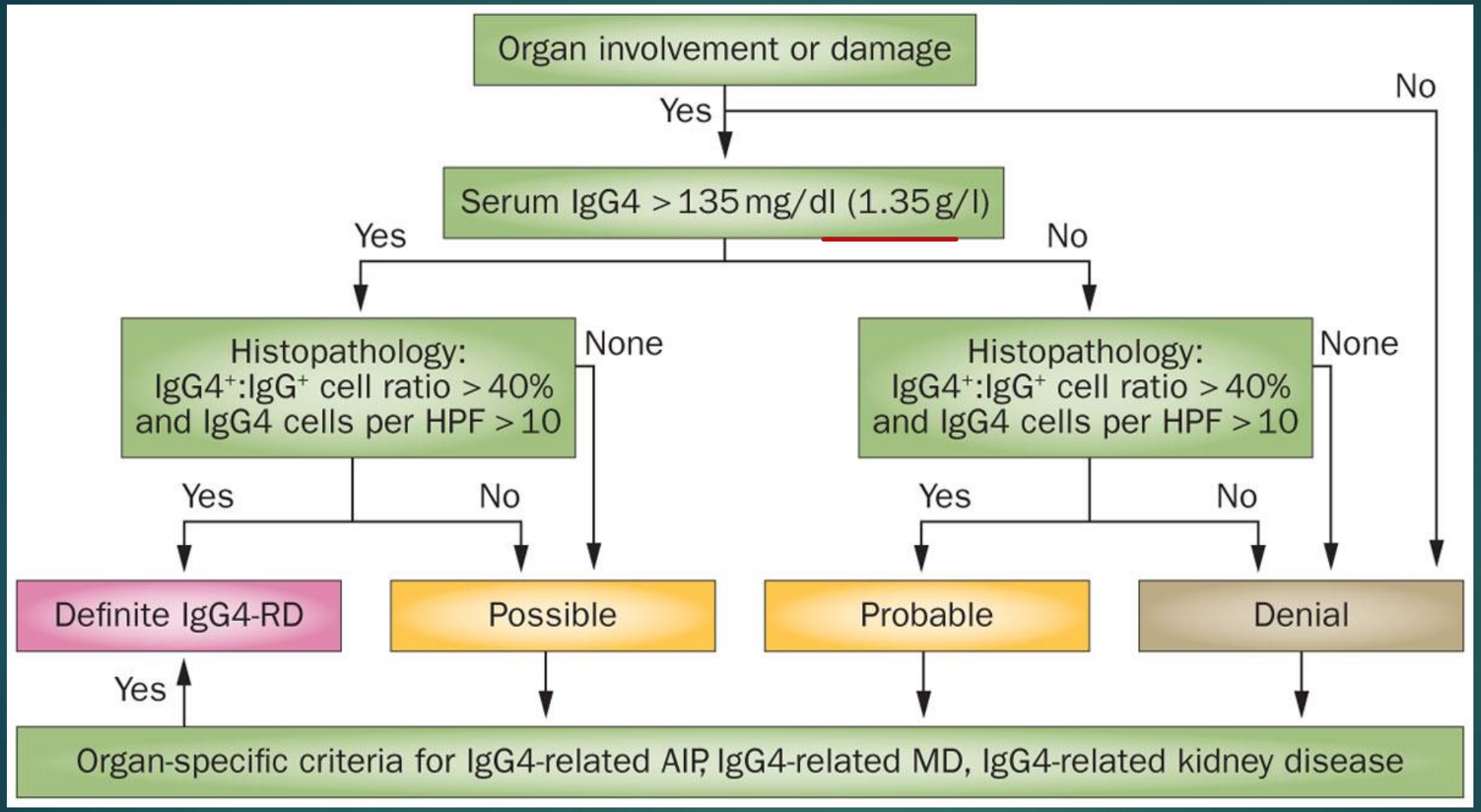
- Immunohistochemistry:
  IgG4 positive plasma cells



Diagnosis

- S-IgG4 > 1,40 g/l:
  - sensitivity 60-70 %
  - specificity 60 %
  - positive predictive value 34 %
  - negatiive predictive value 96 % (Carruthers et al. 2014)
- Histopathology is crucial
  - Dense lymphoplasmacytic infiltration
  - Storiform fibrosis
  - Obliterative phlebitis
  - Often eosinophilia
- Immunostaining IgG4/IgG-proportion >40 %
- NOTA BENE! Granulomatotic imflammation is not typical for IgG4-RD

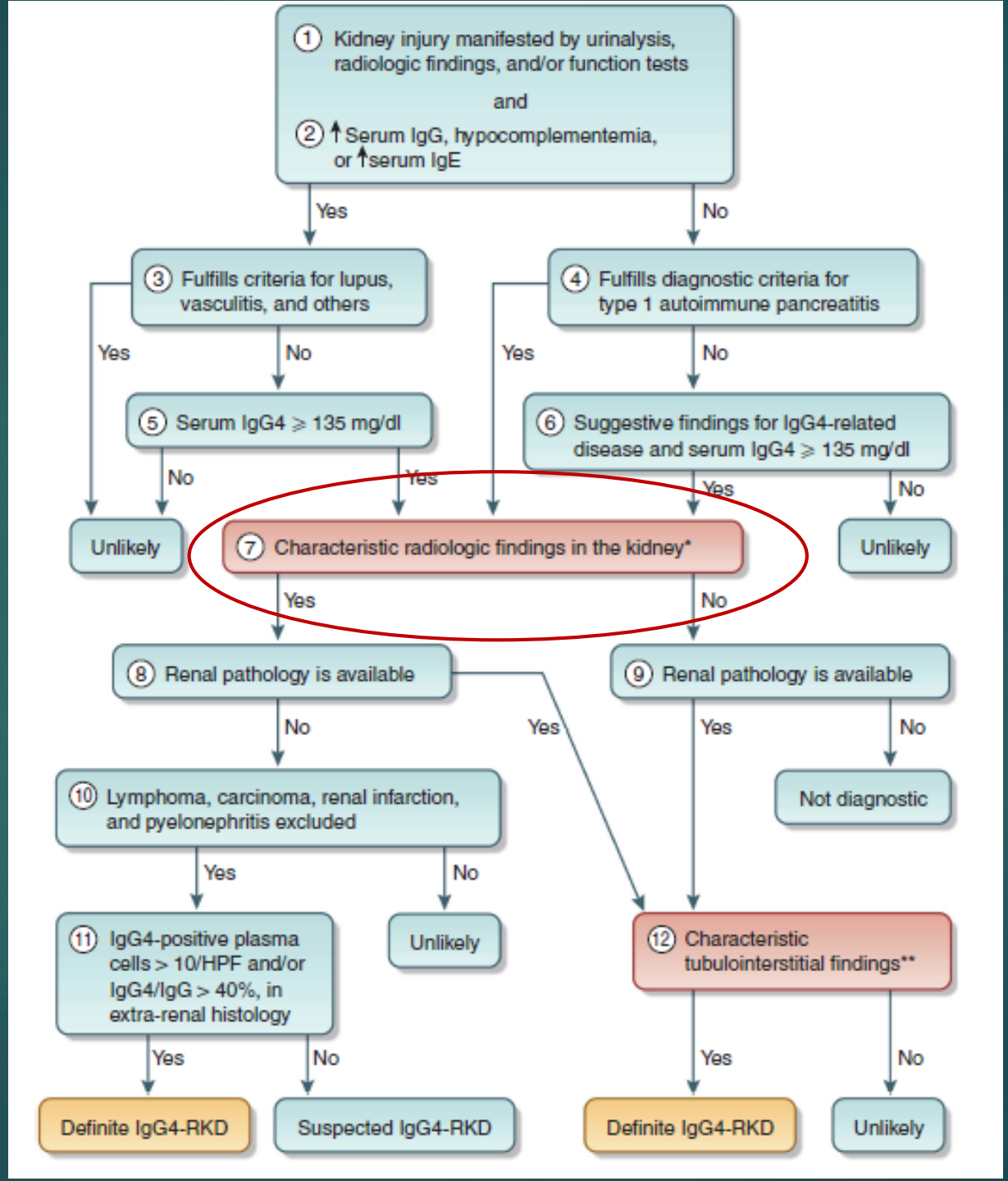
IgG4-RD diagnostic algorithm



Clinics + serology + histopathology = definite
Clinics + histopathology = probable
Clinics + serology = possible

