CASE REPORT

Case Report: IgG4-related kidney disease complicated by interstitial pneumonia [version 1; peer review: 1 approved, 2 approved with reservations]

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Abstract

Immunoglobulin G4 (IgG4)-related disease is a systemic inflammatory disorder characterized by tubulointerstitial nephritis with IgG4-positive plasma cell infiltration. We report the case of an 84-year-old male who presented with a history of dyspnea on exertion and cough. The lymph nodes were palpated in the axilla. Urinalysis revealed mild proteinuria and increased levels of NAG and β2-microglobulin. Blood tests showed hyperglobulinemia with a marked elevation of serum IgG4 levels. Chest computed tomography showed bilateral ground-glass and reticular opacities in the lower and peripheral portions of the lungs. Ga-67 scintigraphy showed kidney uptake.
The patient was diagnosed with IgG4-related kidney disease based on the renal pathology indicative of typical tubulointerstitial nephritis with extensive IgG4-positive plasma cell infiltration. The patient was treated with prednisolone and showed a prompt response in his clinical condition. The patient achieved normalization of serum IgG4 levels 6 months after the initiation of treatment. Although IgG4-related disease is thought to be potentially associated with organ fibrosis, there are few reports on combination of interstitial pneumonia and IgG4-related kidney disease. Our case report presents a possible pattern of IgG4-related disease.

Keywords

IgG4-related kidney disease, tubulointerstitial nephritis, interstitial pneumonia, prednisolone

Open Peer Review

Approval Status ✓ ✓ ?

	1	2	3
version 2 (revision) 27 Sep 2023		✓ view	
version 1 29 Aug 2023	✓ view	? view	? view

1. **Masaru Matsui**, Nara Medical University, Nara, Japan
2. **Tomohito Gohda**, Juntendo University, Tokyo, Japan
3. **Seiji Kishi**, Kawasaki Medical School, Kurashiki, Japan

Any reports and responses or comments on the article can be found at the end of the article.

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Author roles: Mima A: Conceptualization, Data Curation, Formal Analysis, Funding Acquisition, Investigation, Methodology, Project Administration, Resources, Supervision, Validation, Visualization, Writing – Original Draft Preparation, Writing – Review & Editing; **Lee R**: Data Curation, Formal Analysis, Funding Acquisition, Supervision, Validation; **Murakami A**: Investigation, Methodology, Supervision, Visualization; **Gotoda H**: Formal Analysis, Methodology, Validation; **Akai R**: Data Curation, Resources, Supervision, Validation; **Lee S**: Data Curation, Formal Analysis, Supervision

Competing interests: Honoraria: Akira Mima (Eli Lilly); Grants received: Akira Mima (Sumitomo Pharma).

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Introduction

Immunoglobulin G4 (IgG4)-related disease is a systemic inflammatory disease characterized by extensive lymphoplasmacytic infiltration of IgG4-positive cells in various organs.[1–3] Renal involvement has been reported in approximately 10% of patients with IgG4-related disease.[4] Respiratory organ lesions have also been recognized; however, their rate is low and they are often only detected during close examination.[5] Clinical symptoms vary depending on the organs affected by IgG4-related disease; however, they are usually mild. Thus, IgG4-related disease should be diagnosed based on a combination of clinical, serological, and radiological findings, and pathological features.[6] There have only been a few reports on the coexistence of interstitial pneumonia and IgG4-related kidney disease.[7] In this report, we describe the case of a patient who presented with interstitial pneumonia and was diagnosed with IgG4-tubulointerstitial nephritis and IgG4-related kidney disease. Treatment with prednisolone was initiated soon after diagnosis and the patient responded well.

