Biomedical Sciences and Clinical Medicine 2023;62(3):94-105.
doi: 10.12982/BSCM.2023.12
https://heo1.tci-thaijo.org/index.php/CMMJ-MedCMJ/index

BSCM
Biomedical Sciences and Clinical Medicine

Original Article **Open Access**

CT and MRI Manifestations of IgG4-Related Disease in the Abdomen: A Retrospective Review

Sittaya Buathong[1], Kobkun Muangsomboon[1], Voraparee Suvannarerg[1], Patkawat Ramart[2] and Sorranart Muangsomboon[3]

[1]Division of Diagnostic Radiology, Department of Radiology, [2]Division of Urology, Department of Surgery, [3]Department of Pathology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand

Correspondence:
Sittaya Buathong, MD,
Division of Diagnostic Radiology,
Department of Radiology,
Faculty of Medicine Siriraj Hospital,
Mahidol University, Bangkok,
Thailand.
E-mail: sittaya.bua@gmail.com

Received: November 21, 2021;
Revised: June 22, 2023;
Accepted: August 3, 2023

ABSTRACT

OBJECTIVE IgG4-RD is an immune-mediated systemic inflammatory disease that affects multiple organs, including in abdomen and pelvis, and presents with various radiologic appearances. The purpose of this study was to review the imaging manifestations of IgG4-RD in the abdomen at Siriraj hospital.

METHODS This retrospective study was approved by the IRB of Siriraj hospital. Thirty-five patients diagnosed with IgG4-RD with abdominal involvement in the 17-year period 2003-2020 identified by searching hospital radiology and ICD10 data bases were included. Thirty-three CT and three MRI images, including one patient with a CT at the initial presentation and an MRI at a relapse presentation, were reviewed by a radiologist for the presence of organ involvement.

RESULTS A total of 105 abdominal problems were identified among the 35 patients, with many patients having more than one issue. The most common issue was pancreatitis which was diagnosed in 22 patients (62.9%), followed by bile duct in 18 patients (51.4%), retroperitoneum in 16 patients (45.7%) and kidney in 16 patients (45.7%). A minority of patients also had rare liver, mesentery, prostate gland and/or urethral involvement. Various features in each organ were described and characterized.

CONCLUSIONS IgG4-related disease in the abdomen or pelvis can present a wide spectrum of clinical and imaging findings. Recognizing the relevant imaging features facilitates the establishment of an effective diagnosis as well as the differentiation of this disease from other benign or malignant conditions.

KEYWORDS IgG4-related disease, IgG4-related disease in abdomen, IgG4-related disease in pelvis, abdominal involvement of IgG4-related disease, autoimmune pancreatitis, multifocal fibrosclerosis

INTRODUCTION

Immunoglobulin G4-related disease (IgG4-RD) is an immune-mediated, chronic relapsing--remitting inflammatory condition characterized by infiltration of IgG4-positive plasma cells and lymphocytes with associated fibrosis, causing mass-forming lesions within one or more affected organs. Most patients have an increasing level of serum IgG4 (1). The disease was firstly reported in 2001 in a type 1 autoimmune

pancreatitis patient, and was recognized as systemic disease in 2003 (2). The criteria for diagnosis of IgG4-RD developed by a Japanese group in 2011 (1) includes clinical characteristic diffuse or localized swelling or masses in one or more organs, elevated serum IgG4 concentrations (≥135 mg/dL) and histopathologic examination showing marked lymphoplasmacytic infiltration and storiform fibrosis (3). IgG4-RD is one of a small number of diseases for which there is still no data regarding prevalence. The estimated incidence in Japan is around 0.28-1.08/100,000 population (4). The multisystem and organ involvement, however, has been categorized in a number of publications as described in Table 1 which shows radiologic findings of IgG4-RD manifestations in the abdomen and pelvis, including pancreas, bile ducts, gallbladder, liver, retroperitoneum (fibrosis), kidney, and prostate gland.

According to the Japanese criteria, the radiologic characteristics of these organ involvements play an important role in IgG4-RD diagnosis (4). Some of the radiologic findings, however, resemble malignancy, especially the mass-forming pattern in involved organs. Better understanding of these lesions would facilitate the establishment of a more effective strategy for confirming the

Table 1. Radiologic findings of IgG4-RD intra-abdominal manifestation (4-6)

