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CASE REPORT

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IgG4-related disease mimicking renal pelvis tumor with peritoneal carcinomatosis

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Abstract

IgG4-RD may rarely present as a retroperitoneal fibrosis, mimicking carcinomatosis. Clinicians should consider this disease when encountering an idiopathic peritoneal and retroperitoneal fibrosis with renal involvement and hydronephrosis.

KEYWORDS

carcinomatosis, hydronephrosis, IgG4-related disease, laparoscopic surgery, retroperitoneal fibrosis

1 | INTRODUCTION

IgG4-related disease (IgG4-RD) is a rare systemic inflammatory disease with a poorly understood etiology. We present an 84-year-old man who had an accidentally noted renal pelvis tumor. A laparoscopic incisional biopsy revealed peritoneal fibrosis with carcinomatosis-like lesions. The histopathological examination confirmed the diagnosis of IgG4-related disease.

IgG4-related disease is a rare clinicopathological entity that encompasses systemic fibrosis, infiltration of IgG4 positive plasma cells, and serum IgG4 elevation.[1] The etiology of IgG4-RD is still poorly understood, and it is associated with Mikulicz's disease, autoimmune pancreatitis (AIP), inflammatory abdominal aortic aneurysm, chronic sclerosing sialadenitis, sclerosing cholangitis, and retroperitoneal fibrosis.

Retroperitoneal fibrosis is one of the most frequent manifestation of IgG4-RD, accounting for 9.6%-27% of all patients. However, rarely, IgG4-RD can present as a solitary mass lesion within renal pelvis. In some even rarer situations,

it presents as peritoneal carcinomatosis.[2] Definite diagnosis is based on immunohistochemistry. The first line of treatment for IgG4-RD is glucocorticoids. However, frequent recurrence is a major feature of IgG4-related diseases so that further investigation of ideal biomarker to monitor is warranted. Here, we report a rare case of IgG4-RD with presentation of pseudo-renal pelvis tumor combined with suspected peritoneal and retroperitoneal carcinomatosis.

2 | CASE PRESENTATION

An 84-year-old man with underlying diseases of hypertension, diabetes mellitus type II, chronic obstructive pulmonary disease, and benign prostatic hyperplasia suffered from general malaise and poor appetite for 1 month. The physical examination showed mild pale of conjunctiva. Laboratory tests revealed leukopenia (WBC:3.88 × 1000/μL), normocytic anemia (Hgb:11.5 g/μL, MCV:90.2fl), elevated creatinine level (2.15 mg/dL), and proteinuria (3+). The urine cytology revealed suspicion of malignancy. Renal ultrasound suggested left hydronephrosis. In order to rule out urothelial carcinoma, the patient underwent abdominal nonenhanced computed tomography (CT) scans. The results showed extensive left renal pelvis and ureteral malignancy with extension to left peritoneal and retroperitoneal spaces (Figure 1). Therefore, the patient underwent left ureterorenoscopy. However, severe ureter kinking and stricture were found without any intralumenal tumor. Hence, internal dilatation was performed and a 6Fr/24 cm tumor stent was placed.

Based on the above image and surgical results, the patient was referred to Hematology and General Surgery departments for further evaluation. Laparoscopic surgical exploration was performed. Suspected peritoneal carcinomatosis lesion with omental adhesion was found in the operation. (Figure 2). The adhesive lesion was dissected and excised carefully. The operation time was 40 minutes with minimal blood loss. The patient had an uneventful postoperative course and was discharged on postoperative day 1.

