The Spectrum of IgG4-Related Sclerosing Disease in the Abdomen

Poster No.:	C-1111
Congress:	ECR 2019
Type:	Educational Exhibit
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Keywords:	Abdomen, Mesentery, Retroperitoneum, CT, MR, Education, Pathology
DOI:	10.26044/ecr2019/C-1111

Learning objectives

- To review radiological features of IgG4-Related Disease (IgG4-RD) in the abdomen and pelvis and their correlation with physiopathological and clinical features.
- To evaluate the utility of multimodality cross-sectional imaging in its diagnosis.
- To highlight the imaging clues for an appropriate differential diagnosis.

Background

IgG4-related disease (IgG4-RD) is a multisystemic and increasingly diagnosed immunemediated fibroinflammatory condition characterized by diffuse or focal tumor lesions with a dense lymphoplasmacytic infiltrate enriched in IgG4-positive plasma cells associated with obliterative phlebitis and a variable degree of fibrosis. Elevated IgG4 serum levels are found in 60-70% of patients, but they are not pathogenic and only represent a down-regulatory response of the immune system.

IgG4-RD mostly affects men older than 50 years-old. The disease is also increasingly recognized to occur in children. It can synchronously or sequentially involve virtually all the organ systems of the abdomen, being the most common the pancreas, but it can also affect the biliary tree and gallbladder, retroperitoneum, kidney, prostate and lymph nodes.

It is usually a self-limiting condition, but if vital organs are involved, aggressive treatment with glucocorticoids is mandatory since it can lead to serious organ failure. Treatment is effective in the majority of patients, but disease flares are common, so azathioprine, mycophenolate mofetil, and methotrexate are used frequently as glucocorticoid-sparing agents or remission-maintenance drugs.

CT, MR and 18F-FDG PET-CT are the imaging modalities of choice to depict characteristic imaging features and extent of IgG4-RD. Both morphologic and functional imaging are complimentary for evaluation of response to therapy.

Findings and procedure details

IgG4-related Pancreatitis (Fig. 1 on page 8, Fig. 2 on page 8)

IgG4-related pancreatitis is the most common intrabdominal manifestation of the IgG4-RD and it accounts for 5-11% of chronic pancreatitis.

Patients present with similar symptoms of pancreatic adenocarcinoma or chronic pancreatitis, such as mild abdominal pain, weight loss, obstructive jaundice, and new-onset diabetes. Radiological features are key clues in the differential diagnosis along with involving of extrapancreatic organs and responsiveness to glucocorticoids.

On TC, IgG4-related pancreatitis presents as a diffuse enlargement with loss of

pancreatic clefts ("sausage-shaped" sign) or segmental enlargement of the head and uncinate process. A rare form has been described where multifocal hypodense

masses are present within a diffusely enlarged pancreas.

A hypoattenuating halo (capsule-like rim) caused by sclerosis of surrounding fat is frequently seen and the pancreatic duct is diffusely narrowed.

It shows reduced enhancement during pancreatic phase (40 seconds after contrast injection) and delayed enhancement on portal venous phase (70 seconds)

On MR, hypointensity on T1WI and mild hyperintensity on T2WI are seen, with delayed contrast-enhancement and high restriction of MR-diffusion sequences, with ADC values even lower than pancreatic adenocarcinoma.

IgG4-related pancreatitis may be self-limiting in 74% of patients. Glucocorticoid treatment achieve morphological and functional remission in 98% of patients, but recurrence rates are high (24%)

Patients with pancreatic adenocarcinoma present with a hypodense poorly marginated focal mass with heterogeneous enhancement. An extensive desmoplastic reaction, encasement of vessels and dilatation of biliary and pancreatic ducts are also characteristic radiological features.

Hepatobiliary Tract Involvement

IgG4-related sclerosing cholangitis is the most common extrapancreatic manifestation of IgG4-RD in the abdomen. 70% of IgG4-related sclerosing cholangitis is associated with IgG4-related pancreatitis.

Clinical manifestations are similar to those observed in primary sclerosing cholangitis and cholangiocarcinoma.

MR-cholangiography depicts segmental and long strictures with prestenotic dilatation, whereas primary sclerosing cholangitis displays band-like strictures of 1-2 mm with a beaded and pruned-tree appearance and diverticulum-like outpouching. Strictures of the lower common bile duct are also more frequent in IgG4-related sclerosing cholangitis.

There are four types of IgG4-related sclerosing cholangitis according to the location of the biliary tree strictures:

- Type 1: Distal common bile duct stricture.
- Type 2: Distal common bile duct stricture with diffuse intrahepatic cholangiopathy with (2a) or without (2b) prestenotic dilatation.
- Type 3: Hilar and distal common bile duct stricture.
- Type 4: Hilar stricture.

Just like primary sclerosing cholangitis, IgG4-related sclerosing cholangitis can also progress to end-stage liver disease and cholangiocarcinoma.

IgG4-related sclerosing cholecystitis is a rare condition, usually presented along with IgG4-related sclerosing cholangitis, that presents as diffuse thickening of the gallbladder wall or an infiltrating tumour, difficult to differentiate from gallbladder carcinoma.

IgG4-related hepatopathy presents non-specific radiological features like hepatomegaly and periportal edema. Benign pseudotumors have also been described.

Retroperitoneal Fibrosis (Fig. 3 on page 9, Fig. 4 on page 10, Fig. 5 on page 10, Fig. 6 on page 11, Fig. 7 on page 12, Fig. 8 on page 12, Fig. 9 on page 13)

It is present in 10-20% of patients with IgG4-related pancreatitis.

It can manifest 3 types of lesions according to the location of sclerosing inflammation in the aortic adventitia (periaortic), in the submucosal layer of the urinary tract and in the peritoneum/fascia.

On imaging, this condition appears as a soft-tissue mass with a smooth border to the surrounding aorta and its branches or renal parenchyma.

Periaortic type is the most common. It often affects infrarenal abdominal aorta and its branches. An inflammatory abdominal aneurysm or aortic dissection have been described.

Urinary tract type is often associated with unilateral hydronephrosis, usually less severe than the other two types. It seems that the less degree of fibrosis or the epithelium layer spare in this type could explain this feature.

