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REVIEW

IgG4-related disease in the abdomen and pelvis: atypical findings, pitfalls, and mimics

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Abstract

IgG4-related disease (IgG4-RD) is a systemic, autoimmune, fibroinflammatory disease that can cause multi-organ damage. Although there have been many trials and studies since its recognition in 2003, there is still much that is unknown. Furthermore, IgG4-RD can affect any organ in the body and often has many mimics and alternative diagnoses, which can make for a challenging workup. Imaging plays a substantial role in the diagnosis of IgG4-RD and is often the first occasion where IgG4-RD comes into consideration. Thus, knowledge about the imaging findings of various manifestations of IgG4-RD can aid in the diagnosis and have a significant impact on patient management. In this article, we review the wide array of imaging findings, both typical and atypical, as well as possible mimics of IgG4-RD in the abdomen and pelvis.

Keywords IgG4-related disease · IgG4 · Autoimmune pancreatitis · Sclerosing cholangitis · Sclerosing mesenteritis · Retroperitoneal fibrosis · IgG4 vasculitis

Introduction

IgG4-related disease (IgG4-RD) is a systemic, immune-mediated fibroinflammatory disease that results in tissue destruction of multiple organs and was not recognized until 2003 [1]. As a result, much has yet to be discovered about this entity. Epidemiologic studies are sparse; however, it is known that the majority of patients are men generally older than the age of 50 [1, 2]. Early studies from Japan focused on autoimmune pancreatitis where the prevalence is approximately 0.8 per 100,000 patients [3] and was linked to serum IgG4 levels [4]. However, it is now known that IgG4-RD can affect any organ in the body from the pancreas to the kidneys to the retroperitoneum and lymph nodes, and importantly, the histopathology of the disease is extremely similar no matter the organ involved [5]. IgG4-RD is often underdiagnosed and mistaken for malignancy, infection, or other autoimmune conditions. Delayed diagnosis can lead to irreversible multi-organ damage and failure. Thus, it is of utmost importance for radiologists to be aware of this entity in order to facilitate further workup and management. In this article, we describe the imaging findings and mimics of abdominal and pelvic IgG4-RD.

Clinical diagnosis of IgG4-related disease

Although clinical diagnosis of IgG4-RD remains a challenge, Umehara and colleagues have generated a set of comprehensive diagnostic criteria that take into account the clinical history and physical exam, serum IgG4 levels, and characteristic histopathological features which are summarized in Fig. 1 [6, 7]. In patients with definite IgG4-RD, the history, physical exam, and imaging findings

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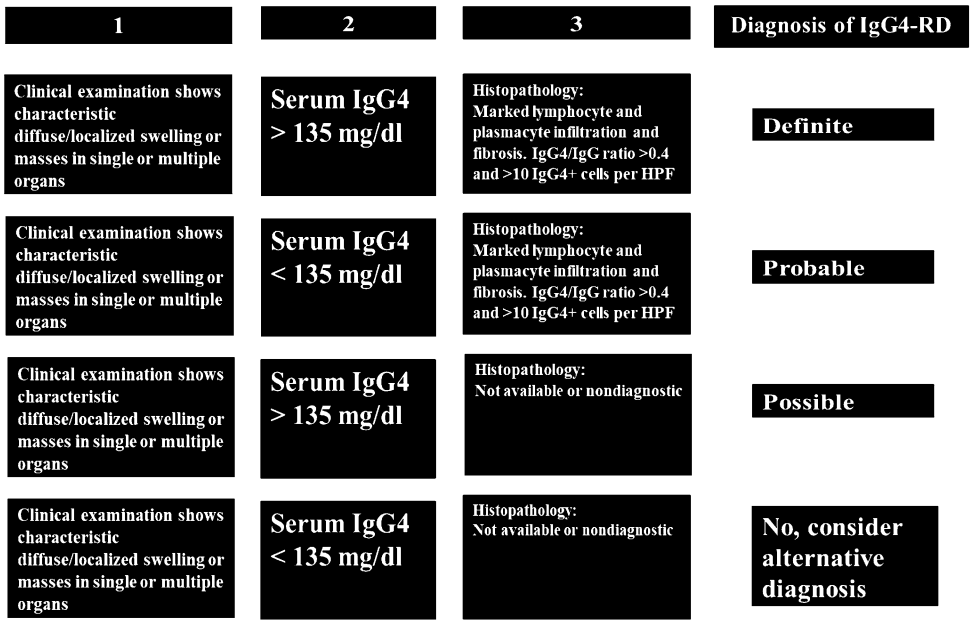

Fig. 1 Summary of clinical, serological, and histological diagnostic criteria for IgG4-related disease

reveal swelling or masses in multiple organs, serum IgG4 levels are at least 135 mg/dl, and histopathologic findings in tissue samples show marked lymphocyte and plasma cell infiltration (specifically IgG4-positive plasma cells) and fibrosis.

Alternatively, IgG4-RD can be diagnosed using organ-specific criteria of which the most notable is the pancreas. The Mayo Clinic HISORt criteria for the diagnosis of autoimmune pancreatitis revolves around the patient belonging to at least 1 of 3 proposed diagnostic groups [8]. The first is the histological group where tissue sampling of the pancreas shows characteristics of lymphoplasmacytic sclerosing pancreatitis which include periductal lymphoplasmacytic infiltrates with obliterative phlebitis and fibrosis and/or at least 10 IgG4-positive cells per high-powered field in one of these infiltrates. The second is the imaging and serology group which must show a diffusely enlarged pancreas with delayed peripheral enhancement, irregular pancreatic duct, and elevated serum IgG4 levels. The third group is the response to steroids where patients have unexplained pancreatic disease after negative workup, elevated IgG4 levels, and resolution or improvement with steroid therapy [9].

IgG4-related disease of the pancreas

IgG4-related pancreatic disease, also known as autoimmune pancreatitis (AIP), makes up a small but not insignificant portion of chronic pancreatitis cases. Although IgG4-related pancreatic disease and autoimmune pancreatitis are often used interchangeably, it is important to note that there are two subtypes of autoimmune pancreatitis. Type 1 resembles the prototypical systemic IgG4-RD that involves the pancreas and often multiple other organs. Type 2 has distinct pathological features and is confined only to the pancreas [10]. On computed tomography (CT), the pancreas is diffusely enlarged with loss of the normal lobulated contour and minimal adjacent fat stranding (Fig. 2). The pancreas also shows diffusely decreased arterial enhancement and increased delayed enhancement [11–14]. On magnetic resonance (MR) imaging, the

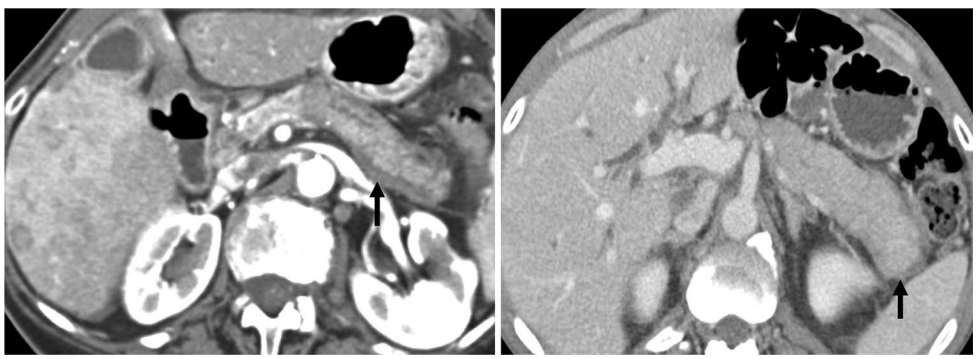

Fig. 2 Axial contrast-enhanced CT images of two patients with pathologically proven IgG4 autoimmune pancreatitis showing a diffusely enlarged pancreas, hypodense rim/halo sign (black arrows), and no peripancreatic fat stranding

pancreas is diffusely T1 hypointense and slightly T2 hyperintense relative to the liver parenchyma with dynamic enhancement characteristics similar to CT [11]. Another characteristic finding is the peripancreatic halo which is hypoattenuating on CT and hypointense with delayed enhancement on MR [11]. On MR cholangiopancreatography (MRCP), there is diffuse or partial narrowing of the pancreatic duct (Fig. 3) [12, 14, 15]. On ^{18}F-fluorodeoxyglucose (FDG) positron emission tomography (PET)/CT, the enlarged pancreas moderately/intensely takes up FDG without pancreatic duct obstruction [16]. Furthermore, FDG PET/CT is valuable in identifying additional sites of disease not apparent on conventional CT as well as evaluating treatment response [16]. Unfortunately, atypical findings of IgG4-related pancreatic disease can muddle the picture. Approximately 25–40% of patients can have focal enlargement or a mass in the pancreas on imaging which can be iso- to hypoattenuating and almost impossible to differentiate from the most dangerous mimic, pancreatic carcinoma (Fig. 4). Additionally, they may both exhibit