The resected specimen measured 4.0 × 3.6 × 0.5 cm in size. Grossly, it was yellowish and soft. A microscopic examination revealed dense lymphoplasmacytic infiltrations in fibroadipose tissue. Higher magnification revealed focal fibrosis (Figure 3). The immunohistochemical study (Figure 4) revealed CD20 (+, follicles), CD3 (+, parafollicles), cyclin D1 (−, follicles), CD138 (+), IgG (+), and IgG4 (+) with plasma cell ratio (IgG4 + /IgG + >40%). The IgG4-related disease was highly suggestive. Serum laboratory evaluation after the surgery revealed high levels of serum IgG (2460 mg/dL) and IgG4 (>1300 mg/dL) with hypocomplementemia (C3:36.3 mg/dL and C4:2.49 mg/dL). The patient is being currently under steroid medication (0.6 mg/

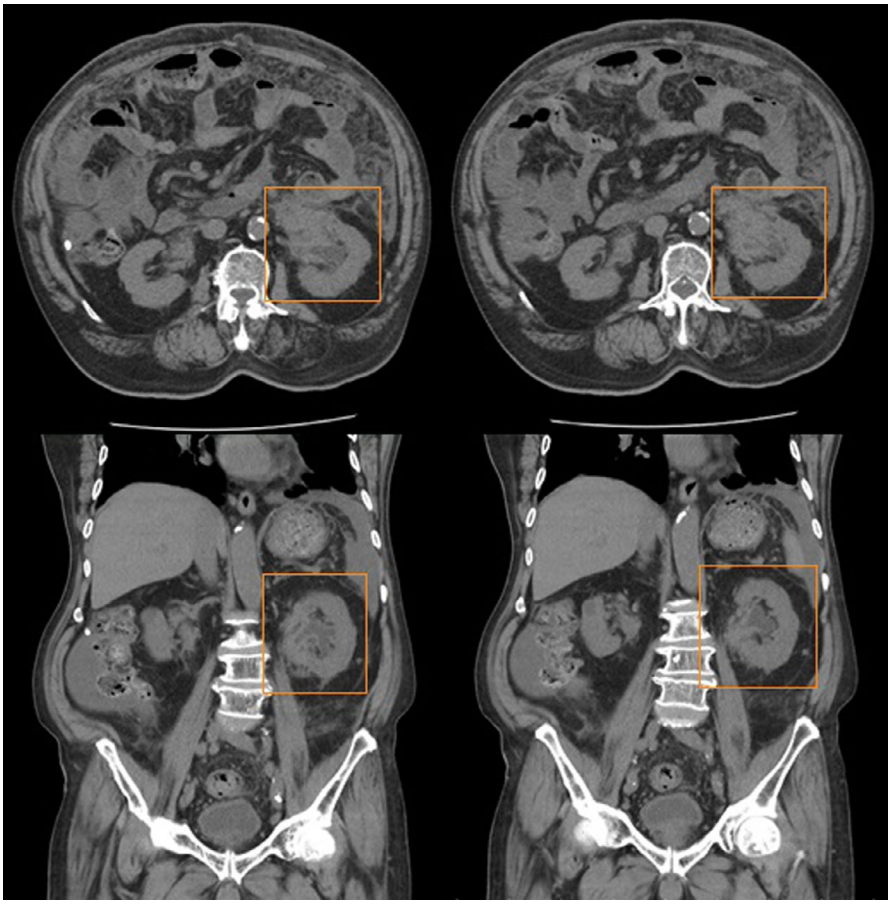

FIGURE 1 Computed tomography (CT). Computed tomography (CT). A CT image reveals a suspicious renal pelvis tumor with hydronephrosis

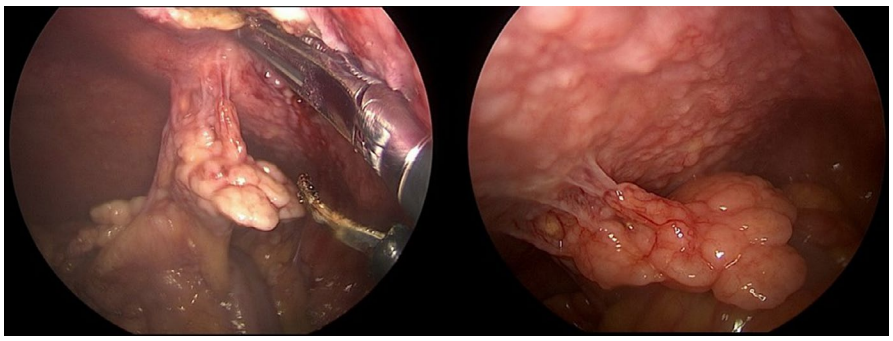

FIGURE 2 Laparoscopic surgical exploration. A laparoscopic surgical exploration revealed suspicious peritoneal carcinomatosis with omentum adhesion

