IgG4-related retroperitoneal fibrosis: Imaging features with clinical correlations.

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Aims and objectives

IgG4-related disease (IgG4-RD) is a recently established disease entity, which has been engaging a lot of investigators over this decade. An Association between serum IgG4 elevation and autoimmune pancreatitis (AIP), the prototype of IgG4-RD, was first reported by Hamano et al. in 2001.\(^1\) They also reported a case of AIP associated by retroperitoneal fibrosis, which had abundant IgG4-bearing plasma cells both in pancreas and retroperitoneal lesion in histopathological examination.\(^2\) Since then, various organ manifestations suggesting the possible association with IgG4 has been published and that led to establish the novel disease entity 'IgG4-related disease'.\(^3-7\)

Irrespective of the affected organ, IgG4-RD shares some clinical features such as frequent occurrence in elderly male dominance, a serum IgG4 elevations, and favorable response to corticosteroid therapy. IgG4-RD can involve systemic organs synchronously and metachronously. The affected organs typically diffusely swollen or show tumorous lesions sometimes led to be symptomatic (i.e. obstructive jaundice in Type 1 AIP, eye bulging in lachrymal lesions). In pathological examination, IgG4-RD is characterized by diffuse lymphoplasmacytic infiltration, obliterative phlebitis, striform fibrosis, and numerous IgG4-positive plasma cells.\(^8\)

While glandular organs such as pancreas, lachrymal gland, and submandibular gland are frequently involved by IgG4-RD, retroperitoneal fibrosis is also major manifestation of that reported as 20% of prevalence.\(^9\) Though, some literatures investigating the IgG4-related retroperitoneal fibrosis has been published, most of them are case reports and whole image of IgG4-related retroperitoneal fibrosis remains unclear.\(^10,11\) So far, IgG4-related retroperitoneal fibrosis has been described as the renal hilar mass or soft tissue mass around the aorta sometimes involve the urinary tract causing hydronephrosis. In our previous reports, IgG4-related retroperitoneal lesions demonstrated periaortic/arterial, periureteral, and plaque-like lesions.\(^5\) In this way, IgG4-related retroperitoneal fibrosis includes several manifestations because of the heterogeneity of the term 'retroperitoneal fibrosis', and it is still unclear that the prevalence or clinical significance of each manifestation. Usually, the diagnosis of IgG4-RD is made based on the serum IgG concentrations, imaging examinations, and pathological examinations. Though, some papers about the imaging features of IgG4-RD have been published, the imaging features of IgG4-related retroperitoneal fibrosis are still unclear.\(^12-17\) In this study, we examined radiological features of IgG4-related retroperitoneal fibrosis with clinical correlations.
Methods and materials

Case selection

A total of 73 cases with IgG4-related retroperitoneal fibrosis were selected from the radiology files of Kanazawa University Hospital, and affiliated institutions including Toyama Prefectural Central Hospital, Fukui Prefectural Hospital, Fukui Saiseikai Hospital, Tonami General Hospital, Kouseiren Takaoka Hospital, and Noto General Hospital, Japan, between January 2005 and December 2013. And we added one consultation case from non-affiliated institution (Toranomon Hospital). Thus, this study consisted of 74 cases with IgG4-related retroperitoneal fibrosis. The patients were 64 males and ten females with an average age of 66 years (range: 35 to 86 years). One patient was reported in an earlier case report, and 17 cases were included our previous study. Clinical records were available for all patients and examined regarding the age, sex, clinical symptoms, treatment, and laboratory data that included serum IgG and IgG4 concentration.

Diagnosis of IgG4-RD

Of 74 patients, 49 were diagnosed as having IgG4-RD based on the histological examination at least in one organ. Histological diagnosis was made based on the IgG4-RD Pathology Consensus Statement: in addition to the abundant IgG4 positive plasma cell infiltration, morphological features, including diffuse lymphoplasmacytic infiltration, storiform fibrosis, and /or obliterative phlebitis were considered as supportive findings of IgG4-RD. The diagnosis for remaining 25 patients were made by combination of typical imaging findings of Type 1 AIP (i.e. diffuse swelling of the pancreas parenchyma, diffuse narrowing of the pancreatic duct and/or capsule-like rim) and serum IgG4 elevation. Type 1 AIP is a prototype of IgG4-RD and the imaging features are established, thus, typical imaging findings of Type 1 AIP and serum IgG4 elevation (>135 mg/mL) can be considered as definitive of type 1 AIP (IgG4-related pancreatitis). Sixteen patients fulfilled both histological and AIP criteria.