Organs and disease	CT	MRI
Pancreas Type 1 autoimmune pancreatitis - Diffuse disease - Focal disease	Non-contrast enhanced CT (NCECT): Hypoattenuation (4)	T1: Hypointense T2: Mildly hyperintense DWI: Restriction (significantly lower than that of pancreatic cancer) (5)
	CE: Delayed enhancement pattern due to the presence of parenchymal fibrosis, capsule-like rim or halo of low attenuation surrounding the pancreas (4)	
	CT, MRCP, ERCP: Diffuse or segmental narrowing of the main pancreatic duct and sometimes stenosis of the bile duct, duct penetrating sign, ice pick sign, absent or mild upstream dilatation of the pancreatic duct (4)	
	Rare findings: calcifications, pseudocyst, severe peripancreatic stranding	
Liver and Bile duct IgG4-related sclerosing cholangitis	MRCP, ERCP: Focal or diffuse bile duct wall thickening, mostly associated with stenosis and upstream dilatation	
	A circular and symmetric ring of tissue encasing the bile duct wall, with relatively smooth margins and homogeneous enhancement in the delayed phase	
Gallbladder	Diffuse acalculous cholecystitis (5)	
IgG4-related inflammatory hepatic pseudotumor	Homogeneous delayed enhancement	T1: Hypointense T2: Hyperintense CE: Variable
Kidney - Tubulointerstitial nephritis (TIN) - Chronic sclerosing pyelitis - Inflammatory pseudotumor of the ureter	IgG4-TIN CECT: bilateral, hypodense lesions	T1, T2: low signal intensity GE: mild enhancement
	1. Bilateral round or wedge-shaped peripheral cortical lesions (the most common) 2. Diffuse patchy involvement 3. Rim of soft tissue around the kidney 4. Bilateral nodules in the renal sinuses 5. Diffuse wall thickening of the renal pelvis (6)	
Prostate Prostatitis	Prostate gland enlargement with or without focal lesion (5)	
Retroperitoneum	A soft-tissue mass, covering the abdominal aorta and its branches (4) with or without aortitis	
Mesentery sclerosing mesenteritis	Soft-tissue mass enveloping the mesenteric vessels, preservation of fat around vessels, "fat ring sign", specks of calcification (20% of the cases) (4)	
Nodes	<2 cm lymphadenopathy mostly at the hilar region (5)	

diagnosis and to institute the appropriate treatment. To that end, this study reviewed imaging findings from CT and MRI scans of the abdomen and pelvis of IgG4-RD patients recorded in Siriraj Hospital.

METHODS

Patients

Patients diagnosed with IgG4-RD in Siriraj Hospital between 1 April 2003 and 31 January 2020 were identified. The study cohort was identified from the institution's radiology database using the searching terms "IgG4" and "IgG4-RD" as well as recognized conditions in the spectrum of IgG4-RD (1,5,6), e.g., autoimmune pancreatitis (AIP), mass-forming pancreatitis, Kuttner's tumor, Mikulicz's disease, sclerosing sialadenitis, sclerosing cholangitis, sclerosing dacryoadenitis, inflammatory pseudotumor, periaortitis, periarteritis, retroperitoneal fibrosis, interstitial nephritis, inflammatory abdominal aneurysm, and multifocal fibrosclerosis, in radiological reports including clinical summaries, imaging findings, diagnoses, and impressions. Additional searches were conducted of the ICD 10 database for the code D803 which indicates the presence of IgG4-RD.

Inclusion criteria

The inclusion criteria used for the diagnosis of IgG4-RD in this study (4) were histology-proven IgG4-RD (including morphological characteristics of typical storiform fibrosis and/or obliterative phlebitis, an increased absolute number of IgG4þ plasma cells, and an elevated IgG4þ/IgGþ plasma cell ratio) (7) or a diagnosis by clinicians of involvement of IgG4-RD in one or more organs with elevated serum IgG4 (>135 mg/dL) (5). For example, type 1 autoimmune pancreatitis (AIP) and IgG4-RD pancreatitis do not always require histological confirmation, rather the diagnosis is based on clinical features and specific imaging features of pancreatic manifestations (Table 1) with elevated IgG4 serum. All patients included in this study had undergone abdominal CT or MRI scanning in Siriraj Hospital at the time of diagnosis.

Clinical features

Electronically stored clinical notes for all patients were retrospectively reviewed for gender, age, past medical history, clinical presentation, and course of treatment. The serum IgG4 level (mg/dL) at the time of diagnosis was also obtained.

Statistics

Data was analyzed using Predictive Analytics Software 18.0 (SPSS Inc., Chicago, IL, USA). Statistical analysis was performed using descriptive statistics (mean, standard deviation, and percentage).

CT and MRI examinations

Of the 35 patients, 33 had undergone CT scanning of the abdomen at the time of presentation. The scanning protocols were varied, with coverage of the scan categorized as whole abdomen (19 cases) or upper abdomen (14 cases). One patient underwent a non-contrast CT scan due to poor renal function. Three patients underwent MR imaging of the abdomen (2 upper abdomen with MRCP and 1 lower abdomen). One patient underwent CT and MRI scanning of the lower abdomen at the time of the first and second new organ presentation, respectively.

The CT and MR images of the patients were retrospectively reviewed for organ involvement by an abdominal radiologist. The number of lesions, laterality, maximal diameter of the lesion in centimeters, location, shape (round or wedge shaped), border, attenuation for CT or signal intensity for MR imaging (hypo- or hyperattenuation of signal intensity of the lesion compared with the adjacent normal parenchyma of that organ), focal (limited to one part of the organ) or diffuse (throughout the whole organ) involvement and mass effect of the lesions were analyzed separately for each organ.

Ethical approval

This retrospective study was approved by the Siriraj Institutional Review Board of Siriraj Hospital NO. Si 716/2020.

RESULTS

Patients

By reviewing the clinical data, imaging, and histology of the patients identified by the database search, 35 cases of IgG4-RD that met the inclusion criteria were finally identified. Of the 35 patients, 21 (60%) had histology-proven

IgG4-RD (10 from an intra-abdominal organ, 12 extra-abdominal). An additional 14 patients (40%) were diagnosed as having possible IgG4-RD based on the Japanese Comprehensive Clinical Diagnostic (CCD) criteria for IgG-4RD using the clinical evaluation and IgG4 level.