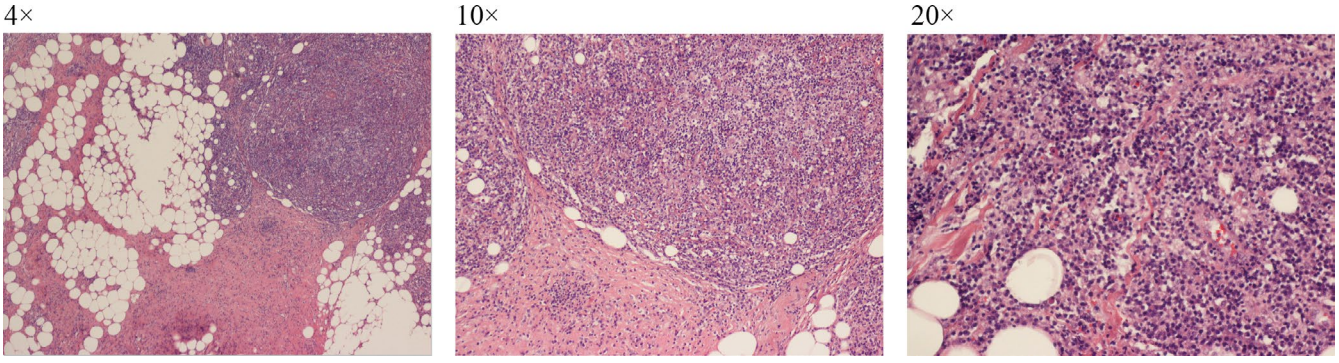

FIGURE 3 Histological examination. The findings of histological examination indicated dense lymphoplasmacytic infiltrations in fibroadipose tissue. Higher magnification revealed focal fibrosis

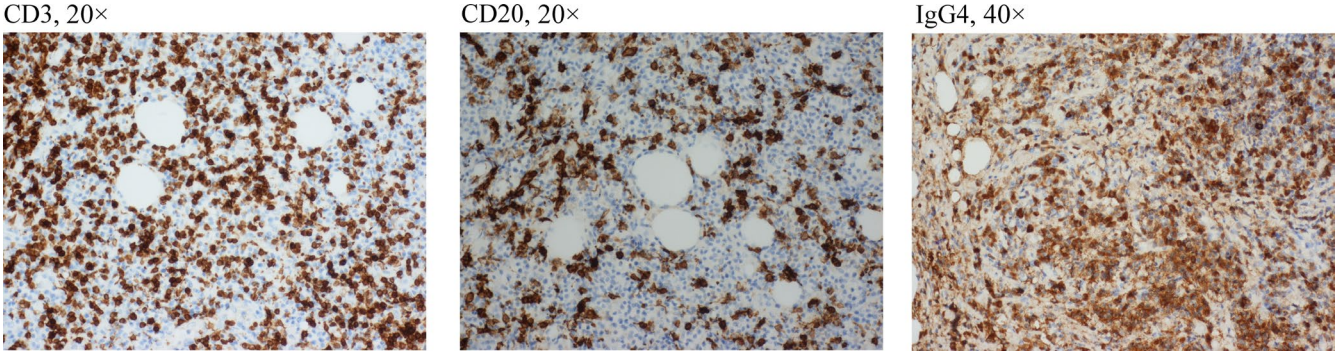

FIGURE 4 The immunohistochemical staining. The immunohistochemical study revealed positive findings of CD3 (parafollicles), CD20 (follicles), and IgG4 (plasma cells)