Radiological examination

Out of 74 patients, all patients underwent computed tomography (CT) through the abdomen to pelvis. Of those, three were performed non contrast-enhanced CT only, and contrast-enhanced CT was performed for 71 patients using multi-detector row CT scanner having at least 8 rows. Except one case (with slice thickness of 10mm), all CT scans were obtained with a section thickness of 2.5-5.0mm. Post contrast-enhanced CT was performed using dual-phase technique. The early phase images were obtained between 35- and 45-second delays after the administration of 100-150 mL of nonionic...
contrast medium at the rate of 3-4.5 mL/sec with a power injector. After that, late phase images were obtained between 90- and 150-second delays after the starting the injection. Because of the multi-institutional retrospective nature of this study, the scanning protocols were not consistent.

Image analysis

All images were reviewed by two radiologists (D.I. and K. Y., with 13 and 12 years of abdominal CT and MRI imaging experience, respectively), and decisions were reached by consensus. Anatomical structure (aorta, urinary tract, and others) mainly involved by the lesion was recorded in all cases. If two or more anatomical sites were involved, centered structure was defined as mainly involved site. The characteristics of the lesion (wall thickening, mass forming, and plaque-like), presence or absence of cystic change or calcification, hydronephrosis (none, mild, and severe), inflammatory aneurysm were recorded. If the hydronephrosis was identified, responsible lesion was also noted. In the cases of urinary tract centric lesions, the involved segment (renal pelvis, upper urinary tract, and lower urinary tract), the characteristic of luminal surface (smooth or irregular), border to the surrounding fat tissue or renal parenchyma (smooth or irregular) were also evaluated. Follow-up images available for 57 patients were analyzed with regard to the change of the lesions (no change, improved, and worsened), and the development of IgG4-related lesions in other site.

Radiopathologic correlation

Pathological specimens of retroperitoneal fibrosis were available for 15 patients. Five were obtained by surgical resection of inflammatory abdominal aneurysm and resected specimen contained all aortic layer structures. In one patient, left total nephrectomy was performed under suspicious of renal pelvic cancer. In these six cases, radiopathological correlations were examined by two radiologists and one pathologist focusing on the location of inflammatory process and how the imaging examinations reflect it and decisions were reached consensus. In remaining nine cases, histological specimens were obtained by surgical biopsy (n=4) or needle biopsy (n=5). These specimens did not contain specific anatomical structures.
Results

Clinical presentation and laboratory data

Patients were male dominant adults. Fifty one patients were symptomatic at first presentation, of those, 16 had symptom presumably related to retroperitoneal fibrosis including back pain, abdominal pain or edema of lower extremities. Thirty five patients presented clinical symptoms caused by other IgG4-related lesion: submandibular swelling, lachrymal swelling, obstructive jaundice, or worsening of diabetes mellitus due to AIP. On the other hand, remaining 23 were asymptomatic or had symptoms presumably not related to IgG4-related lesions. These patients found to have IgG4-related retroperitoneal fibrosis during CT examination for routine medical work-up or follow-up of previously diagnosed IgG4-RD or other diseases. Serum IgG (normal #1600 mg/dL) and IgG4 (normal #135 mg/dL ) concentrations were examined in 73 patients and elevated in 60 (82%) and 72 (99%) with mean value of 2333 mg/dL and 678 mg/ dL, respectively.