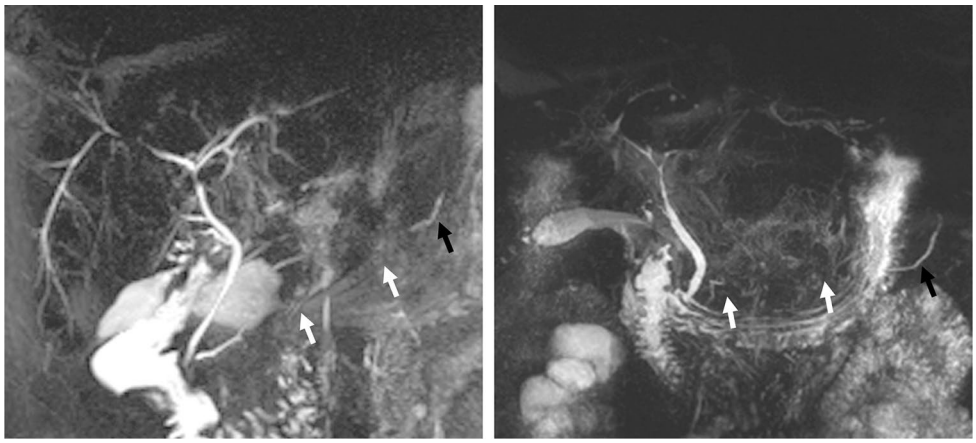

Fig. 3 Magnetic resonance cholangiopancreatography (MRCP) images of two patients with IgG4 autoimmune pancreatitis show non-visualization of a long segment of the main pancreatic duct (white arrows) with a normal upstream main pancreatic duct (black arrows)

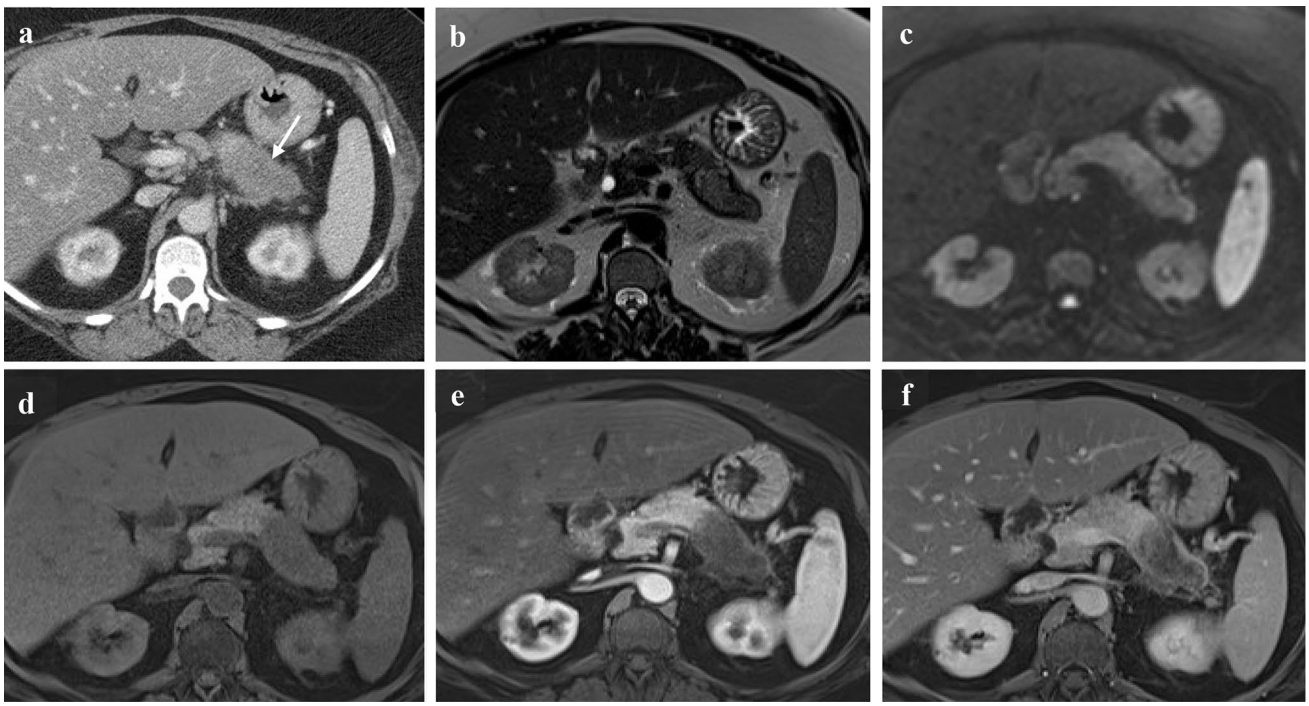

Fig. 4 Axial (**a**) contrast-enhanced CT image shows a subtle focal hypodensity (arrow) in the pancreatic tail. Axial T2-weighted (**b**), diffusion-weighted (**c**), T1 pre-contrast (**d**), post-contrast T1 early phase (**e**), and delayed phase (**f**) MR images show a T1 hypointense and mildly T2 hyperintense lesion with no significantly increased DWI signal and hypoenhancement on early phase with mildly increased enhancement on delayed phase. These characteristics fit with either IgG4-related pancreatic disease or adenocarcinoma. This lesion was biopsied and shown to be pancreatic adenocarcinoma

increased signal on diffusion-weighted imaging (DWI), but IgG4-related pancreatic disease has been shown to have a significantly decreased apparent diffusion coefficient (ADC) with a cut-off value that is still controversial [17, 18]. Enhancement of the main pancreatic duct wall, also known as the enhanced duct sign, and a thickness of the enhancing wall greater than 1 mm can help distinguish IgG4-related pancreatic disease from pancreatic carcinoma [19]. The enhanced duct sign is strongly associated with and highly specific for AIP [19]. One other useful imaging finding in focal AIP is the lack of upstream pancreatic duct dilatation, which is often seen in pancreatic adenocarcinoma (Fig. 3). Another potential pitfall is that up to 5–20% of patients can have a normal or atrophic-appearing pancreas with nonspecific calcifications (Fig. 5) [13, 14]. A potential mimic of pancreatic IgG4-RD is acute pancreatitis (Fig. 6); however, considering the patient's lack of history of alcohol intake or gallstones, none to minimal peripancreatic inflammatory changes, and the presence of the peripancreatic halo can help radiologists lean more towards IgG4-related pancreatitis rather than typical acute pancreatitis.

IgG4-related sclerosing cholangitis

IgG4-related sclerosing cholangitis (IgG4-SC) is a distinct entity that is separate from primary and secondary sclerosing cholangitis and is often associated with IgG4-related pancreatic disease [20]. It shares similar pathologic characteristics including elevated serum IgG4 levels as well as dense lymphocytic infiltrates and IgG4-positvie plasma cells in the bile duct walls [21]. The epidemiology of IgG4-SC is unknown but has been extrapolated to be around 2 per 100,000 cases based on autoimmune pancreatitis studies [22]. Clinically, the disease is most prevalent in men between the ages of 60–70, and the most common presentation is obstructive jaundice [23]. Separating IgG4-SC from other forms of sclerosing cholangitis as well as pancreatic cancer and cholangiocarcinoma can sometimes be difficult but crucial to management since IgG4-SC responds well to steroid therapy [24]. Classification of IgG4-SC is based on four patterns of bile duct involvement (Fig. 7) and each has a separate differential. Type 1 IgG4-SC is isolated distal common bile duct stenosis which has a differential that includes pancreatic cancer, cholangiocarcinoma, and chronic

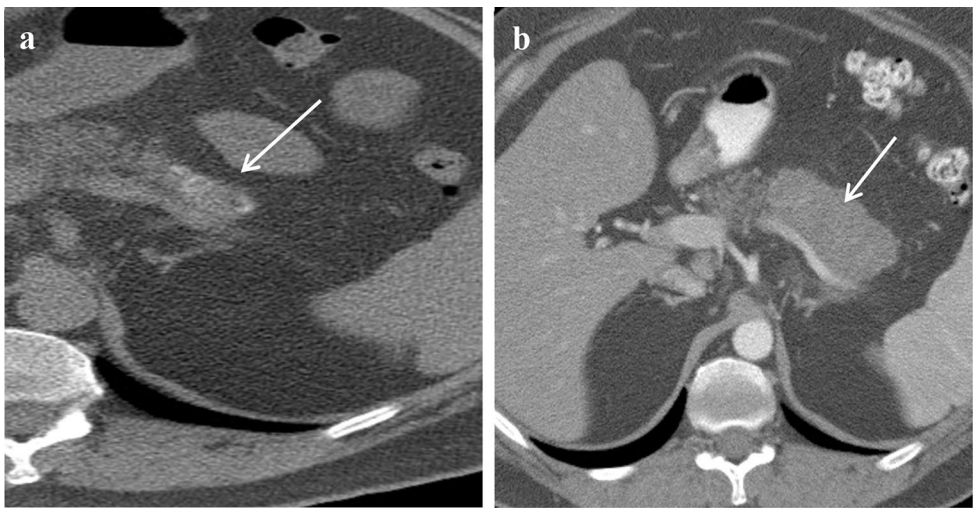

Fig. 5 Axial contrast-enhanced CT images from time of presentation (**a**) show retraction of the pancreatic tail and calcifications, and 6 years prior (**b**) show pancreatic enlargement that was never called in this patient who presented with vague abdominal pain and was never treated for IgG4-related pancreatic disease