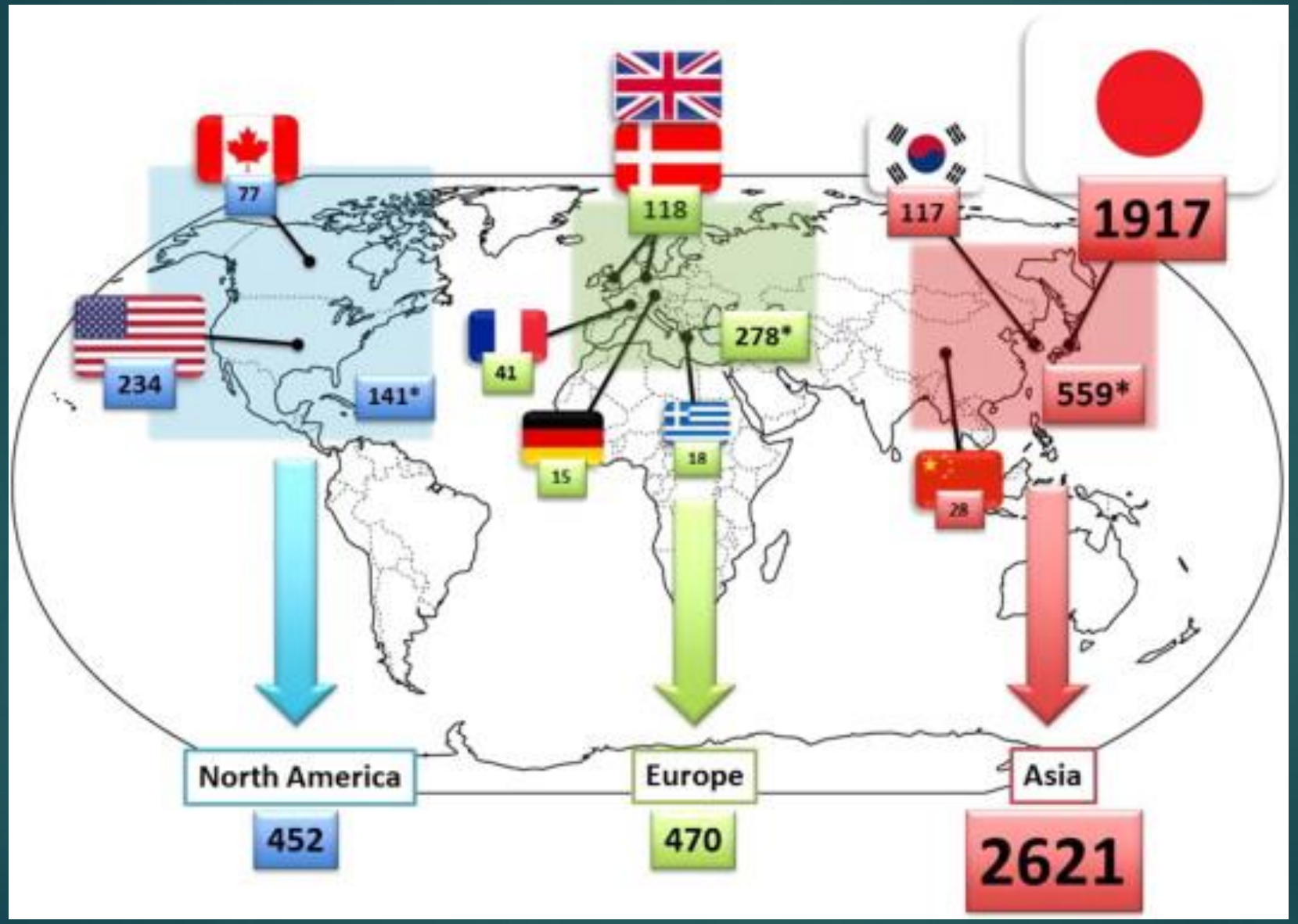
Yamamoto, M. *et al. Nat. Rev. Rheumatol.* 2013.

IgG4-RKD diagnostic algorithm



Kawano M. *et al. Clin Exp Nephrol.* 2011.

Prevalence of IgG4-RD



Pilar Brito-Zerón et al. The clinical spectrum of IgG4-related disease Autoimmunity Reviews, 2014

Treatment 1

- Corticosteroids - almost always good response
  - Prednisolone 0,6 mg/kg/day 2-4 weeks
  - Gradual dose reduction ad 5 mg after 3-6 months.
  - Continuation 2,5-5 mg/vrk for 3 years
- Reduction of IgG4-levels
- Relapses in 20-30 %

Treatment 2

- Another immunosuppressive medicine if corticosteroids fail or intolerance
  - azathioprine first line
  - Alternative: mycophenolate, methotrexate, even bortezomib
- Lack of prospective data
- Risk of malignancy X 3.5!
- Treatment of resistant disease: rituximab
  - (Khosroshahi A et al. Arthritis Rheum 2010;62:1755-62.)

Rituximab in IgG4-RD

- 30 patients
- Rituximab 1000 mg, 2 doses
- 87 % did not use corticosteroids, in 13 % corticosteroids had been paused for at least 2 months
- Treatment response in 97 %
- Complete remission after 6 months 77 %, 12 months 40 %
- Conclusion: Rituximab is efficient in IgG4-RD, also without concomitant corticosteroid treatment

*Carruthers MN et al. Ann Rheum Dis Febr 2015, epub

Case report

78-year-old man

- COPD, asthma, longtime smoker, alcohol abstinence since 1990, nursing aid at home, physically inactive, good cognition

- 2/2012 serum creatinine normal 86 umol/liter
- 11/2013 creatinine 161
- 3/2014 creatinine increase to 226

- Anemia, Creatinine, high sed rate
  → referred to consultant in March 2014

Ikä ajopäivänä 78 v
VERIRYHMÄ: Ei tiedossa
VERIRYHMÄVASTA-AINEET: Ei tiedossa

			B-Hb	B-HKR	B-Eryt	MCV	RDW	MCH
PERUSVERENKUVA			134-167	39-50	4.25-5.7	82-98	<14	27-33
			g/l	%	E12/l	fl	%	pg
4102	22.04.14	1042	113	33	3.75	89	14	30

			MCHC	B-Leuk	B-Trom
			320-355	3.4-8.2	150-360
			g/l	E9/l	E9/l
4102	22.04.14	1042	339	12.0	389

			B-Neut	Neut	B-Ly	Lymf	B-Mono	Mono
LEUKOSYYTTIEN ERITTELY (AUTOMAAT.)			1.5-6.7	41-81	1.3-3.6	20-45	0.2-0.8	1-11
			E9/l	%	E9/l	%	E9/l	%
4102	22.04.14	1042	6.17	52	3.24	27	1.21	10

			B-Eos	Eos	B-Baso	Baso	Erblast
			0.03-0.44	1-6	0-0.1	0-1	
			E9/l	%	E9/l	%	E9/l
4102	22.04.14	1042	1.13	9	0.20	2	0.00

			P-CRP	B-La	P-K	P-Na	S-pH
AKUUTTI VAIHE, NESTETASAPAINO			<3	<30	3.3-4.9	137-145	
			mg/l	mm/h	mmol/l	mmol/l	
4102	22.04.14	1042	10	95	3.9	134	7.31

			S-Ca-Ion	S-Ca-IonA	P-Krea	Pt-GFRe-MD
			1.16-1.3		60-100	>60 ml/min/1.73m2
			mmol/l/pH7.4	mmol/l	umol/l	
4102	22.04.14	1042	1.18	1.24	234	24 ml/min/1.73m2

Tuloskertymä (Jatkuva)
Ajalta: 22.04.2014 - 22.04.2014
Ajoaika: 13.05.2015 10:13

Ikä ajopäivänä 78 v

			P-AFOS	S-IgLcK-V	S-IgLcL-V	S-K/L-s-V
KEMIALLISET TUTKIMUKSET			35-105	6.9-25.6	8.6-26.5	0.52-1.4
			U/l	mg/l	mg/l	
4102	22.04.14	1042	155	400	183	2.19

Myeloma was suspected
Hematologist was consulted

”One can not outrule that monoclonal kappa light chains could be the underlying cause of kidney failure”

”The next diagnostic procedure should be a kidney biopsy, and from the biopsy an electromicroskopic investigation should be made as well”

Transferred to a nephrologist...

220936-491K Ikä ajopäivänä 78 v
VERIRYHMÄ: Ei tiedossa
VERIRYHMÄVASTA-AINEET: Ei tiedossa

PERUSVERENKUVA	B-Hb	B-HKR	B-Eryt	MCV	RDW	MCH
	134-167	39-50	4.25-5.7	82-98	<14	27-33
	g/l	%	E12/l	fl	%	pg
41121 16.06.14 1004	116	35	3.83	91	15	30

	MCHC	B-Leuk	B-Trom
	320-355	3.4-8.2	150-360
	g/l	E9/l	E9/l
41121 16.06.14 1004	333	11.3	449

AKUUTTI VAIHE, NESTETASAPAINO	P-CRP	B-La	P-K	P-Na	S-pH
	<3	<30	3.3-4.9	137-145	
	mg/l	mm/h	mmol/l	mmol/l	
41121 16.06.14 1004	6	98	4.3	135	7.34

	S-Ca-Ion	S-Ca-IonA	fP-Pi	P-Krea	Pt-GFRe-MD
	1.16-1.3		0.71-1.23	60-100	>60 ml/min/1.73m2
	mmol/l/pH7.4	mmol/l	mmol/l	umol/l	
41121 16.06.14 1004	1.24	1.28	1.03	253	22 ml/min/1.73m2

	P-Alb
	34-45
	g/l
41121 16.06.14 1004	31.8

GLUKOOSITASAPAINO	U-AlbKrea	U-Alb	U-Krea	B-HbA1c	B-GHb-A1C
	<2.5	<25	2.3-23.5	20-42	4-6
	mg/mmol	mg/l	mmol/l	mmol/mol	%
41121 16.06.14 1004	8.8	38	4.4	39	5.7

HORMONIT,VITAMIINIT, KASVAINMERKKIAINEET	fP-PTH 15-65 ng/l	S-Aldos-P <520 pmol/l
41121 16.06.14 1004	36	490

ALLERGIATUTKIMUKSET	S-IgE 0-110 kU/l	S-ECP <16 ug/l
41121 16.06.14 1004	493	8.8

VIRTSAN SEULONTA	Ottotapa	Rakkoa	Gluk	Keto	Suhti	pH	Hb	Prot	Nitr
41121 16.06.14 1004	Keskisuihkuvirtsa	3 h	neg	neg	1.015	6.0	+	+	neg