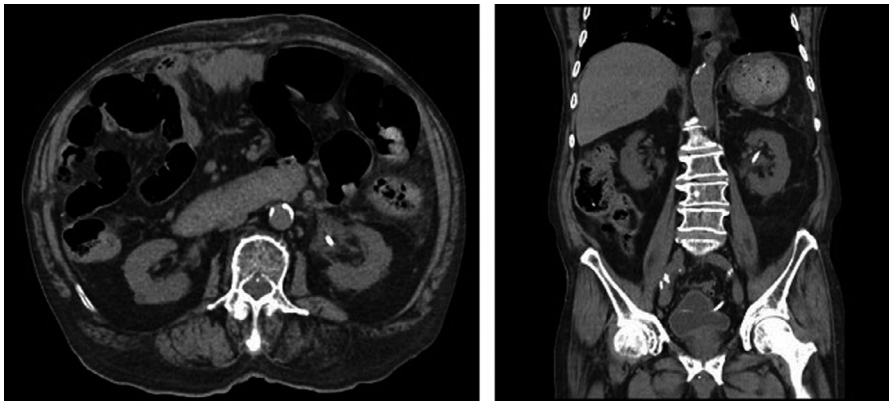

FIGURE 5 Two-month post-operative computation tomography (CT). CT images demonstrated regression of left retroperitoneal fibrosis and hydronephrosis

TABLE 1 Clinical summary of reported similar IgG4-related disease cases

Age (y)	Sex	Lesion location	Biopsy	Treatment	References
84	M	Left renal pelvis mass Peritoneum and retroperitoneum	Laparoscopic incisional biopsy	Oral prednisolone	Our case
71	M	Left ureteropelvic junction mass	N/A	Oral prednisolone	12
51	F	Left renal pelvic mass	N/A	Left nephroureterectomy	13
75	M	Right renal pelvis mass	N/A	Right nephroureterectomy	14
49	F	Left renal pelvis mass	N/A	Left nephroureterectomy	15
53	F	Right renal pelvis and calyces	N/A	Right nephroureterectomy	16

Abbreviations: F, female; M, male; N/A, Not applicable.

kg/day) after 6-month follow-up. General malaise and poor appetite improved gradually. Interval shrinkage of his retroperitoneal fibrosis and regression of the hydronephrosis was found in 2-month follow-up abdomen computed tomography (Figure 5). His renal function improved as well with postoperative creatinine level of 1.27 mg/dL.

3 | DISCUSSION

IgG4-related disease is a systemic disease that gains more attention in the last two decades. It is also known as IgG4-related sclerosing disease, IgG4-related systemic sclerosing disease, IgG4-related autoimmune disease, hyper-IgG4 disease, and IgG4-related systemic disease. Most IgG4-RD cases were presented in males (62%-83%) and in age older than 50 years.[3] Moreover, up to 90% male predominance has been reported in IgG4-RD with kidney and retroperitoneum involvement.[4] The most common presentations of IgG4-RD are autoimmune pancreatitis (AIP) and Mikulicz's disease (MD). However, involvement of other various organs has been recorded elsewhere including salivary gland, bile duct, lung, kidney, orbit, lymph node, and retroperitoneum.

Lesions in our case are presented in kidney, peritoneum, and retroperitoneum, mimicking renal tumor extension to peritoneal and retroperitoneal spaces. Retroperitoneal fibrosis (RPF) is one of the lesion sites of IgG4-RD. The representative clinical manifestations are flank pain, abdomen pain, lower extremities edema, low-grade fever, decreased urine output, weight loss, and poor appetite..[5] It may also accompany with unilateral or bilateral hydronephrosis.

Laboratory findings show that high concentration of serum IgG4 is the most important features in IgG4-RD patients (87.5%). However, normal concentration of IgG4 may be encountered. Therefore, high concentration of IgG4 is not mandatory for the diagnosis. Another feature of IgG4-RD is hypocomplementemia, which is presented in half of the patients according to previous population cohort study.[6] Impaired renal function may also be seen in these patients. We did not consider the possibility of IgG4-RD before the incisional biopsy because urothelial carcinoma was initially suspected due to the malignant cell in urine cytology. Therefore, no related serum test was performed before the biopsy.