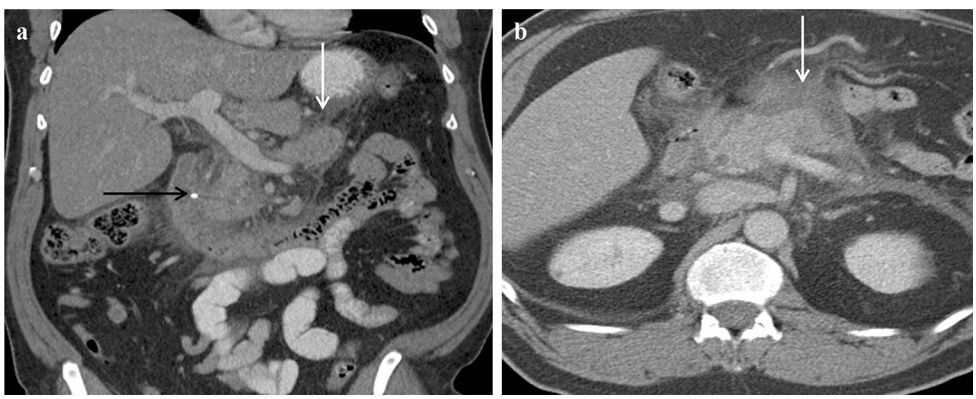

Fig. 6 Coronal (**a**) and axial (**b**) contrast-enhanced CT images show diffuse pancreatic enlargement, extensive peripancreatic fat stranding (white arrows), and a stone in the ampulla (black arrow) causing acute pancreatitis

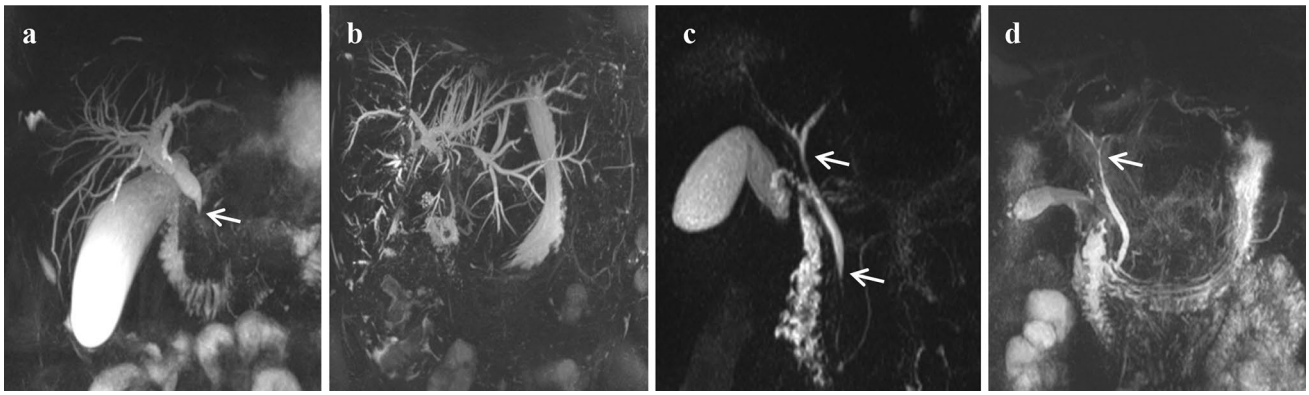

Fig. 7 MRCP images show the four types of IgG4-related sclerosing cholangitis. Type 1 (**a**) is stenosis of the distal common bile duct (CBD). Type 2 (**b**) is diffuse intra and extrahepatic bile duct stenosis. Type 3 (**c**) is stenosis of the hilar bile ducts and distal CBD. Type 4 (**d**) is stenosis of only the hilar bile ducts

pancreatitis. Type 2 is diffuse stenosis of the intra and extrahepatic bile ducts with or without prestenotic dilation, Type 2a and 2b, respectively. The primary differential for Type 2 is primary sclerosing cholangitis (PSC) as well as HIV-related cholangiopathy. Type 3 is stenosis of the hilar hepatic ducts as well as the distal common bile duct while Type 4 is isolated stenosis of the hilar hepatic ducts, and the primary differential for both is cholangiocarcinoma [25]. Imaging findings that favor IgG4-SC include multifocal strictures, gallbladder involvement, biliary wall thickening > 2.5 mm, smooth inner and outer margins of the lumen, and long segment narrowing (Fig. 8) [26, 27]. PSC and cholangiocarcinoma are potential mimics and distinguishing them from IgG4-SC can sometimes be a challenge. The classic findings of multifocal short segment biliary strictures and dilation with a beaded, pruned-tree appearance favor PSC [28]. A solitary, irregular lesion, abrupt transition, eccentric or marked bile duct wall thickening, and an obliterated lumen are all findings that would favor cholangiocarcinoma [29]. Finally, paying attention to extra-biliary manifestations such as pancreatic involvement (Fig. 9) can also help add confidence to the diagnosis of IgG4-SC.

IgG4-related disease of the appendix

IgG4-related disease affecting the appendix is rare. To date, there have only been three published case reports. Clinical presentation is similar with right lower quadrant pain and other features of appendicitis or appendiceal tumor; though notably, there was no leukocytosis or fever. Histologic findings correlate with IgG4-RD in other organs and most notably spare the mucosa. CT findings are nonspecific with one case report that showed mass-like swelling of the appendix with periappendiceal fat stranding [30]. The second case report showed CT findings of a markedly dilated appendix with thickened walls and intraluminal fluid suspicious for a mucocele [31]. Finally, the third case report showed CT findings of a mass-forming lesion arising from the appendix without features associated with appendicitis or a mucocele [32]. Because IgG4-related appendiceal disease can have any permutation of nonspecific features such as mass-like growth of the appendix, thickened walls, periappendiceal/perimesenteric infiltration, and fat stranding (Fig. 10), distinguishing it from appendicitis and neoplasms can be challenging. However, paying attention to the clinical presentation and initial lab findings as well as keeping the possibility of IgG4-RD in the differential can aid in preventing unnecessary surgery.

IgG4-related disease of the mesentery and lymph nodes

IgG4-related disease of the mesentery and lymph nodes can be divided into 2 main manifestations. The first is diffuse mesenteric nodularity and lymphadenopathy (Fig. 11). This manifestation can be associated with other organ involvement or may be the initial presentation or the only manifestation. If initial, the differential includes lymphoma, metastases, and Castleman disease; however, the lymph nodes in IgG4-RD are often < 2 cm, and patients usually do not exhibit the clinical features of the aforementioned differentials [33]. Interestingly, IgG4-related lymphadenopathy differs from the typical pathology in that they do not exhibit phlebitis or sclerosis [34].