Peritoneum/fascia type often presents as a plaque-like soft-tissue mass in presacral space, with infiltration of pelvic organs.

Differential diagnosis with other retroperitoneal masses is important (lymphoma, large-vessel vasculitis, syphilis, and sarcoidosis-induced aortitis). Smooth borders of the mass and less severe hydronephrosis are key characteristics of IgG4-related retroperitoneal fibrosis. Besides, 95% of patients with IgG4-related retroperitoneal fibrosis have lesions in other locations.

Renal Involvement (Fig. 10 on page 14, Fig. 11 on page 14, Fig. 12 on page 15)

It is present in about one-third of patients with IgG4-related pancreatitis.

IgG4-RD most frequently appears as multiple round or wedge-shaped renal cortical nodules, hypointense both on T1 and T2WI with delayed contrast-enhancement.

Differential diagnosis includes pyelonephritis, vascular insult or metastases.

Renal involvement may also appear as diffuse patchy involvement, a rim of soft tissue around the kidney, bilateral nodules in the renal sinuses and diffuse wall thickening of the renal pelvis wall.

Lymph Node Involvement

It is present in 80% of patients with IgG4-RD, either generalized lymphadenopathy or localized disease around the affected organ.

Radiological features of the lymph nodes are non-specific and diagnosis is based on histology and involvement of another abdominal organ.

The differential diagnosis in patients with generalized lymphadenopathy includes sarcoidosis, multicentric Castleman disease, infection (eg, tuberculosis), and lymphoma or other malignancy.

Others

IgG4-related sclerosing mesenteritis appears as a soft-tissue mass encasing the mesenteric vessels with a fat ring around them. It can lead to small bowel obstruction.

Radiological features of lymphoplasmacytic gastritis include loss of fundal folds, so stomach adopts a narrow tubular morphology, similar to those observed in other types of atrophic gastritis.

Patients with IgG4-related prostatitis present with enlarged gland with heterogeneous contrast-enhancement and multiple adenopathies.

Images for this section:

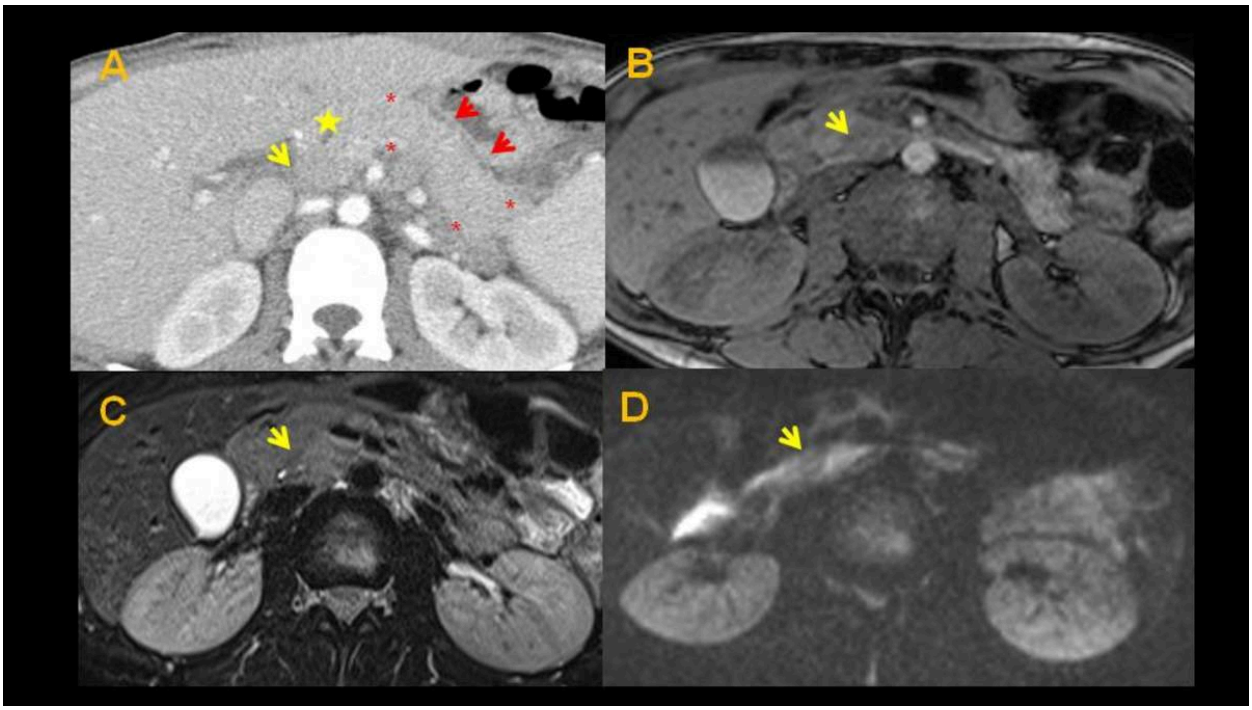

Fig. 1: 27 years-old woman presented with abdominal pain and high levels of amylase. Axial contrast-enhanced CT (a) shows a globulous pancreatic gland (sausage-shape sign, red asterisks) with an hypodense halo on sclerosis (red arrows), but with a diffuse enlargement of pancreatic duct (yellow asterisk) and a slightly hypondense area of hypodensity in the head of the pancreas (yellow arrow) Axial T1WI (b), T2WI with fat suppression (c) and diffusion (d) show a hypointense area on T1WI, hyperintense on T2WI with fat suppression and with restriction on diffusion at the head of the pancreas (yellow arrow on b, c and d)