Case presentation

An 84-year-old unemployed Japanese man presenting with dyspnea on exertion and cough was referred to our hospital. The patient had a history of hypertension and hypothyroidism, but an unremarkable family history of any related pathology. Examination results of the patient were found to be negative for arthralgia, skin rash, macrohematuria, and hemoptysis. Upon admission, body temperature was recorded to be 36.5 °C; blood pressure, 128/72 mmHg; heart rate, 72 bpm; oxygen saturation, 98%; weight, 60.5 kg; height, 164.9 cm; and BMI, 21.1 kg/m^2. Initial laboratory and diagnostic workup revealed blood urea nitrogen 18 mg/dL (normal range: 8-20 mg/dL), creatinine 0.98 mg/dL (normal range: 0.65-1.07 mg/dL), estimated glomerular filtration rate 56 mL/min/1.73 m^2 (normal range: $\geq$ 60 mL/min/1.73 m^2), calcium 9.4 mg/dL (normal range: 8.8-10.4 mg/dL), total protein 9.1 g/dL (normal range: 6.5-8.0 g/dL), albumin 3.6 g/dL (normal range: 3.9-4.9 g/dL), alkaline phosphatase 60 IU/L (normal range: 50-350 IU/L), aspartate transaminase 27 IU/L (normal range: 7-38 IU/L), alanine transaminase 11 IU/L (normal range: 4-44 IU/L), total cholesterol 182 mg/dL (normal range: 120-220 mg/dL), triglyceride 175 mg/dL (normal range: 50-149 mg/dL), WBC 11.5$\times$10^3/μL (normal range: 3.1-8.4$\times$10^3/μL), RBC 3.97$\times$10^6/μL (normal range: 4.2-5.7$\times$10^6/μL), hemoglobin 12.5 g/dL (normal range: 14-18 g/dL),

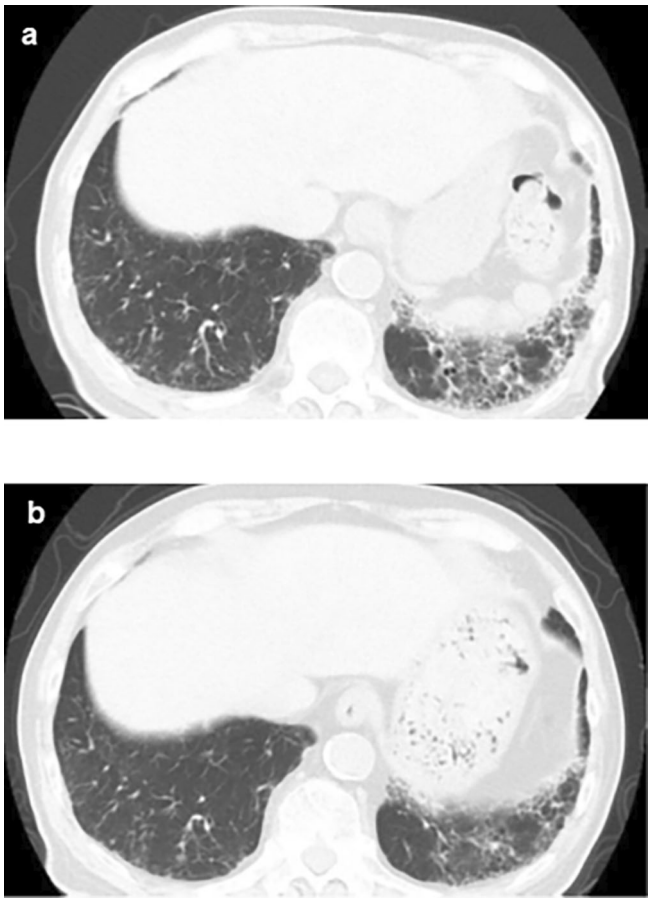


Figure 1. Computed tomography findings. (a) Plain chest CT showing the reticular pattern and bronchial dilatation in the bilateral lower lung fields before therapy; (b) After therapy, the interstitial pattern nearly disappeared from the bilateral lung fields. CT: computed tomography.