The majority of the patients were more than 50 years old, with a male-female ratio of 4:1. The majority of the cohort had a clinical presentation (97%). The symptoms were attributed to jaundice in 12 patients (34.3%), while 10 patients (28.6%) had nonspecific abdominal symptoms such chronic abdominal pain and epigastric pain. Seven (20.0%) presented with a mass in the head and neck region. Other clinical presentations included weight loss (n=2, 5.8%) acute kidney injury (n=1, 2.9%), pleural effusion (n=1, 2.9%), and prolonged fever (n=1, 2.9%). One patient was incidentally found to have IgG4-RD in the form of retroperitoneal fibrosis during surveillance of alcoholic cirrhosis.

Other medical diseases of the study cohort were type 2 diabetes mellitus (9 patients), chronic viral hepatitis (2 patients), and prior malignancy (5 patients: 2 prostate cancers, 1 thyroid cancer and 2 hematologic malignancies). One patient was found to have Hashimoto thyroiditis.

Organ manifestations

Among the 35 patients, a total of 105 abdominal imaging manifestations were identified at the time of diagnosis. The pancreas was the most frequently affected organ, involved in 22 cases (62.9%), with a majority (14 cases) presenting in a diffuse form. This was followed by bile duct involvement in 18 patients (51.4%), with an even distribution between focal and diffuse forms. Kidney and retroperitoneal involvement were each seen in 16 patients (45.7%), with the kidney cases split between parenchymal and non-parenchymal involvement, while all retroperitoneal cases exhibited periaortitis and 5 also had additional areas of involvement in the retroperitoneal space. Gallbladder involvement was observed in 10 patients (28.6%), all of whom had diffuse wall thickening. Mesenteric involvement occurred in 7 patients (20.0%), all presenting with mass formation, and the same number had lymph node involvement characterized by enlarged nodes with homogeneous density. Liver involvement was noted in 4 patients (11.4%), primarily in a diffuse form. The least common were prostatic and urethral involvements, each seen in only one patient (2.9%), both exhibiting in a diffuse form (Tables 2 and 3).

DISCUSSION

IgG4-RD is a chronic inflammatory disease that can affect multiple organs, including head and neck, thorax, abdominal area and pelvis as well as skin. The most common presentation is a mass-like lesion or soft tissue infiltration that mimics neoplasm.

The study population was mostly late middle age to elderhood with males predominating. The findings of this study resemble a study of 235 cases of IgG4-RD in Japan by Inoue et al. (8). The initial clinical presentations of the patients in this study were abdominal-related or extra abdominal-related (head and neck, thorax) symptoms and non-specific symptoms (weight loss and fever). Around 1/3 of the cohort had a non-abdominal-related presentation with intra-abdominal involvement discovered by imaging. This is concordant with a prior study which stated that in many cases involvement of other organs is asymptomatic and can only be found by comprehensive imaging of the chest and abdomen (9). Thus, performing a thorough imaging, including the abdomen, is necessary for assessment of disease at the time of diagnosis.

This study presents the abdominal imaging findings in IgG4-RD cases. The majority of those cases involved more than one abdominal organ. The pancreas was the most commonly involved organ, follow by the bile duct, retroperitoneum and kidney, findings similar to a study by Inoue et al. (8), where involvement of the pancreas, kidney, bile duct and retroperitoneum were found in 60%, 23%, 13%, and 4% of cases, respectively.

Only 3 patients (8.6%) in this study had isolated organ involvement in the pancreas, retroperitoneum, and kidney, fewer than that in studies by Okazaki et al. (10) and Inoue et al. (8) which reported single organ involvement in approximately 10-20% and 42% of patients, respectively. The remaining 32 patients (91.4%) in the current study had multiple organ manifestations, both intra- and extra-abdominal.

Table 2. Patient data including age, sex, IgG4 level, extra-abdominal organ involvement, diagnosis and imaging modality at presentation

Patient data	n (%)
Age (years)	Mean 63.89 [IQR 58-70]
IgG4 level (mg/dL)	median 1,290.00
Sex	2
- Male	8 (80.0)
- Female	7 (20.0)
Extra abdominal organ involvement	
- Salivary gland	9 (25.8)
- Orbital pseudotumor	5 (14.3)
- Lung	4 (11.4)
Japanese Comprehensive Clinical Diagnostic criteria (4)	
- Definitive: Pathology + Clinicals/Imagings + IgG4 level	21 (60.0)
- Possible: Clinicals/Imagings+IgG4 level	14 (40.0)
Imaging at modality at clinical presentation	
- CT	32 (91.4)
- MRI	2 (5.7)
- CT and MRI	1 (2.9)
Organ involvement	
- Pancreas	22 (62.9)
- Bile duct	18 (51.4)
- Kidney	16 (45.7)
- Retroperitoneum	16 (45.7)
- Gallbladder	10 (28.6)
- Mesentery	7 (20.0)
- Lymph nodes	7 (20.0)
- Liver	4 (11.4)
- Prostate gland	1 (2.9)
- Urethra	1 (2.9)