IgG4-related disease at other sites

IgG4-related lesion in other organs were identified in 70 patients (95%) and shown in Table 1 on page 8 . Most of such lesions were detected at the same time as the retroperitoneal fibrosis, but 12 lesions (AIP; 3 cases, bile duct lesion; 3 cases, submandibular gland lesion; 2 cases, lung lesion; 2 cases, vascular lesion; 2 cases) had developed during the follow-up period after the retroperitoneal fibrosis. On the other hand, in 10 patients, IgG4-related retroperitoneal fibrosis appeared during follow-up of other IgG4-related lesions.

Radiological findings

Mainly involved anatomical structures

A total 98 lesions of IgG4-related retroperitoneal fibrosis were detected in 74 patients. The most common site was abdominal aorta; periaortic type (52 lesions; 53%), followed renal pelvis to upper urinary tract; urinary tract type (31 lesions; 32%). Of remaining 15 lesions (15%), 13 were located along with the intra pelvic peritoneum, and two were seen along with the left renal fascia; peritoneum/fascia type Fig. 1 on page 8 . As shown in table, 60 patients had only one type of lesion, while 13 had two types. In one patient, all 3 types were identified Table 2 on page 9 .

Characteristics of CT findings
The radiological features of periaortic type lesion were circumferential or partial wall thickening of the aorta with homogeneous enhancement in the late phase of the contrast-enhanced CT Fig. 2 on page 10. Most of the lesions were located in the infra-renal portion and some were extended in the common iliac artery Fig. 2 on page 10. In the early phase images, small vessels such as inferior mesenteric artery or lumbar artery were penetrating the lesion without stenosis Fig. 2 on page 10. Calcification of the aortic intima was seen between the lesion and aortic lumen. Intra-lesional calcification or cystic change was not seen. Urinary tract was involved at the edge of the lesion causing hydronephrosis in 15 cases Fig. 3 on page 11. Urinary tract type lesion was characterized by the wall thickening of the renal pelvis and urinary tract. Though, one lesion showed stranding to the surrounding fat tissue, remaining lesions had smooth border to the surrounding fat tissue Fig. 4 on page 12 and Fig. 5 on page 13. All but one lesion involved urinary tract circumferentially and urinary tract centered in the lesions Fig. 6 on page 14. One lesion demonstrated mass lesion partially involved the right urinary tract Fig. 7 on page 15. The luminal surface was smooth in all lesions and luminal irregularity or papillary projection was not observed Fig. 8 on page 16. Vessel encasement was not noted in all lesions. Bilateral lesions were identified in 10 cases, and remaining 14 lesions involved unilateral urinary tract with 10 in left and 4 in right side Fig. 9 on page 17. All lesions were located in renal pelvis to upper urinary tract and lower urinary tract lesion was not identified. The characteristic radiological findings of peritoneum/fascia type lesion were homogeneously enhanced soft tissue mass along with the intra pelvic peritoneum located in front of external iliac artery, vein and presacral space Fig. 10 on page 18. Lesions were isolated from intra pelvic organs or external iliac vessel, however urinary tract was involved in the lesion causing hydronephrosis in two cases Fig. 11 on page 19. Two lesions were seen as ill-bordered soft tissue along with left renal fascia and extended in the perirenal fat tissue Fig. 12 on page 20.

Hydronephrosis was noted in 21 patients (28% Table 3 on page 21. In 12 patients, hydronephrosis was seen in unilaterally (left in 8 and right in 4), and 9 patients had bilateral hydronephrosis. The responsible lesion of hydronephrosis was periaortic type lesion in 15 patients (15/21, 71%), urinary tract type lesion in 4 (4/21, 19%), and peritoneal/fascia type lesion in 2 (2/21, 10%). Of a total 30 hydronephrotic lesions, the severity was mild in 6 lesions, moderate in 14, and severe in 10, all mild hydronephrosis was caused by urinary tract type lesions, in the contrary, all but one hydronephrosis classified in moderate to severe were seen in priaortic or peritoneum/fascia type lesion and urinary stent placement or percutaneous nephrostomy were performed for seven and one patients, respectively. Inflammatory abdominal aortic aneurysm were identified in nine cases (9/74, 12%) and all was seen in periaortic type lesion Fig. 13 on page 22. Of these patients, four were performed surgical graft-replacement at the first presentation, and remaining five were followed up with or without steroid therapy.