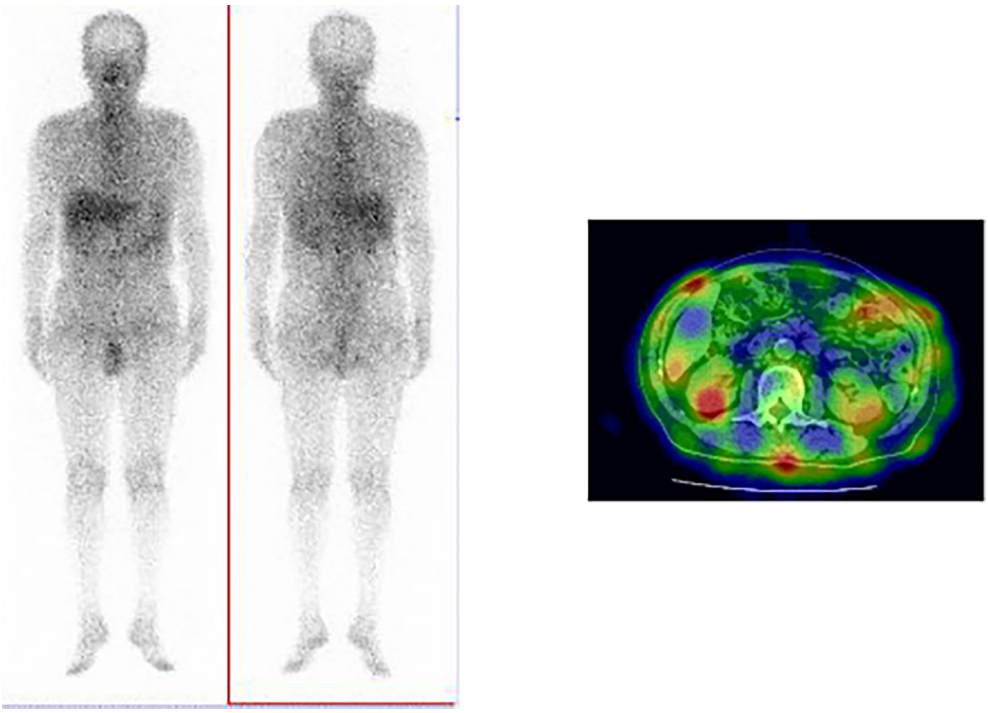


Figure 2. Ga-67 scintigraphy findings. Uptake by kidney revealed using Ga-67 scintigraphy.

platelets 200×10^3/μL (normal range: 150-330$\times10^3$/μL), eosinophils 3% (normal range: 0-5%), and urinalysis negative for protein, RBC, and cell casts. Urinary N-acetyl-beta-D-glucosaminidase (NAG)/creatinine 17.1 IU/gCr (normal range: 1.6-5.8 IU/gCr) and urinary β2 microglobulin 371 mg/L (normal range: ≤289 mg/L). Antineutrophil cytoplasmic antibodies screening was found to be negative, with low C3=68 mg/dL, low C4=7.4 mg/dL, and negative for anti-SSA, anti-SSB, anti-RNP, Scl-70, anti-Sm, and ds-DNA antibodies. Antinuclear antibodies (ANA) antibodies were found to be ×1280. Hyperglobulinemia was determined with an IgG level of 3719 mg/dL (normal range: 870-1700 mg/dL) and an IgG4 level of 1290 mg/dL (normal range: 4-108 mg/dL). Rheumatoid factor (≤15 IU/mL) was elevated at 24 IU/mL, and KL-6 (<500 IU/mL) was significantly increased at 623 IU/mL. Computerized tomography (CT) revealed bilateral ground-glass and reticular opacities predominantly in the lower and peripheral portions of the lungs (Figure 1a). Furthermore, bronchial wall thickening, and enlarged cervical, mediastinal, and axillary lymph nodes were identified. However, renal, pancreatic, or salivary gland inflammation was not observed. Ga-67 scintigraphy revealed accumulation in the kidneys (Figure 2). Consequently, the patient was diagnosed with IgG4-related kidney disease based on the renal pathology with massive tubulointerstitial nephritis, characteristic fibrosis (bird's eye pattern) (Figure 3a and b), and IgG4-positive cell infiltration, wherein the number of IgG4 positive plasma cells was >10/hpf, and IgG4/IgG ratio was 61.9% (Figure 3c). Deposition of globulin or complement, and evidence of glomerular sclerosis were not observed in the glomeruli. Treatment was initiated by administering oral prednisolone at 30 mg/day for one month, followed by prompt alleviation of cough and dyspnea on exertion. With a subsequent decrease (after one month prednisolone treatment) in urinary NAG and β2 microglobulin and IgG4 levels, prednisolone was decreased from 2.5 to 5 mg every 2 to 4 weeks for 4 weeks. One year after the initiation of treatment, the patient achieved normalization of serum IgG4 levels, and chest CT revealed the interstitial pattern was found to have nearly disappeared (Figure 1b). Figure 4 shows the clinical course of this patient.

