IgG4 related Cholangiopathy and Pancreatitis

Dhiraj Yadav, MD MPH

Associate Professor

Division of Gastroenterology & Hepatology

University of Pittsburgh

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Some publications from UPMC on this subject

- Raina A, Yadav D, Krasinskas A, et al. Evaluation and Management of Autoimmune Pancreatitis: Experience at a large US center. Am J Gastroenterol. 2009;104:2295-306.
- Raina A, Slivka A, Sanders M, et al. Application of International Consensus Diagnostic Criteria (ICDC) for Autoimmune Pancreatitis (AIP) to a US cohort. Pancreas 2012 (abstract).
- Hart PA, Kamisawa T, Brugge WR, et al. Long-term outcomes of autoimmune pancreatitis: a multicentre, international analysis. Gut. 2012 Dec 11 [Epub]. PMID:23232048
- Nasr J, Nalesnik M, Rabinowitz M. A comparative study of orthotopic liver transplant for sclerosing cholantitis patients with and without elevated serum IgG4 levels. Gastroenterology 2011 (abstract).
- Krasinskas A, Raina A, Khalid A, et al. Autoimmmune Pancreatitis. Gastroenterol Clin North Am 2007;36:239-57.
- Raina A, Yadav D, Krasinskas A. Autoimmune Pancreatitis. NEJM. 2007;356:1587.
- Raina A, Krasinskas A, Greer J, et al. Serum immunoglobulin F fraction 4 levels in pancreatic cancer: elevations are not associated with autoimmune pancreatitis. Arch Pathol Lab Med 2008;132:48-52.
- Raina A, Greer JB, Whitcomb DC. Serology in autoimmune pancreatitis. Minerva Gastroenterol Dietol. 2008 Dec;54:375-87.

Autoimmune Pancreatitis

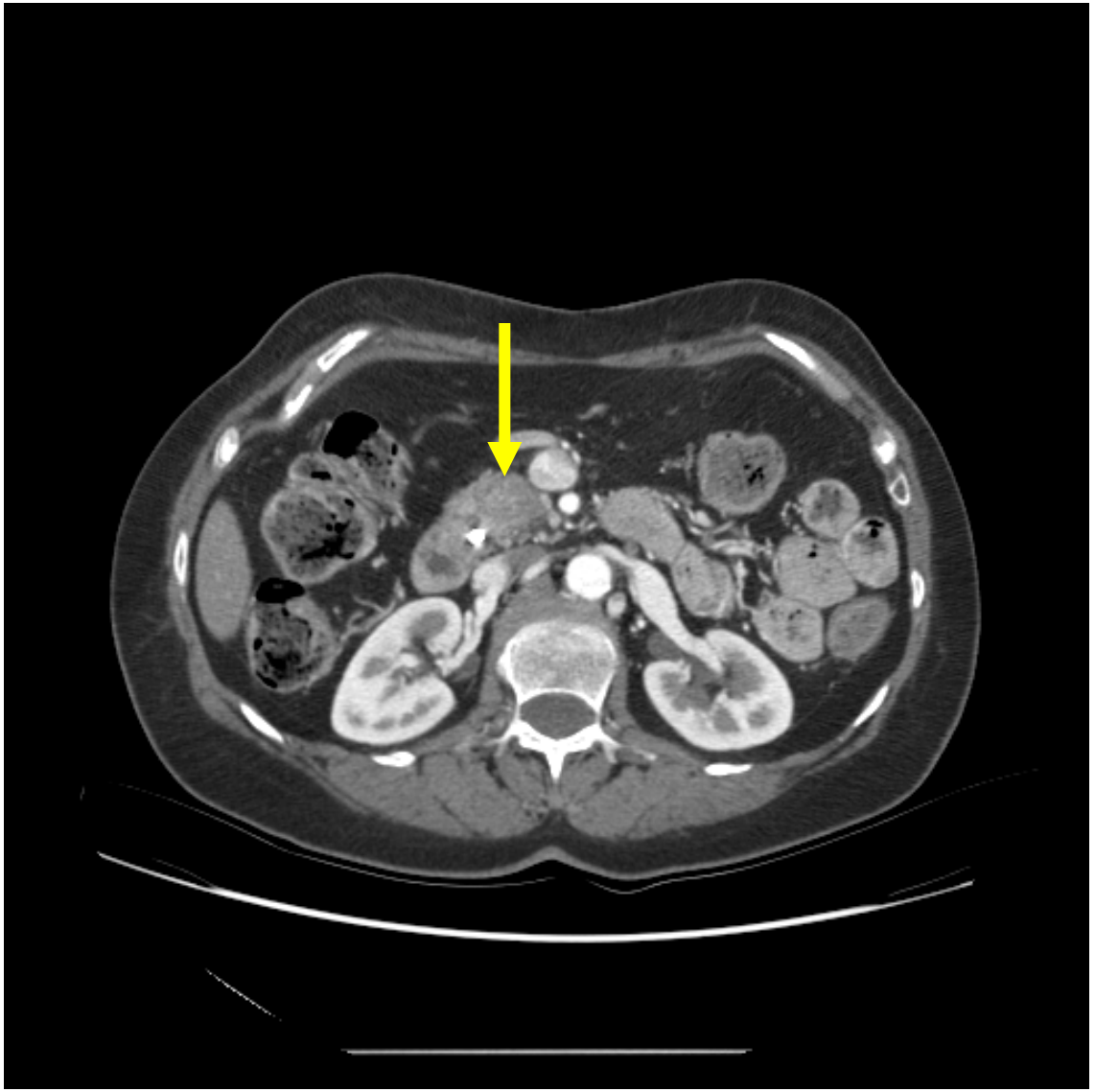
- Autoimmune disorder
- First described as a distinct entity in 1995
- Rare disease
  - Exact prevalence in Western countries unknown
  - ~2500 cases in the US if we extrapolate from Japanese data