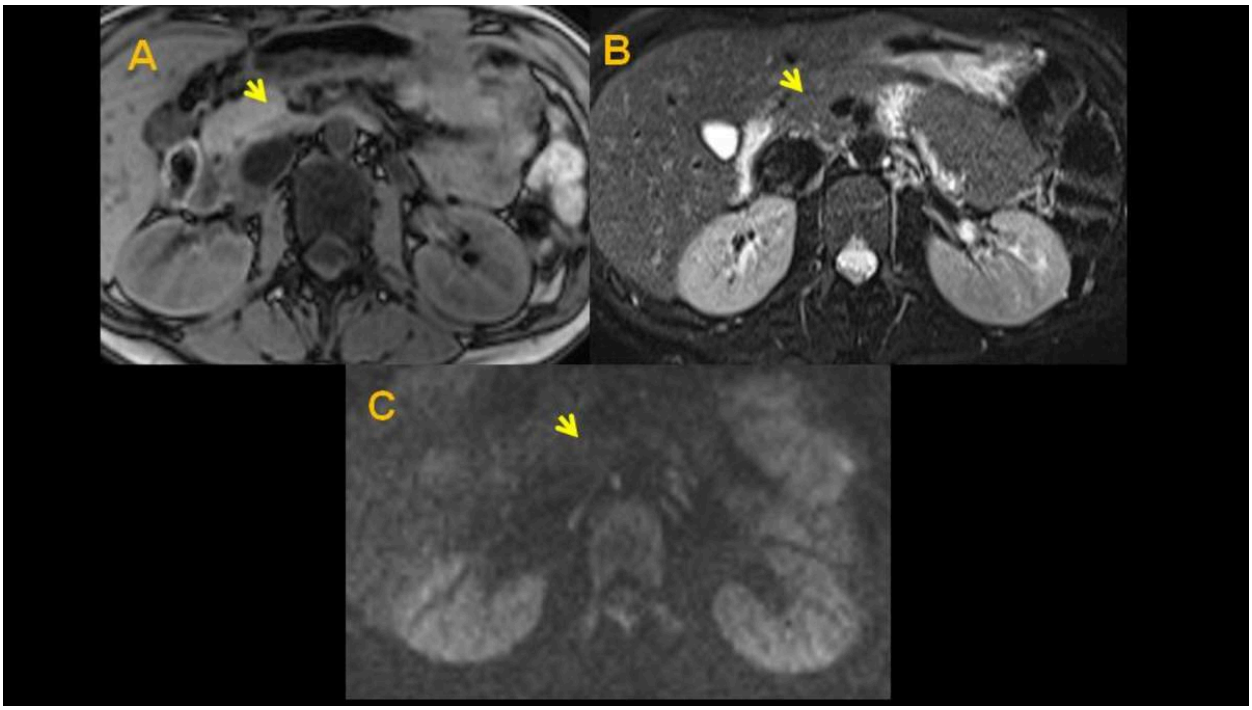

Fig. 2: Follow-up of the previous patient, 15 months after the diagnosis and treatment with glucocorticosteroids. Axial T1WI (a), T2WI with fat suppression (b) and diffusion (c) show a resolution of the lesion at the head of the pancreas (arrows in a, b and c)

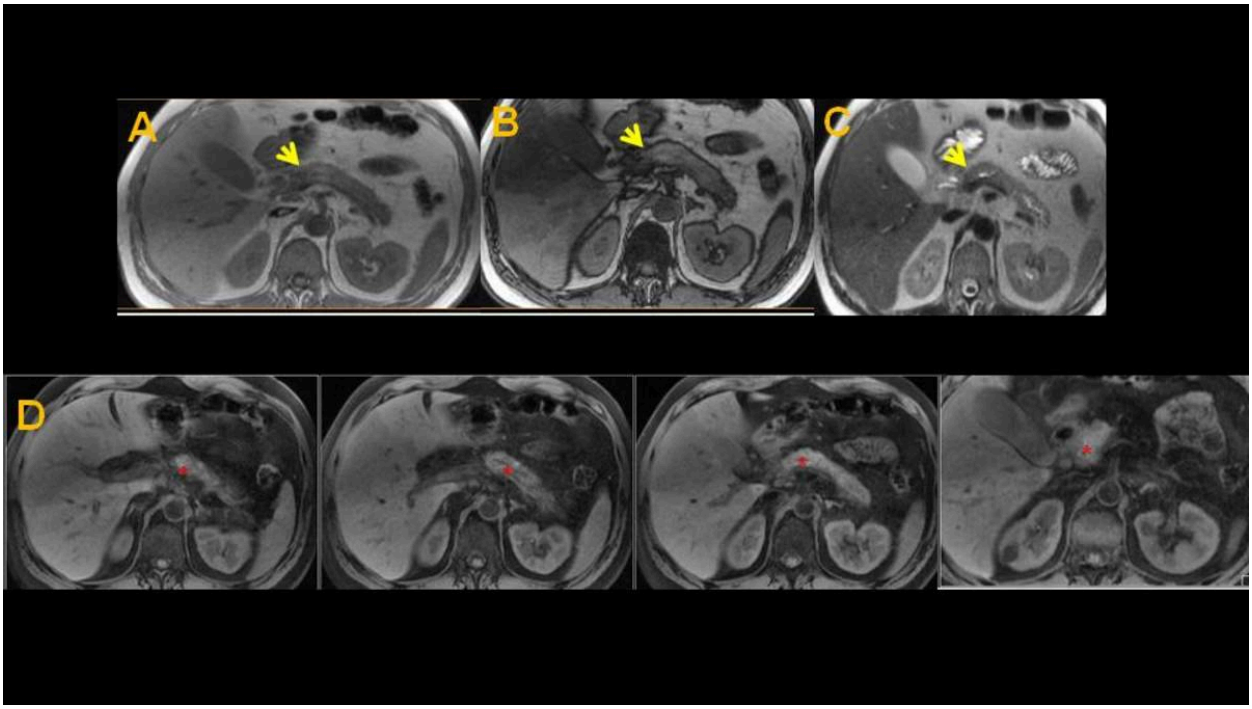

Fig. 3: 53 years-old man presented with right hypochondrial pain, ictericia, coluria and acolia. Axial T1WI in and out of phase (a,b), T2WI (c) and early (d) and delayed (e) post-contrast T1WI show a globulous pancreatic gland (sausage-shape sign, arrows in a,b,c) with delayed contrast-enhancement (asterisks in d)