Discussion

IgG4-related diseases should be differentiated from diseases caused by excessive inflammatory cytokine production, such as interleukin-6 (IL-6)-produced Castleman's disease and autoimmune disorders.[8] Usually, IgG4-related diseases are observed in middle-aged men. Most patients with this disease present with associated extrarenal lesions, such as in the salivary glands, lymph nodes, and pancreas.[9] Therefore, the clinical manifestations of the disease vary according to the organ involved. The most characteristic features of IgG4-related kidney disease are presence of IgG4 positive plasma cell-rich tubulointerstitial nephritis and fibrosis, which are sometimes concurrent with glomerular lesions.[10,11]

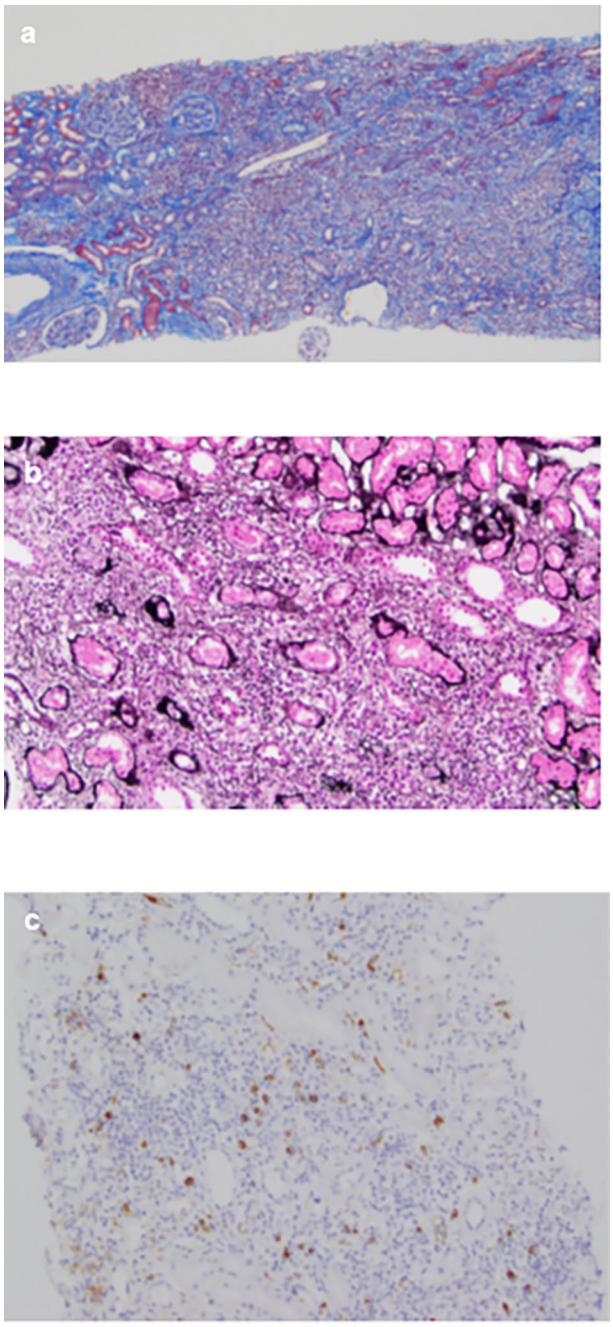
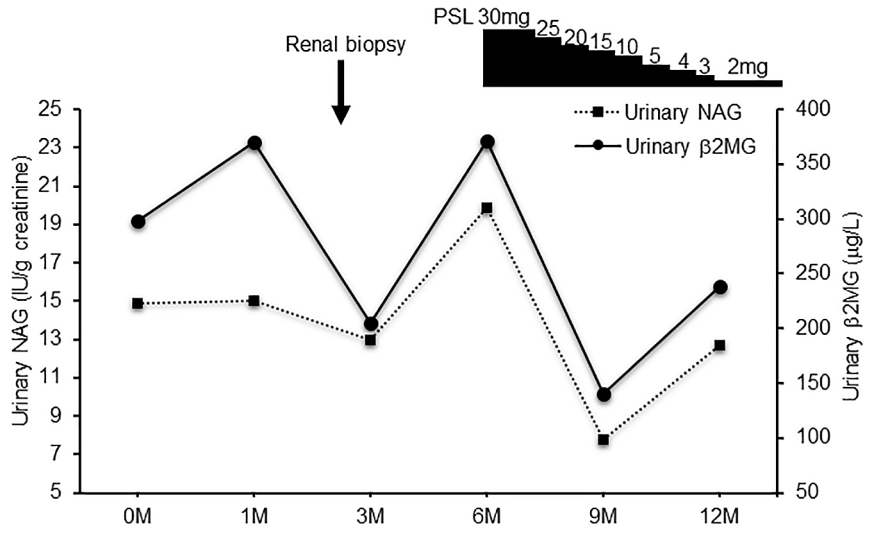