	Leuk
41121 16.06.14 1004	neg

VIRTSAN SOLUT	Ottotapa	Rakkoa	Eryt <20 E6/l	Leuk <10 E6/l	Epit <10 E6/l
41121 16.06.14 1004	Keskisuihkuvirtsa	3 h	8	1	1

LEUKOSYYTTIEN ERITTELY (AUTOMAAT.)	B-Neut 1.5-6.7 E9/l	Neut 41-81 %	B-Ly 1.3-3.6 E9/l	Lymf 20-45 %	B-Mono 0.2-0.8 E9/l	Mono 1-11 %
4101 08.05.14 0716	4.47	52	2.04	24	0.88	10

	B-Eos 0.03-0.44 E9/l	Eos 1-6 %	B-Baso 0-0.1 E9/l	Baso 0-1 %	Erblast E9/l
4101 08.05.14 0716	1.11	13	0.14	2	0.00

vB-HAPPOEMÄSTASE, -pO2 ja oksimetria		pH	pCO2	pO2	Be	HCO3-St
		7.32-7.42	5.3-7.3 kPa	4-6.7 kPa	-2.5-2.5 mmol/l	24-28 mmol/l
41121	16.06.14 1004	7.33	5.3	3.1	-4.4	21

KEMIALLISET TUTKIMUKSET		P-AFOS	P-ALAT	P-Urea	S-IgG1	S-IgG2	S-IgG3
		35-105 U/l	10-70 U/l	3.5-8.1 mmol/l	4.9-11.4 g/l	1.5-6.4 g/l	0.2-1.1 g/l
41121	16.06.14 1004	166	37	13.0	16.2	0.99	0.72

16.06.14 1004 Lausunto S-IgG-Sc : IgG4-taso vahvasti koholla, Myös IgG1-taso koholla. Vahvasti koholla oleva IgG4-taso haittaa myös muiden alaluokkien määritystä. Tämä näkyy siinä että alaluokkien summa on korkeampi kuin kokonais-IgG.
(Hanna Jarva)

		S-IgG4	P-C3	P-C4
		0.08-1.4 g/l	0.71-1.41 g/l	0.12-0.34 g/l
41121	16.06.14 1004	43.1	1.10	0.16

IMMUNOLOGIA		S-ANAAb	S-DNAAb
		<320 titteri	<10 IU/ml
41121	16.06.14 1005	<80	<10

VASKULIITIT		S-ANCA	S-Pr3AbG	S-MPOAbG	S-C-ANCIF	S-P-ANCIF
			<2 IU/ml	<3.5 IU/ml	<20 Titteri	<20 Titteri
41121	16.06.14 1005	Lausunto	<1	<1	<20	<20

16.06.14 1005 Lausunto S-ANCA : Normaali löydös. Ei vaskuliittiin viittaavaa.
(Antti Väkevä)

Radiological findings - Ultrasound

- Kidney size slightly reduced 9 cm
- The kidney parenchyma is also reduced
- A large gall stone
- The intrahepatic ducts were enlarged
- The liver was irregular
- Poor visibility of the pancreas

First visit to the nephrologist 27.6.14

"Female confidant was present"

"Clinical investigation did not yield any significant findings. Cachexia, weight 59 kilogram"

"Did not wish to undergo kidney biopsy"

How should we continue??????

First visit to the nephrologist 27.6.14

"Female confidant was present"

"Clinical investigation did not yield any significant findings. Cachexia, weight 59 kilogram"

"Did not wish to undergo kidney biopsy"

"Prednisolone 40 mg X 1 was started"

Anything else???

First visit to the nephrologist 27.6.14

"Female confidant was present"

"Clinical investigation did not yield any significant findings. Cachexia, weight 59 kilogram"

"Did not wish to undergo kidney biopsy"

"Prednisolone 40 mg X 1 was commenced

Calcium + vitamin D3 increased to 500 mg/400 IU X 2
Pantoprazole 20 mg X 1"

"Follow-up every 2-4 months…

Les feuilles mortes...

I´m dreaming of a white christmas...

I love Paris in the springtime...

Visit to the nephrologist 4.4.15

"Female confidant was present again"

"The patient was very content with the situation, weight increased by 10 kg"

"Media otitis a few times"

"Prednisolone had been reduced to 7.5 mg X 1
Calcium + vitamin D3 continues 500 mg/400 IU X 2
Pantoprazole 20 mg X 1"

PERUSVERENKUVA

	B-Hb	B-HKR	B-Eryt	MCV	RDW	MCH
	134-167	39-50	4.25-5.7	82-98	<14	27-33
	g/l	%	E12/l	fl	%	pg
41121 30.03.15 0934	135	38	4.23	91	14	32

	MCHC	B-Leuk	B-Trom
	320-355	3.4-8.2	150-360
	g/l	E9/l	E9/l
41121 30.03.15 0934	352	13.5	344

AKUUTTI VAIHE, NESTETASAPAINO

	P-CRP	B-La	P-K	P-Na	S-pH
	<3	<30	3.3-4.9	137-145	
	mg/l	mm/h	mmol/l	mmol/l	
41121 30.03.15 0934	3	18	4.2	137	7.46

	S-Ca-Ion	S-Ca-IonA	P-Mg	fP-Pi	P-Krea
	1.16-1.3		0.71-0.94	0.71-1.23	60-100
	mmol/l/pH7.4	mmol/l	mmol/l	mmol/l	umol/l
41121 30.03.15 0934	1.25	1.22	0.91	1.01	235

	Pt-GFReEPI	P-Alb
	>83 ml/min/1.73m2	34-45
		g/l
41121 30.03.15 0934	22 ml/min/1.73 m2	40.3

GLUKOOSITASAPAINO

	U-AlbKrea	U-Alb	U-Krea	B-HbA1c	B-GHb-A1C
	<2.5	<25	2.3-23.5	20-42	4-6
	mg/mmol	mg/l	mmol/l	mmol/mol	%
41121 30.03.15 0715	5.1	32	6.3		
41121 30.03.15 0934				40	5.9

vB-HAPPOEMÄSTASE, -pO2 ja oksimetria	pH	pCO2	pO2	Be	HCO3-St
	7.32-7.42	5.3-7.3 kPa	4-6.7 kPa	-2.5-2.5 mmol/l	24-28 mmol/l
41121 30.03.15 0934	7.44	4.7	6.1	-0.3	24

MUU HEMATOLOGIA	fP-Trfesat	fP-Fe	fP-Transf	P-Ferrit
	17-52 %	9-34 umol/l	1.75-3.13 g/l	10-220 ug/l
41121 30.03.15 0934	37	28.1	2.89	81

KEMIALLISET TUTKIMUKSET	P-AFOS	P-ALAT	P-Urea	P-Uraat	S-IgG4
	35-105 U/l	<50 U/l	3.5-8.1 mmol/l	230-480 umol/l	0.08-1.4 g/l
41121 30.03.15 0934	42	27	11.6	351	5.60

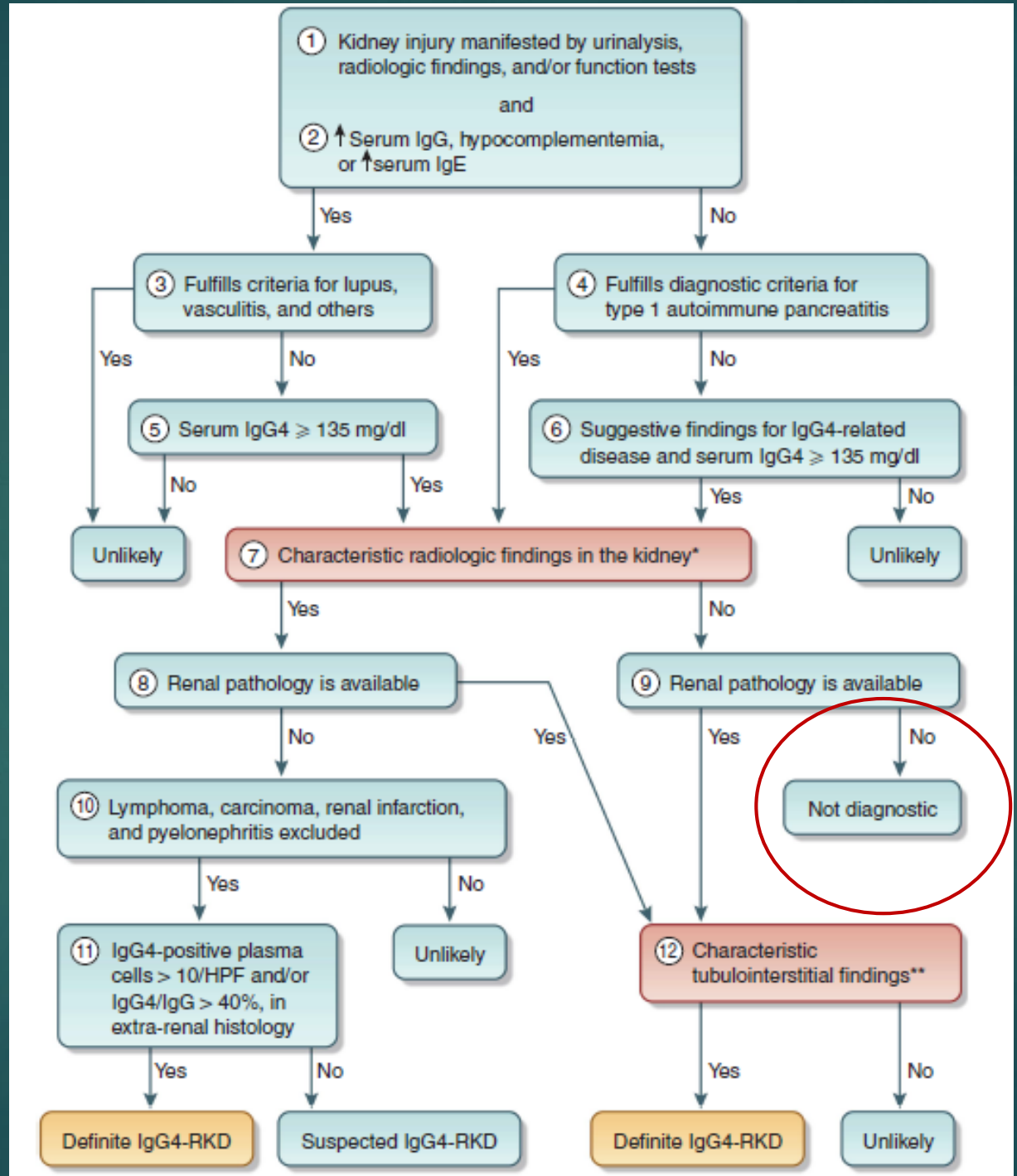
HORMONIT,VITAMIINIT, KASVAINMERKKIAINEET	fP-PTH
	15-65 ng/l
41121 30.03.15 0934	69