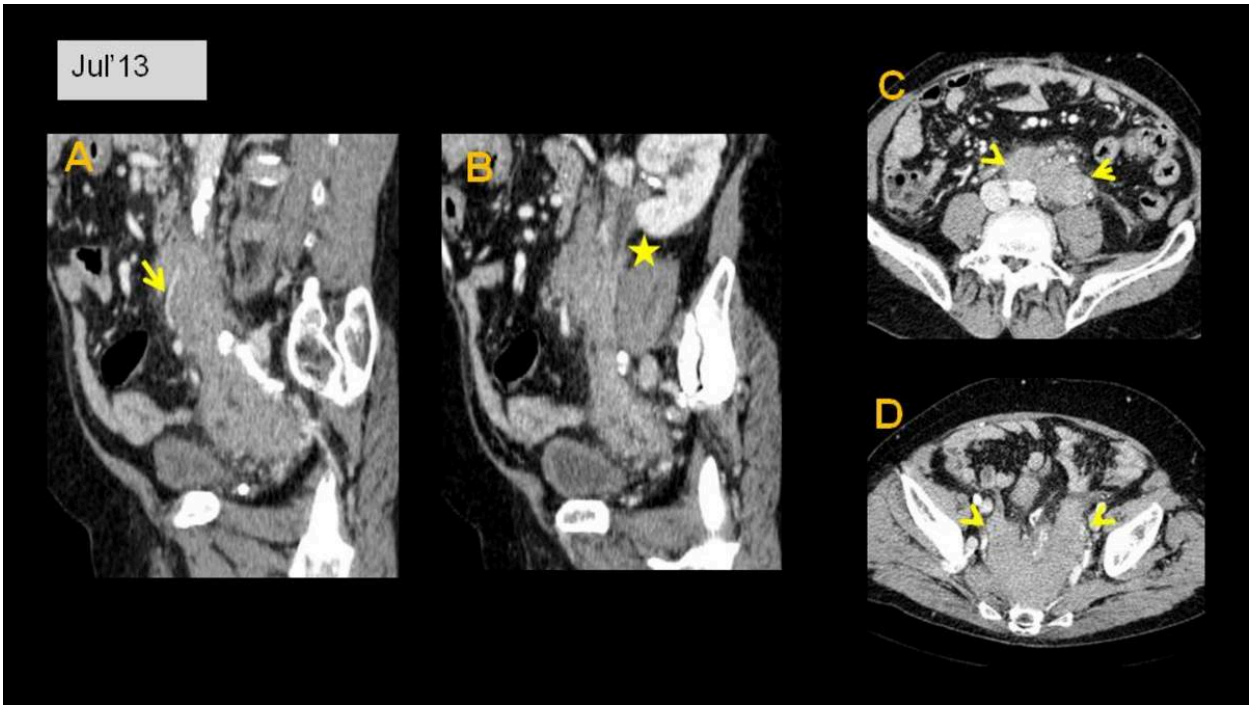

Fig. 4: 74 years-old male with IgG4-RD retroperitoneal fibrosis. Sagittal (a and b) and axial (c and d) contrast-enhanced CT show retroperitoneal soft tissue enlargement (arrowheads) with encasement of superior mesenteric artery with hipodense halo of fat sparing (arrow) and encasement of the left ureter, with secondary hydronephrosis (asterisk) Diagnosed based on high serum levels of IgG4.

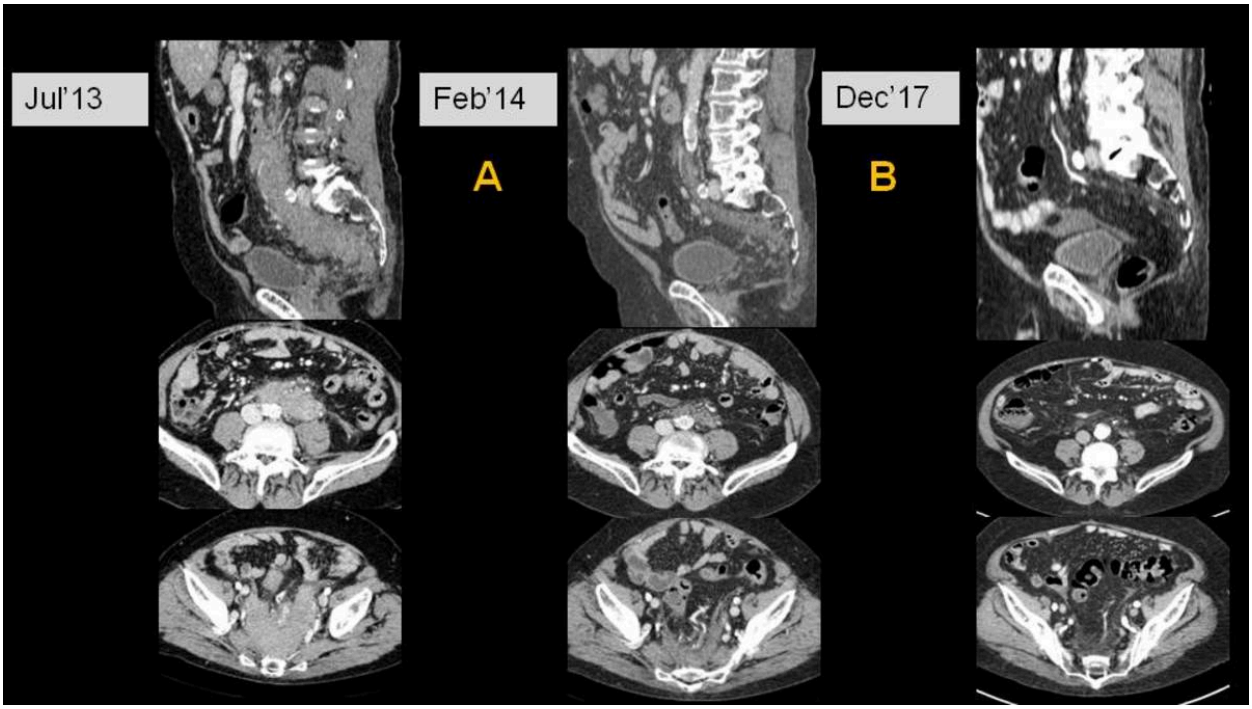

Fig. 5: Partial response after treatment with mycophenolate after the first 6 months (a) and complete response after 4 years follow-up (b).