Figure 3. Microscopy findings of the renal biopsy. (a) The interstitium shows mononuclear cell infiltration and interstitial fibrosis with tubular atrophy with Masson's trichrome stain (×40); (b) PAM stain in the interstitium shows bird's eye pattern of fibrosis (×200); (c) Immunohistochemical analysis for IgG4 shows dominant IgG4+ plasma cell filtration, with an IgG4+/IgG+ ratio of >40% (×100).

Similar to the present case, approximately 30% of the patients diagnosed with IgG4-related kidney disease do not show any abnormality on a CT scan. In contrast, previous reports indicated that approximately 70% of patients with IgG4-related kidney disease show some kind of abnormality.[9,12] The discrepancy between these findings can be owing to the presence or absence of contrast-enhanced CT, which is necessary within renal function tolerance. Ga-67 scintigraphy and FDG-PET have been reported to be useful for its diagnosis. However, contradictory to the present case, positive accumulation in the kidney during Ga-67 scintigraphy has been reported to be only 11%.[9] Another useful method of analysis for IgG4-related kidney disease is T2-weighted and diffusion-weighted MR imaging.[13]



IgG (mg/dL)	3719	3593	3043	3068	1123	729
IgG4 (mg/dL)	1290	811	733	625	148	31.3
KL-6 (IU/mL)	623		488	573		

Figure 4. The clinical course of the patient. Clinical course treatment was initiated by administering prednisolone at 30mg/day, followed by prompt alleviation of the dyspnea on exertion and cough. Urinary NAG and β2 MG, and serum IgG4 were significantly decreased after prednisolone treatment. NAG, N-acetyl-β-D-glucosaminidase; β2 MG, β2 microglobulin; PSL, prednisolone.

CT imaging findings of the lungs in IgG4-related diseases have been classified into four types: ground-glass opacity, diffuse reticular, bronchial wall thickening, and nodular patterns.[14] The ground-glass opacity and diffuse reticular patterns potentially suggest lymphocyte and plasma cell infiltration of the alveoli and interstitium. Bronchial wall thickening pattern indicates plasma cells infiltration of the bronchial vascular bundles, alveoli, and interstitium. Finally, nodular sclerosing inflammation of the bronchial glands was prominently observed to be associated with the nodular pattern.[14] Although we did not perform a lung biopsy in the present case, the CT findings of diffuse reticular and bronchial wall thickening confirmed pulmonary involvement in IgG4-related diseases.

Inflammatory cytokines, such as IL-5 and tumor necrosis factor (TNF)-α, reportedly correlate with IgG4-related diseases.[15,16] Furthermore, our previous reports also indicate that the inflammatory cytokines play a potentially pivotal role in the development of renal fibrosis.[17] T helper cells type 2 (Th2) and regulatory T cells (Tregs) have been reported to be involved in IgG4-related tubulointerstitial fibrosis.[18] Treg cells can increase the regulatory cytokines, such as transforming growth factor-β (TGF-β), which has also been identified in renal fibrosis signaling.[18,19] However, many aspects of this disease, especially complications caused by interstitial pneumonia, remain unclear with limited reports on this disease type; hence, further studies are warranted.