Table 3. Image findings of abdominal organ involvement

Organ involvement	Number (%)		
Pancreatic involvement	22 (62.9)	Focal form (8)	Diffuse form (14)
Bile duct involvement	18 (51.4)	Focal form (9)	Diffuse form (9)
Tenal involvement	16 (45.7)	Parenchymal involvement (9)	Non- parenchymal involvement (7)
Retroperitoneal involvement	16 (45.7)	Periaortitis (16)	Periaortitis and other areas of retroperitoneal space (5)
GB involvement	10 (28.6)	Diffuse wall thickening (10)	
Mesenteric involvement	7 (20.0)	Mass formation (7)	
Lymph nodes	7 (20.0)	Enlargement, homogeneous density nodes (7)	
Liver involvement	4 (11.4)	Focal form (1)	Diffuse form (3)
Prostatic involvement	1 (2.9)	Diffuse form	
Urethral involvement	1 (2.9)	Diffuse form	

Most patients had multi-organ involvement at the time of initial diagnosis. One patient had known IgG4-RD in multiple organs including pancreas, retroperitoneum, kidney, liver and gallbladder. The clinical status of remission in that individual was followed by chronic persistent disease and the patient subsequently presented with a periurethral mass seven years after the initial diagnosis.

In the group with multi-organ involvement, some multiple abdominal organ involvement had been found. Bile duct involvement was found with pancreas or gallbladder involvement in 63.6% and 90% of cases, respectively. Renal involvement with retroperitoneal involvement and lymph node enlargement was found in 56.3% and 71.4% of patients, respectively. Almost half the patients (n=15, 42.8%) had extra-abdo-

minal involvement including the head and neck (sialadenitis and orbital pseudotumor) and thorax (pleural effusion, lung nodules, consolidation and mediastinal lymphadenopathy).

Abdominal manifestation

Pancreatic involvement

Pancreatic involvement was found in 22 patients. Four patients who were suspected of having a pancreatic mass subsequently underwent surgery with result of finding IgG4-related pancreatitis. Fourteen patients (63.6%) had a diffuse form of pancreatic involvement which appeared as a diffuse enlargement and loss of pancreatic lobulation or as a diffuse pattern (Fig. 1A). Eight patients (36.3%) had a focal form of pancreatic involvement (head=5, body=2 and tail=1). The proportion of these patterns was similar to that in another study which reported diffused enlargement among 11%-56% and focal or mass-like enlargement among 28%-59% of patients (11). In another series, a 'mixed' appearance of diffuse and focal enlargement was found in 56% of patients (12). However, no clear examples of the mixed form were found in the present study and only one case of diffuse enlargement with the predominating area at the head, neck or uncinate process was depicted.

Most CT scans of the affected pancreatic parenchyma showed hypoenhancement or delayed/late enhancement, whereas normal enhancement was found in only 2 patients. Of the 2 patients with MR images, pancreatic parenchyma was slightly diffuse hypointense on T1-weighted MR images and hypointense on T2-weighted MR images in addition to restricted diffusion. Normal gadolinium enhancement was observed and no pancreatic duct involvement was identified. Christoph et al. described late enhancement, a classical finding of autoimmune pancreatitis, in 25% of patients with CT scans and 74% of patients with MRI (12). The restricted diffusion was possibly an indication of active disease (13).

Additional instances of diffuse patterns were found frequently, e.g., peripancreatic fat stranding (n=5, 35.7%) and a capsule like rim around the pancreas (rim halo sign) (n=8, 57.1%). This capsule-like rim around pancreas was found in a greater proportion (57.1%) of cases in this study than in other studies (25-40%) (14). Other features were less frequent seen, e.g., focal peripancreatic fluid (n=1, 0.07%) and multiloculated cystic lesion at the tail of the pancreas (n=1, 0.07%). Three patients (21.4%)