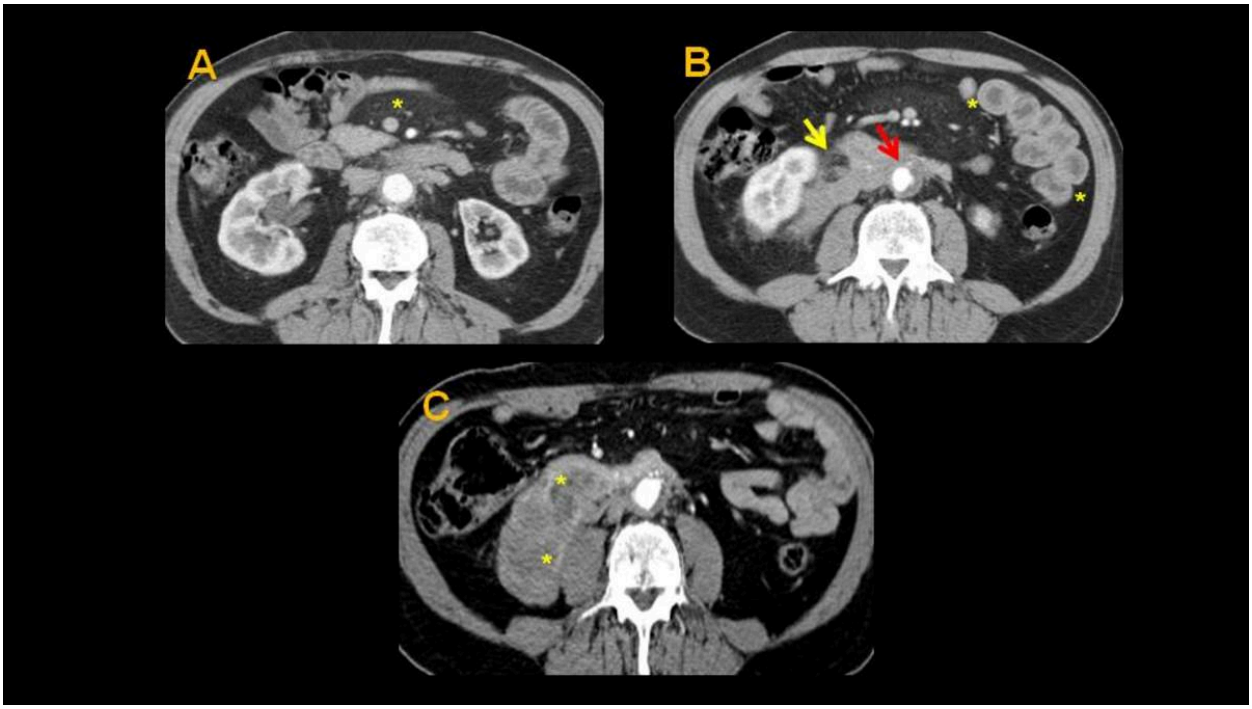

Fig. 6: 56 years-old male with IgG4-RD retroperitoneal fibrosis. Axial contrast-enhanced CT show sclerosing mesenteritis with nodular enlargement (asterisk in a) and concentric

thickening of yeyunal wall (asterisk in b). There is also a retroperitoneal soft tissue enlargement with encasement of the right ureter, with secondary hydronephrosis (yellow arrow in b). It partially encases the aortal and inferior mesenteric artery with concentric thickening of the aorta wall (red arrow in b) After 7 years of follow-up, after treatment with Rituximab ®, there is a change in internal density of the soft tissue mass (asterisks in c). No biopsy was performed. High serum levels of IgG4 was detected.