VIRTSAN SEULONTA	Ottotapa	Rakkoa	Gluk	Keto	Suhti	pH	Hb	Prot	Nitr
41121 30.03.15 0715	Keskisuihkuvirtsa	>4 h	neg	neg	1.015	6.5	neg	+	neg

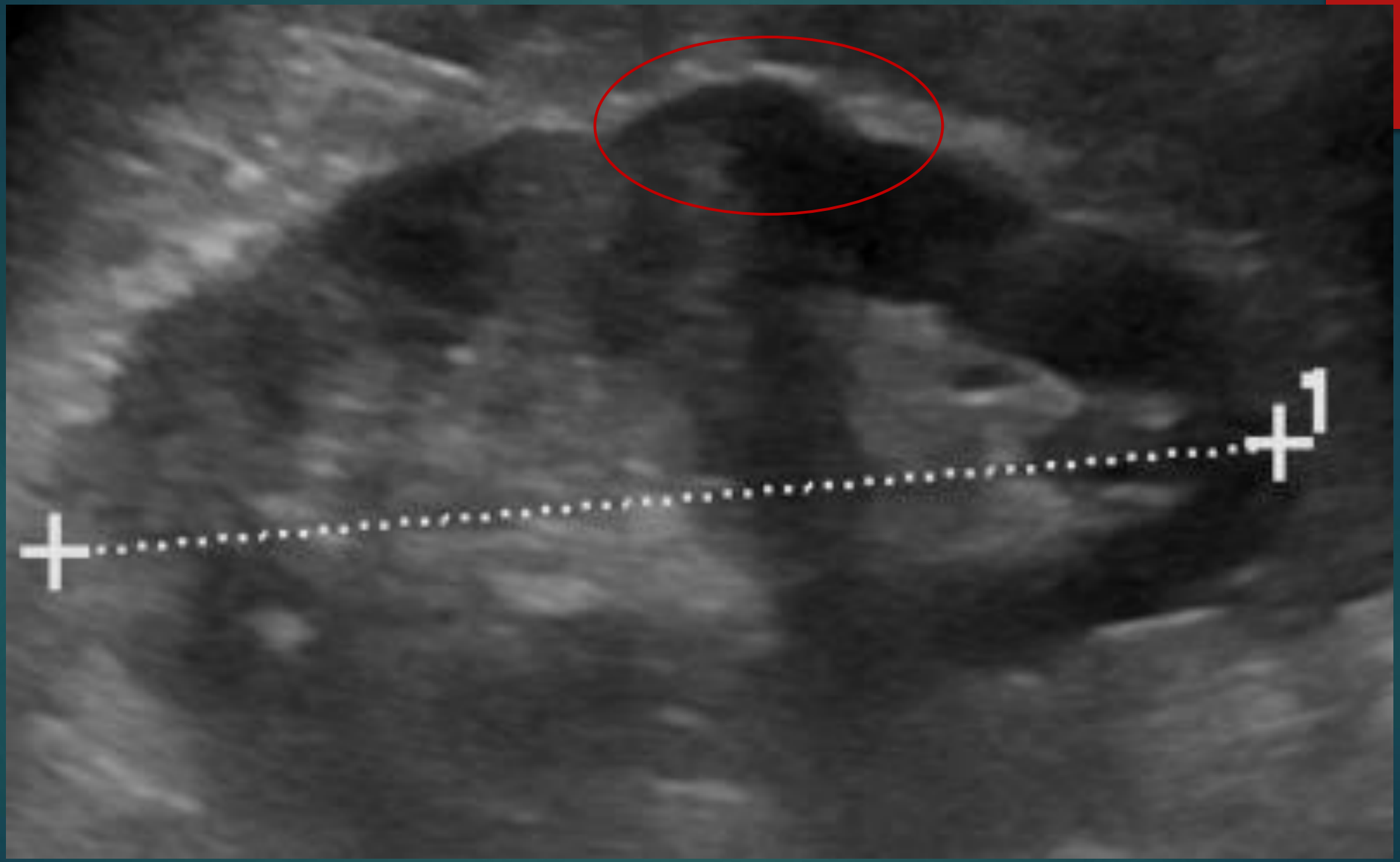
	Leuk
41121 30.03.15 0715	neg

VIRTSAN SOLUT	Ottotapa	Rakkoa	Eryt	Leuk	Epit
			<20 E6/l	<10 E6/l	<10 E6/l
41121 30.03.15 0715	Keskisuihkuvirtsa	>4 h	7	1	3

Was it a definite IgG4-RKD?



Kawano M. *et al. Clin Exp Nephrol.* 2011.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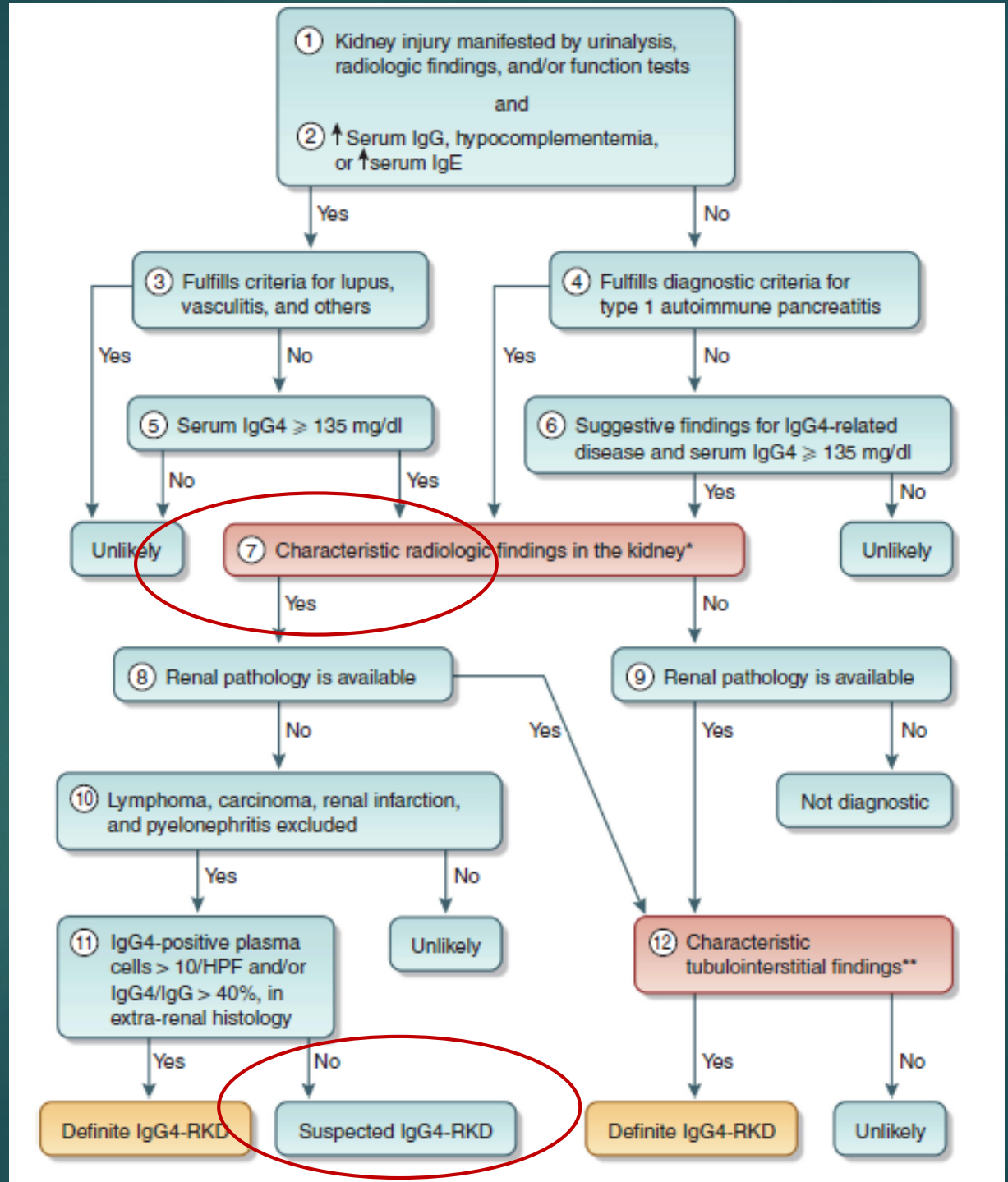


