IgG4-related Sclerosing Diseases Involving Abdominal Organs; Radiologic Findings and Differential Diagnosis

Young-Hwan Lee, MD, Seri Kang, MD, Youe Ree Kim, MD, Hye Ji Rue, MD, Kwon-Ha Yoon, MD

Wonkwang University Hospital, Iksan, South Korea

Learning Objectives

1. To illustrate imaging findings of IgG4-related sclerosing diseases affecting various abdominal organs including Liver, biliary tract, pancreas, retroperitoneum, kidneys, lymph nodes.

2. To inform the imaging features of IgG4-related diseases of abdomen which can be helpful to differentiate from many of tumorous or other inflammatory abdominal diseases.

Background

- Immunoglobulin G4 (IgG4)–related disease is a recently proposed clinical-pathologic entity characterized by fibroinflammatory lesions rich in IgG4-positive plasma cells and, often but not always, elevated serum IgG4 concentrations.

- Although definitive diagnosis requires histopathologic analysis, imaging plays an important role in demonstrating infiltration and enlargement of involved organs.

- Because IgG4-related disease usually shows a marked response to corticosteroid therapy, radiologists should be familiar with its clinical and imaging manifestations to avoid a delayed diagnosis and unnecessary surgical interventions.

Imaging Findings Or Procedure Details

- In this exhibit, we'll discuss the clinical manifestations and pathophysiology of various IgG4-related sclerosing diseases of abdomen.

- We classified IgG4-related diseases into 7 groups according to the involved abdominal organs; Pancreas, liver, biliary tree, kidney, small bowel mesentery, retroperitoneum and lymph nodes.

IgG4-related Diseases of Abdomen and their Radiologic Mimics

Organs	IgG4-related Diseases	Mimics
Pancreas	Autoimmune pancreatitis (AIP)	Focal form of AIP - pancreatic malignancy Diffuse form of AIP - pancreatitis
Liver	IgG4-related inflammatory pseudotumor, Hepatopathy	Malignant hepatic tumors
Bilary tree	IgG4-related sclerosing cholangitis	Primary sclerosing cholangitis, cholangiocarcinoma
Kidney	Tubulointerstitial nephritis, Membranous glomerulonephritis, Inflammatory pseudotumors, chronic sclerosing pyelitis	Bilateral - lymphoma, metastases, Unilateral – renal cell carcinoma, transitional cell carcinoma Wedge shape – infarct, pyelonephritis
Small bowel mesentery	IgG4-related sclerosing mesenteritis	Lymphoma, carcinoid tumor, carcinomatosis
Retroperitoneum	IgG4-related retroperitoneal fibrosis	Lymphoma, large-vessel vasculitis, syphilis, sarcoidosis-induced arteritis
Lymph nodes	IgG4-related Lymphadenopathy	Lymphoma, multicentric Castleman disease, disseminated malignancy

IgG4-related Autoimmune Pancreatitis

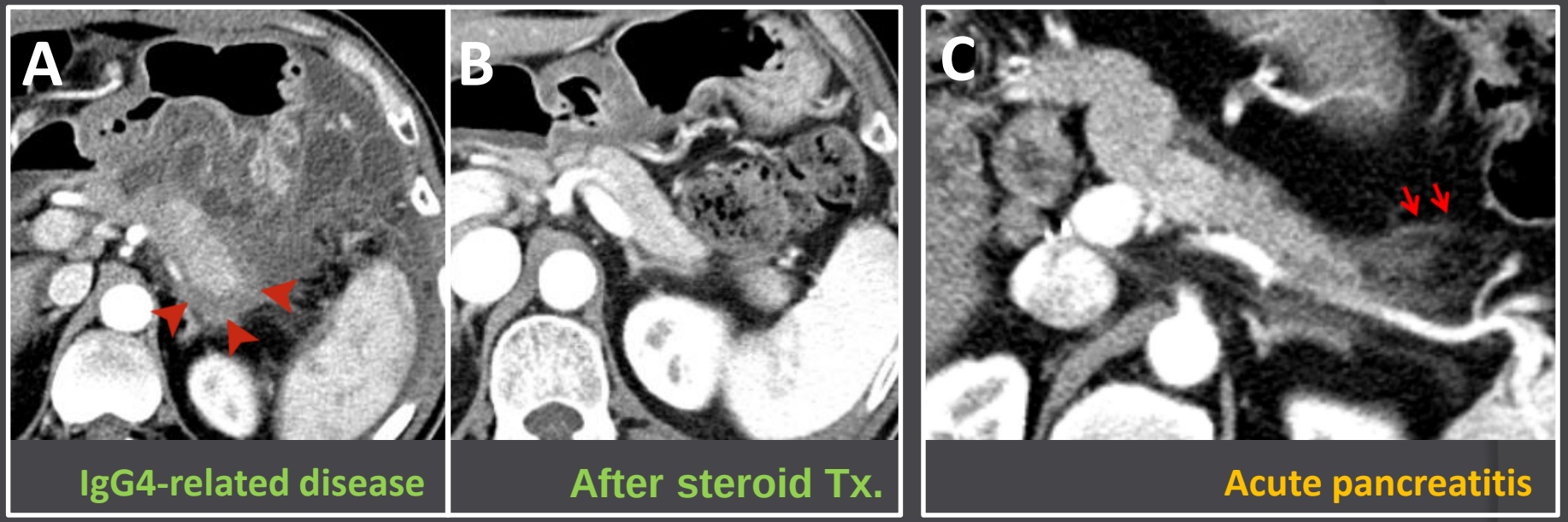


Fig. 1. IgG4-related disease in a 50-year-old man (A,B).
Acute pancreatitis in a 42-year-old woman (C).
Axial contrast-enhanced (A) CT show swelling of the pancreatic tail with peripancreatic hypoattenuating halo(arrowhead). This patient shows marked elevation of **IgG4 level with 883g/L**. Follow-up CT image(B) obtained after steroid administration shows a **marked response to treatment**, with resolution of the hypoattenuating peripancreatic halo. Another patient with acute pancreattiis reveals **peripancreatic fat strands** on enhanced CT (C, arrows).