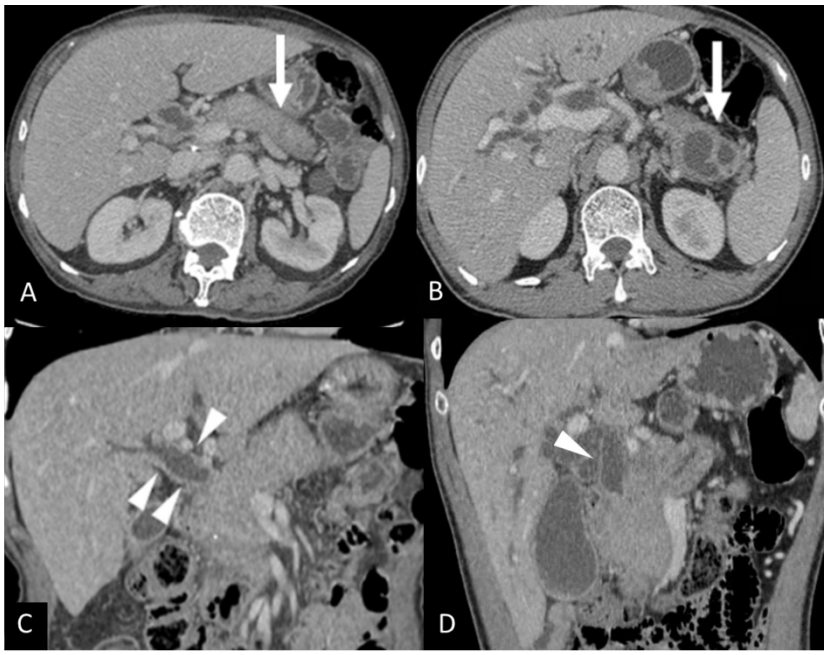

Figure 1. Pancreas and bile duct involvement A. IgG4-related pancreatitis, diffuse pancreatic involvement (arrow) B. IgG4-related pancreatitis, diffuse pancreatic enlargement and multiloculated cyst or probably wall-off necrosis at tail of pancreas (arrow) and distal CBD narrowing (arrowheads) C, D. IgG4-related cholangitis, CBD wall thickening (arrowheads)

were suspected of having splenic vein thrombosis. Multiloculated cystic lesion (Fig. 1B) can be found in case reports of autoimmune pancreatitis (15). For one patient in the present study, underlying chronic alcoholic disease was cited. Despite the high serum IgG4 levels and CT images which revealed diffuse pancreatic and distal common bile duct (CBD) involvement, the nature of this cystic lesion was still uncertain due to the lack of a definitive biopsy. Other probable co-existing diagnoses were alcoholic chronic pancreatitis with pancreatic pseudocyst and pancreatic cystic neoplasm.

In this study, the pancreatic duct was not a significant imaging feature for detection in either CT or MRI, e.g., pancreatic dilatation and duct penetrating sign, probably due to limitations of the CT imaging protocol or to the small number of MRIs in the study. In the case of the diffuse form of IgG4-RD pancreatitis, less visualization of the pancreatic duct was noted and it was presumed to be an indication of extrinsic ductal narrowing secondary to peri-ductal edema or inflammation.

Bile duct involvement

Of the 18 patients with bile duct involvement, 16 underwent CT scans and 2 had MRI scans. Those are not the investigations of choice for patients with biliary involvement (16). Other findings were identified as diffuse involvement (n=9, 50.0%) and focal involvement (n=9, 50%). The majority of the findings were compatible with common features of sclerosing cholangitis, i.e., smooth bile duct wall thickening (Figs. 1C, 1D) as well as progressive enhancement and variable luminal narrowing. Focal involvement appeared as focal smooth wall thickening of the bile duct and various segments of the biliary tract including the entire extrahepatic bile duct (EHD) in 6 patients (66.7%) and in one patient with distal CBD, confluence of the intrahepatic bile duct (IHD) and multifocal short segments involving the IHD and EHD. One focal form showed infiltrated soft tissue lesions or mass-forming involving the hepatic duct confluence and proximal CBD causing upstream dilatation, resembling malignancy such as infiltrative hilar cholangiocarcinoma (17).

Renal involvement

Of the 16 patients with renal involvement (all CT scans), 9 patients (56.3%) had renal parenchymal involvement and 7 (43.7%) had perirenal, renal sinus, or renal pelvis. This finding differs from one study that reported a much greater proportion of parenchymal involvement (75% of 48 cases) (6). One patient with pathologically proven IgG4-related tubulointerstitial nephritis had only a non-contrast CT scan, which revealed nonvisualized lesions. Almost all patients (n=13) had bilateral involvement. Only two patients were found to have unilateral involvement where in both patients the lesions were seen in the right kidney.

Renal parenchymal lesions had the same variation in patterns reported in other studies, most of which were identified as well-defined multiple wedge- or round-shaped cortical lesions (n=6), less commonly as multiple small (subcentimeter) peripheral cortical nodules (n=2) and rarely as diffused patchy infiltration (n=1). On CT scans, the renal parenchymal lesions were low attenuation areas compared with the normal renal cortex during the first and the delayed enhancement phases. None of the lesions were visible on non-enhanced CT scans. Two patients with cortical involvement were found to have perirenal fat stranding. Still, most of the findings were found to have many differential diagnostic considerations. For instance, multiple wedge- or round-shaped cortical lesions (Fig. 2A) had indications of pyelonephritis (18) and vascular insults. Other diseases that also have bilateral renal hypodense lesions, especially metastasis and lymphoma, should be identified in the differential diagnosis, as should other renal inflammatory diseases such as Wegener's granulomatosis (19). A perirenal soft tissue thickening or soft tissue rim sign (Fig. 2B) was also found in one patient where the images resemble lymphoma, retroperitoneal fibrosis, and Erdheim-Chester disease (20).