Autoimmune Pancreatitis

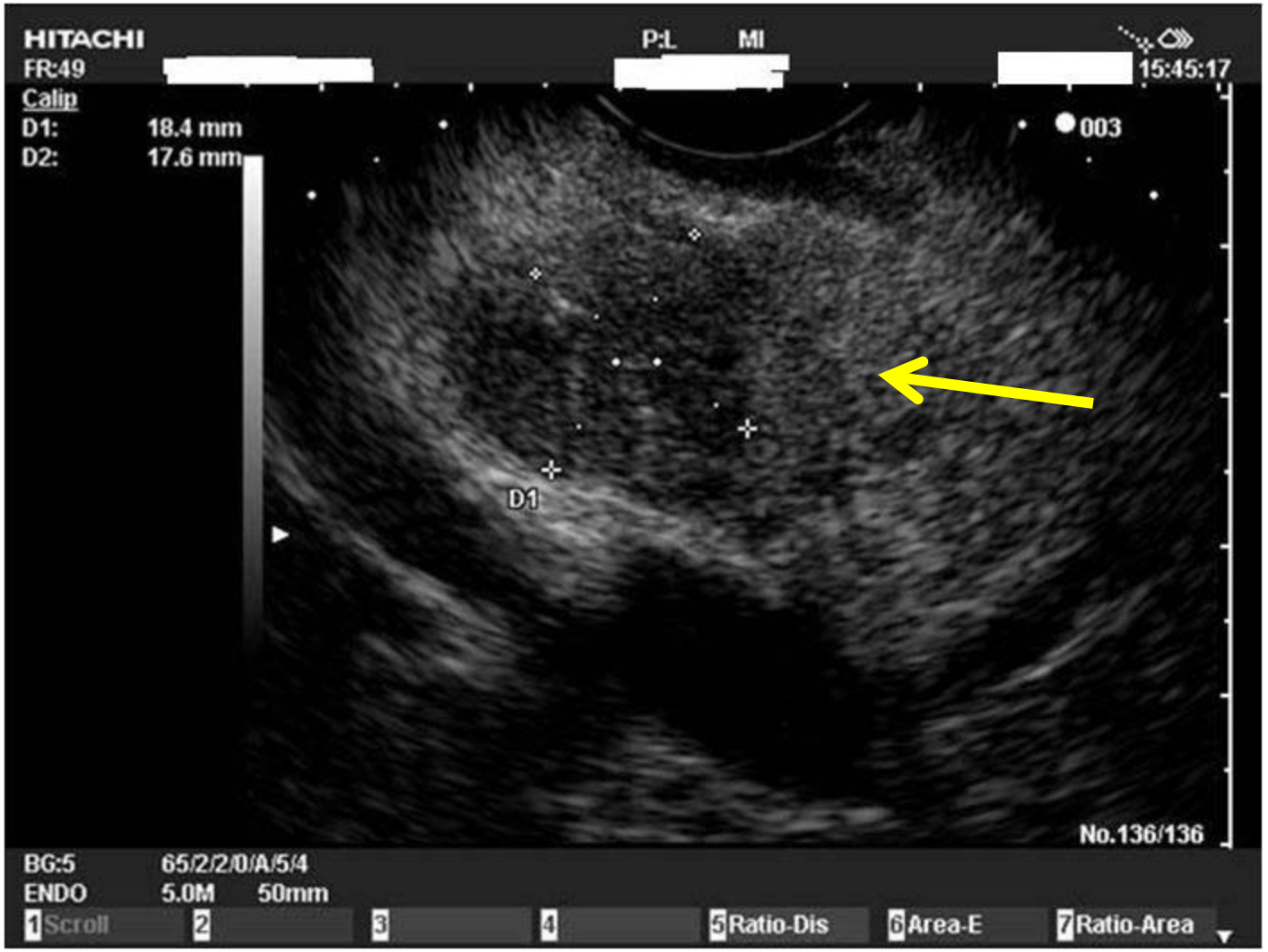
- Clinical presentation mimics Pancreas cancer
- Less common
  - Pancreatitis, persistent pancreatic mass, scarred or shrunken pancreas, malabsorption
- Elevation of serum IgG4 levels
- Typical appearance on imaging tests and biopsy
- Patients often have involvement of other organs
- Two forms have been recognized - Type I and II