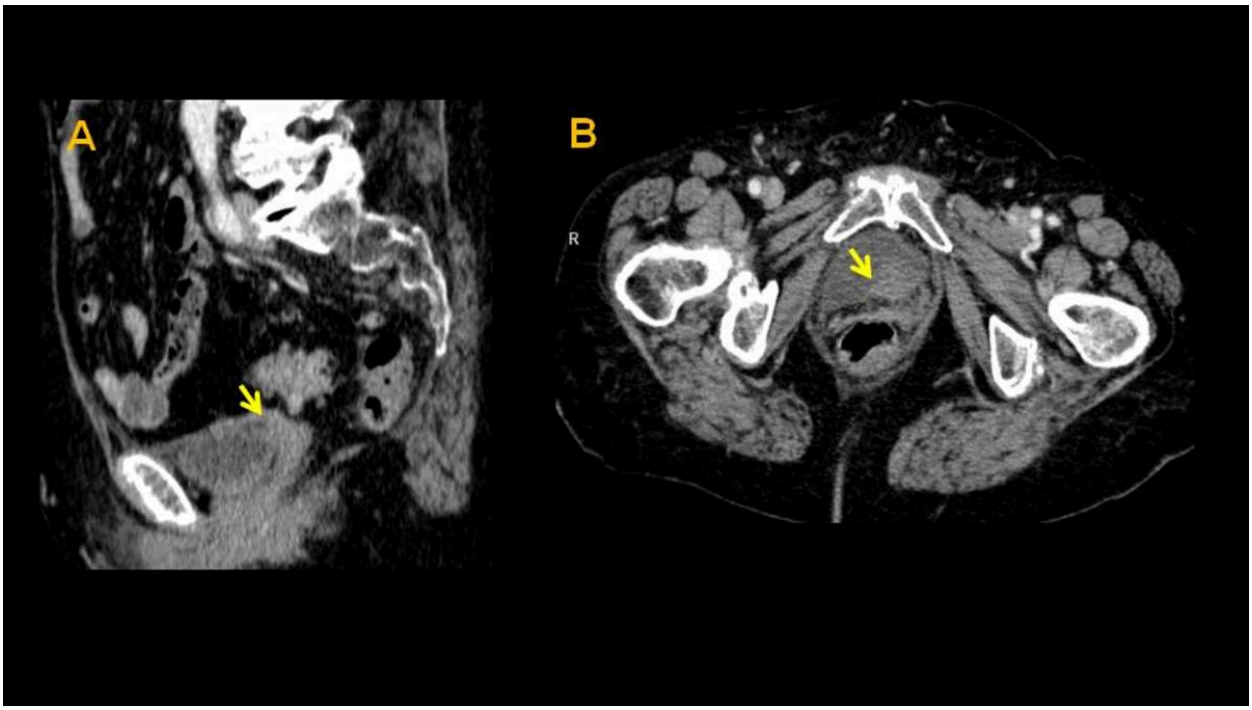

Fig. 7: 85 years-old female with IgG4-RD of the vaginal vault, asymptomatic. Sagittal (a) and axial (b) contrast-enhanced CT show a focal thickening of the bladder wall (arrowheads). Biopsy by transurethral resection demonstrated inflammatory infiltrate enriched with 12,5% of IgG4 plasma cells. There was no progression in 5 years follow-up without treatment.

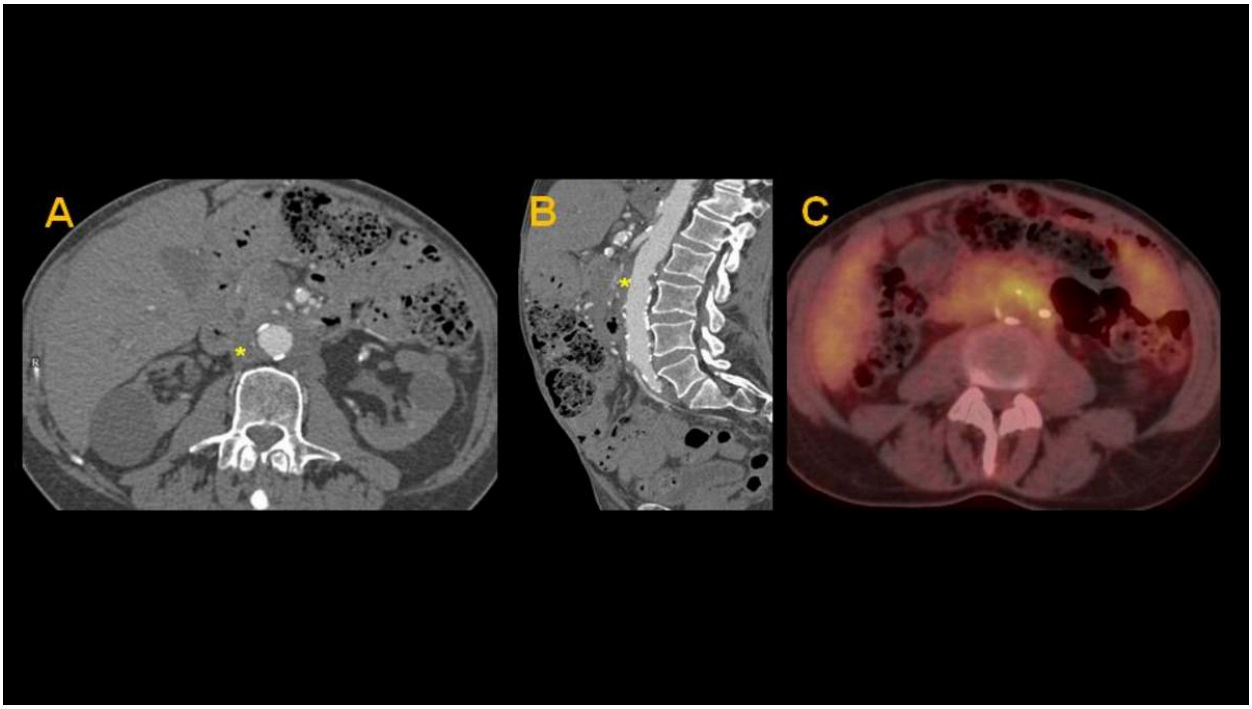

Fig. 8: 69 years-old male with IgG4-RD retroperitoneal fibrosis. Axial and sagittal contrast-enhanced CT show retroperitoneal soft tissue enlargement with encasement of the aorta which presents irregular plaques of fibrolipid atheroma (asterisks in a and b). Axial FDG-18 PET-TC (c) shows avid uptake of radiotracer.