The optimal treatment for IgG4-related kidney disease has not been established; however, most patients, including the one in the present case, respond to prednisolone. Saeki *et al.* showed that the induction of prednisolone led to rapid improvement in renal function and serological abnormalities 1 month after the initiation of therapy, and that maintenance therapy with low-dose prednisolone successfully resulted in long-term suppression of disease activity in 43 Japanese patients with IgG4-related kidney disease.[9]

Similar to the present case, even in patients without diagnosis of renal localized IgG4-related disease, favorable outcomes can be achieved with the same treatment modalities as those employed for the patients diagnosed with the disease.

IgG4-related kidney disease is an emerging disease with recently identified pathological features. Generally, patients respond rapidly to prednisolone and present a relatively favorable prognosis. The present case of IgG4-related kidney disease associated with interstitial pneumonia provides a novel rationale for its pathophysiology.

Consent

Written informed consent was obtained from the patient for publication of the details of their medical case and any accompanying images.

The study protocol for the patient record review was reviewed and the need for approval was waived by Institutional Review Board of Osaka Medical and Pharmaceutical University, as a retrospective review of patient data did not require ethical approval in accordance with local guidelines.

Data availability

All data underlying the results are available as part of the article and no additional source data are required.

Acknowledgements

The author thanks Dr. Yoshinobu Hirose and Dr. Tatsuhiko Mori (Osaka Medical and Pharmaceutical University) for valuable discussions on the case pathology. We would like to thank Honyaku Center Inc. for English language editing.

References

1. Hamano H, Kawa S, Horiuchi A, *et al.*: **High serum IgG4 concentrations in patients with sclerosing pancreatitis.** *N. Engl. J. Med.* 2001; **344**: 732–738.
Publisher Full Text

2. Stone JH: **IgG4-related disease: nomenclature, clinical features, and treatment.** *Semin. Diagn. Pathol.* 2012; **29**: 177–190.
PubMed Abstract | Publisher Full Text

3. Umehara H, Okazaki K, Masaki Y, *et al.*: **Research Program for Intractable Disease by Ministry of Health, Labor and Welfare (MHLW) Japan G4 team. A novel clinical entity, IgG4-related disease (IgG4RD): general concept and details.** *Mod. Rheumatol.* 2012; **22**: 1–14.
PubMed Abstract | Publisher Full Text | Free Full Text

4. Saeki T, Nishi S, Imai N, *et al.*: **Clinicopathological characteristics of patients with IgG4-related tubulointerstitial nephritis.** *Kidney Int.* 2010; **78**: 1016–1023.
PubMed Abstract | Publisher Full Text

5. Masaki Y, Dong L, Kurose N, *et al.*: **Proposal for a new clinical entity, IgG4-positive multiorgan lymphoproliferative syndrome: analysis of 64 cases of IgG4-related disorders.** *Ann. Rheum. Dis.* 2009; **68**: 1310–1315.
PubMed Abstract | Publisher Full Text

6. Deshpande V, Zen Y, Chan JK, *et al.*: **Consensus statement on the pathology of IgG4-related disease.** *Mod. Pathol.* 2012; **25**: 1181–1192.
PubMed Abstract | Publisher Full Text

7. Adachi H, Okuyama H, Yamaya H, *et al.*: **A case of IgG4-related kidney disease complicated by eosinophilic lung disease.** *CEN Case Rep.* 2015; **4**: 162–168.
PubMed Abstract | Publisher Full Text | Free Full Text

8. Nishimoto N, Terao K, Mima T, *et al.*: **Mechanisms and pathologic significances in increase in serum interleukin-6 (IL-6) and soluble IL-6 receptor after administration of an anti-IL-6 receptor antibody, tocilizumab, in patients with rheumatoid arthritis and Castleman disease.** *Blood.* 2008; **112**: 3959–3964.
PubMed Abstract | Publisher Full Text

9. Saeki T, Kawano M, Mizushima I, *et al.*: **The clinical course of patients with IgG4-related kidney disease.** *Kidney Int.* 2013; **84**: 826–833.
Publisher Full Text