IgG4-related Autoimmune Pancreatitis

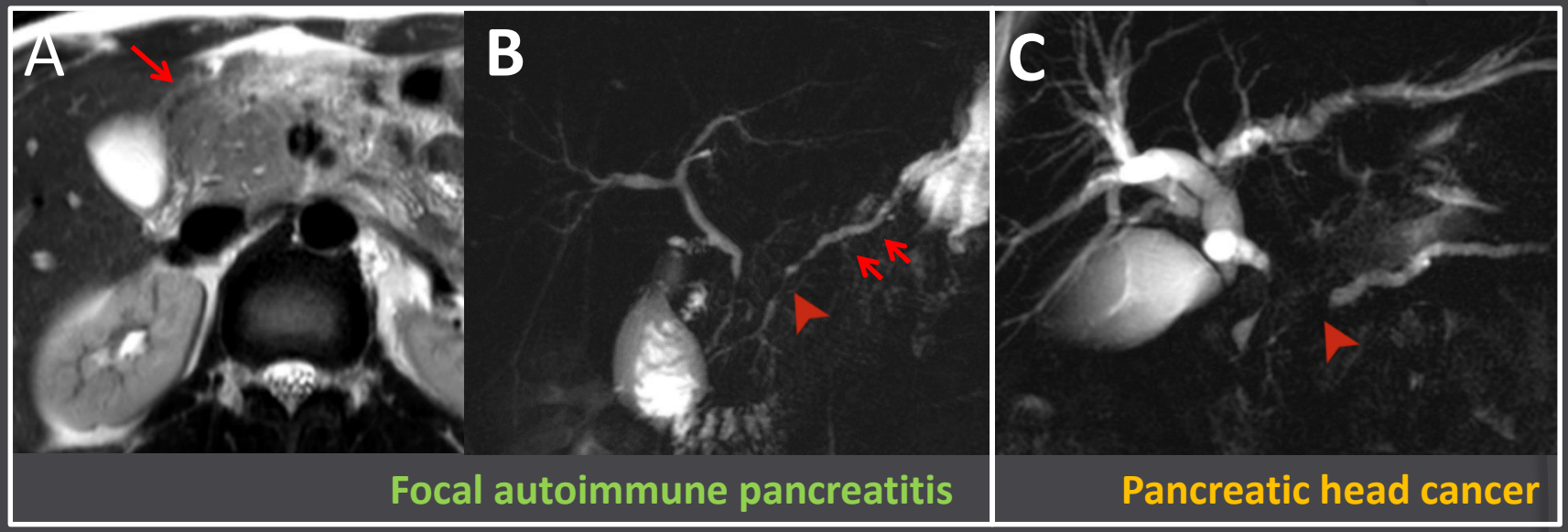


Fig. 2. **Focal autoimmune pancreatitis** in a 29-year-old man (A,B).
Pancreatic head cancer in a 69-year-old woman (C).
Axial T2-weighted MR images(A) show well-demarcated focal enlargement and mild hyperintensity of pancreatic head portion (arrow), reflecting an edematous component. Coronal MRCP image (B) shows **smooth, tapered stenosis** in the main pancreatic duct(arrowhead), with upstream pancreatic duct dilatation (arrows, ice pick sign). Another patient with pancreatic head cancer reveals **abrupt obstruction** in the main pancreatic duct (arrowhead) with dilatation of upstream pancreatic duct and bile duct(double duct sign) on MRCP (C).

IgG4-related Autoimmune Pancreatitis

- Specific finding

- Capsulelike rim or halo of low attenuation surrounding pancreas, presumed to represent a fluid collection, a phlegmon, or fibrosis.

- At imaging

- Hypoechoic at US, hypoattenating at CT, midly hyperintense at T2-weighted MR imaging with distinctive delayed enhancement.

- Two main recognized patterns of autoimmune pancreatitis;
  - → Diffuse diseases; a uniformly enlarged pancreas with sharp margin and loss of lobular contours, resulting in a featureless sausage like appearance.
  - → Focal disease; focal enlargement of pancreas, resulting in a masslike appearance.

IgG4-related Autoimmune Pancreatitis

Differential diagnosis

- Pancreatic cancer

; no penetration of the pancreatic duct through the mass (“duct penetrating sign”)

; abrupt narrowing of the pancreatic duct and dilatation of upstream pancreatic duct just distal to the pancreatic lesion (“ice pick sign”)

; higher apparent diffusion coefficient (ADC) on diffusion-weighted MR imaging.

- Acute pancreatitis

; peripancreatic stranding, peripancreatic fat necrosis and lack of a peripancreatic halo.