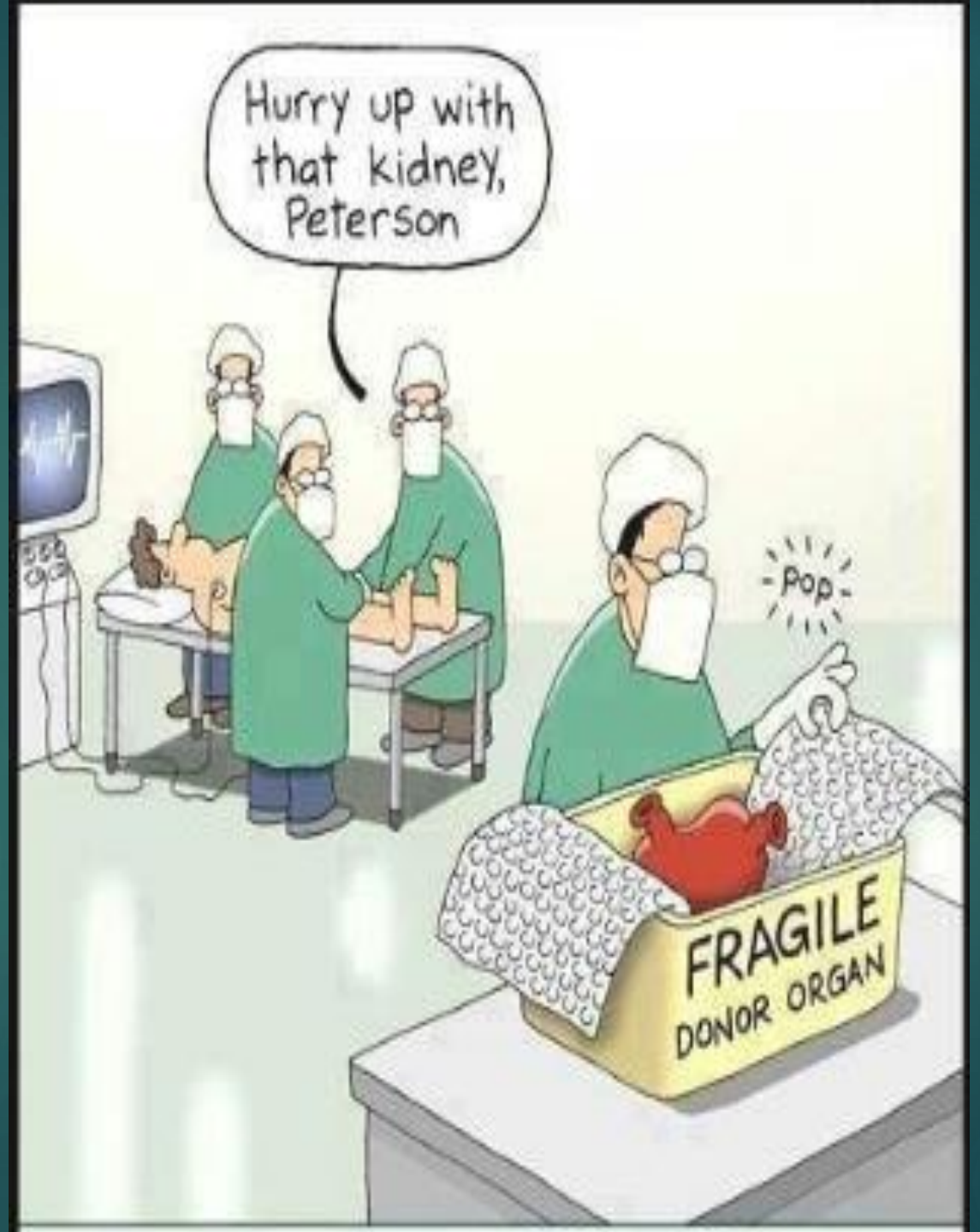
Kawano M. *et al. Clin Exp Nephrol.* 2011.

IgG4-RD - Take home message

1. A systemic fibroinflammatory condition in middle-aged and elderly men.
2. A great "imitator"
3. Most common manifestations: autoimmune pancreatitis, sclerosing cholangitis , Mikulicz' disease, nephropathy
4. Elevated S-IgG4 is a suggestive finding
5. Definite diagnosis is based upon histological and immunohistochemical findings
6. The most important differential diagnoses: other inflammatory diseases, lymphoma and other neoplasms
7. Good response to corticosteroids

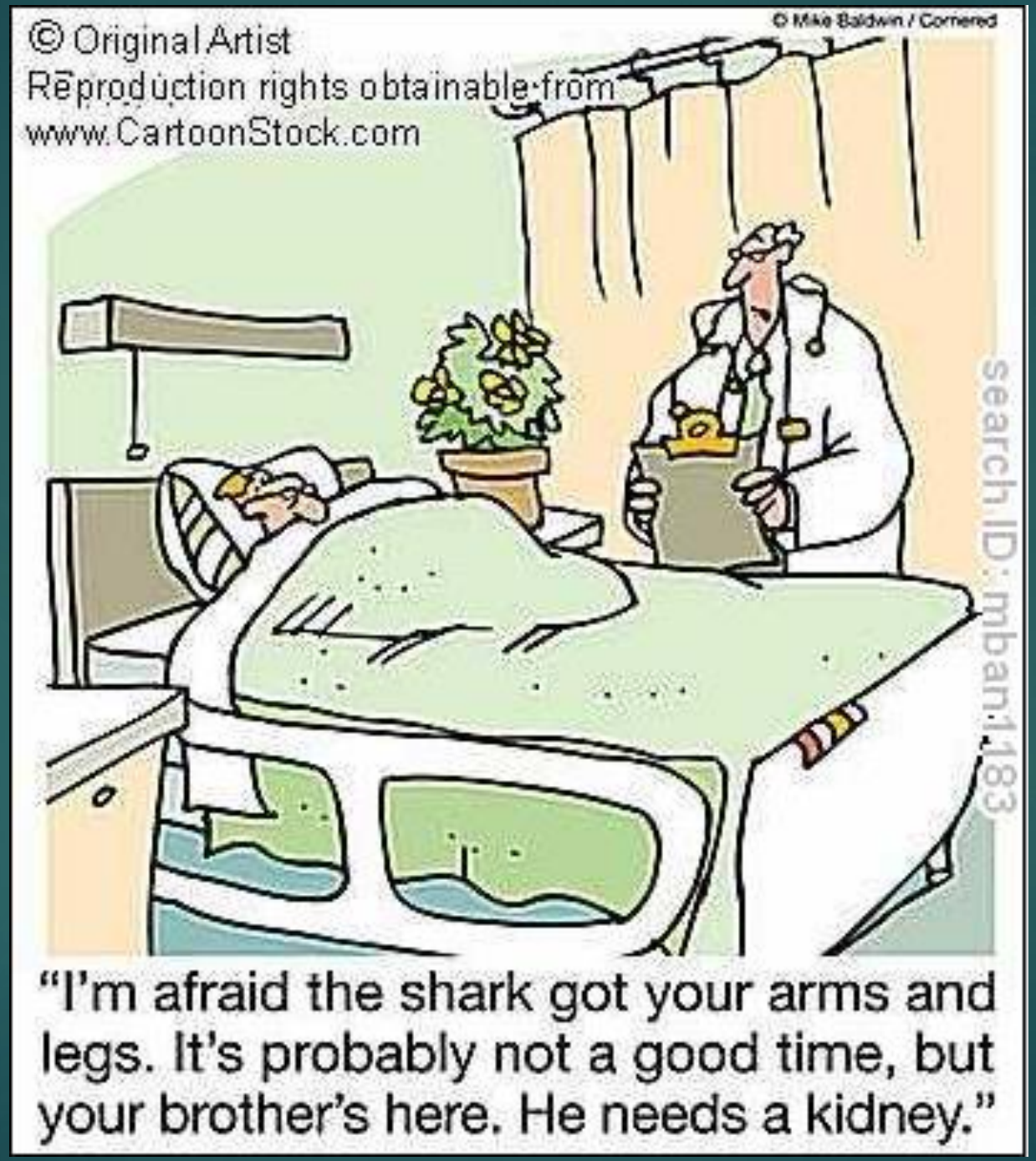
A final clinical quiz…

Diagnosis?