10. Saeki T, Kawano M: **IgG4-related kidney disease.** *Kidney Int.* 2014; **85**: 251–257.
Publisher Full Text

11. Raissian Y, Nasr SH, Larsen CP, *et al.*: **Diagnosis of IgG4-related tubulointerstitial nephritis.** *J. Am. Soc. Nephrol.* 2011; **22**: 1343–1352.
PubMed Abstract | Publisher Full Text | Free Full Text

12. Kawano M, Saeki T, Nakashima H, *et al.*: **Proposal for diagnostic criteria for IgG4-related kidney disease.** *Clin. Exp. Nephrol.* 2011; **15**: 615–626.
Publisher Full Text

13. Ono H, Murakami T, Mima A, *et al.*: **Successful treatment of highly advanced immunoglobulin G4-related kidney disease presenting renal mass-like regions with end-stage kidney failure: a case study.** *BMC Nephrol.* 2017; **18**: 261.
PubMed Abstract | Publisher Full Text | Free Full Text

14. Inoue D, Zen Y, Abo H, *et al.*: **Immunoglobulin G4-related lung disease: CT findings with pathologic correlations.** *Radiology.* 2009; **251**: 260–270.
PubMed Abstract | Publisher Full Text

15. Takekawa M, Imai K, Adachi M, *et al.*: **Hypereosinophilic syndrome accompanied with necrosis of finger tips.** *Intern. Med.* 1992; **31**: 1262–1266.
PubMed Abstract | Publisher Full Text

16. Campbell HD, Tucker WQ, Hort Y, *et al.*: **Molecular cloning, nucleotide sequence, and expression of the gene encoding human eosinophil differentiation factor (interleukin 5).** *Proc. Natl. Acad. Sci. U. S. A.* 1987; **84**: 6629–6633.
PubMed Abstract | Publisher Full Text | Free Full Text

17. Mima A: **Inflammation and oxidative stress in diabetic nephropathy: new insights on its inhibition as new therapeutic targets.** *J. Diabetes Res.* 2013; **2013**: 248563.

18. Nakashima H, Miyake K, Moriyama M, *et al.*: **An amplification of IL-10 and TGF-beta in patients with IgG4-related tubulointerstitial nephritis.** *Clin. Nephrol.* 2010; **73**: 385–391.
PubMed Abstract | Publisher Full Text

19. Mima A, Abe H, Nagai K, *et al.*: **Activation of Src mediates PDGF-induced Smad1 phosphorylation and contributes to the progression of glomerulosclerosis in glomerulonephritis.** *PLoS One.* 2011; **6**: e17929.
PubMed Abstract | Publisher Full Text | Free Full Text

Open Peer Review

Current Peer Review Status: ✔ ? ?

Version 1

Reviewer Report 20 September 2023

https://doi.org/10.5256/f1000research.144701.r203748

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Seiji Kishi
Department of Nephrology and Hypertension, Kawasaki Medical School, Kurashiki, Japan

This case report presents an IgG4-related disease complicated by pulmonary involvement. The association with pulmonary lesions is discussed as a novel finding.

Please allow me to ask the following questions to improve the paper and make it more meaningful to the reader:

1. Are there any other findings besides imaging that can be evaluated in relation to steroid therapy? Physical examination, walking distance, oxygen saturation, pulmonary function tests, and even other blood tests would be acceptable.

2. Can you discuss more about IgG4-related diseases and pulmonary involvement? For example, the classification and frequency of interstitial pneumonia, the prediction of steroid response, and whether the findings are predictive of recovery of renal function.

Is the background of the case's history and progression described in sufficient detail?
Yes

Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?
Yes

Is sufficient discussion included of the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?
Partly

Is the case presented with sufficient detail to be useful for other practitioners?
Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: kidney disease, acute kidney injury, chronic kidney disease

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 21 Sep 2023

AKIRA MIMA

Reviewer:
Are there any other findings besides imaging that can be evaluated in relation to steroid therapy? Physical examination, walking distance, oxygen saturation, pulmonary function tests, and even other blood tests would be acceptable.

Authors' response:
The reviewer raised important question regarding evaluation of steroid therapy in our case. Oxygen saturation was quickly restored to 100% when started steroid therapy. We have added this information to the "Case Presentation" section.

Reviewer:
Can you discuss more about IgG4-related diseases and pulmonary involvement? For example, the classification and frequency of interstitial pneumonia, the prediction of steroid response, and whether the findings are predictive of recovery of renal function.