The second manifestation is IgG4-related sclerosing mesenteritis. This is a rare entity characterized by focal or diffuse fibrosis and inflammatory changes in the small bowel mesentery which can appear as a soft tissue mass that will narrow or encase the adjacent blood vessels (Fig. 12) [33, 35] and can also cause bowel obstruction [36]. They avidly take up FDG on PET [37, 38]. Potential mimics include lymphoma and carcinoid or neuroendocrine tumors which

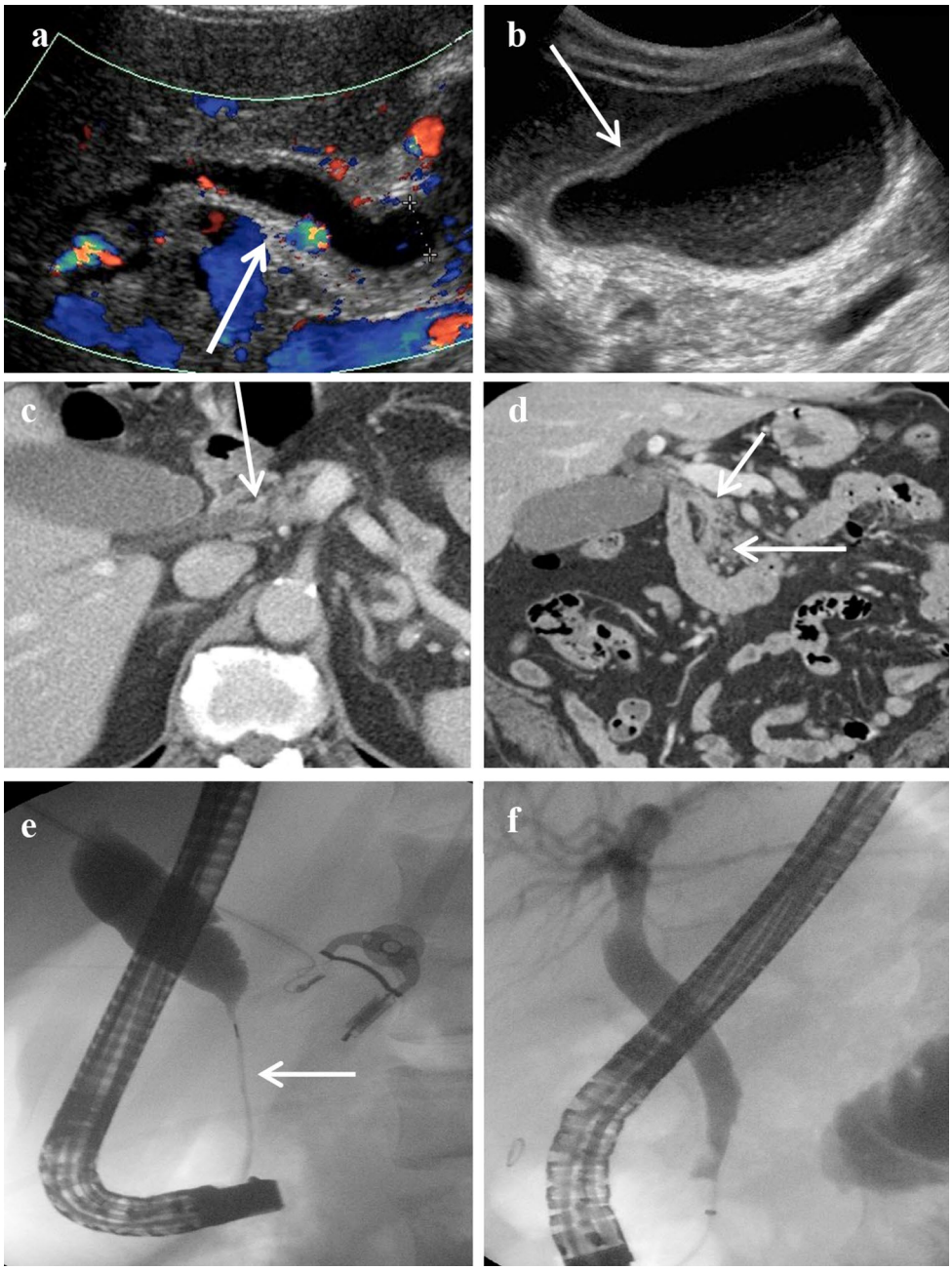

Fig. 8 Ultrasound images show thickening of the common bile duct wall (**a**) and gallbladder wall (**b**) in this IgG4-related sclerosing cholangitis patient who presented with pain and jaundice. Axial (**c**) and coronal (**d**) contrast-enhanced CT images of a second patient presenting with jaundice show long segment narrowing and mural thickening of the CBD. ERCP images before (**e**) and after (**f**) steroid treatment show smooth narrowing of the distal CBD with dilatation of the proximal duct and significant improvement after steroid therapy

will also exhibit FDG avidity on PET imaging. One useful finding is the fat ring sign which is preservation of the fat around the mesenteric vessels seen in IgG4-related mesenteritis [33].

IgG4-Related Renal Disease

IgG4-related kidney disease (IgG4-RKD) can present as acute or chronic renal failure and/or a mass seen on imaging [39] and is found in about one third of patients with autoimmune pancreatitis [40–42]. Histologically, the majority of IgG4-RKD is tubulointerstitial rather than glomerular [43]. Additionally, in IgG4-related renal disease, complement levels have been shown to be an indicator of disease activity [9]. Imaging findings can be divided into parenchymal and extra-parenchymal lesions. Parenchymal lesions come in 5 distinct patterns, each with their own set of differentials. Small peripheral cortical nodules and well or ill-defined round lesions [40, 42] could also represent lymphoma, metastases, or granulomatosis with polyangiitis (formerly known as Wegener's). Hypodense wedge-shaped lesions (Fig. 13) [40–42] and diffuse patchy involvement (Fig. 14) [40] may also represent pyelonephritis or a vascular insult [33]. Finally, a single mass-like lesion may be difficult to

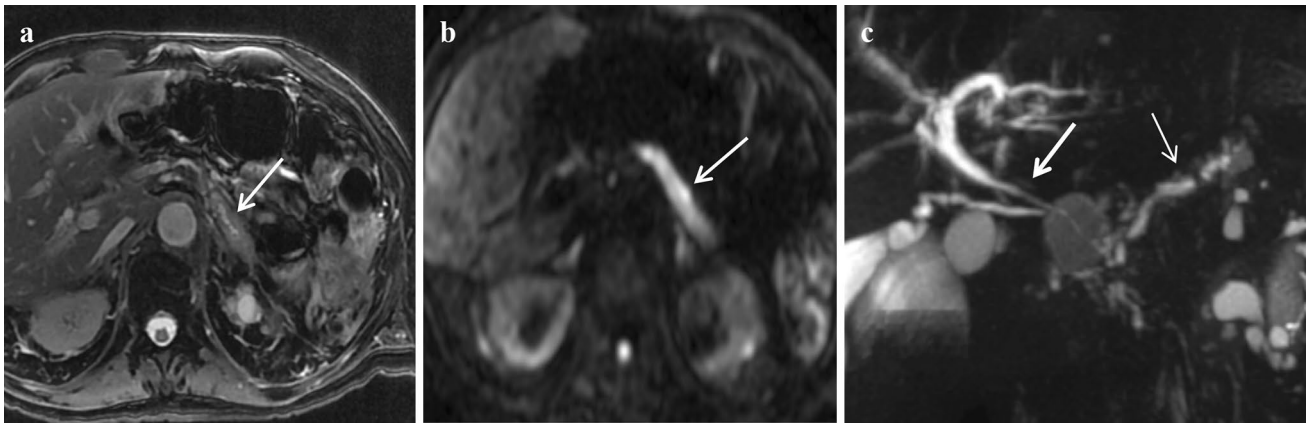

Fig. 9 Axial T2-weighted (**a**) MR image in this patient with IgG4-related pancreatic disease and sclerosing cholangitis shows a featureless pancreas with increased T2 signal relative to the liver. Axial diffusion-weighted (**b**) image shows increased signal in the pancreas suggestive of active inflammation. Coronal MRCP (**c**) image shows focal narrowing of the distal common bile duct (thick arrow) and dilation and irregularity of the pancreatic duct (thin arrow)

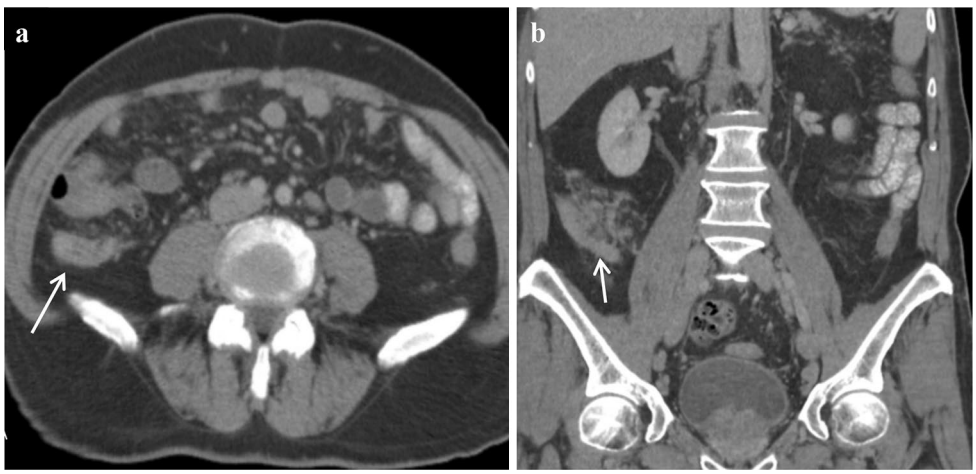

Fig. 10 Axial (**a**) and coronal (**b**) contrast-enhanced CT images show a diffusely enlarged appendix with adjacent thickened infiltration of the mesoappendix. This appendix was surgically removed and confirmed on histopathologic examination to be IgG4-related disease

differentiate from renal cell carcinoma (Fig. 15) [42]. Extraparenchymal lesions can be divided into a diffuse rim of soft tissue around the kidney, irregular nodules in the sinuses, and diffuse renal pelvic wall thickening [40]. On CT, IgG4-RKD lesions are all hypoattenuating on early phases and gradually show mild-enhancement, becoming less distinct, and reaching near isoattenuation on delayed phases (Fig. 16) [40, 44]. On MRI, these lesions are T1 isointense, T2 hypointense, and hyperintense on DWI and exhibit contrast dynamics similar to CT [40, 44, 45].