Image study remains crucial for diagnosis of retroperitoneal fibrosis and kidney disease. Computational tomography (CT) and magnetic resonance imaging (MRI) allow specific lesion detections. Low intensity of kidney lesions in CT scans and hypointense in T2-weighted MRI are usually presented in IgG4-related disease. In our case, left renal pelvis with soft tissue intensity could be found in noncontrast abdominal CT. We did not perform computational tomography with contrast due to impaired renal function.

To confirm the diagnosis, tissue proof is essential. Three major histological features could be seen in IgG4-related disease tissues. The first feature is cellular fibrosis with stortiform pattern. The second is obliterate phlebitis. The third is dense lymphoplasmacytic infiltrates. If two of the above histologic findings are presented, IgG4-RD is highly suggestive. Moreover, the ratio of IgG4-bearing plasma cells to IgG-bearing plasma cells over 40% or IgG4-positive plasma cells > 10/high-power field could assist with the diagnosis.[7]

The gold standard treatment of IgG4-RD is glucocorticoid. Maintenance dose is essential for its high frequency of recurrence. The optimal dose is 0.6 mg/kg for initial dose.[8] Other immunologic agents such as azathioprine, mycofenolate mofetil, methotrexate, or combinations could be applied as the maintenance regimen. Rituximab, an Anti-CD20 monoclonal antibody, could deplete B cells and further leads to decreased IgG4 serum concentrations.[9] Serum IgG4 antibody is not a sensitive biomarker for monitoring relapse. Hypocomplementemia is more sensitive than serum IgG4, which is suggested in case series.[10] Further research in evaluation of serum complements as a biomarker is required. Serum GDF-15, a growth differentiation factor 15, also known as macrophage inhibitory cytokine-1, secreted by activated macrophage could act as a fibrotic degree in IgG4-RD.[11]

To diagnose solitary IgG4-related disease with or without retroperitoneal fibrosis is a challenge for surgeons because they mimic malignant tumors. Renal pelvic tumors or

lymphomas should also be listed in differential diagnosis. In Table 1, we review and list some similar cases of IgG4-RD published in the literature. Most of the previous cases received nephroureterectomy.[12-16] Despite the fact that our case is not the first IgG4-RD with retroperitoneal fibrosis and renal mass, it is the first case showing omental involvement that mimics carcinomatosis. In previous case reports, most omental involvement IgG4-RD is associated with small bowel or colons.[2,17]

Because of its rarity and no specific imaging consensus,[18] even experienced surgeons could misdiagnose IgG4-related diseases as renal pelvis tumor, retroperitoneal tumor or lymphoma. In this case, urothelial carcinoma was highly suspicious initially based on urine cytology and computed tomography. However, peritoneal and retroperitoneal infiltrates are less likely presented simultaneously in urothelial carcinoma. Fortunately, transperitoneal laparoscopic incisional biopsy was performed and the patient avoided unnecessary operation.

4 | CONCLUSION

In conclusion, in suspicious of retroperitoneal tumor with renal involvement, IgG4-RD should be taken into consideration. Serum test of IgG4 and complements might be helpful for the diagnosis. Here, we presented a rare case of IgG4-related disease with peritoneal and retroperitoneal fibrosis that mimics renal pelvis tumor. In order to confirm the diagnosis of IgG4-RD and to avoid unnecessary operation, biopsy should be performed before surgical resection. In our case, good response was noted after immediate administer of corticosteroid.

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CONFLICT OF INTEREST

None declared.

AUTHORS' CONTRIBUTIONS

JJ and CS: performed the surgery. YL and ST: analyzed and interpreted the patient's image of CT. KT: examined and interpreted the pathology. CC: reviewed the related articles and was a major contributor in writing the manuscript. All authors: read and approved the final manuscript.

ETHICAL APPROVAL

Approval for the study was obtained from the institutional review board of Kaohsiung Municipal Siaogang Hospital.

CONSENT FOR PUBLICATION

Informed consent was obtained from the patient for the publication of this case report.

DATA AVAILABILITY STATEMENT

The authors do not wish to share the patient's data. The privacy of this participant should be protected.