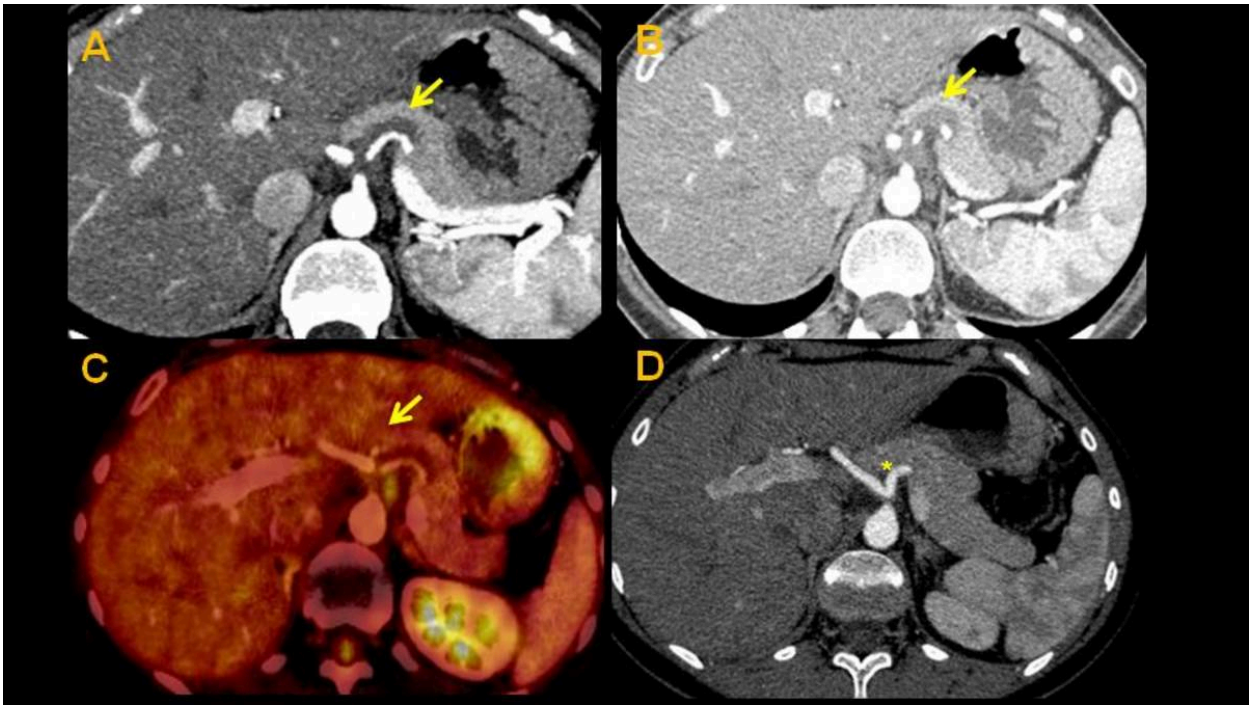

Fig. 9: 41 years-old female with IgG4-RD periarteritis. Axial contrast-enhanced CT shows celiac trunk and splenic artery encasement by a rim of soft tissue thickening (arrow in a, b and c). This periarterial soft tissue thickening shows avid uptake of FDG 18. Complete response after treatment with prednisone (asterisk in d).

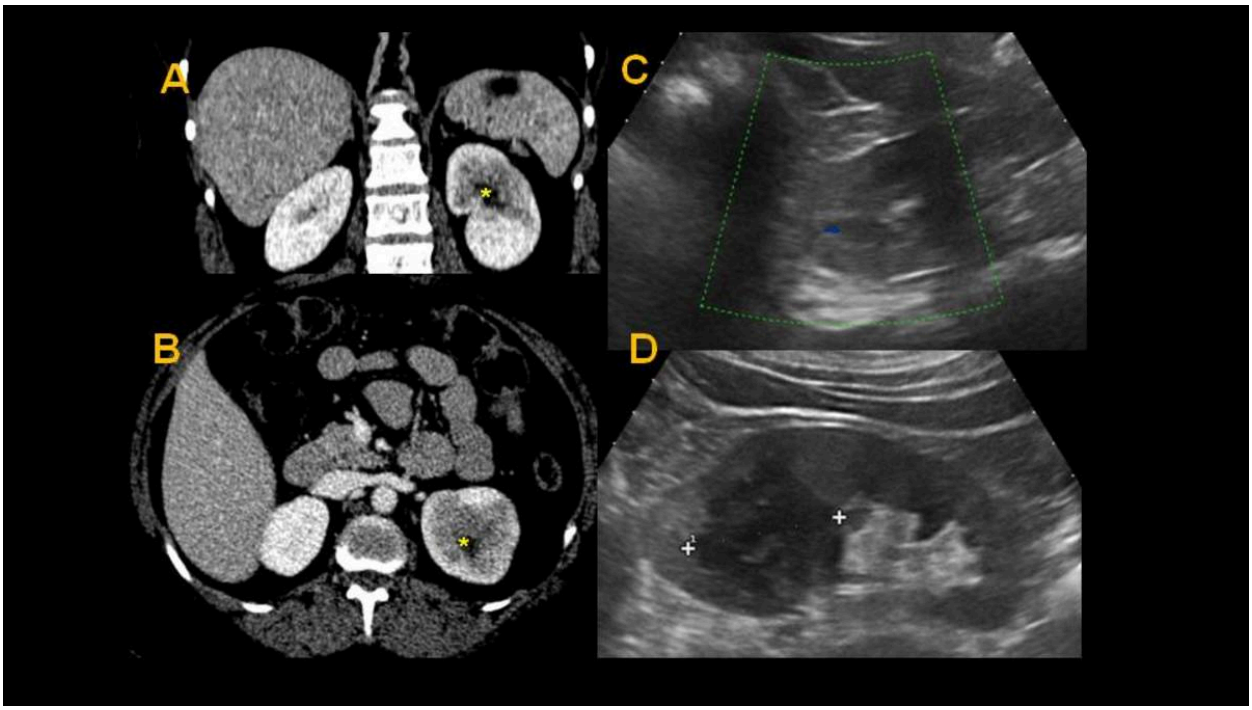

Fig. 10: 53 years-old female with IgG4-RD renal pseudotumor. Coronal (a) and axial (b) contrast-enhanced CT show a renal pseudotumor in the upper pole of left kidney with calyceal dilatation (asterisk). An ill-defined mass without colour Doppler is observed in ultrasonography (c and d)