IgG4-related Inflammatory Pseudotumor

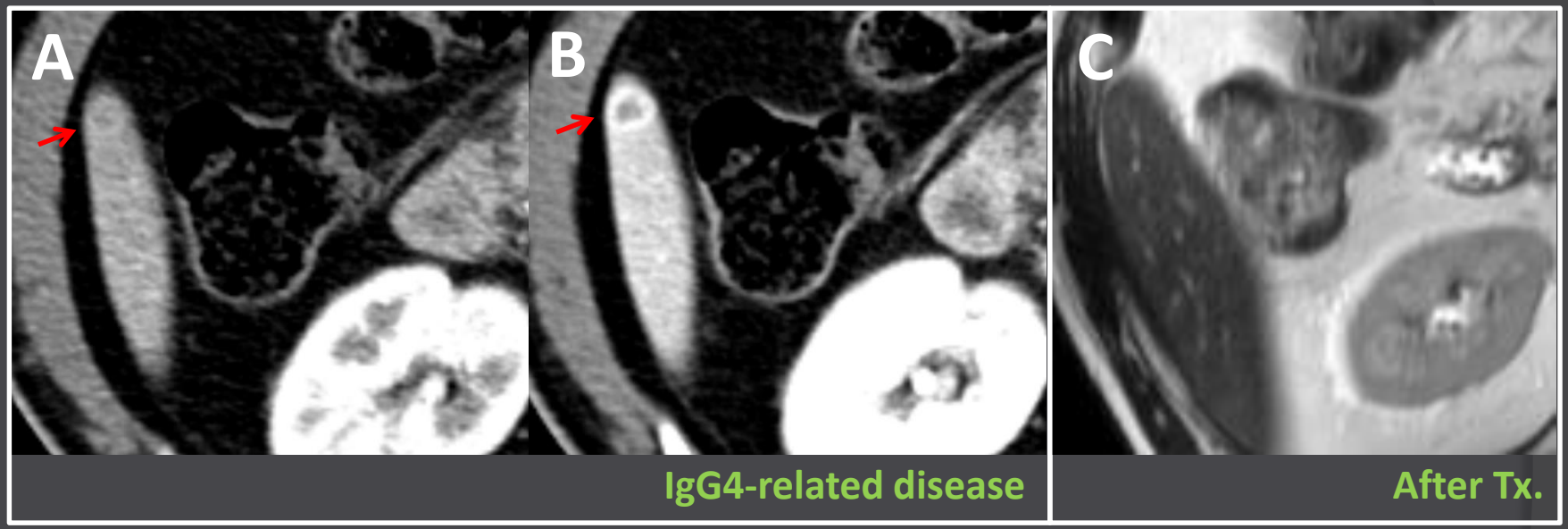


Fig. 3. **IgG4-related disease** in 29-year-old man.

Axial CT reveals a arterial enhancing nodule (arrow) in the liver segment 6 (A) with further **enhancement in the delayed phase** (B). 6 Months after treatment with steroid, hepatic nodule disappeared on T2-weighted MR image (C).

IgG4-related Hepatopathy

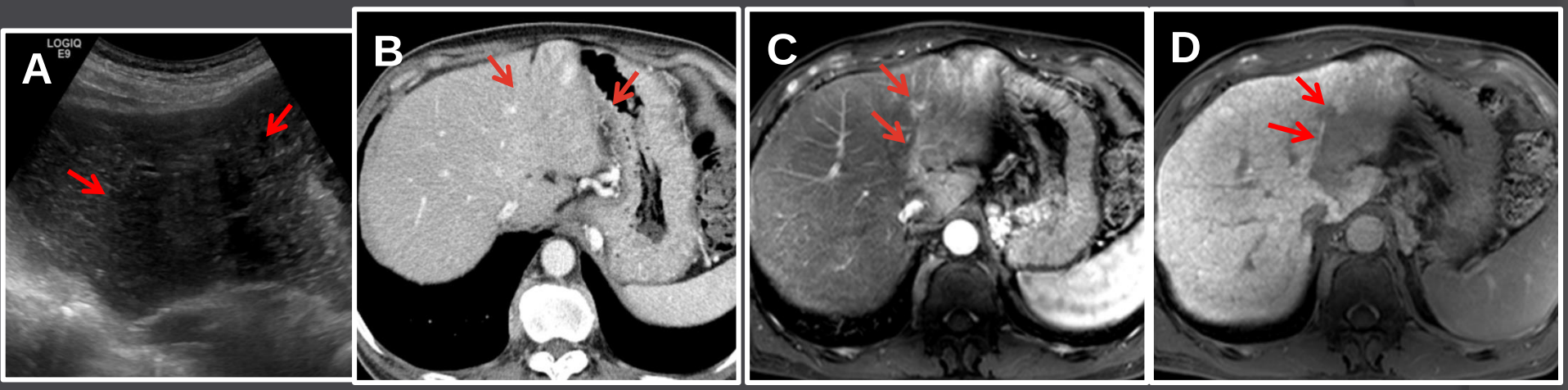


Fig.4. **IgG4-related hepatopathy** in a 54-year-old man.
Transabdominal ultrasound (A), contrast enhanced CT (B), axial fat saturated T2-weighted image (C) and Gd-EOB enhanced hepatobiliary phase image (D) show ill defined infiltrative hypoechoic hepatic mass (arrows) with mild arterial enhancing and delayed washout, EOB defect, T2 hyperintensity, diffusion restriction (not shown) at lateral segment of left hepatic lobe and atrophic change of left portal vein is noted.

IgG4-related Diseases of the Liver

- Two types of IgG4-related inflammatory pseudotumors;
  - → fibrohistiocytic
  - → lymphoplasmacytic : more strong association

- Image findings

- hypointense on T1-weighted MRI.
- hyperintense on T2-weighted images with variable enhancement.

Differential diagnosis

- Malignant hepatic tumor

; delayed enhancement on CT is rarely seen.
biopsy is needed.

IgG4-related Sclerosing Cholangitis

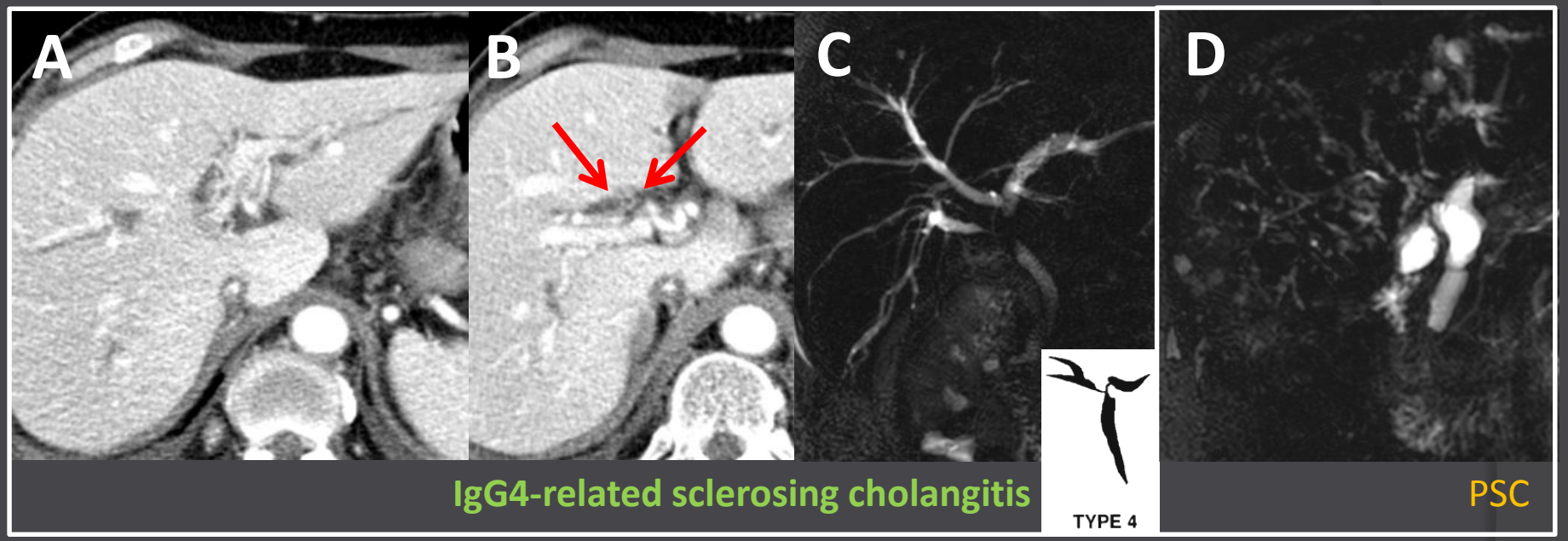
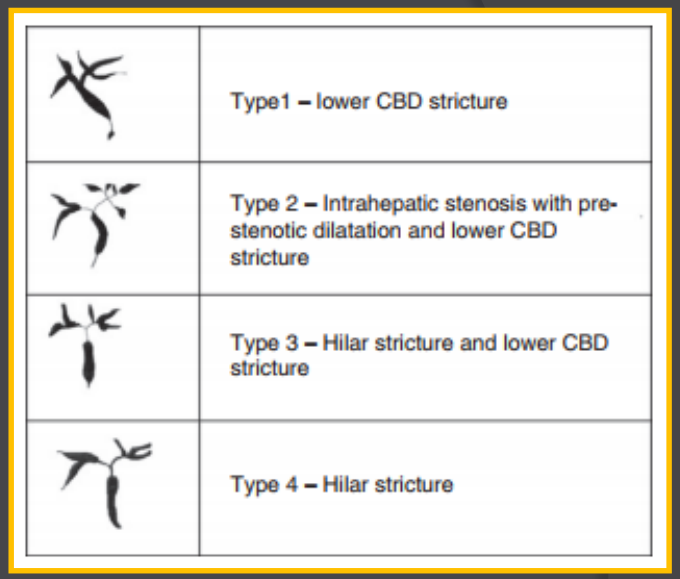