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REFERENCES

1. Takahashi H, Yamamoto M, Suzuki C, Naishiro Y, Shinomura Y, Imai K. The birthday of a new syndrome: IgG4-related diseases constitute a clinical entity. *Autoimmun Rev*. 2010;9(9):591-594.
2. Coulier B, Montfort L, Beniuga G, Pierard F, Gielen I. Small bowel obstruction caused by peritoneal immunoglobulin g4-related disease mimicking carcinomatosis: case report. *Korean J Radiol*. 2014;15(1):66-71.
3. Stone JH, Zen Y, Deshpande V. IgG4-related disease. *N Engl J Med*. 2012;366(6):539-551.
4. Zen Y, Onodera M, Inoue D, et al. Retroperitoneal fibrosis: a clinicopathologic study with respect to immunoglobulin G4. *Am J Surg Pathol*. 2009;33(12):1833-1839.
5. Kawano M, Saeki T, Nakashima H. IgG4-related kidney disease and retroperitoneal fibrosis: an update. *Mod Rheumatol*. 2019;29(2):231-239.
6. Evans RDR, Cargill T, Goodchild G, et al. Clinical manifestations and long-term outcomes of IgG4-related kidney and retroperitoneal involvement in a United Kingdom IgG4-related disease cohort. *Kidney Int Rep*. 2019;4(1):48-58.
7. Montironi R, Scarpelli M, Cheng L, et al. Immunoglobulin G4-related disease in genitourinary organs: an emerging fibroinflammatory entity often misdiagnosed preoperatively as cancer. *Eur Urol*. 2013;64(6):865-872.
8. Khosroshahi A, Wallace ZS, Crowe JL, et al. International Consensus Guidance Statement on the Management and treatment of IgG4-related disease. *Arthritis Rheumatol*. 2015;67(7):1688-1699.
9. Khosroshahi A, Carruthers MN, Deshpande V, Unizony S, Bloch DB, Stone JH. Rituximab for the treatment of IgG4-related disease: lessons from 10 consecutive patients. *Medicine (Baltimore)*. 2012;91(1):57-66.
10. Kihara M, Sugihara T, Hosoya T, Miyasaka N. Clinical significance of complement as a biomarker of disease activity in 4 cases of IgG4-related disease with retroperitoneal fibrosis. *Clin Exp Rheumatol*. 2013;31(6):947-949.
11. Kawashiri SY, Origuchi T, Umeda M, et al. Association of serum levels of fibrosis-related biomarkers with disease activity in patients with IgG4-related disease. *Arthritis Res Ther*. 2018;20(1):277.
12. Yoshino T, Moriyama H, Fukushima M, Sanda N. A case of IgG4-related retroperitoneal fibrosis mimicking renal pelvic cancer. *Urol Int*. 2013;90(3):365-368.
13. Wang Y, Chen X, Luo R, et al. IgG4-related systemic disease mimicking renal pelvic cancer: a rare case. *World J Surg Oncol*. 2014;12:395.

14. Park HG, Kim KM. IgG4-related inflammatory pseudotumor of the renal pelvis involving renal parenchyma, mimicking malignancy. *Diagn Pathol*. 2016;11:12.
15. Kuroda N, Nakamura S, Miyazaki K, et al. Chronic sclerosing pyelitis with an increased number of IgG4-positive plasma cells. *Med Mol Morphol*. 2009;42(4):236-238.
16. Zhang H, Ren X, Zhang W, Yang D, Feng R. IgG4-related kidney disease from the renal pelvis that mimicked urothelial carcinoma: a case report. *BMC Urol*. 2015;15:44.
17. Vadi SK, Parihar AS, Kumar R, et al. IgG4-related disease simulating carcinoma colon with diffuse peritoneal Carcinomatosis on 18F-FDG PET/CT. *Clin Nucl Med*. 2018;43(7):e247-e249.
18. Forestier A, Buob D, Mirault T, et al. No specific imaging pattern can help differentiate IgG4-related disease from idiopathic retroperitoneal fibrosis: 18 histologically proven cases. *Clin Exp Rheumatol*. 2018;36(3):371-375.

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