Follow-up imaging
Follow-up images were available in 57 patients, of whom 45 were treated with steroid for initial daily dose of 20-40 mg. Of these 45, one patient was treated with steroid for the hydronephrosis after surgical graft-replacement. Remaining 14 were followed up without steroid therapy because of the less clinical symptoms or severe diabetes mellitus. Steroid therapy was effective for all lesions but in one case with inflammatory abdominal aortic aneurysm, dilatation of the aorta was progressed and surgical graft-replacement was required Fig. 14 on page 23. Follow-up images in patients having hydronephrosis after steroid therapy were obtained for 11 patients (20 hydronephrotic lesions). Of these, 13 lesions were completely improved, whereas six lesions were remnant while responsible lesions were improved Fig. 15 on page 24. Renal parenchymal atrophy was developed in 2 lesions.

**Radiopathologic correlations**

In six cases including five cases of priaortic type, and one urinary type lesion, radiological findings were compared with surgically resected specimen. In the periaortic type lesions, inflammatory process composed of severe lymphoplasmacytic infiltrations and fibrosis were mainly located in the adventitia and intima and media were preserved in histopathological specimens. In contrast-enhanced CT, these pathological findings were reflected as wall thickening of the aorta, and representing the inflammation in the adventitia, high density layer was identified between the lesion and aortic lumen or mural thrombus Fig. 16 on page 25 and Fig. 17 on page 26. In urinary tract type lesions, marked inflammatory process composed of lymphoplasmacytic infiltrations and fibrosis were identified in the submucosal layer. Interestingly, despite of the severe submucosal inflammation, epithelium was rarely involved. These findings were reflected in the contrast-enhanced CT as wall thickening of the renal pelvis and urinary tract. The lack of the epithelial involvement was correlated with the smoothness of luminal surface in imaging examination Fig. 18 on page 27 and Fig. 19 on page 28.

In surgical (n=4) or needle (n=5) biopsied specimen obtained in nine patients, marked lymphoplasmacytic infiltrations and fibrosis were detected, and IgG4-bearing plasma cells were easily identified, with IgG4/IgG ratio over 40%. Necrosis or calcification was not seen. The imaging findings of homogeneous enhancement in late phase images were considered reflecting these pathological conditions Fig. 20 on page 29 and Fig. 21 on page 30.
Table 1: Table 1. Extra-retroperitoneal lesion observed in 70 patients.

<table>
<thead>
<tr>
<th>Extra retroperitoneal lesions</th>
<th>Number of lesions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pancreas</td>
<td>41</td>
</tr>
<tr>
<td>Submandibular gland</td>
<td>25</td>
</tr>
<tr>
<td>Lacrymal gland</td>
<td>16</td>
</tr>
<tr>
<td>Kidney</td>
<td>15</td>
</tr>
<tr>
<td>Bile duct</td>
<td>14</td>
</tr>
<tr>
<td>Lung/pleura</td>
<td>13</td>
</tr>
<tr>
<td>Arteries</td>
<td>6</td>
</tr>
<tr>
<td>perineural lesion</td>
<td>3</td>
</tr>
<tr>
<td>para vertebral</td>
<td>7</td>
</tr>
<tr>
<td>Pituitary glands</td>
<td>2</td>
</tr>
<tr>
<td>Lymph node</td>
<td>9</td>
</tr>
</tbody>
</table>

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Fig. 1: Figure 1. Typical imaging findings of 3 types, (a) periaortic type (arrow), (b) urinary tract type (arrow), and (c) peritoneum/fascia type (arrows) are shown.

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Table 2. Number of each manifestation in 74 patients.