Fig. 5. IgG4-related sclerosing cholangitis in a 62-year-old man (A, B, C).
Primary sclerosing cholangitis (PSC) in a 66-year-old woman (D).

Axial contrast-enhanced CT image demonstrate **concentric mild enhancing wall thickening** of the common hepatic duct (B, arrows) with prestenotic intrahepatic bile duct dilatation(A). MRCP image also show stricture of extrahepatic bile duct and right intrahepatic bile duct at hepatic hilum(C). Another patient with primary sclerosing cholangitis reveals multifocal and short strictures of both intrahepatic bile duct with **beaded appearance** (D).

IgG4-related Sclerosing Cholangitis



- Most common involved segment
  - the intrapancreatic portion of the CBD.
- Focal or diffuse bile duct wall thickening with stenosis and upstream dilatation.
- A circular and symmetric rind of tissue encasing the bile duct wall with relatively smooth margins and homogeneous enhancement in the delayed phase of CT and MRI.
- Gallbladder involvement
  - diffuse wall thickening with decreased echogenicity at US and low signal intensity at T2-weighted MRI with late enhancement.

IgG4-related Sclerosing Cholangitis

Differential diagnosis

- At ERCP ;
  - Primary sclerosing cholangitis: multifocal and short strictures with beaded or “pruned-tree” lesions
  - IgG4-related sclerosing cholangitis: long and continuous strictures, or Isolated strictures of the distal CBD.

- In presence of a soft-tissue mass, producing stenosis of the hilar hepatic bile duct
  - Cholangiocarcinoma: hepatic capsular retraction due to desmoplastic growth.
  - IgG4-related sclerosing cholangitis

  : tumor infiltration is confined to the bile ducts.

  : luminar irregularities and stenosis of the biliary and pancreatic ducts.