GCNA 2008;37:439-60; Pancreas 2012;41:835-9; Pancreas 2011;40:352-8

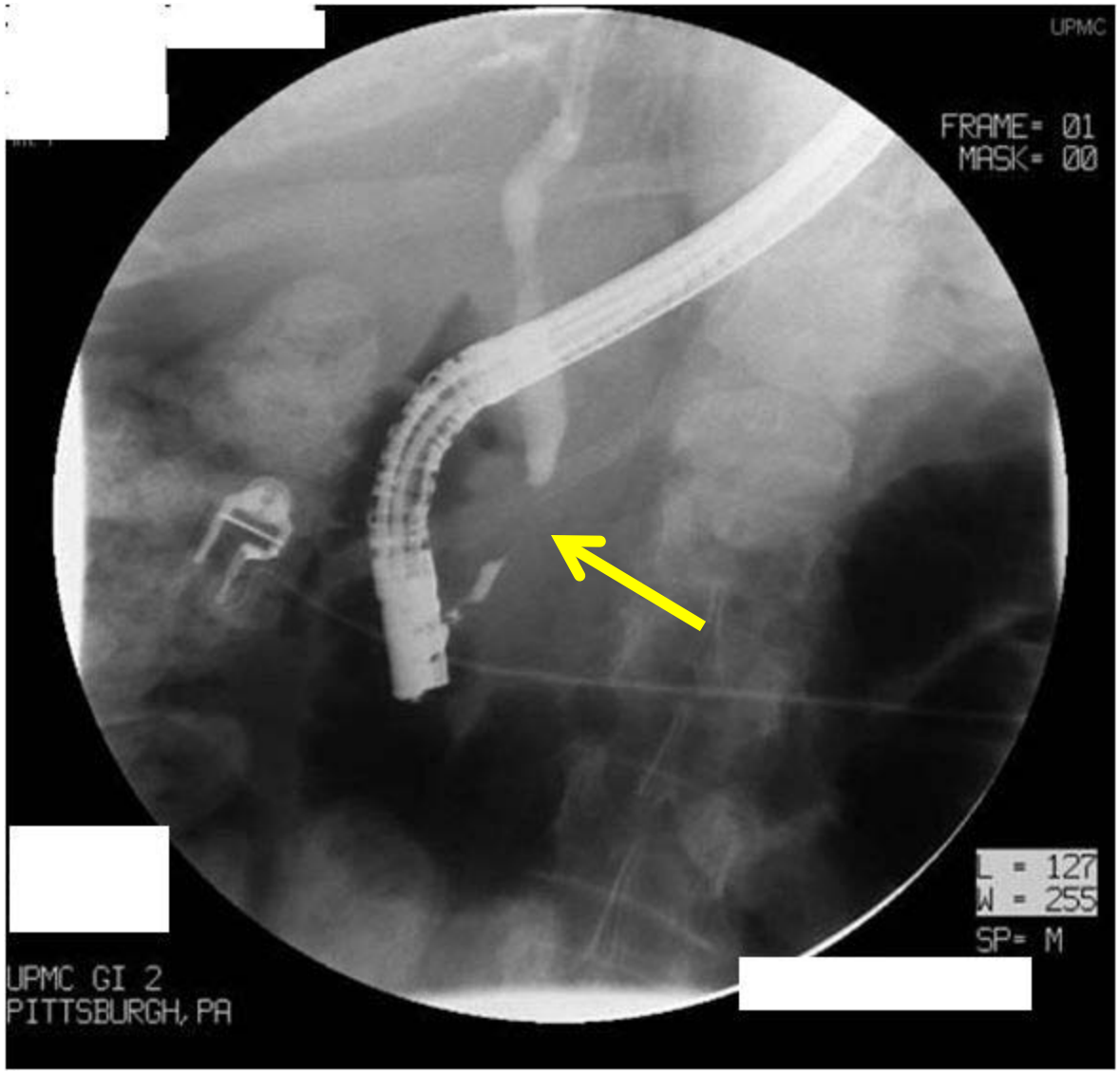
Autoimmune Pancreatitis



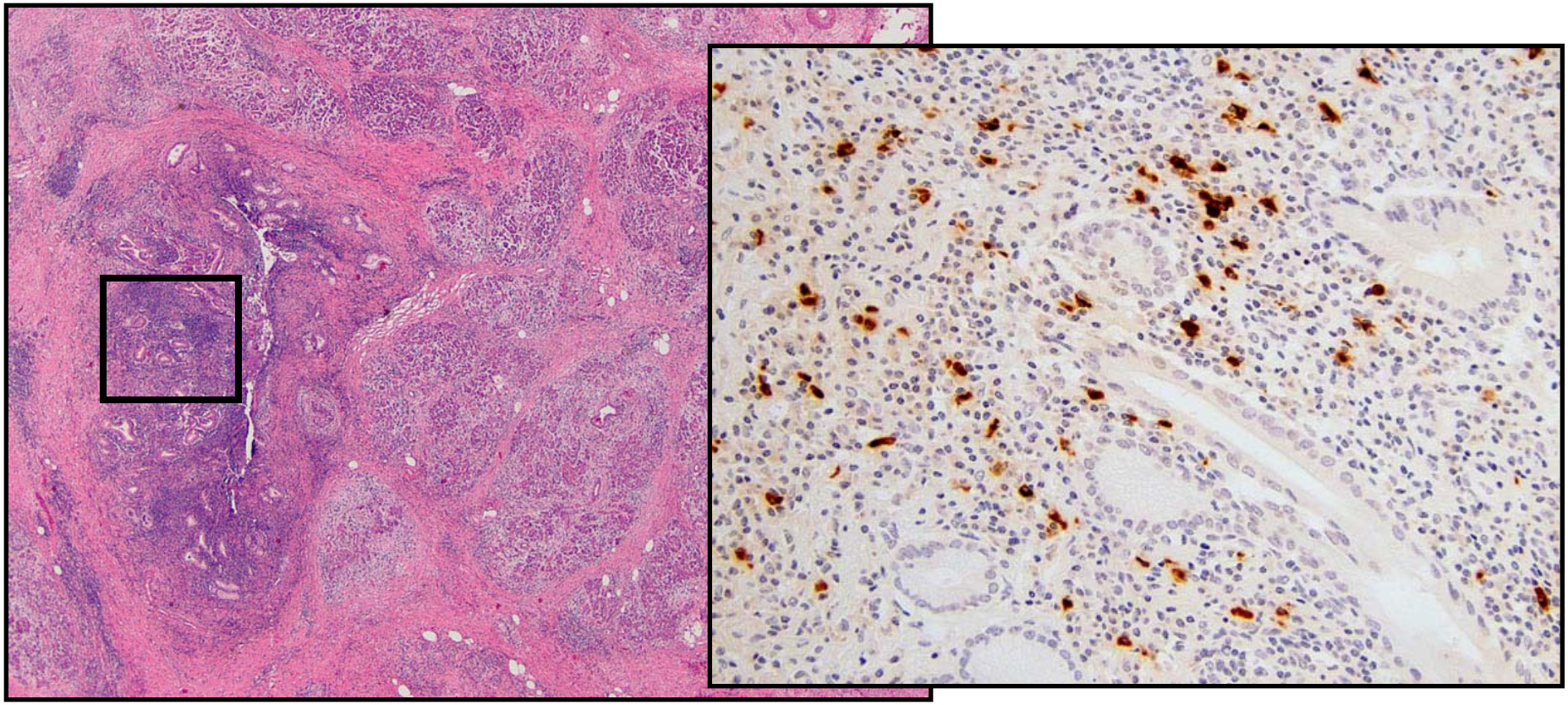
Autoimmune Pancreatitis



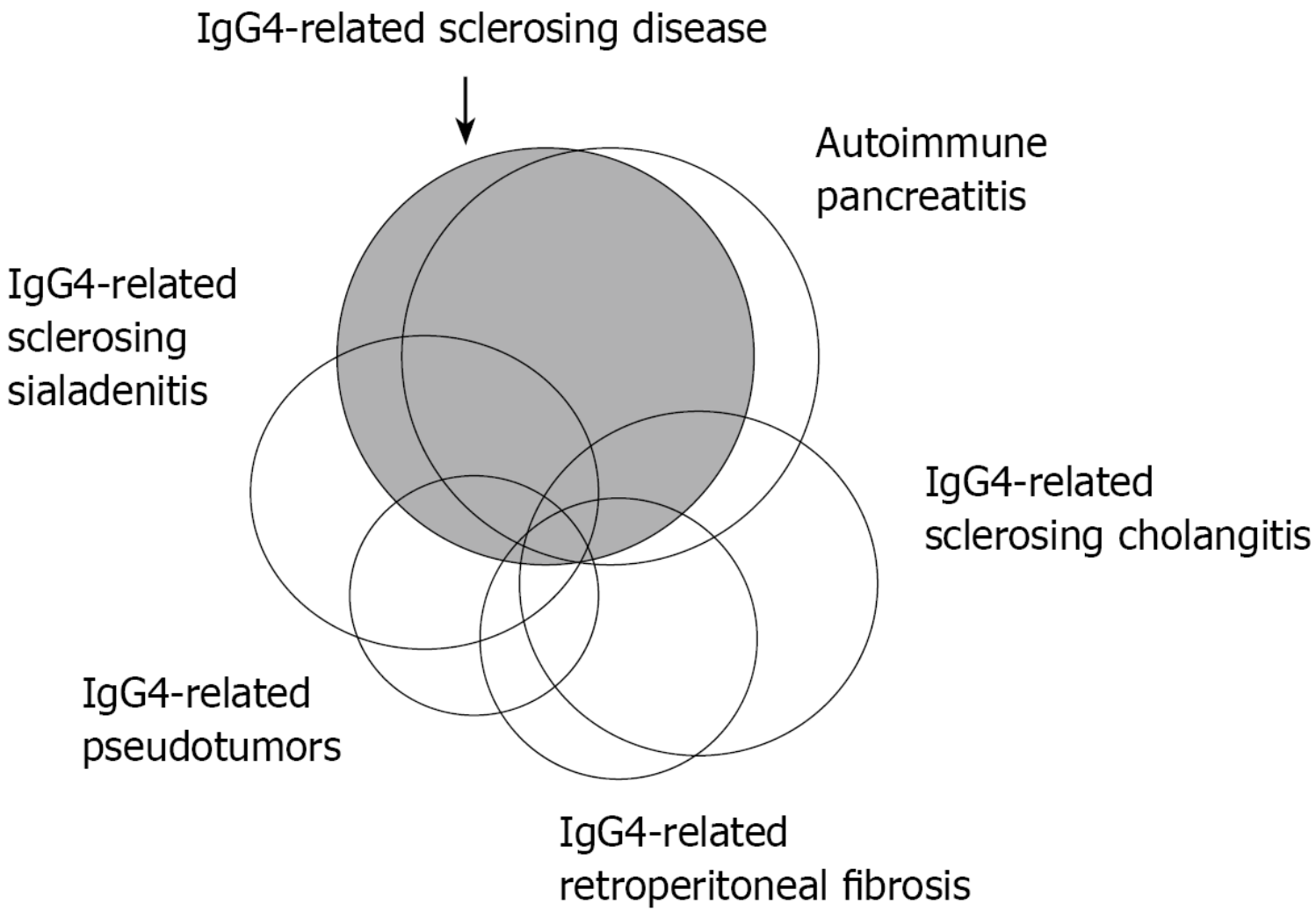
Autoimmune Pancreatitis



Autoimmune Pancreatitis



IgG4 related Disease



WJG 2008;14:3948-55

Organs involved in IgG4 related disease

Disease	Organ
Mikulicz's syndrome	Salivary and lachrymal glands
Kuttner's tumour	Submandibular glands
Riedel's thyroiditis	Thyroid
Hashimoto's thyroiditis	Thyroid
Autoimmune pancreatitis	Pancreas
Eosinophilic angiocentric fibrosis	Orbit and upper respiratory tract
Multifocal fibrosclerosis	Orbit, thyroid, retroperitoneum, mediastinum
Inflammatory pseudotumor	Orbit, lungs, liver, kidneys
Mediastinal fibrosis	Mediastinum
Retroperitoneal fibrosis	Retroperitoneum
Interstitial pneumonitis	Lungs
Inflammatory aortic aneurysm	Abdominal aorta
Idiopathic hypocomplementemic tubulointerstitial nephritis	Kidney
Periaortitis and periarteriris	Aorta
Autoimmune hypophysitis	Hypophysis
Cutaneous pseudolymphoma	Skin
Rosai-Dorfman disease	Glands