IgG4-Related Retroperitoneal Fibrosis

Retroperitoneal fibrosis is an inflammatory condition which has many underlying causes such as drugs, radiation, trauma, and infection but it can also be idiopathic. It is believed that more than two-thirds of idiopathic cases are due to IgG4-RD [46]. Roughly 20% of autoimmune pancreatitis cases are associated with retroperitoneal fibrosis [47]. On imaging, lesions usually manifest as a periaortic (Fig. 17), periureteral, or perinephric (Fig. 18) soft tissue mass which can result in aortic aneurysms and hydronephrosis, respectively [33, 44, 47]. On MR imaging, lesions are usually T1 hypo/isointense with variable T2 signal where a higher signal indicates more active inflammation and vice versa (Fig. 19) [44, 48]. Distinguishing between the potential mimics such as lymphoma and other malignancies is difficult yet crucial, and although still controversial, absence of aortic elevation is usually a sign of retroperitoneal fibrosis rather than malignancy [48]. Furthermore, PET may be helpful in differentiating between the two entities due to lower FDG uptake in retroperitoneal fibrosis relative to lymphoma and metastases [49].

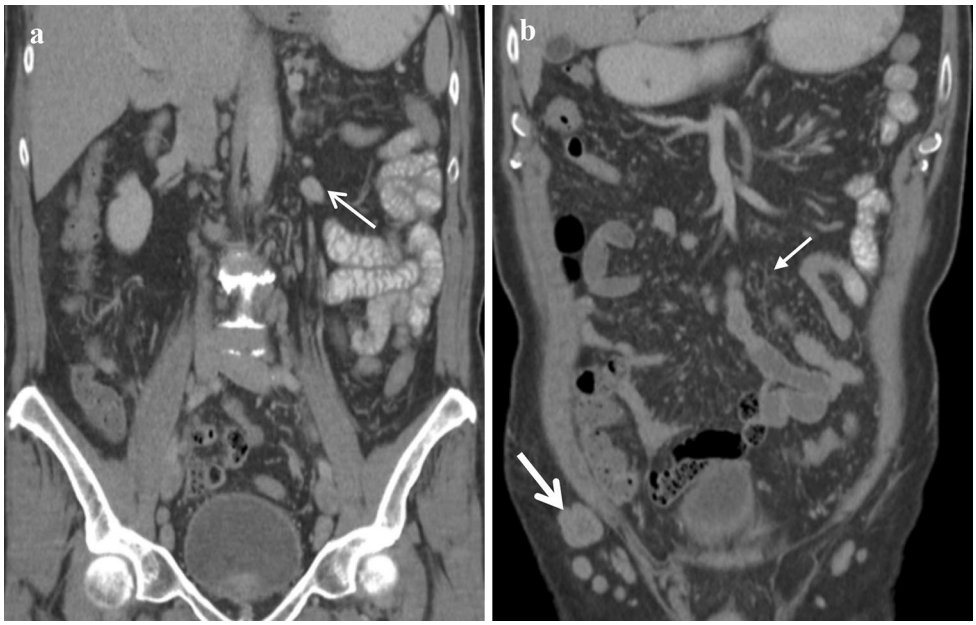

Fig. 11 Coronal contrast-enhanced CT images show multiple enlarged retroperitoneal lymph nodes (**a**) as well as diffuse mesenteric nodularity (thin arrows) and enlarged bilateral inguinal lymph nodes (thick arrow) (**b**) in this patient with IgG4-related mesenteric disease and lymphadenopathy

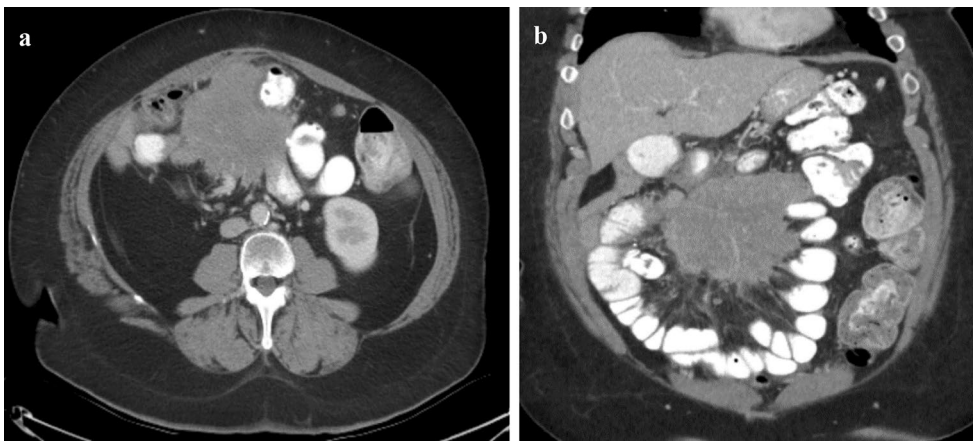

Fig. 12 Axial (**a**) and coronal (**b**) contrast-enhanced CT images show a sclerosing mesenteric mass mimicking a malignancy that was biopsied and shown to be IgG4-related sclerosing mesenteritis

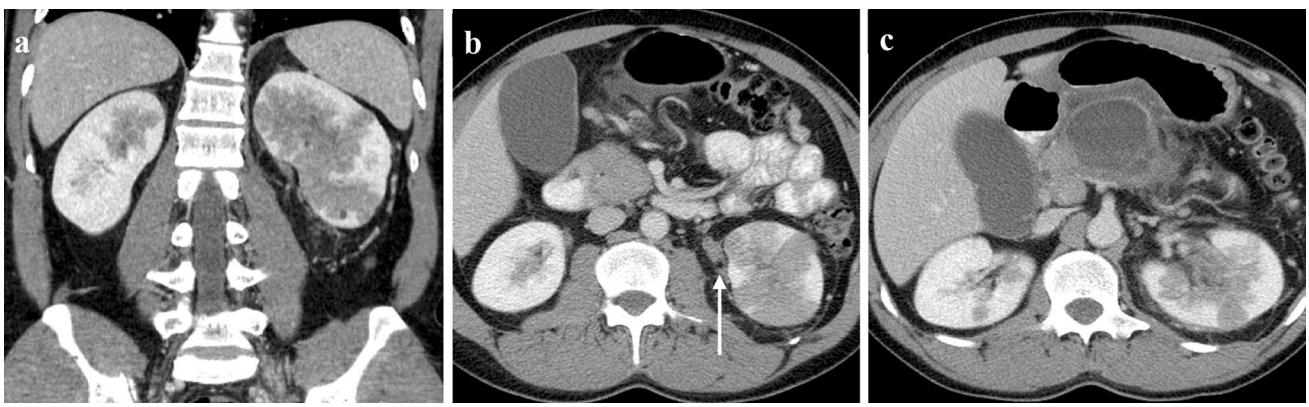

Fig. 13 Coronal (**a**) and axial (**b** and **c**) contrast-enhanced CT images in a patient with a history of autoimmune pancreatitis show diffuse bilateral patchy renal hypodensities suggestive of IgG4-related renal disease as well as a pancreatic pseudocyst (**c**), a complication from pancreatitis. There are also associated perinephric soft tissue nodules (arrow)

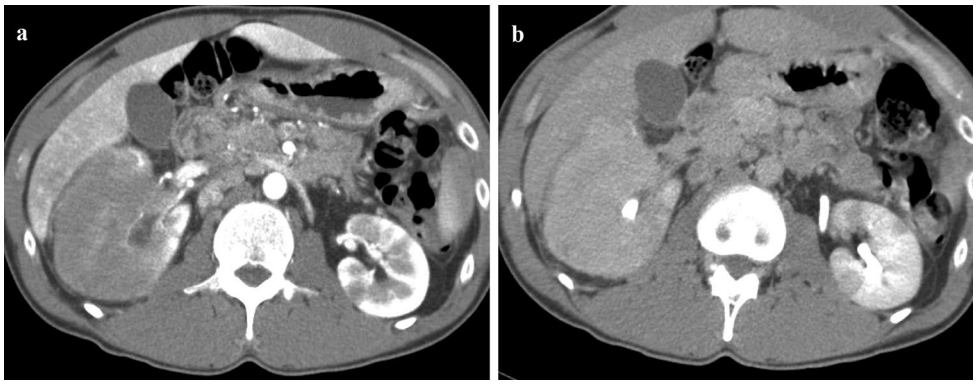

Fig. 14 Axial contrast-enhanced CT images in the arterial (**a**) and excretory phases (**b**) show diffuse enlargement of the right kidney with patchy hypoattenuation and hypoenhancement with small scattered hypodensities in the left kidney. These lesions proved to be IgG4-related tubulointerstitial nephritis on biopsy