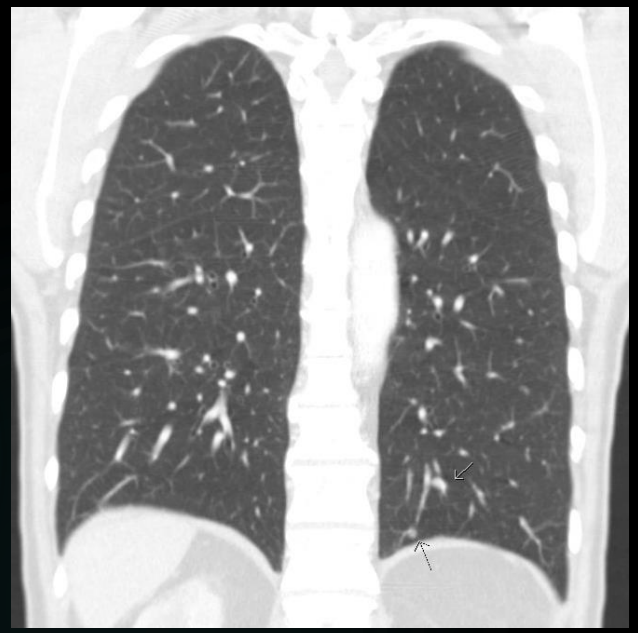

Hurry up with that kidney, Peterson
Pop
FRAGILE
DONOR ORGAN
Obsessive Compressive Disorder: The irresistible urge to burst bubble wrap

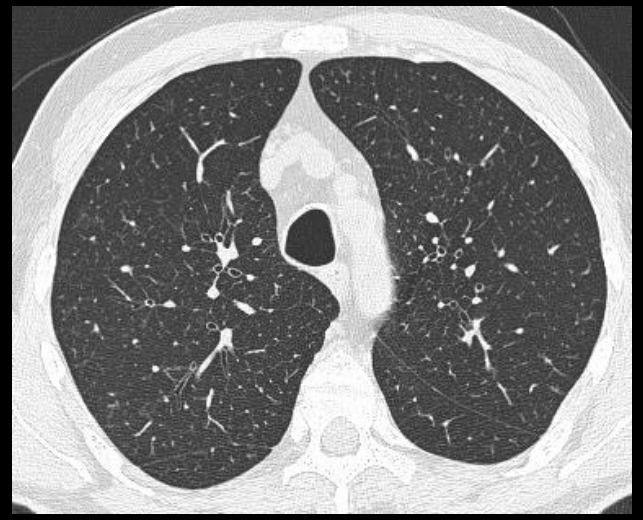
Thank you for your attention!

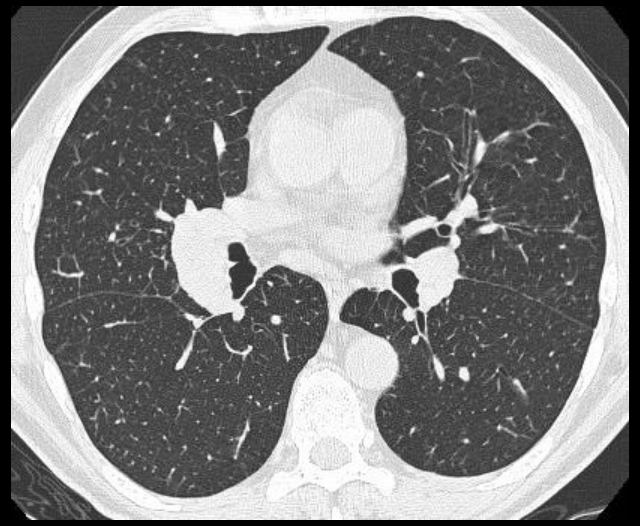


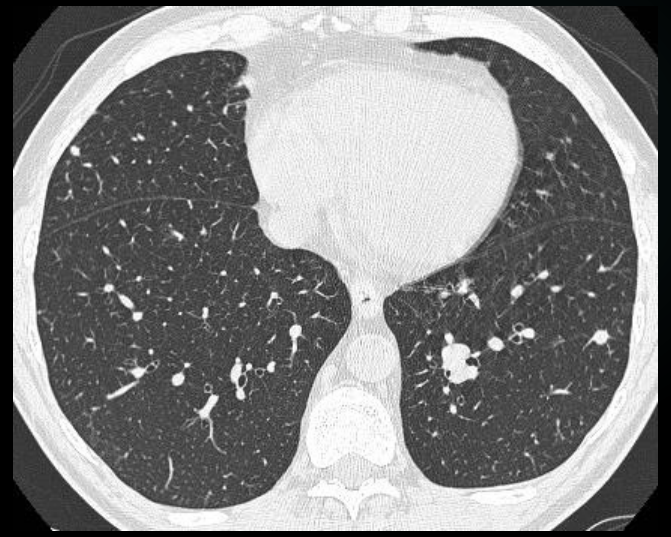
Good luck with your career!

Keuhkoissa retikulaarisia ja nodulaarisia muutoksia









Munuainen

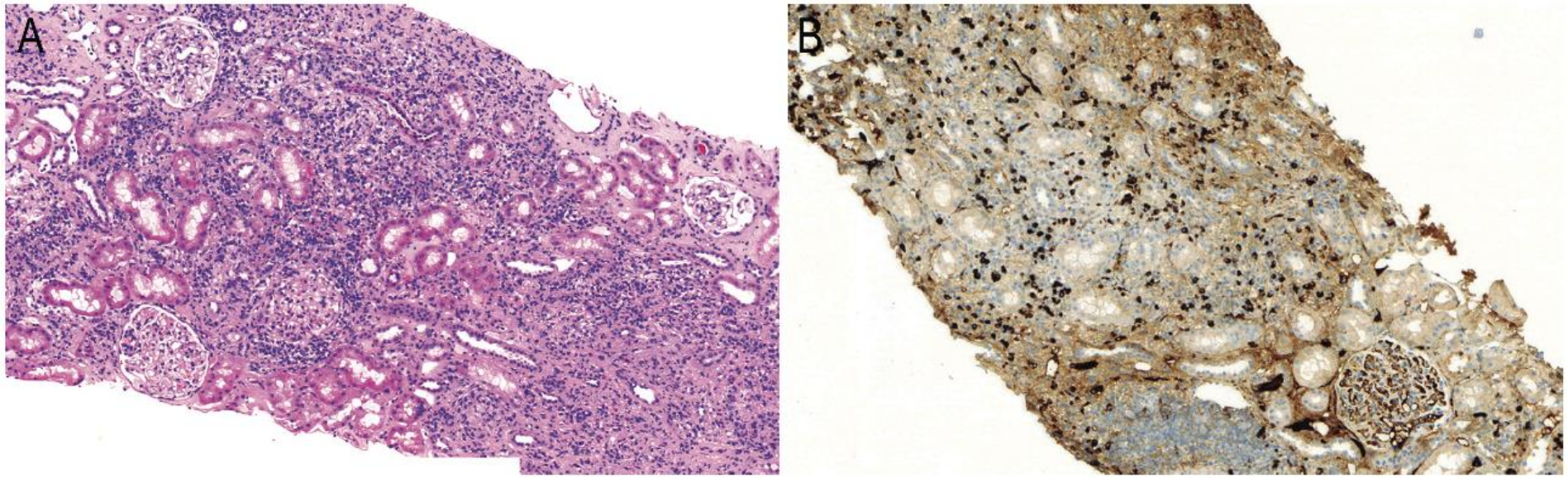
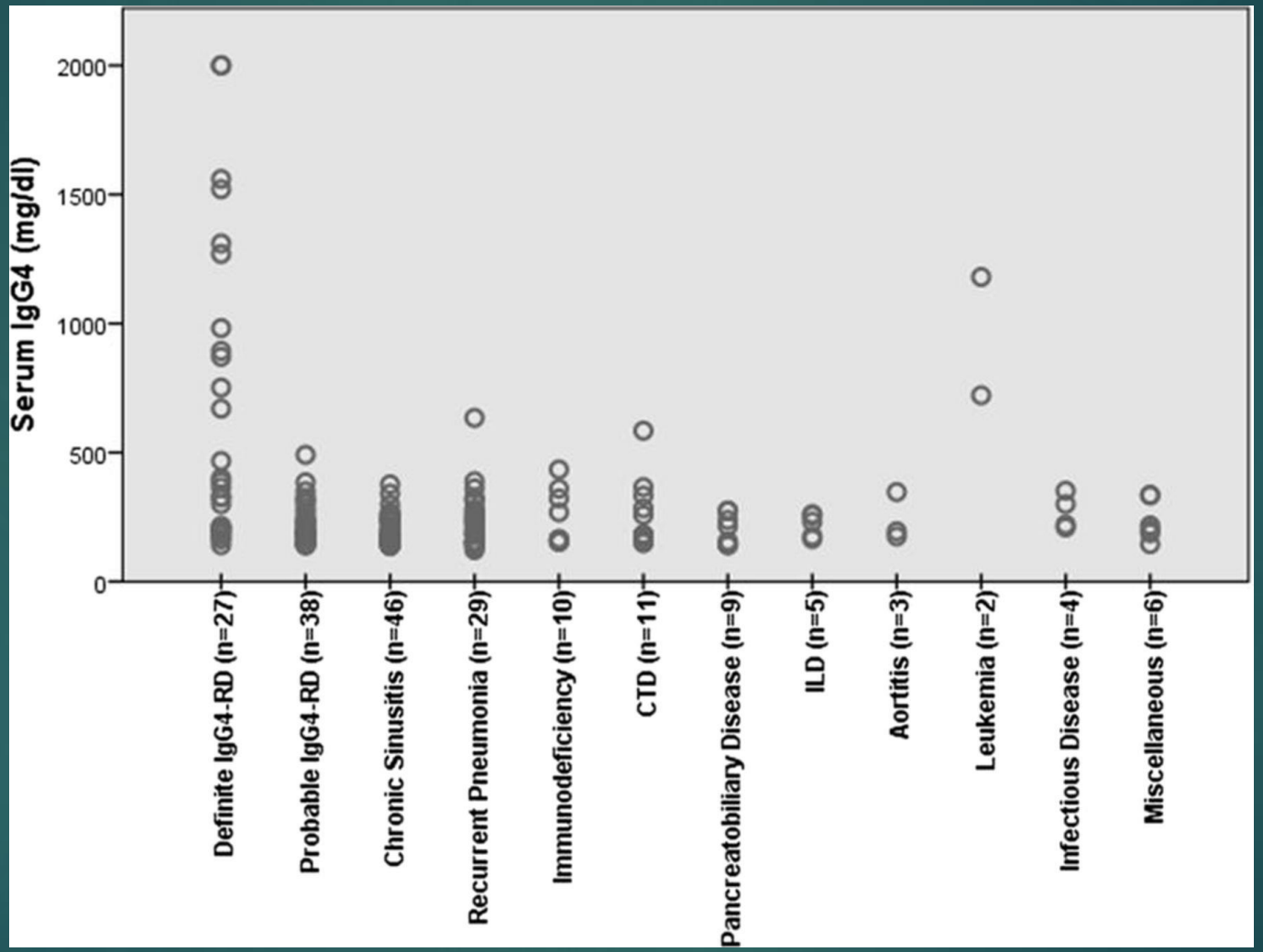


Fig. 10. Tubulointerstitial nephritis (TIN) secondary to IgG4-RD. **A.** Diffuse lymphoplasmacytic infiltration between the tubuli and glomeruli. Atrophy af the renal tissue and fibrosis are noted (H&E). **B.** TIN with less pronounced fibrosis than in Fig. 10A. IgG4-positivity of numerous plasma cells (IgG4 immunostaining).