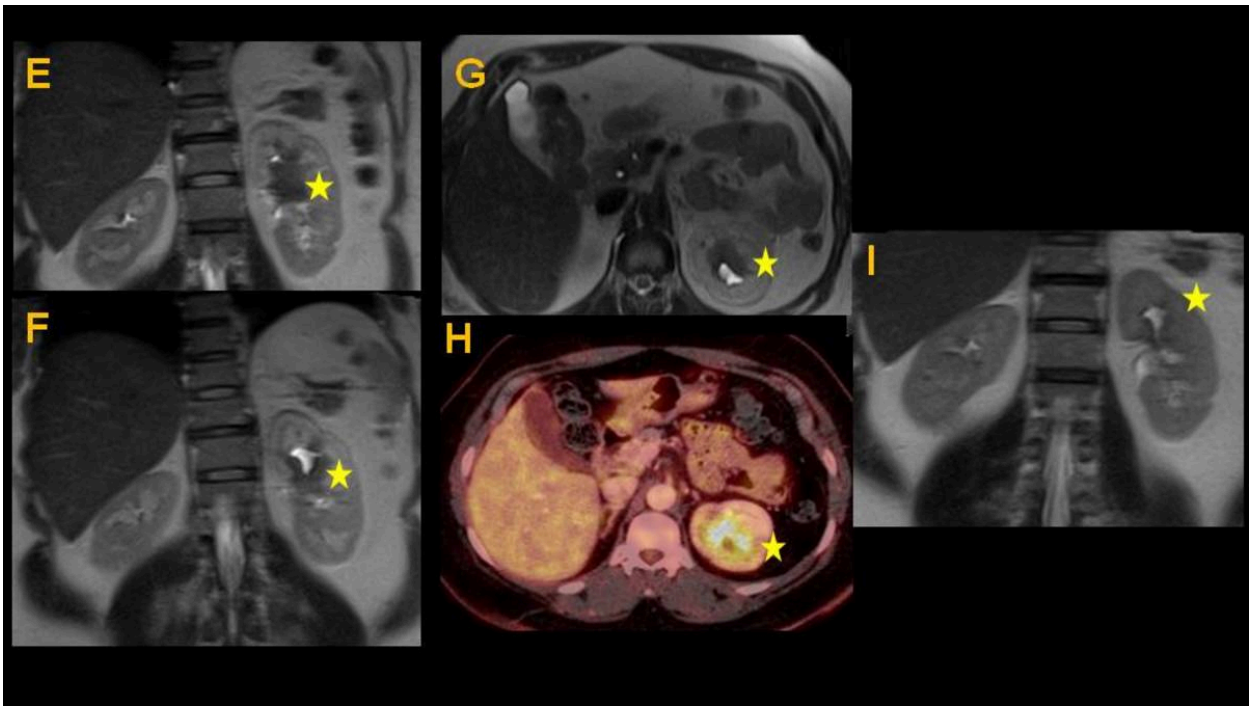

Fig. 11: Same patient as previous figure. Coronal (a, b) and axial (c) T2WI show a renal mass in left kidney. Axial FDG-18 PET-TC (d) shows avid uptake of radiotracer.

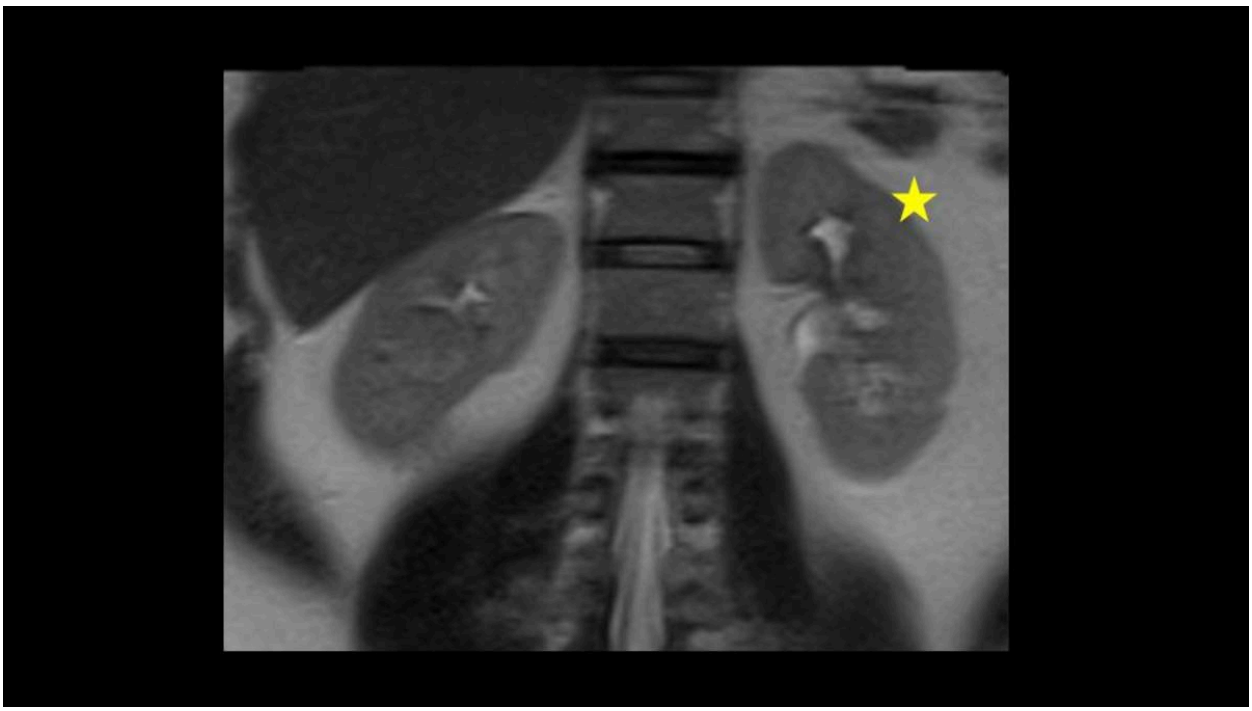

Fig. 12: Follow-up of previous patient, after 24 months of treatment with glucocorticoids, completed response was observed.

Conclusion

IgG4-RSD is a multisystemic fibroinflammatory condition that mimics many neoplastic, infectious and inflammatory disorders.

Radiologists should be able to recognize key radiological features and frequent multiorgan involvement of the disease to establish an accurate and timely diagnosis in combination with clinical history and serologic markers and to avoid unnecessary invasive procedures.

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References

- Kamisawa T, Funata N, Hayashi Y, et al. A new clinicopathological entity of IgG4-related autoimmune disease. J Gastroenterol. 2003;38:982-4.
- Hedgire SS, McDermott S, Borczuk D, et al. The spectrum of IgG4-related disease in the abdomen and pelvis. AJR Am J Roentgenol. 2013;201:14-22.
- Sun GF, Zuo CJ, Shao CW, et al. Focal autoimmune pancreatitis: radiological characteristics help to distinguish from pancreatic cancer. World J Gastroenterol. 2013;19:3634-41.
- Stone JH, Zen Y, Deshpande V. IgG4-related disease. N Engl J Med. 2012;366:539-51.
- Kamisawa T, Takuma K, Anjiki H, et al. Differentiation of autoimmune pancreatitis from pancreatic cancer by diffusion-weighted MRI. Am J Gastroenterol. 2010;105:1870-5.
- Khalili K, Doyle DJ, Chawla TP, et al. Renal cortical lesions in patients with autoimmune pancreatitis: a clue to differentiation from pancreatic malignancy. Eur J Radiol. 2008;67:329-35.