Patterns of renal involvement of other than the parenchyma were also observed. One patient had irregular enhancement of soft tissues in the bilateral renal sinuses with adjacent fat stranding (Fig. 2C). Diffuse wall thickening of the renal pelvis (Fig. 2D), similar to those reported in another study (6), was present in eight patients. Six of these patients had renal pelvic wall thickening extending to the ureter. No hydronephrosis was seen. One study (6) reported renal pelvic wall involvement without

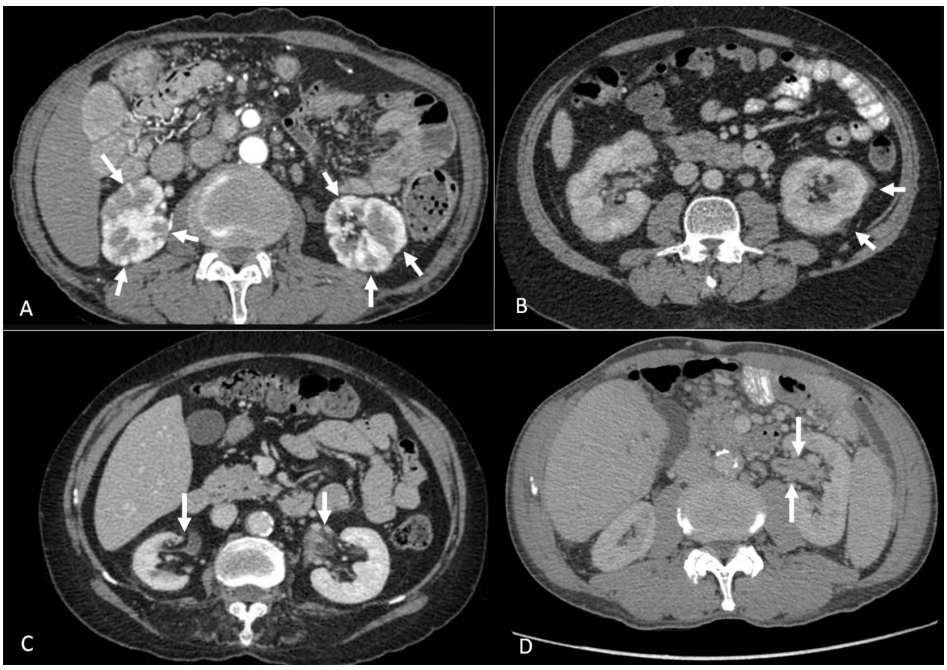

Figure 2. Axial CT images from different patients show renal involvement A. Wedge-shaped peripheral cortical lesions (arrows), B. Diffuse patchy parenchymal involvement with perinephric hypodense soft tissue (arrows) C. Ill-defined soft tissue at renal sinus (arrows), D. Diffuse wall thickening of the renal pelvis (arrows)

retroperitoneal fibrosis and that mild hydronephrosis was observed in about 10% of cases. In cases of marked renal pelvis wall thickening, a differential diagnosis of other infiltrative diseases, e.g., pyeloureteritis and urothelial neoplasms, including infiltrative transitional cell carcinoma, should be considered (21).

Three patients demonstrated two patterns of involvement at initial presentation, either diffuse renal pelvis wall thickening together with patterns of cortical nodules or diffuse patchy and soft tissue at the renal sinus which could indicate the possibility of coexisting lesions in this disease.

Retroperitoneal involvement

All 16 patients with retroperitoneal lesions were visualized as having soft tissue characteristically surrounding the infrarenal part of the abdominal aorta and/or the iliac arteries classical features of retroperitoneal fibrosis which is also called IgG4-related periaortitis (4,22). Five patients had other areas of soft tissue formation within various regions of the retroperitoneum including the posterior pararenal space (n=1), the presacral space (n=1), the renal pelvis (n=2) and the paracaval region (n=1).

The locations of aortic involvement were mostly the infrarenal aorta to the proximal common iliac artery (15 patients), while one patient also had a short-segmented lesion at the origin level of the renal artery. All the lesions were asymmetrical circumferential soft tissue thickening with progressive delayed enhancement (Fig. 3A). The average maximal thickness was 0.7 cm (range 0.5 to 1.8 cm). There was mild dilatation of the affected aorta in 1 patient (about 2.5 cm at the infrarenal aorta), while the rest of the patients had a normal diameter aorta. A varied degree of calcified plagues in the affected aorta was visualized in 12 patients. These findings are similar to those reported in a study of 22 patients by Dai et al. (22). However, a few divergences from that study were noted, e.g., a slightly lower average maximal thickness of the lesions in the present study (mean 0.7 cm compared to 11 mm) and significantly less luminal involvement with mild dilatation of the aorta which was found in only one case compared to 7 of 22 cases in another study (22). One patient in this study with aortic ectasia (IgG4-related pancreatitis and periaortitis) was a 76-year-old man who had underlying diseases including cardiovascular disease and hypertension, so in this case, the aortic ectasia might be related to aging and underlying diseases more than to IgG4-RD luminal involvement. Additionally, three patients with soft tissue formation at the paracaval and presacral