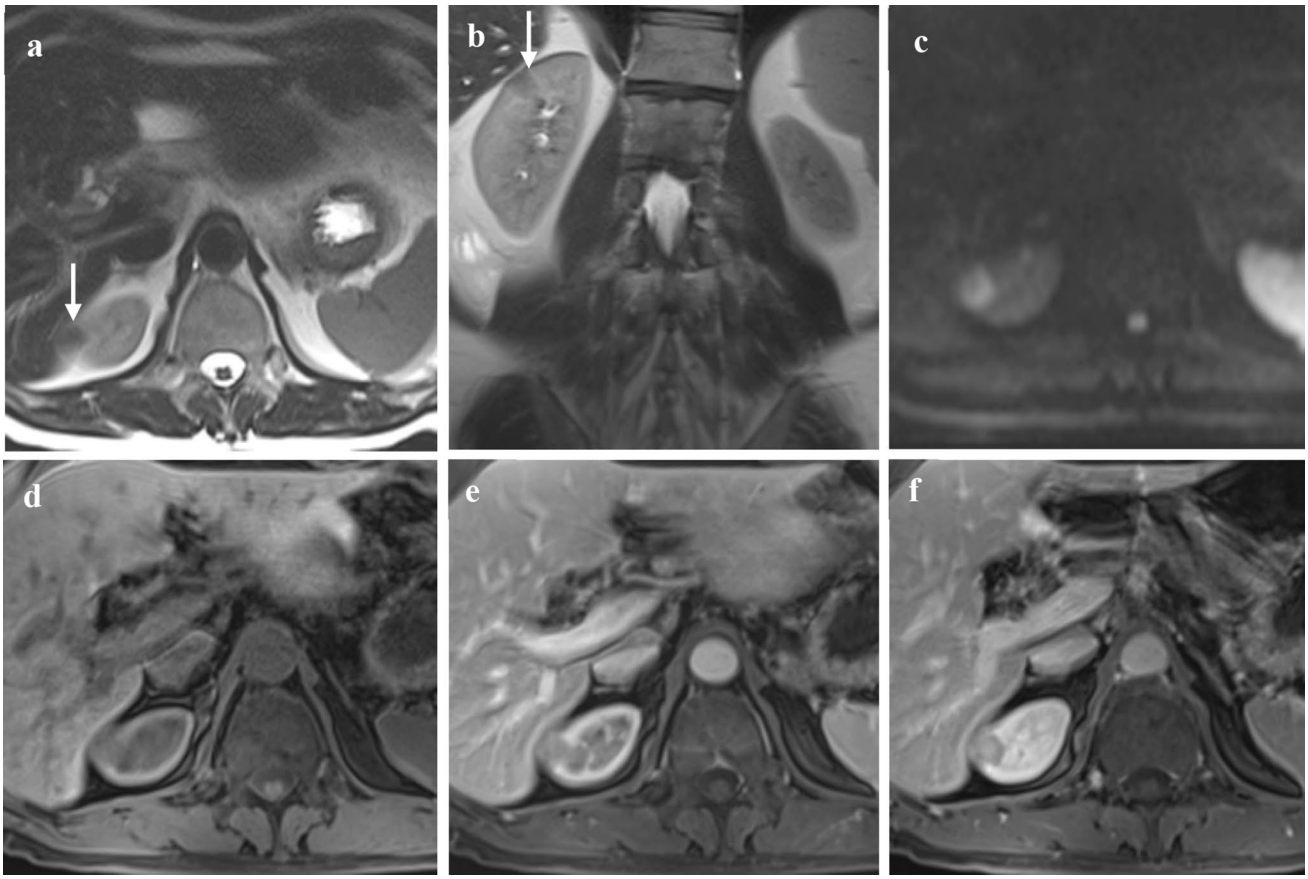

Fig. 15 Axial (**a**) and coronal (**b**) T2-weighted, axial diffusion-weighted (**c**), pre (**d**)-, and post (**e** and **f**)-contrast MR images in this patient found to have a renal mass on CT. There is a T2 hypointense, mildly enhancing cortical wedge-shaped lesion with restricted diffusion in the right kidney which was found to be IgG4-related renal disease, not a malignancy

IgG4-Related Prostatitis

Prostate involvement in IgG4-RD is uncommon and is associated with roughly 8% of autoimmune pancreatitis cases [50]. Patients usually present with lower urinary tract symptoms mistakenly thought to be due to benign prostatic hypertrophy [51, 52]. On imaging, the prostate is nonspecifically diffusely enlarged sometimes indenting into the bladder [53]. The prostate gland may show diffusely increased FDG uptake on PET/CT which could help distinguish it from focal increased uptake with malignancy (Fig. 20) [16]. Nonetheless, differentiating from malignancy is still difficult since serum prostate-specific antigen (PSA) levels are variable in IgG4-related prostatitis with some cases being normal and some elevated [52, 54]. Despite this, it is important to keep the possibility of IgG4-RD in the differential, especially in

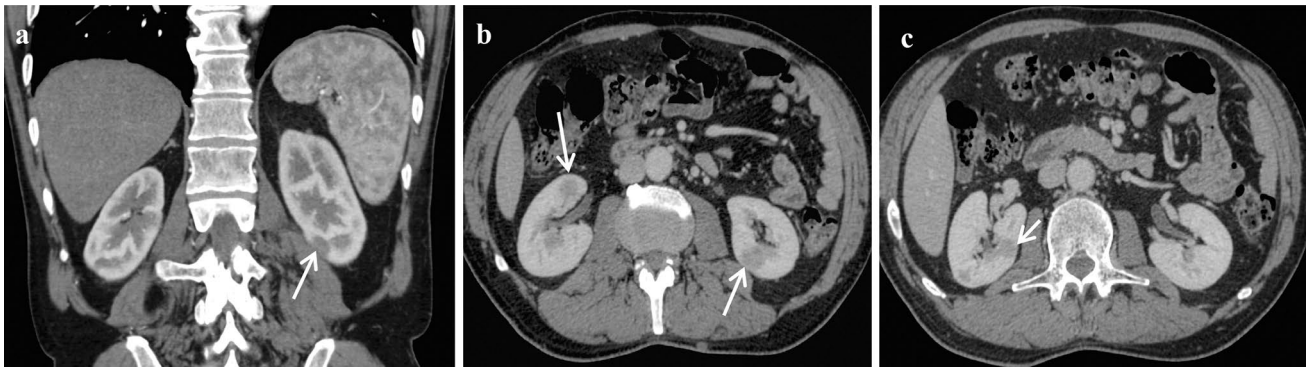

Fig. 16 Coronal corticomedullary phase (**a**) and axial nephrogenic phase (**b** and **c**) contrast-enhanced CT images show multiple bilateral hypodense lesions that are well defined in the corticomedullary phase and more indistinct in the later nephrogenic phase in this patient with IgG4-related disease

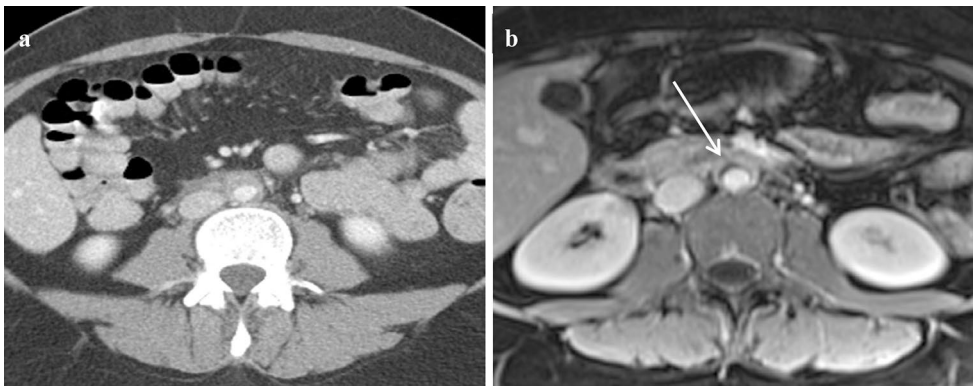

Fig. 17 Axial contrast-enhanced CT (**a**) and axial post-contrast MR (**b**) images in a patient with a history of autoimmune pancreatitis show a rim of soft tissue around the aorta and IVC, and this rim is separate from the enhancing aortic wall (arrow) which is compatible with IgG4 retroperitoneal fibrosis