IgG4-related Renal Involvement

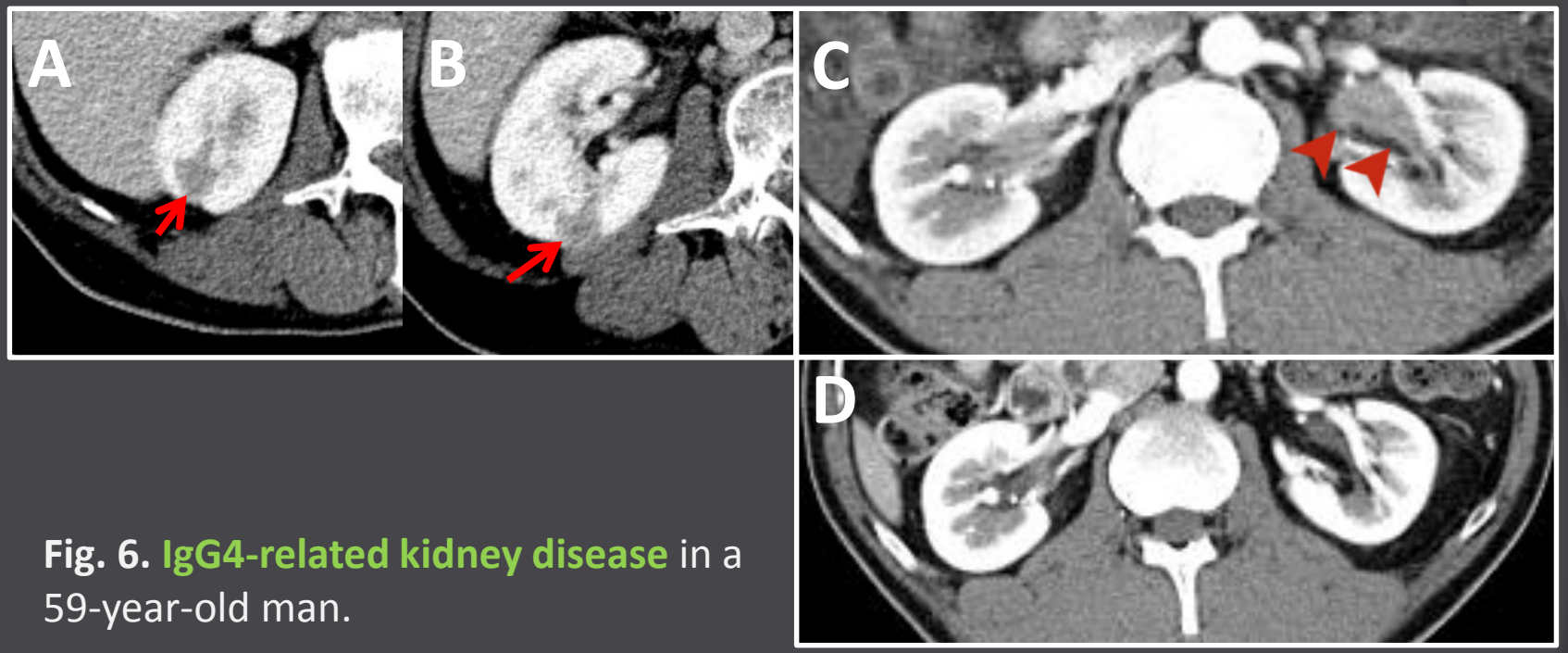


Fig. 6. **IgG4-related kidney disease** in a 59-year-old man.

Axial contrast-enhanced CT images show multiple **enhancing solid masses** (arrow) in the right kidney (A, B) and also demonstrates ill defined enhancing **soft tissue lesion along the left renal pelvis** (C, arrowhead). This patient reveals marked elevation of **serum IgG4 level with 6280g/L** and **IgG4 positive plasma cell** in biopsy. Two months after steroid therapy, soft tissue lesion along the left renal pelvis is almost not seen (D).

IgG4-related Renal Involvement

- Five patterns of disease ;

1) bilateral round or wedge-shaped peripheral cortical lesions(the most common)
2) bilateral nodules in renal sinuses
3) a rim of soft tissue around the kidney
4) diffuse patchy involvement
5) diffuse wall thickening of renal pelvis.

- At CT ;

- hypoattenuating during the arterial phase, becoming isoattenuating relative to the surrounding parenchyma during later phases.

- At MRI ;

- low signal intensity on both T1- and T2-weighted images, with mild enhancement on T1-weighted images.

Renal Involvement

Differential diagnosis

- Multiple round or wedge-shaped cortical nodules,
  - pyelonephritis, vascular insult, metastases, and lymphoma.
  - pyelonephritis : wedge-shaped areas peak in the renal calices and enhance poorly.
  - renal infarction and vasculitis :show low-density, wedge shaped lesions corresponding to specific vascular territories

- Solitary round lesion,
  - renal cell carcinoma, transitional cell carcinoma.
    - renal cell carcinoma : hypervascular
    - IgG4-related ureteropelvic lesions : normal intimal epithelium differently from ureteropelvic cancers, originating from the intimal epithelium.

Renal Involvement; mimics

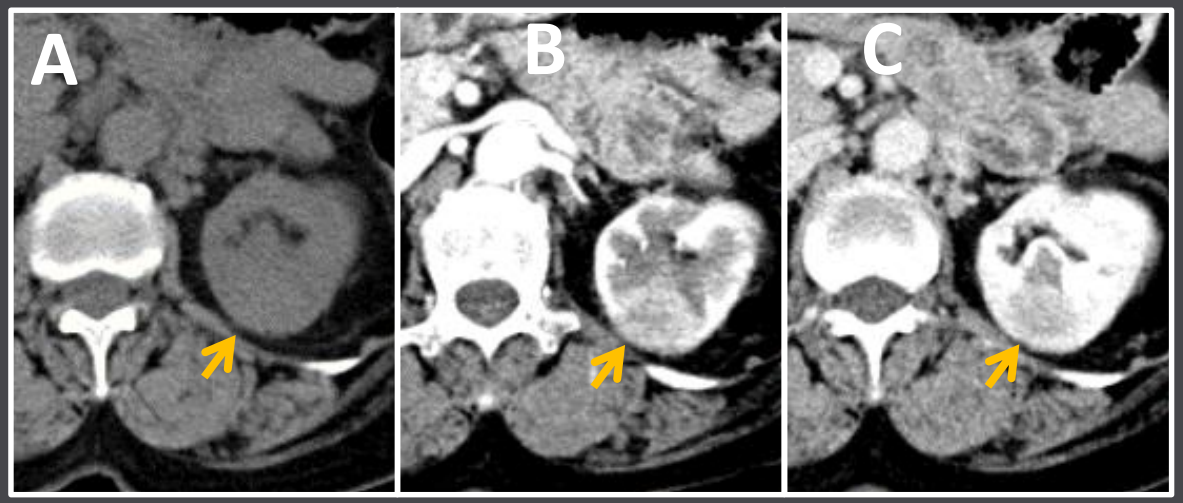


Fig. 7. Renal cell carcinoma in a 68-year-old woman.

Axial CT reveals a **enhancing nodule** (arrow) in left kidney(B) with subtle **washout on delayed phase** image (C), a nodule that is not seen in non enhanced image (A).

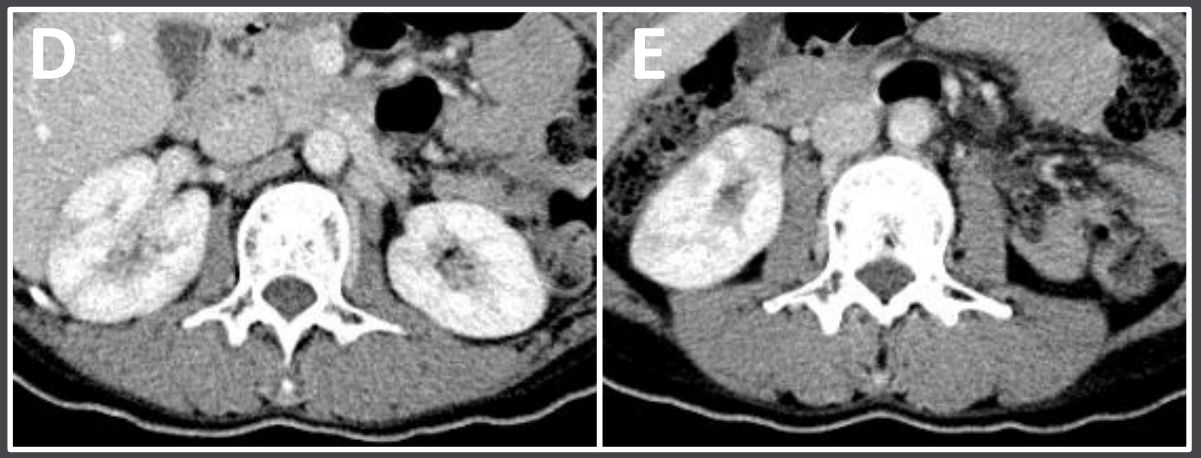


Fig. 8. Acute pyelonephritis in a 44-year-old woman.