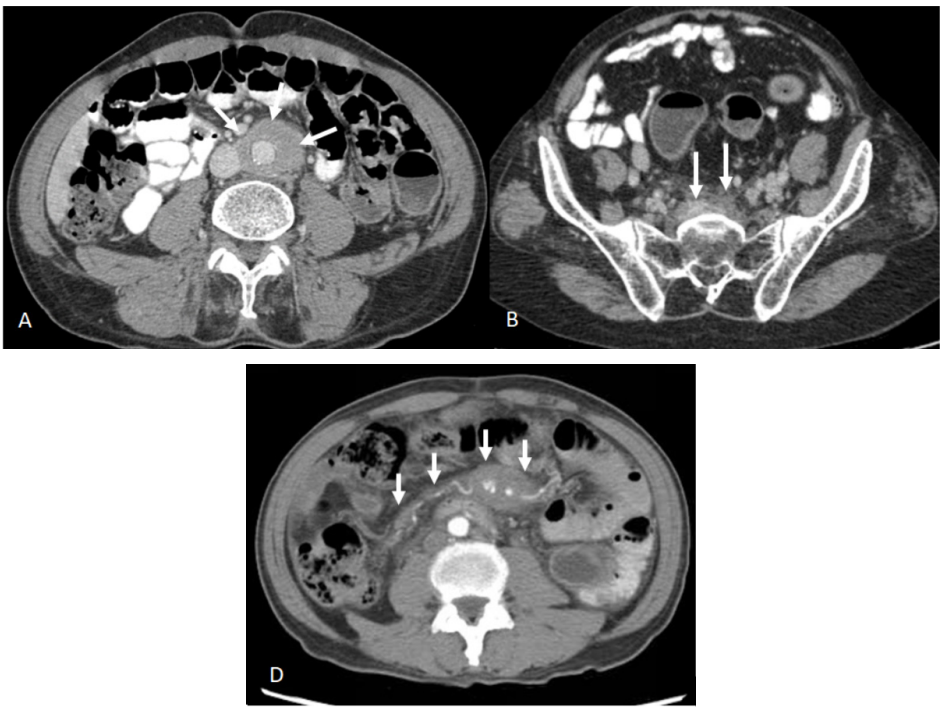

Figure 3. Axial CT images of retroperitoneum and mesenteric involvement A. Periaortic soft tissue density or periaortitis (arrow), B. Soft tissue thickening at presacral region (arrow), C. Soft tissue thickening around mesenteric vessels (arrow)

region (Fig. 3B) and the renal pelvis had bilateral proximal peri-ureteric soft tissue thickening without hydronephrosis or hydroureter.

Other intra-abdominal organ involvement. Other less frequent intra-abdominal organ involvements were found in this study, including gallbladder, mesentery, liver, prostate gland and urethra. Diffused gallbladder wall thickening was visualized in 10 patients of whom only one patient had pericholecystic fat stranding. This feature cannot be differentiated from other cause of chronic cholecystitis. However, 90% of the cases of gallbladder involvement were associated with bile duct involvement as well. It is possible that the accompanying evidence of bile duct involvement could be important for diagnosis.

Mesenteric involvement was found in 7 patients. The lesions were characterized by fat stranding and enhancing soft tissue formation at the mid abdomen, enveloping the mesenteric vessels including the superior mesenteric artery (n=6) and the inferior mesenteric artery (n=1) (Fig. 3C), which is characteristic of sclerosing mesenteritis (4). Peritoneal thickening was found in 3 patients, although several conditions can mimic this appearance in CT scans including lymphoma, carcinoid tumor, carcinomatosis, primary mesenteric mesothelioma, and mesenteric edema (23).

Liver parenchymal lesions were visualized in 4 patients. The lesions were described as a large, ill-defined wedge-shaped area involving the entire hepatic lobe, with heterogenous enhancement in 3 patients. Another patient was found to have an ill-defined hypodense mass which was associated with mild IHD dilatation (Fig. 4A), however, that is non-specific and could be described as infiltrative liver neoplasm (24).

Intra-abdominal lymph node enlargement (greater than 1 cm in the short axis) was found in 7 patients. The enlarged lymph nodes were found in various regions, mostly at the paraaortic and mesenteric regions. Most of the lymph nodes had an oval shape and homogeneous density with a size less than 2 cm. These findings could be nonspecific, but may represent an inflammatory process related to IgG4-RD (4). This study had a limitation in complete nodal evaluation because of the lack of pathology-proven evaluation of the lymph nodes, so the lymph node enlargement could have been a reactive node resulting from a chronic disease.

Prostatic involvement was pathologically proven in one patient with IgG4-RD of the salivary gland and lacrimal gland. The CT revealed