Authors' response:
The reviewer asked more detailed information for IgG4-RD. From a pathological perspective, it has been observed that certain distinct features, such as the presence of lymphocytes and IgG4-positive plasma cells, exhibit a distribution pattern consistent with the findings in imaging. Nevertheless, in certain lymphoproliferative disease unrelated to IgG4-RD, comparable findings are evident in both CT imaging and histopathology. This similarity poses a challenge in distinguishing them from the respiratory manifestations of IgG4-RD should consider clinical presentation, imaging results, and pathological characteristics. Relatively good response to corticosteroid has been reported for the treatment of IgG4-RD lung lesions. These pieces of information are added to the "Discussion" section.

Competing Interests: No competing interests were disclosed.

Reviewer Report 11 September 2023

https://doi.org/10.5256/f1000research.144701.r203747

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Tomohito Gohda
Department of Nephrology, Faculty of Medicine, Juntendo University, Tokyo, Japan

This case report is well written. However, I suggest the authors to respond to the following comments:

1. The quality of microscopy findings of renal biopsy seems to be poor.

2. Please describe in more detail how to differentiate normal IP from IgG4-related lung disease in the absence of lung biopsy findings.

3. Please describe any differences from previous reports in cases of IgG4-related renal and respiratory disease.

Is the background of the case's history and progression described in sufficient detail?
Yes

Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?
Yes

Is sufficient discussion included of the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?
Partly

Is the case presented with sufficient detail to be useful for other practitioners?
Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: diabetic kidney disease

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 21 Sep 2023

AKIRA MIMA

Reviewer:
The quality of microscopy findings of renal biopsy seems to be poor.

Authors' response:
First of all, we would like to thank the reviewer's careful review. As the reviewer points out, the image quality is not good. We are very sorry; this is a limitation of the image capture machine. However, we believe the images are sufficient for pathological diagnosis.

Reviewer:
Please describe in more detail how to differentiate normal IP from IgG4-related lung disease in the absence of lung biopsy findings.

Authors' response:
The reviewer raised important question regarding features of IgG4-RD-induced IP. Pathologically, characteristic findings such as lymphocyte and IgG4-positive plasma cell infiltrates have been reported to have the same distribution as the imaging findings. However, in some lymphoproliferative diseases other than IgG4-RD, similar findings are seen on chest imaging or histopathology, and it is difficult to differentiate them from respiratory involvement of IgG4-RD, suggesting that respiratory involvement of IgG4-RD should be diagnosed comprehensively from the clinical picture, imaging findings and pathological aspects.

Reviewer:
Please describe any differences from previous reports in cases of IgG4-related renal and respiratory disease.

Authors' response:
It has been reported that most imaging studies of the lungs in IgG4-RD showed a variety of pathologic patterns, including solid nodule density, ground-glass opacity, bronchiectasis, honeycombing, and bronchiolar vesicle thickening. Our case showed the reticular pattern and bronchial dilatation. Hence, our case is considered a pulmonary lesion similar to those reported in the past, although there have been only a few reports to date.

Competing Interests: No competing interests were disclosed.

Reviewer Report 11 September 2023

https://doi.org/10.5256/f1000research.144701.r203749

Masaru Matsui
Department of Nephrology, Nara Medical University, Nara, Japan

This case report focuses on the topic that interstitial pulmonary diseases are a rare complication of IgG4-related diseases. As the authors acknowledge, lung biopsy was required for showing IgG4

cells infiltration in interstitium of lungs, and therefore the pathological association between lung and kidney may not be evident. This reviewer was curious about changes in KL-6 after steroid treatment.

Is the background of the case's history and progression described in sufficient detail?
Yes

Are enough details provided of any physical examination and diagnostic tests, treatment given and outcomes?
Yes

Is sufficient discussion included of the importance of the findings and their relevance to future understanding of disease processes, diagnosis or treatment?
Yes

Is the case presented with sufficient detail to be useful for other practitioners?
Yes

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: CKD

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Author Response 12 Sep 2023

AKIRA MIMA

We appreciate reviewer's careful review .

Competing Interests: No competing interests were disclosed.