<table>
<thead>
<tr>
<th>Lesion types</th>
<th>Number (cases)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Periaortic lesion only</td>
<td>39</td>
</tr>
<tr>
<td>Urinary tract lesion only</td>
<td>16</td>
</tr>
<tr>
<td>Peritoneum/fascia lesion only</td>
<td>5</td>
</tr>
<tr>
<td>Periaortic lesion + Urinary tract lesion</td>
<td>6</td>
</tr>
<tr>
<td>Periaortic lesion + peritoneum/fascia lesion</td>
<td>7</td>
</tr>
<tr>
<td>Urinary tract lesion + peritoneum/fascia lesion</td>
<td>0</td>
</tr>
<tr>
<td>Periaortic lesion + Urinary tract lesion + peritoneum/fascia lesion</td>
<td>1</td>
</tr>
</tbody>
</table>

**Table 2:** Table 2. Number of each manifestation in 74 patients.

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Fig. 2: (a) Circumferential wall thickening of the aorta is demonstrated. (b) The lesion is extended to the common iliac artery (a, b; white arrows). Lumbar artery is penetrating the lesion without stenosis (a; red arrow).

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Fig. 3: A 82-year-old man with hydronephrosis caused by periaortic type lesion. (a) Bilateral hydronephrosis is revealed. (b) Urinary tract is involved in periaortic lesion at arrows.

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Fig. 4: (a), (b) The wall thickening of renal pelvis and upper urinary tract is seen (arrows).

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Fig. 5: Same case with Figure 4. Coronal image of urinary tract type lesion, the wall thickening of renal pelvis and upper urinary tract is demonstrated (arrows).

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Fig. 6: Contrast-enhanced CT images of a 66-year-old man with urinary tract type lesion (a, b; axial image, c; coronal image, and d; sagittal image). Remarkable wall thickening of the bilateral renal pervis and upper urinary tract is demonstrated (a-d, arrows). Moderate hydronephrosis is seen in left kidney (a, c). Urinary tract can be detected in the center of the lesion (b, d; arrows).

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**Fig. 7:** A mass lesion partly involving the right urinary tract is seen (arrow).

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**Fig. 8:** Bilateral wall thickening of the renal pelvis is demonstrated (a, b; arrows). Luminal surface is smooth in both lesions.

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Fig. 9: A Unilateral urinary type lesion. Right renal pelvic wall is thickening (arrow).

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**Fig. 10:** Two cases with peritoneal/fascia type lesion. Plaque-like soft tissue is demonstrated (a, b; arrows). Both lesions are enhanced homogenously.

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Fig. 11: A case of hydronephrosis caused by penetrium/fascia type lesion. (a) Left hydronephrosis is seen. (b) Left urinary tract is involved in soft tissue in the presacral soft tissue. (c) Plaque-like soft tissue is demonstrated along with the intra pelvic penetrium.

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**Fig. 12:** Plaque-like soft tissue is seen along with the left renal fascia (a, b; white arrows). Periaortic type lesion is also revealed (b; red arrow).

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Table 3: Detailed profiles and follow-up data in 21 patients with hydronephrosis.

<table>
<thead>
<tr>
<th>Case No</th>
<th>Responsible lesion</th>
<th>Laterality</th>
<th>Affected side</th>
<th>severity</th>
<th>Intervention</th>
<th>Follow-up</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Periaortic type</td>
<td>Unilateral</td>
<td>left</td>
<td>moderate</td>
<td>stent</td>
<td>improved</td>
</tr>
<tr>
<td>2</td>
<td>Periaortic type</td>
<td>Unilateral</td>
<td>right</td>
<td>moderate</td>
<td>-</td>
<td>improved</td>
</tr>
<tr>
<td>3</td>
<td>Periaortic type</td>
<td>Bilateral</td>
<td>left</td>
<td>severe</td>
<td>-</td>
<td>remnant</td>
</tr>
<tr>
<td>4</td>
<td>Periaortic type</td>
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<td>left</td>
<td>moderate</td>
<td>stent</td>
<td>improved</td>
</tr>
<tr>
<td>5</td>
<td>Periaortic type</td>
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<td>right</td>
<td>moderate</td>
<td>stent</td>
<td>improved</td>
</tr>
<tr>
<td>6</td>
<td>Periaortic type</td>
<td>Bilateral</td>
<td>left</td>
<td>severe</td>
<td>-</td>
<td>remnant</td>
</tr>
<tr>
<td>7</td>
<td>Periaortic type</td>
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<td>severe</td>
<td>-</td>
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<tr>
<td>8</td>
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<td>moderate</td>
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<tr>
<td>9</td>
<td>Periaortic type</td>
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<td>severe</td>
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<td>10</td>
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<td>improved</td>
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<tr>
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<td>remnant</td>
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<tr>
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<td>Periaortic type</td>
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<td>moderate</td>
<td>-</td>
<td>improved</td>
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<tr>
<td>13</td>
<td>Periaortic type</td>
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<td>14</td>
<td>Periaortic type</td>
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<tr>
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<td>improved</td>
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<tr>
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<td>moderate</td>
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</tr>
<tr>
<td>21</td>
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<td>Bilateral</td>
<td>left</td>
<td>severe</td>
<td>stent</td>
<td>remnant</td>
</tr>
</tbody>
</table>