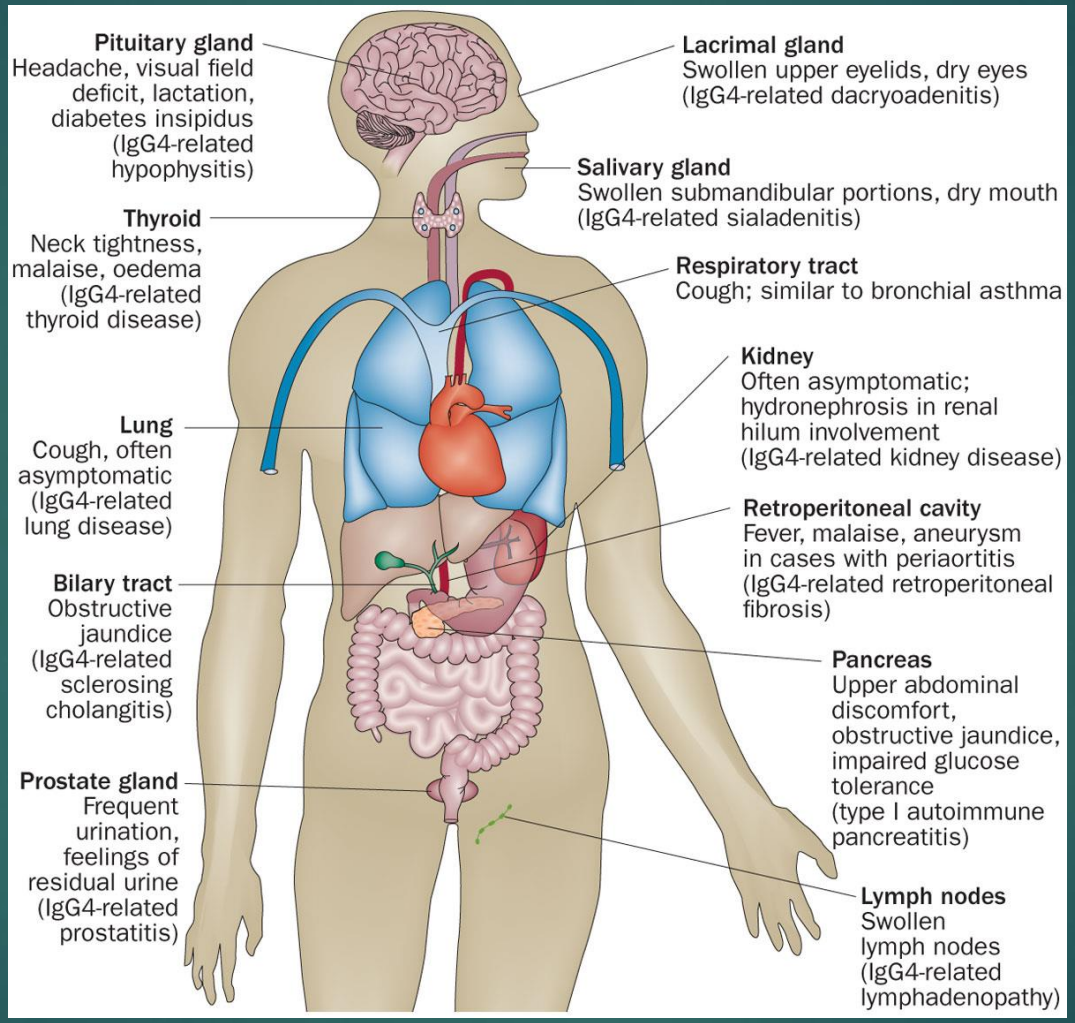
Diseases associated with elevated serum IgG4 levels are shown.



Carruthers M N et al. Ann Rheum Dis
doi:10.1136/annrheumdis-2013-204907

ARD

Systemic organ involvement in IgG4-related disease



Yamamoto, M. *et al.* (2013) Mechanisms and assessment of IgG4-related disease: lessons for the rheumatologist
Nat. Rev. Rheumatol. doi:10.1038/nrrheum.2013.183