Axial contrast enhanced CT (D, E) reveals multifocal **wedge shaped** less enhancing lesion that **peak in the renal calices** in right kidney with mild **edematous swelling** of right kidney.

IgG4-related Sclerosing Mesenteritis

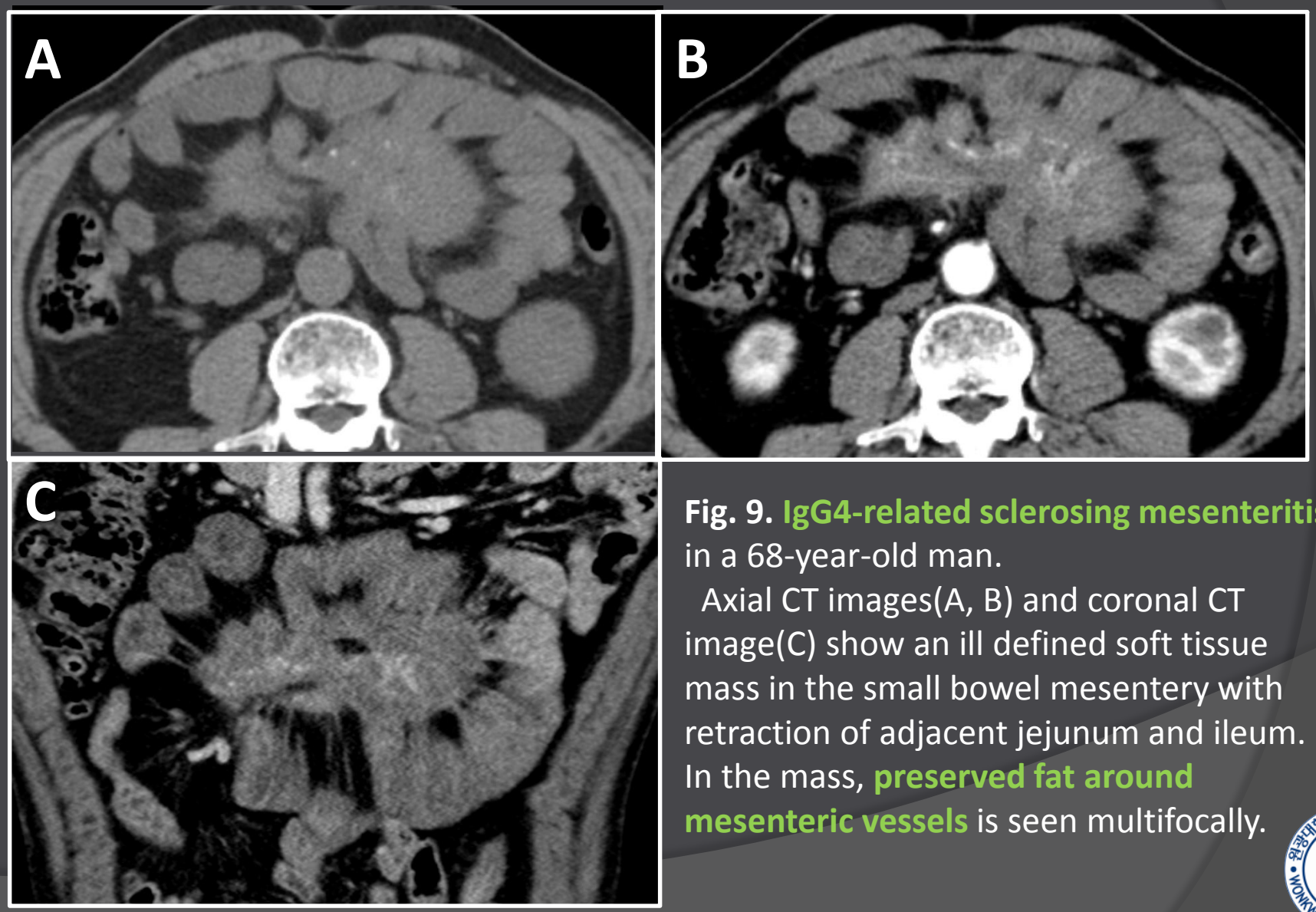


Fig. 9. **IgG4-related sclerosing mesenteritis** in a 68-year-old man.
Axial CT images(A, B) and coronal CT image(C) show an ill defined soft tissue mass in the small bowel mesentery with retraction of adjacent jejunum and ileum. In the mass, **preserved fat around mesenteric vessels** is seen multifocally.

IgG4-related Sclerosing Mesenteritis

- Soft tissue mass enveloping the mesenteric vessels than can induce partial or complete obstruction of the small intestine, occasionally.

- Preservation of fat around the mesenteric vessels (“fat ring sign”).

Differential diagnosis

- Lymphoma, carcinoid tumor, carcinomatosis.

  - mesenteric lymphoma : (“sandwich sign”).

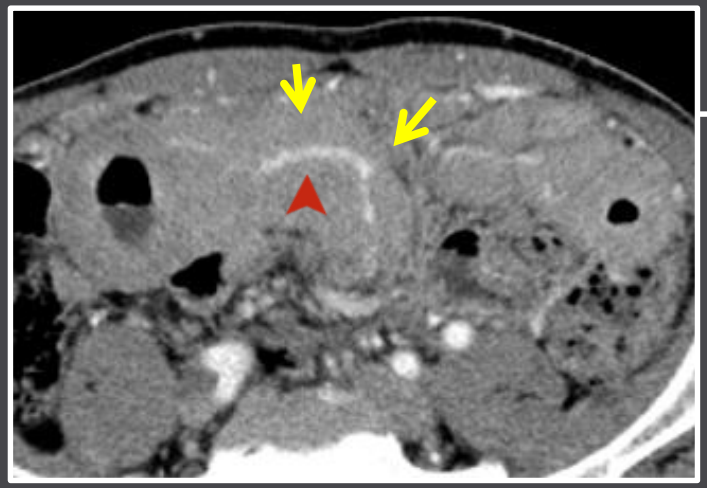


Fig. 10. **Lymphoma** in 61-year-old man.