Table 3: Table 3. Detailed profiles and follow-up data in 21 patients with hydronephrosis.

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**Fig. 13:** An inflammatory abdominal aortic aneurysm seen in the periaortic type lesion. The aortic aneurysm with the wall thickening is revealed (a, b; arrows). The thickened wall is enhanced homogenously (b; arrow).

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**Fig. 14:** An abdominal aortic aneurysm with wall thickening is seen (a; arrow). (b) The CT image after steroid therapy reveals the improvement of wall thickening, however aneurysmal diameter is increased (arrows).

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Fig. 15: Contrast-enhanced CT at initial presentation (a, b), and after steroid therapy (c, d). Bilateral hydronephrosis is seen (a). Bilateral urinary tracts are involved in the periaortic lesion (b; arrows). After steroid therapy, hydronephrosis is remnant despite of the improvement of the periaortic lesion (c, d; arrows).

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Fig. 16: Radio-pathologic correlation of the inflammatory aortic aneurysm. (a) Contrast-enhanced CT, (b) Hematxylin & eosin stained specimen, (c) Elastica van Gieson stained specimen. The wall thickening of the aorta is corresponding to the sclerosing inflammation in the adventitia (a, b; arrows). The high density thin layer between thickened wall and mural thrombus (a; red arrow) is corresponding to the aortic media (c; red arrow) and intima.

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**Fig. 17:** Figure 17. Radio-pathologic correlation of the inflammatory aortic aneurysm. (a) Contrast-enhanced CT, (b) Hematxylin & eosin stained specimen, (c) Elastica van Gieson stained specimen, (d) IgG4 stained specimen. The thickening of the aneurysmal aortic wall (a; arrow) is corresponding to the sclerosing inflammation in the aortic adventitia (b). The aortic media/intima is spared the inflammation (b; arrow). Abundant IgG4-positive cells are revealed (d).

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Fig. 18: Contrast-enhanced CT of a 52-year-old woman. Remarkable wall thickening of the left renal pelvis is demonstrated (a-c; arrows). Pre-operative diagnosis was suspicious of the renal pelvic cancer.

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Fig. 19: Figure 19. Radio-pathologic correlation of the urinary tract type lesion (same case with figure 18). (a) Contrast-enhanced CT, (b) Hematxylin & eosin stained specimen, (c) IgG4 stained specimen. The wall thickening seen in the CT image is corresponding to the submucosal inflammation consisted of the lymphoplasmacytic infiltrations and fibrosis (a, b). In the pathologic specimen, the epithelial layer is being spared the inflammation and this finding is correlated to the luminal smoothness of the affected renal pelvis demonstrated in the CT image (a-c; arrows). Abundant IgG4-positive plasma cells are revealed (c).

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Fig. 20: Figure 20. Radio-pathologic correlation of the periaortic type lesion. (a) Contrast-enhanced CT, (b) Hematxylin & eosin stained specimen, (c) IgG4 stained specimen. The wall thickening of the right iliac artery is seen (a; arrow). In pathologic specimen, this lesion is consisted of the lymphoplasmacytic infiltrations and fibrosis. This sclerosing inflammation is corresponding to the homogenous enhancement in the late phase of the contrast-enhanced CT. IgG4-positive plasma cells are easily detected (c).