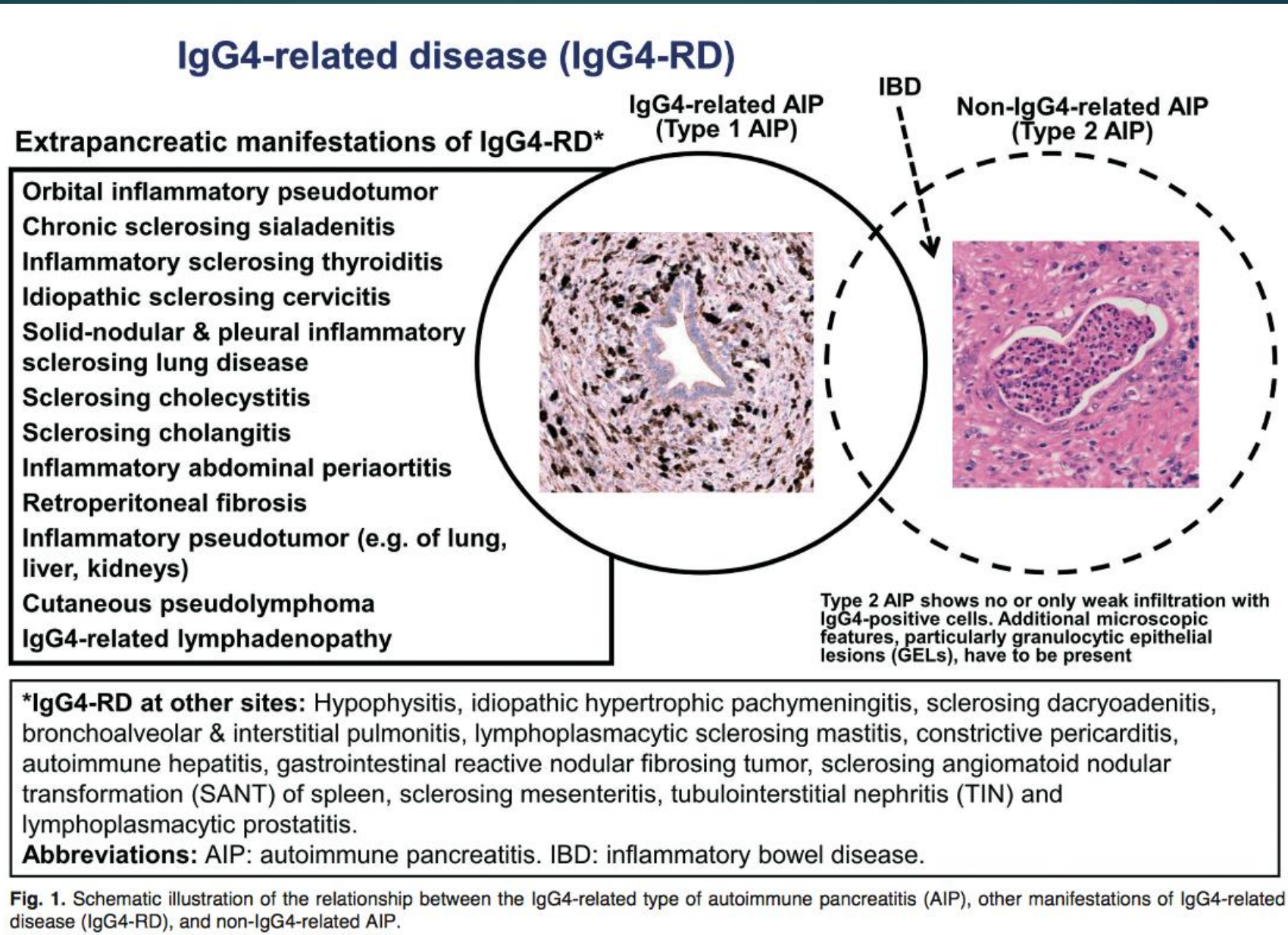


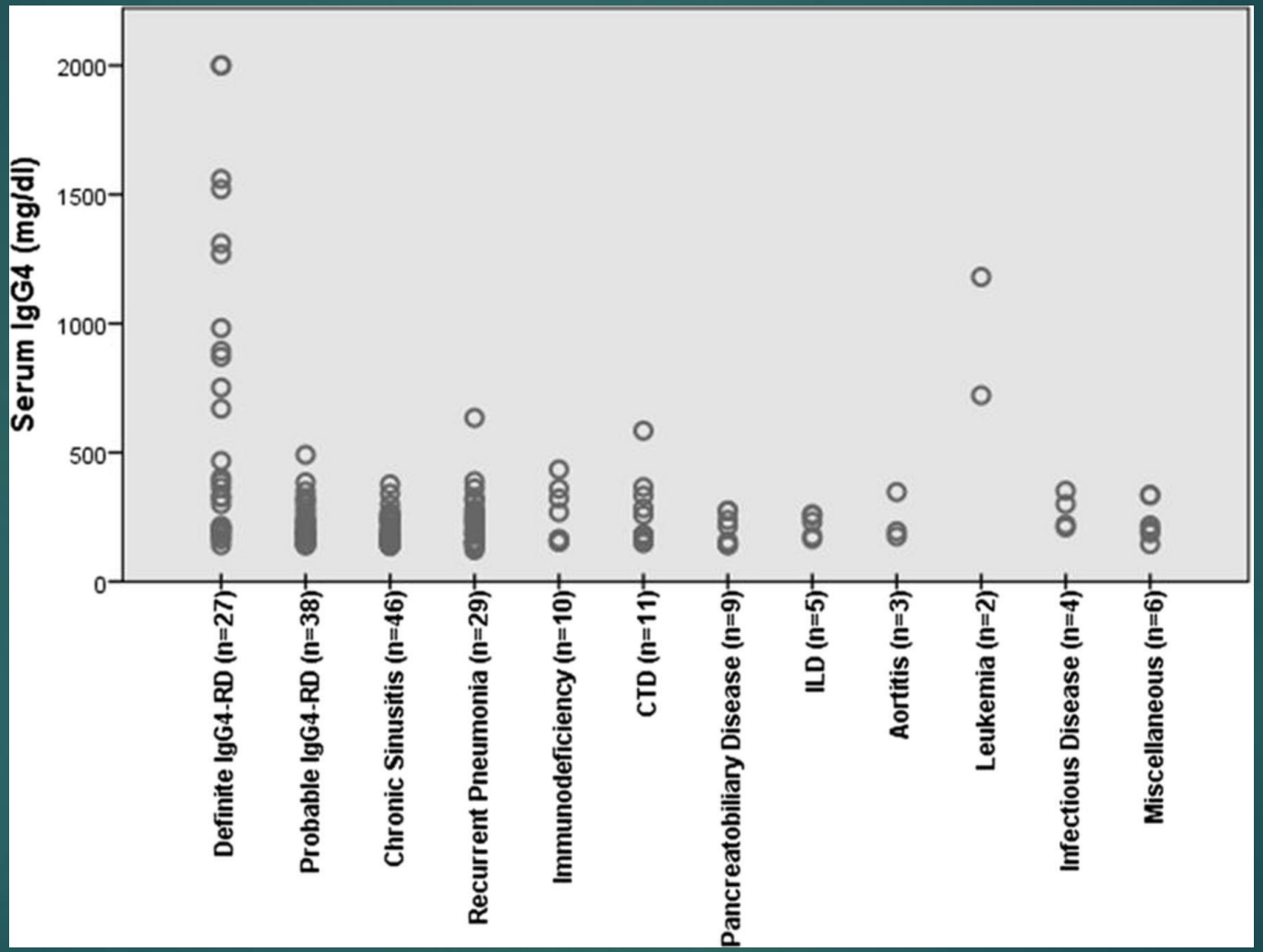
Fig. 1. Schematic illustration of the relationship between the IgG4-related type of autoimmune pancreatitis (AIP), other manifestations of IgG4-related disease (IgG4-RD), and non-IgG4-related AIP.

IgG4-related disease: a systemic condition with characteristic microscopic features.

Detlefsen S.

Histol Histopathol. 2013 May;28(5):565-84. Review.

Diseases associated with elevated serum IgG4 levels are shown.



Carruthers M N et al. Ann Rheum Dis
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ARD

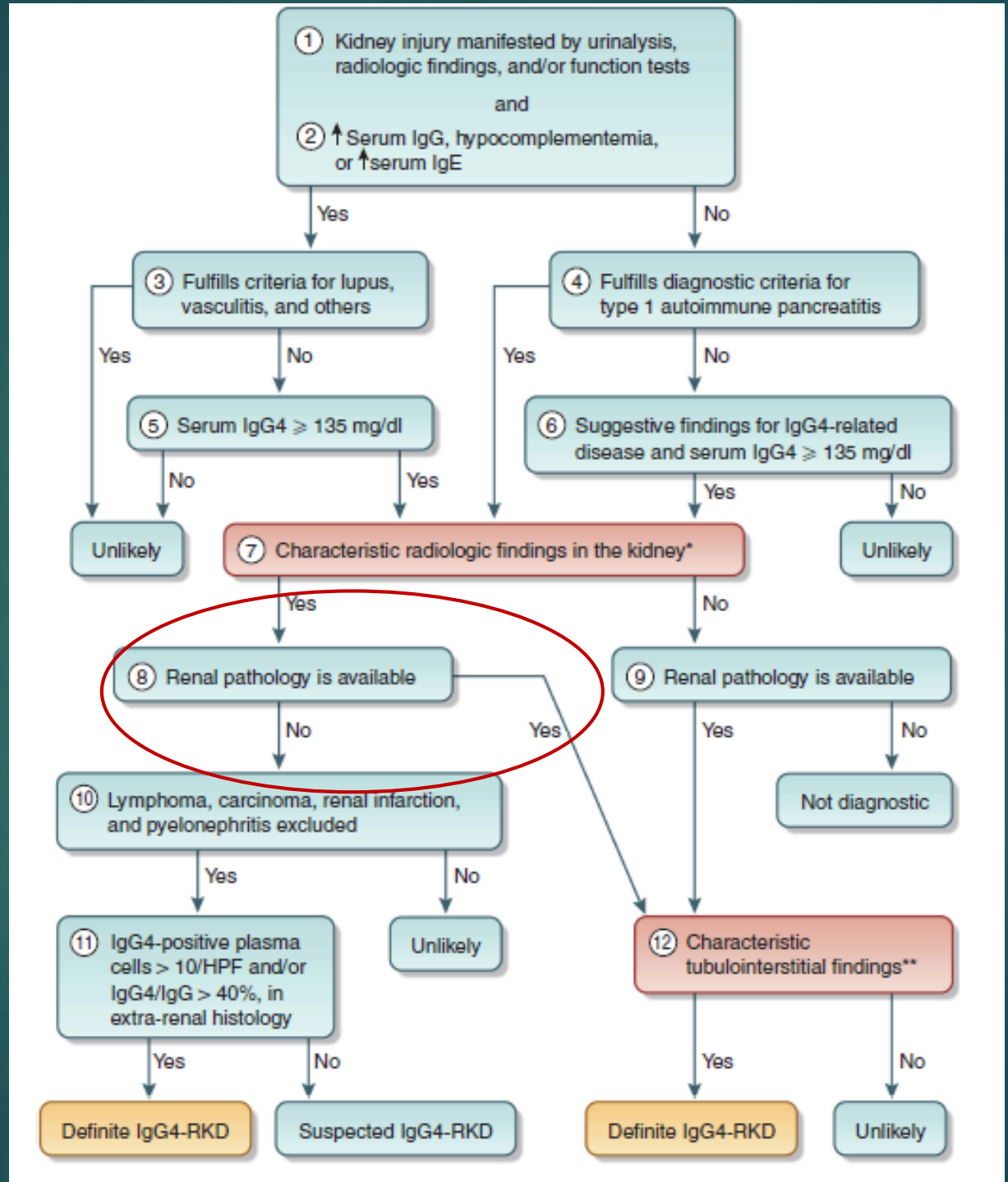
Table 1 | Major organ manifestations of IgG4-related disease

Pancreas	Type 1 autoimmune pancreatitis
Salivary glands	Sialadenitis
Eye/orbit/lacrymal glands	Orbital inflammation/pseudotumor and dacryoadenitis
Aorta/artery/retroperitoneum periaortitis	Periaortitis/periarteritis and retroperitoneal fibrosis
Kidney	Tubulointerstitial nephritis and pyelitis
Lymph nodes	Lymphadenopathy
Lung	Lung disease (inflammatory pseudotumor, alveolar interstitial disease, and pleuritis)
Biliary system	Sclerosing cholangitis and cholecystitis
Liver	Pseudotumor and hepatopathy
Central/peripheral nervous system	Pachymeningitis and infraorbital nerve swelling
Endocrine system	Hypophysitis and thyroiditis
Others	Prostatitis, mastitis, mediastinitis, and pericarditis skin (nodules and papules)

Table 2 | Diagnostic criteria for IgG4-TIN proposed by Raissian *et al.*[10]

Histology	Plasma cell–rich TIN with >10 IgG4+ plasma cells/HPF field in the most concentrated field[a] TBM immune complex deposits by immunofluorescence, immunohistochemistry, and/or electron microscopy[b]
Imaging	Small peripheral low-attenuation cortical nodules, round or wedge-shaped lesions, or diffuse patchy involvement
Serology	Elevated serum IgG4 or total IgG level
Other organ involvement	Characteristic findings of IgG4-RD in other organs

IgG4-nefropatia diagnostinen algoritmi



Kawano M. *et al. Clin Exp Nephrol.* 2011.