Axial contrast-enhanced CT image reveals soft tisse mass (arrows) enveloping ileocolic artery (arrowhead), presenting sandwich sign, a specific finding of mesenteric lymphoma.

IgG4-related Retroperitoneal Fibrosis

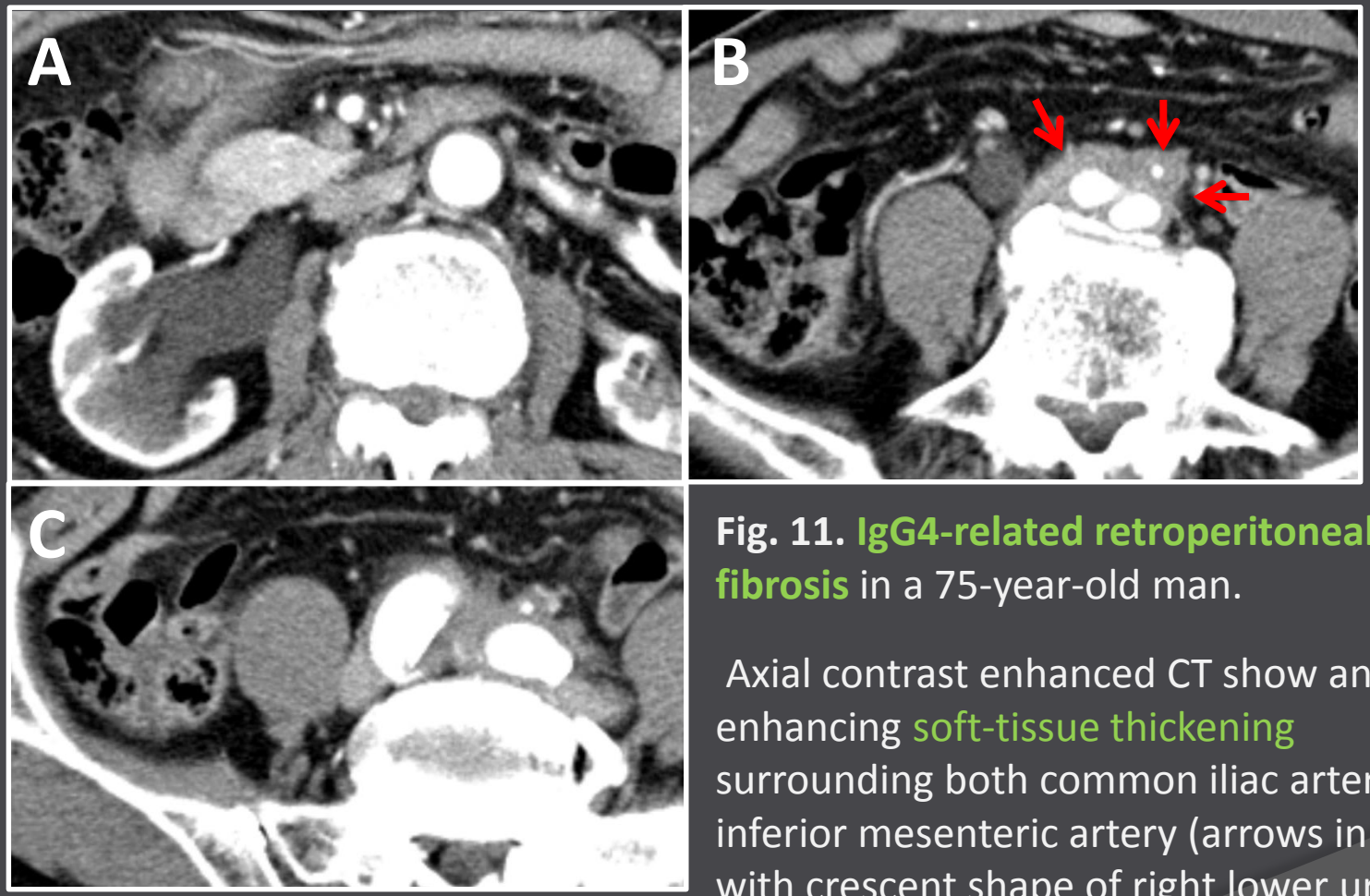


Fig. 11. **IgG4-related retroperitoneal fibrosis** in a 75-year-old man.

Axial contrast enhanced CT show an enhancing soft-tissue thickening surrounding both common iliac artery and inferior mesenteric artery (arrows in B) with crescent shape of right lower ureter (C) due to adjacent fibrosis, producing hydronephrosis (A).

IgG4-related Retroperitoneal Fibrosis

- Three patterns of IgG4-retroperitoneal fibrosis ;
  - a periaortic or arterial mass.
  - periureteral mass, producing hydronephrosis and hydroureter.
  - plaquelke mass.
- At US, a hypoechoic soft tissue surrounding the aorta and its branches.
- At MRI, variable signal intensity depending on the degree of active inflammation and variable enhancement pattern depending on the maturity of the fibrous tissue.

IgG4-related Retroperitoneal Fibrosis

Differential diagnosis

- Lymphoma, large-vessel vasculitis, syphilis and sarcoidosis-induced arteritis.
  - lymphoma : suprarenal level extension.
  - retroperitoneal fibrosis : pelvic extension, medial ureteral bowing
    no displacement of aorta