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**Fig. 21**: Radio-pathologic correlation of the periaortic type lesion. (a) Contrast-enhanced CT, (b) Hematxylin & eosin stained specimen, (c) IgG4 stained specimen. Lymphoplasmacytic sclerosing inflammation is corresponding to the homogeneous enhancement of the lesion demonstrated in the late phase image of the CT (a; arrows, b). Abundant IgG4-positive plasma cells are revealed (c).

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Conclusion

IgG4-RD is recently established disease entity and several organs such as pancreas, submandibular and lachrymal gland, lung, aorta/artery, and nervous system has been recognized as target organs of it. Thinking about target organs of 3 types in IgG4-retroperitoneal fibrosis in this study, periaortic type lesion can be considered as belonging the entity IgG4-related periaortitis/periarteritis or IgG4-related inflammatory aneurysm with targeting the aorta/artery, and urinary tract type is corresponding to IgG4-related pyelitis with involving the renal pelvis to the urinary tract.(16, 18, 19) Regarding the peritoneum/fascia type lesion, even though there is controversy that if the peritoneum or fascia is the target organ of IgG4-RD or not, it is possibly enough that peritoneum can be a target organ like pulmonary pleura has been recognized as a target of it.(20)

Irrespective of the 3 types, we suppose that important differential diagnoses of IgG4-related retroperitoneal fibrosis are malignant lymphoma and non IgG4-related retroperitoneal fibrosis. The presence or absence of IgG4-related lesions could be helpful for discrimination, because 95% of patients had extra-retroperitoneal lesions in this study. Examining the serum IgG4 value also should be considered, because of high frequency (99%) of elevation of serum IgG4 concentrations were identified in this study. Therefore, if IgG4-related retroperitoneal fibrosis is suspected radiologically, we should seek IgG4-related lesions in other sites using imaging examinations and examine serum IgG4 value. However, pathological examination is needed in the cases without extra-retroperitoneal lesions or elevation of serum IgG4 concentrations. In urinary type lesions, renal pelvic or urinary cancer should be considered as differential diagnosis, like one case performed total nephrectomy with preoperative diagnosis of suspicious of renal pelvic cancer. In addition to the exist of IgG4-related lesions in other sites and serum IgG4 value, radiologically, smoothness of the luminal surface due to the lack of the epithelial involvement could be most useful findings for discrimination. Absence of vessel encasement and smooth border to surrounding fat tissue or renal parenchyma, less frequency of severe hydronephrosis also might be radiological clue to differentiate it from renal pelvic or urinary tract cancer, usually arising from epithelium and growth invasively, leads to severe hydronephrosis. Hydronephrosis were seen in 21 cases (28%), irrespective of the 3 types, however, there were some differences regarding the radiological severity and the degree of the improvement of hydronephrosis. Interestingly, hydronephrosis caused by urinary tract type lesion tended to be milder than that seen in another 2 types, even though the fact that urinary tract is the target organ of this type. It is supposed to related to the fact that epithelium layer is spared in this type. Another possible reason is there might be deference for the degree of fibrosis among these types. In fact, of 17 cases with hydronephrosis caused by priaortic type or peritoneum/fascia type lesions, remnant hydronephrosis or renal atrophy was developed in five cases, despite of the improvement of the responsible lesions.
This study has some limitations. First of all, because of the retrospective and multi-center study, CT protocol was not consistent. Second, follow-up images were not available for all patients. If these images were available, more IgG4-related extra-retroperitoneal lesions might be identified. Third, pathological specimens of retroperitoneal lesions were obtained only a limited case, the pathological deference including the degree of fibrosis could not be performed. Lastly, to more clarify the utility of serum IgG4 concentrations or radiological findings in IgG4-related retroperitoneal fibrosis, comparison study with non IgG-related retroperitoneal fibrosis or malignant lymphoma.

In conclusion, IgG4-related retroperitoneal fibrosis could manifest 3 types of lesion reflecting the sclerosing inflammation in the aortic adventitia, submucosal layer of the urinary tract, and peritoneum/fascia. Clinical characteristics also defer among these types, we should pay attention to the involved anatomical structures in IgG4-related retroperitoneal fibrosis.
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