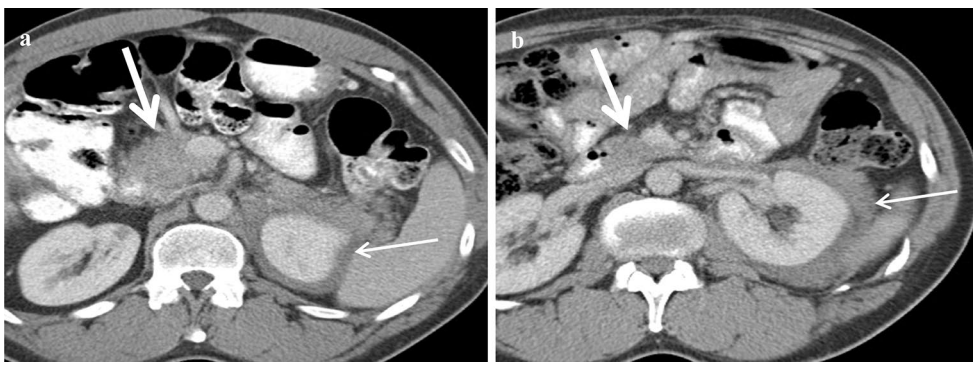

Fig. 18 Axial contrast-enhanced CT images before (**a**) and after (**b**) steroid therapy in this patient with autoimmune pancreatitis and retroperitoneal fibrosis show swelling and hypoattenuation of the pancreas (thick arrows) which decreases with therapy. The left perinephric soft tissue mass (thin arrows) remains unchanged

the presence of other organ involvement, due to its marked response to steroid therapy which could prevent unnecessary extraneous interventions and surgeries.

IgG4-Related Vasculitis

IgG4-related vasculitis (IgG4-RV) can affect the whole spectrum of vessels from small coronaries [55] to the aorta causing aneurysms [56] to everything in between. Due to the difficulty in obtaining tissue samples of the vessel wall as well as nonspecific clinical features, imaging plays a central role detecting as well as diagnosing IgG4-RV. The abdominal aorta and iliac arteries are the most common locations for IgG4-RV [57]. Furthermore, the most dreaded complication is rupture of a developing aneurysm, which is possible even after steroid therapy, and IgG4-RV accounts for roughly 5–6% of all surgical abdominal aortic aneurysms [56, 58]. Imaging findings include diffuse wall thickening > 2 mm, homogeneous wall enhancement, and exaggerated atherosclerotic changes and may or may not display associated luminal dilatation (Fig. 21) [57, 59]. Coronary involvement is also important to keep in mind

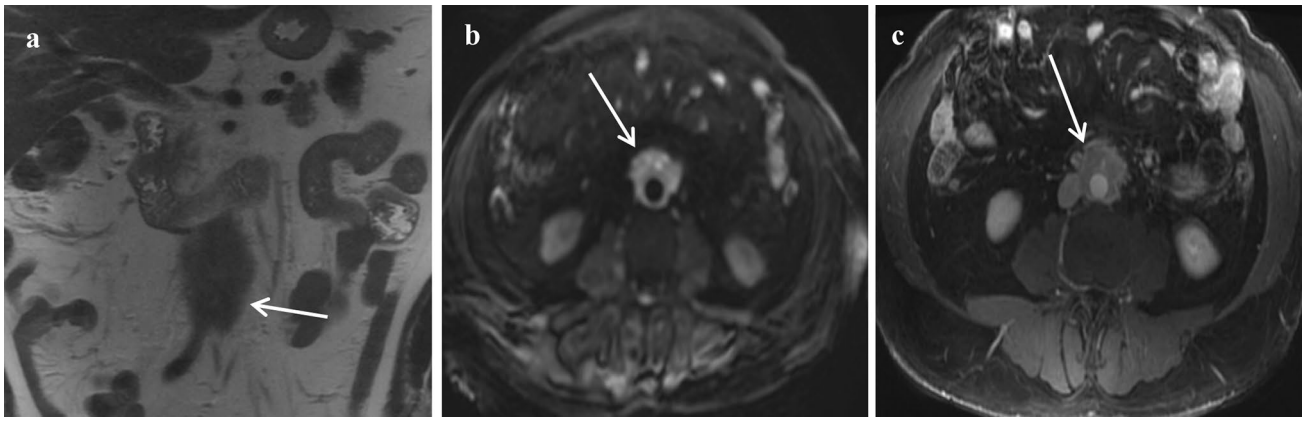

Fig. 19 Coronal T2 (**a**), axial diffusion (**b**), and axial post-contrast T1 (**c**)-weighted MR images show a T2 hypointense, mildly enhancing para-aortic soft tissue mass with restricted diffusion (arrows). Subsequent biopsy demonstrated IgG4/IgG ratio < 0.4, but other histologic findings consistent with IgG4-related retroperitoneal disease. The low ratio is suggestive of no active inflammation corresponding to the T2 hypointensity

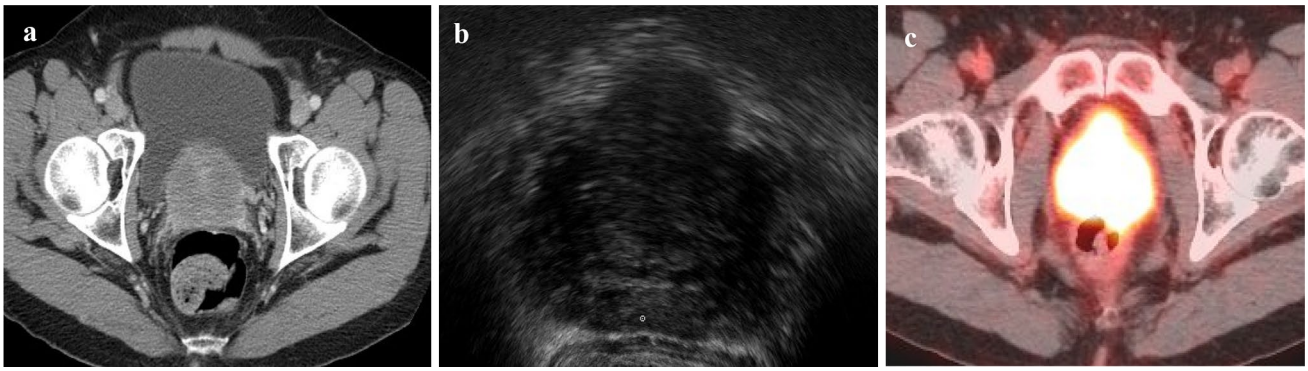

Fig. 20 Axial contrast-enhanced CT (**a**), grayscale ultrasound (**b**), and axial PET/CT (**c**) images show a diffusely enlarged prostate which indents the base of the bladder and has diffusely increased FDG uptake. Prostate biopsy confirmed the diagnosis of IgG4-related prostatitis

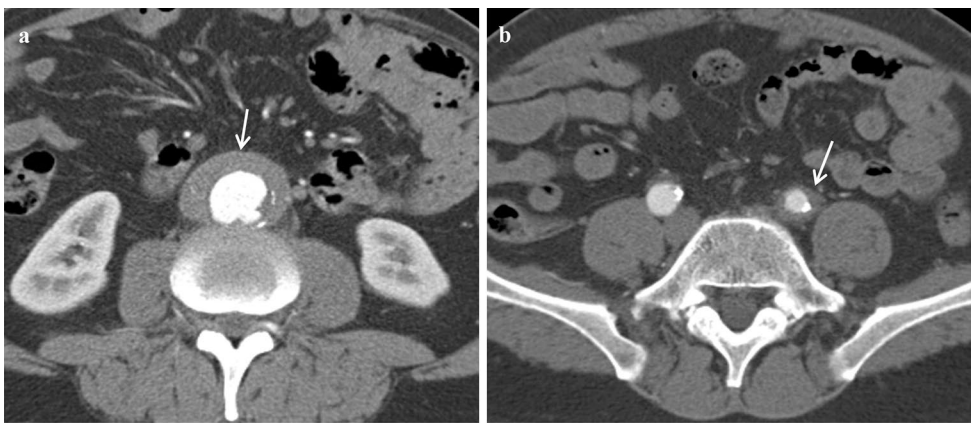

Fig. 21 Axial contrast-enhanced CT images in a patient with a history of autoimmune pancreatitis show well-circumscribed thickening of the aortic wall (**a**) and left iliac artery (**b**) with associated focal luminal dilatation, exaggerated atherosclerotic changes, and homogeneous enhancement, which are all characteristic features of inflammatory abdominal aortic aneurysms related to IgG4-related disease

and is present in roughly 5% of patients with IgG4-RD [56]. A fearful consequence of coronary IgG4-RV is myocardial infarction leading to sudden cardiac death [60–62]. Furthermore, when coronary artery involvement and dilatation are present, electrocardiographically-gated CT as well as a delayed phase on traditional CT can distinguish