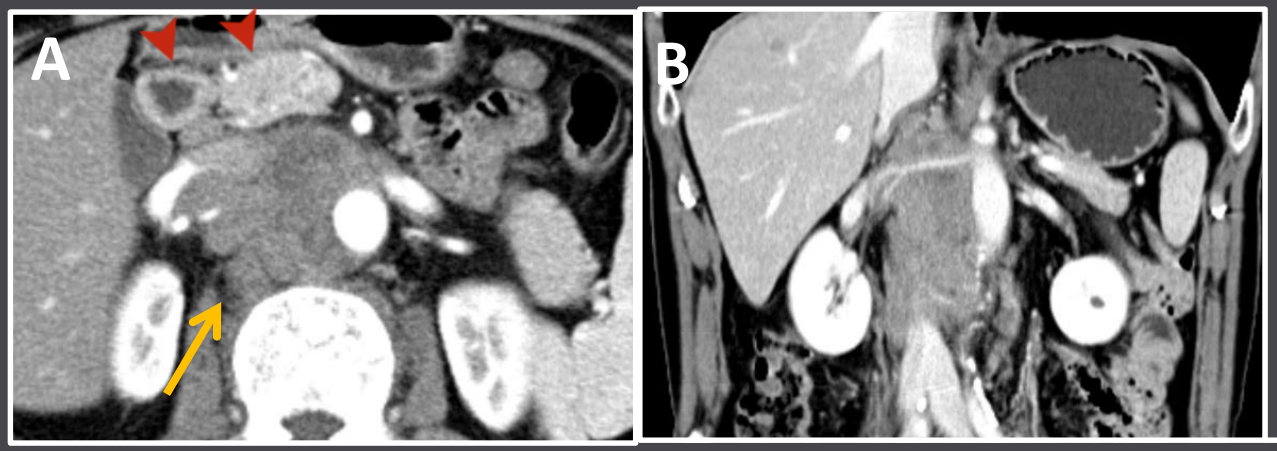


Fig. 12. Lymphoma in a 75-year-old man.

Axial CT imges (A, B) show soft tissue density mass (arrow) with central necrotic portion, **displacing pancreas and duodenum** (arrowheads, mass effect). Coronal contrast enhanced CT image (C) shows **suprarenal level extension of mass**, encasing right renal artery.

IgG4-related Lymphadenopathy

Fig. 13. **IgG4-related lymphadenopathy** in a 62-year-old man.
Coronal contrast-enhanced CT images (A, B, C) show multiple enlarged LNs at pancreaticoduodenal, pericaval, para-aortic nodal stations. Also, there are mild enhancing soft tissue mass with perilesional infiltration along renal vein (arrow), IVC, renal pelvis and ureter.

IgG4-related Lymphadenopathy

- Abdominal(retroperitoneal, peripancreatic, mesenteric), mediastinal, hilar, and cervical lymphadenopathy have been reported.

Differential diagnosis

- lymphoma, Castleman disease, disseminated malignancy.
  - IgG4-related disease : small lymph node <2 cm), no fever or weight loss.
  - disseminated malignancy : omental cake, stranding and distortion of mesentery

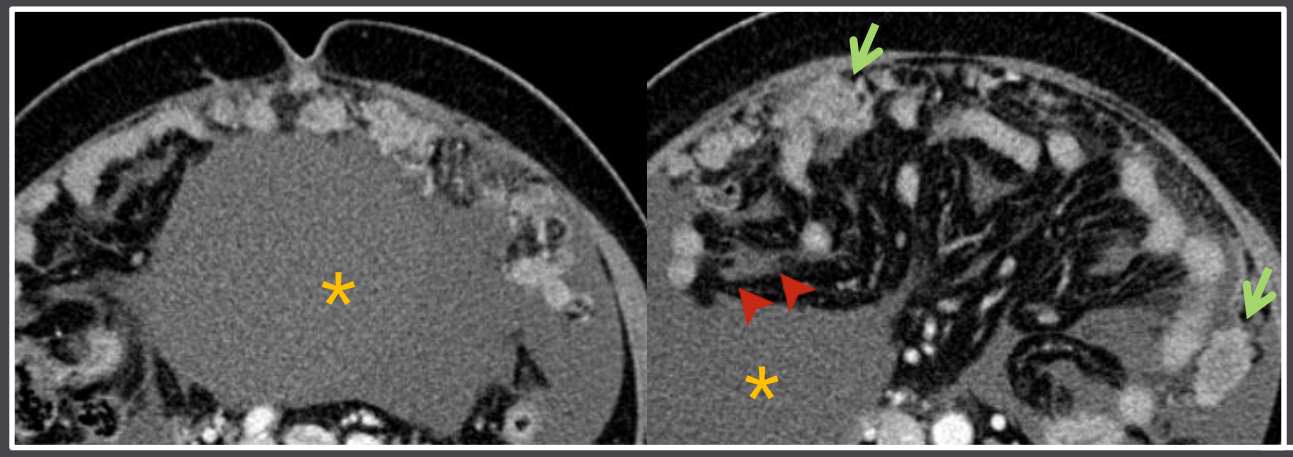


Fig. 14. ovarian cancer with peritoneal seeding in a 56-year-old man.

Large amount of ascites (asterisk), mesenteric strandings (arrowheads) with nodular peritoneal thickening and multiple solid enhancing nodules (arrows) at peritoneum (>2cm) is seen.

Conclusions

- IgG4-related disease is a unique and distinct systemic disease that is frequently misdiagnosed as neoplastic and other inflammatory processes.

- The recognition of the typical imaging patterns in each abdominal organ can raise the suspicion of the disease, and the combination of radiologic, serologic, and histologic findings can lead to correct diagnosis, ensuring effective treatment.

References

- IgG4-related Sclerosing Disease: Autoimmune Pancreatitis and Extrapancreatic Manifestations; RadioGraphics 2011; 31:1379–1402
- IgG4-related Disease from Head to Toe; RadioGraphics 2015; 35:2007–2025
- IgG4-related Disease; Springer Japan 2014; Hisanori Umehara et al.
- The Spectrum of IgG4-Related Disease in the Abdomen and Pelvis; AJR 2013; 201:14–22
- Biliary and hepatic involvement in IgG4-related disease; Alimentary pharmacology and therapeutics; Volume 40, Issue 11-12; December 2014; Pages 1251–1261
- IgG4-related hepatic inflammatory pseudotumor with sclerosing cholangitis: a case report and review of the literature; Cases Journal 2009, 2:7029
- Differentiation of Lymphoma Presenting as Retroperitoneal Mass and Retroperitoneal Fibrosis: Evaluation with Multidetector-row Computed Tomography; Chinese Medical Journal ¦ March 20, 2017 ¦ Volume 130 ¦ Issue 6
- Imaging appearance of fibrosing diseases of the retroperitoneum: can a definitive diagnosis be made?; Abdom Radiol (NY). 2017 Aug 28