Best Pract Res Clin Rheum 2012;26:425-38

IgG4 related disease

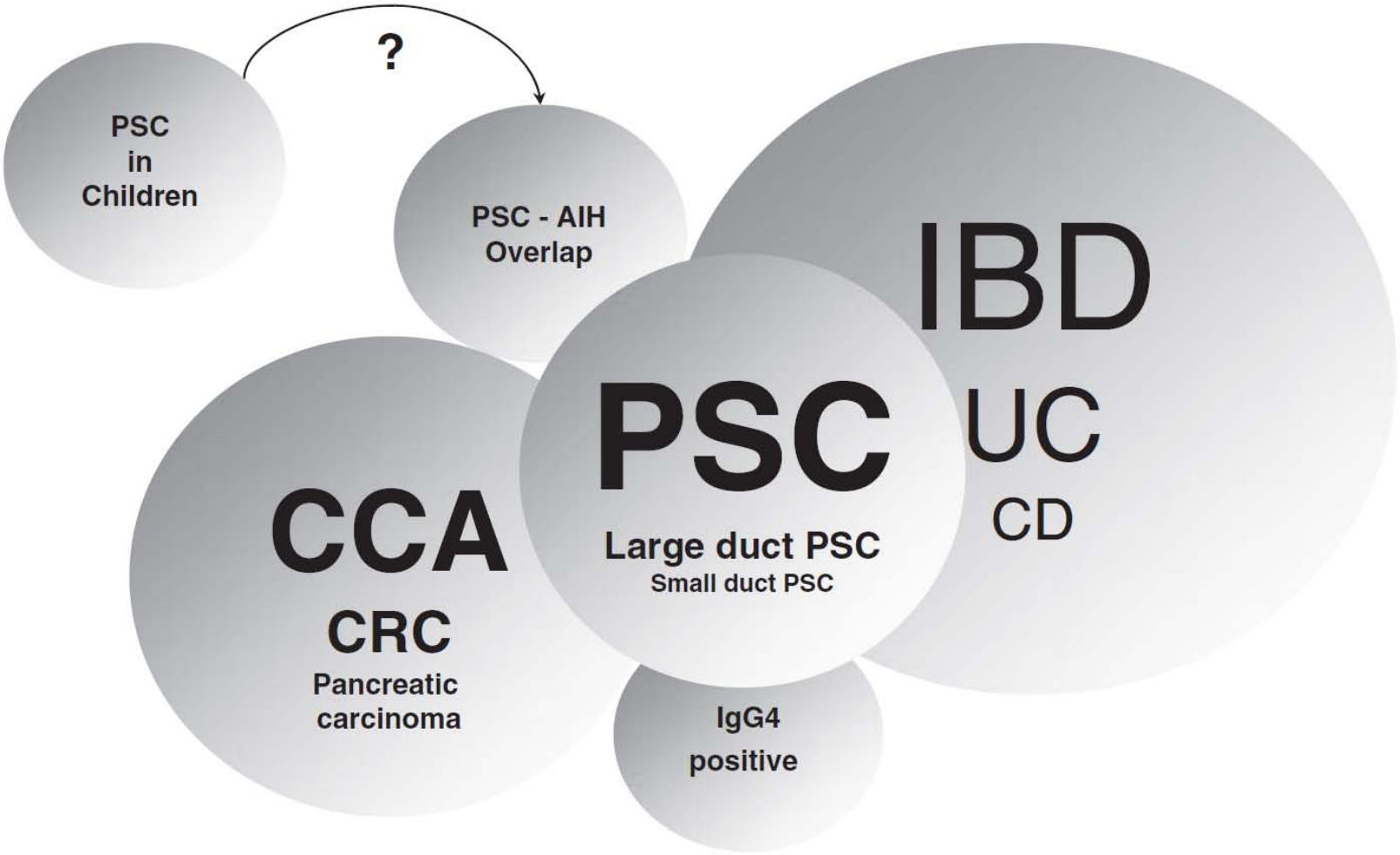
- Systemic disease - First recognized in 2003
- Can involve virtually any organ(s)
  (Pancreas, bile ducts, salivary glands, periorbital tissue, kidneys, lungs, lymph nodes, meninges, aorta, breast, prostate, thyroid, pericardium, skin)
- Elevation of serum IgG4 levels
- Pathology findings are characteristic
  - Dense lymphoplasmacytic infiltration; storiform fibrosis; mild-moderate eosinophil infiltration; rich in IgG4-positive plasma cells
- Excellent response to steroids

NEJM 2012;366:539-51

IgG4 related Sclerosing Cholangitis

- IgG4 related disease involving the bile ducts
- ~90% cases also have Autoimmune Pancreatitis
- Usually elderly male presenting with painless jaundice
- Elevation of serum IgG4 levels
- Imaging findings mimic PSC and cholangiocarcinoma
- Bile duct biopsies show IgG4-positive plasma cells

PSC and elevated serum IgG4



Liver Int 2012;32:352-69

PSC and elevated serum IgG4

- Elevated IgG4 are seen in ~10% PSC patients
- No special features to identify them from patients with normal IgG4 levels
- Have more aggressive and severe disease
- Shorter time to transplantation
- Show good response to steroids – however, the role of steroids and other immunosuppressive treatments still poorly defined

Am J Gastroenterol 2006;101:2070-75; Am J Ther 2011;18:198-205

Summary

- IgG4 related disease is an increasingly recognized clinical entity
- Can involve multiple organs
- Elevations in serum IgG4 levels common
- Has typical pathology findings
- Excellent response to steroid treatment

Summary

- Autoimmune Pancreatitis is the most common manifestation of IgG4 related disease
- ~1 in 3 patients can have bile duct involvement
- Disease relapse often is seen in these patients and can require medications to suppress the immune system
- A subset of patients with PSC have elevations in serum IgG4 levels – signifies more aggressive disease