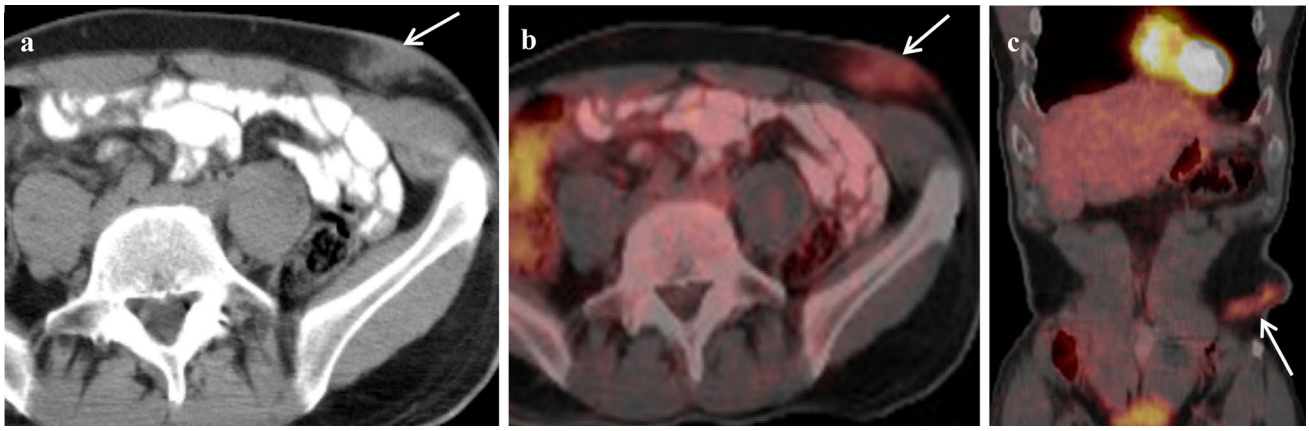

Fig. 22 Axial non-enhanced CT (**a**) image of the abdomen in a patient with widespread IgG4-related disease shows focal soft tissue thickening involving the left anterior abdominal wall. Axial (**b**) and coronal (**c**) fused PET/CT images show the FDG avidity of this soft tissue density

between a coronary thrombus and a thickened wall [57]. The differential for IgG4-RV is extensive, ranging from giant cell arteritis to systemic lupus erythematosus to syphilis to Kawasaki disease and may be difficult to tease out on imaging alone. However, keeping in mindspecific distributions such as IgG4-RV favoring the abdominal aorta as well as multi-organ involvement can help.

Other Rare Locations of IgG4-Related Disease and Multi-organ Involvement

Hepatic parenchymal involvement of IgG4-RD is rare. One type of involvement is IgG4-associated autoimmune hepatitis which can be classified as either a subtype of classic autoimmune hepatitis or a hepatic manifestation of systemic IgG4-RD [63]. The other type of involvement is the IgG4-associated inflammatory pseudotumor, of which, there is the fibrohistiocytic type as well as the lymphoplasmacytic type [64]. The latter is more closely related to the histopathology of IgG4-RD. On CT, the pseudotumor usually presents as a hypodense mass with variable enhancement patterns including delayed homogenous enhancement [65] or peripheral enhancement [66]. On MRI, the lesion is T1 hypointense and T2 hyperintense [65] with variable enhancement [44, 67]. On FDG PET/CT, it avidly takes up FDG [68]. Also, it is important to keep in mind that IgG4-RD can involve any part of the body, even the abdominal wall (Fig. 22). Furthermore, a common theme of IgG4-RD is the presence of multi-organ involvement (Fig. 23). In fact, 92% of patients with autoimmune pancreatitis had at least one other associated extra-pancreatic lesion [47]. Thus, multi-organ involvement can be a helpful clue, directing the radiologist to the possibility of IgG4-RD, especially in cases where the multitude of findings initially seems unrelated.

Management of IgG4-Related Disease and Conclusion

The primary treatment for IgG4-RD is glucocorticoid therapy with some patients requiring a combination of glucocorticoids and an immunosuppressive agent such as azathioprine or methotrexate [69]. Although response to therapy is usually very good with a remission rate of nearly 98% [70], about 23% of patients will relapse even when on maintenance therapy [70]. Studies involving rituximab have shown promising results with 83% of patients with relapsing disease achieving complete remission [71]. There is no single, comprehensive method of assessing treatment response, but the IgG4-RD Responder Index [72] is one quantitative method that takes into account all organ system involvement and has been used in many studies to monitor treatment response. Because the prognosis is favorable for IgG4-RD relative to other alternative entities and mimics, confirming the diagnosis is of utmost importance and can prevent unnecessary treatment. Imaging, along with history, physical exam, and laboratory studies, is sometimes not enough to confidently establish the diagnosis, making tissue sampling necessary. Even in these cases, cross-sectional imaging can provide the most optimal biopsy target. Radiologists play a central role in the diagnosis and management of IgG4-RD, and although there are many mimics and a vast differential, bringing IgG4-RD to the table as a consideration can have a major impact on the patient's outcome.

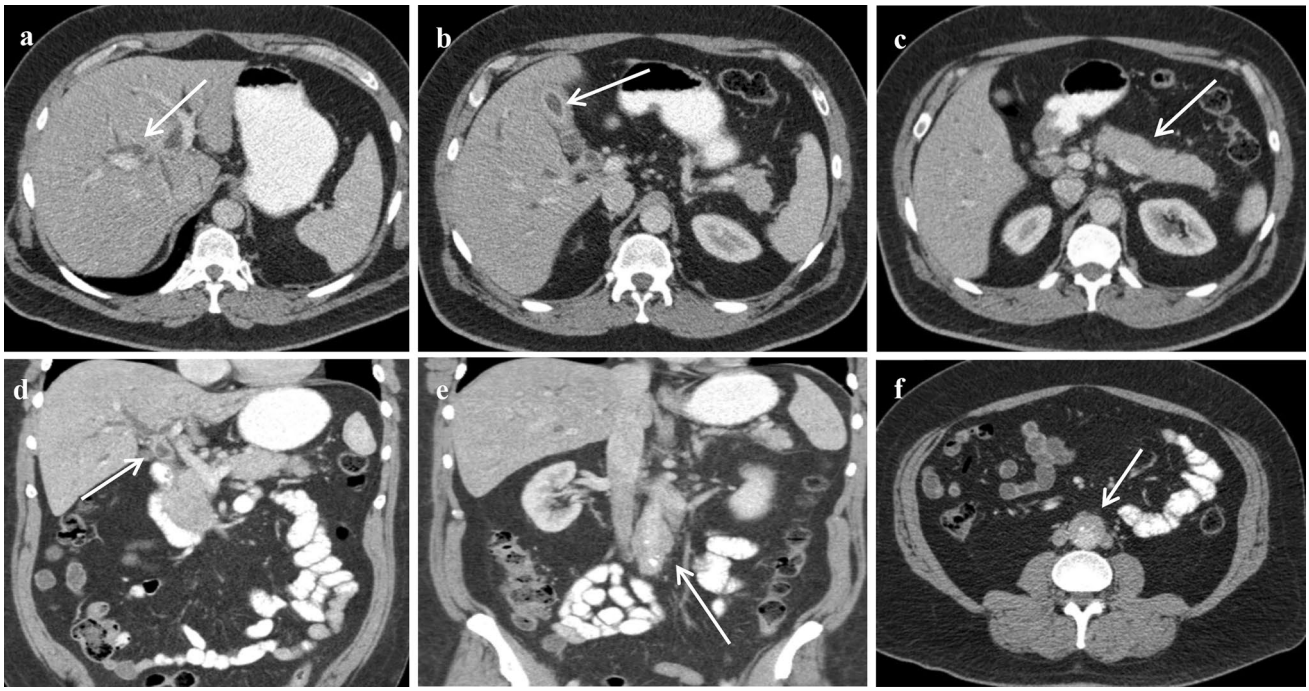

Fig. 23 Axial and coronal contrast-enhanced CT images in a patient with IgG4-related multi-organ involvement show (**a**) bile duct wall thickening (**b**, **d**) gallbladder wall thickening, (**c**) diffuse enlargement of the pancreas, (**e**, **f**) and a para-aortic soft tissue mass

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