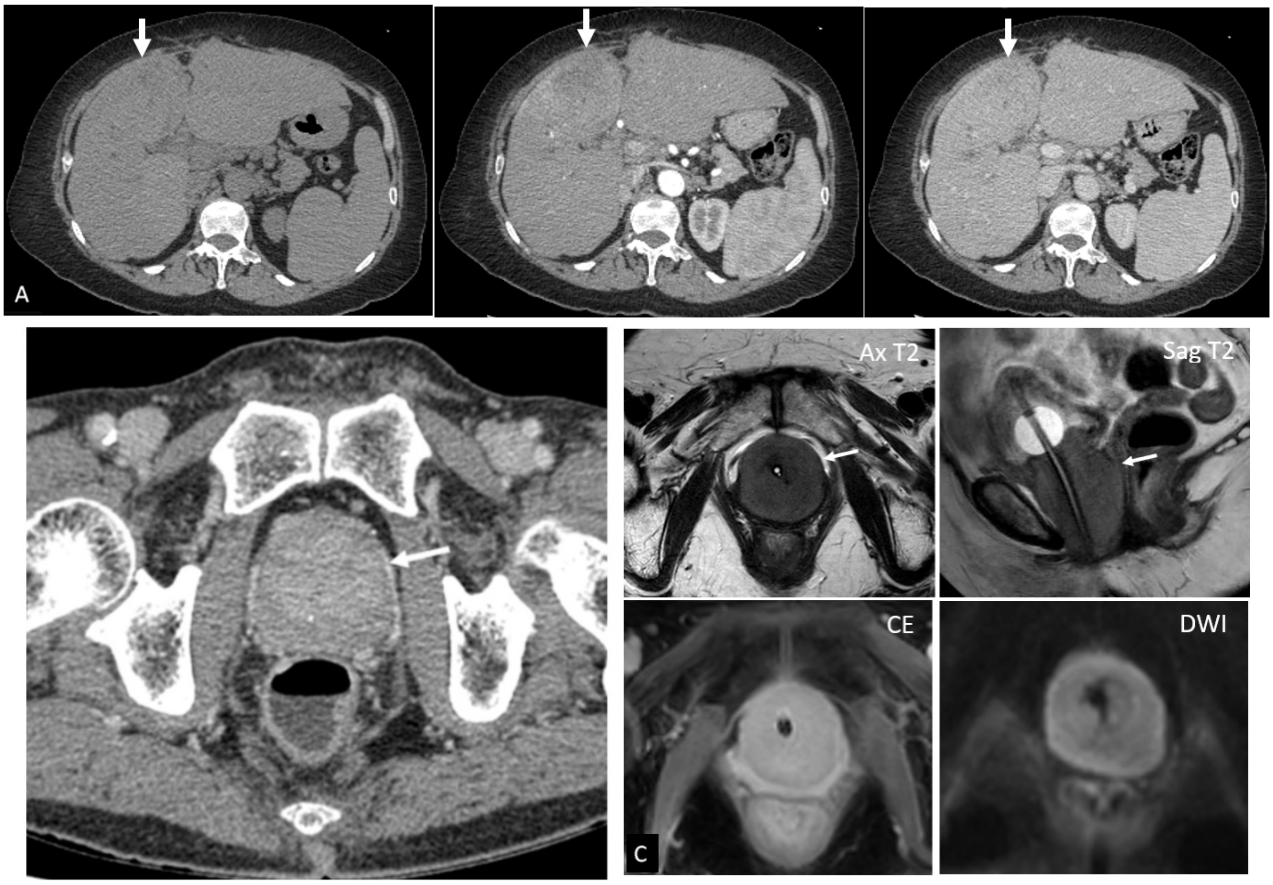

Figure 4. IG4-RD from different patients with liver, prostate gland and urethral involvement A. Inflammatory pseudotumor at liver, the ill-defined mass with delayed enhancement (arrows), B. IgG4-related prostatitis, generalized prostate enlargement and no focal lesion (arrow), C. IgG4-related pseudotumor at urethra, the circumferential peri-urethral soft tissue mass with hypo T2 signal intensity, homogeneous faint enhancement and restricted diffusion (arrows)

an enlarged prostate gland with homogenous enhancement (Fig. 4B). No focal lesion was noted. The serum prostatic surface antigen (PSA) at that time was 6.59 ng/dL. The patient had a lower urinary tract symptom and underwent transurethral resection of the prostate (TURP). However, this CT finding could also be visualized in other prostatitis, including infection, and should be differentiated from malignancy.

An IgG4-related pseudotumor at the urethra visualized in one patient was pathologically proven to be a lesion resulting from a chronic persistent disease over many years and a newly developed urethral lesion. The MR scan of this lesion revealed an oval bulging mass at the urinary bladder neck and membranous urethra which showed homogenous intermediate signal intensity on a T1W image, hyposignal intensity on T2W images, homogenous enhancement and restricted diffusion (Fig. 4C). The appearances are similar to those found in another case report (25). However, those imaging findings also overlap with those of malignant tumors such as urethral neoplasm (26).

Finally, the study showed that IgG4-related disease in the abdomen mainly reveals multi-organ involvement at the initial presentation. One patient can have multi-organ involvement in different time frames. Some subtle radiographic findings or lesions are tumor-like mimics. Typical features are a homogeneous pattern and faint or delayed enhancement on both CT and MRI and hypointensity on T2W MR images. The restricted diffusion on MRI is probably indicative of an active disease. A limitation of this study is the lack of pathologic evaluation of other associated abnormal lesions. However, due to the characteristically excellent response of IgG4 to steroid therapy, follow-up imaging might be helpful for making a more complete diagnosis during post treatment evaluation.

CONCLUSIONS

IgG4-related disease in the abdomen and pelvis presents a wide spectrum of clinical and imaging findings, and may affect many different organs in different ways. Diagnosis requires maintaining a high degree of suspicion. Definitive diagnosis should be based on pathologic, laboratory and radiologic findings. It is also important that the radiologist recognize imaging features in order to effectively establish an accurate diagnosis which leads to appropriate management.

ACKNOWLEDGMENTS

The authors would like to thank Dr. Saowalak Hunnangkul, Clinical Epidermology Unit, Faculty of Medicine, Siriraj Hospital, Mahidol University, for assistance with statistical analysis and data interpretation. The co-authors were supported by a Chalermprakiat Grant, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand.

FUNDING

The co-authors were supported by a Chalermprakiat Grant, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand.

CONFLICTS OF INTEREST

The authors have no conflicts of interest to report.

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