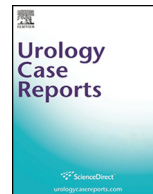




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Oncology

IgG4-related pseudo-tumor of the kidney and multiple organ involvement mimicked malignancy



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ABSTRACT

Immunoglobulin G4-related disease (IgG4-RD) is an increasingly recognized systemic condition characterized by particular clinical, serologic, and pathologic features that are consistent across a wide range of organ systems. Herein, we present a rare case of IgG4-RD presenting as multiple inflammatory pseudotumors involving the kidney and other organs involvement mimicking urothelial cell carcinoma with liver, lymph node and lung metastasis. The final diagnosis was made based on characteristic histopathological finding and analysis of IgG4 immunostaining that can distinguish from other conditions. Greater awareness of this disease is needed to ensure diagnoses, which can prevent unnecessary surgical intervention.

Introduction

Immunoglobulin G4-related disease (IgG4-RD) is an increasingly recognized systemic condition characterized by particular clinical, serologic, and pathologic features, include tumor-like formation of involved organs, often but not always, elevated serum concentrations of IgG4 and a characteristic “storiform” histologic pattern with lymphoplasmacytic infiltrate enriched in IgG4-positive plasma cells.¹ However, in rare incidences, the disease can present as mass-like lesions and may affect more than one organ which can often pose a diagnostic challenge since these lesions mimicking malignancy. To the best of our knowledge, renal involvement of IgG4-RD is extremely rare. Herein, we present a case of IgG4-RD in a 52-year-old Thai male patient presenting as multiple inflammatory pseudotumors involving the kidney and other organs involvement mimicking urothelial cell carcinoma with liver, lymph node and lung metastasis.

Case presentation

A 52-year-old man presented with painless gross hematuria and anemic symptoms for 5 months. He also experienced with anorexia, low-grade fever and weight loss for 5 kgs. The physical examination and initial laboratory investigations revealed markedly anemia (Hb 7 g/dL),

mildly elevated alkaline phosphatase (189 U/L) with normal AST, ALT, and bilirubin. The hyperglobulinemia (10.6 g/dL) was also found and serum protein electrophoresis was shown polyclonal gammopathy. Initial urinalysis was found only the red blood cell 0–1 cells/HPF.

For further evaluation, the contrast-enhanced computed tomography (CECT) scan was performed and revealed a 7.5 × 7.9 × 8.5 cm infiltrative heterogeneous hypo-enhancing lesion involved upper to mid pole of right kidney with slightly irregular delayed rindlike perinephric soft tissue surrounding right kidney (Fig. 1A and B). A 6.8 × 3.8 cm partially-defined lobulate contour of heterogeneous hypo-enhancing lesion in hepatic segment IVa/VIII was also found (Fig. 1C). Moreover, multiple lymph nodes at bilateral paraaortic, paracaval, aortocaval, retrocaval, gastrohepatic and left retrocaval region together with several enlarged mediastinal, bilateral supraclavicular, right internal mammary, bilateral axillary, right anterior superior and middle diaphragmatic lymph nodes, as well as multiple various sized nodules scattered in both lungs were also found (Fig. 1D). Findings of these results were highly suggestive for malignancy included lymphoma with multi organ involvement, and urothelial carcinoma of the right kidney with liver, lymph node and lung metastases.

The liver biopsied showed lymphoplasmacytic infiltrates with plasma cells and extensive replacement of the liver parenchyma by storiform fibrosis (Fig. 2A). Because urothelial carcinoma could not be

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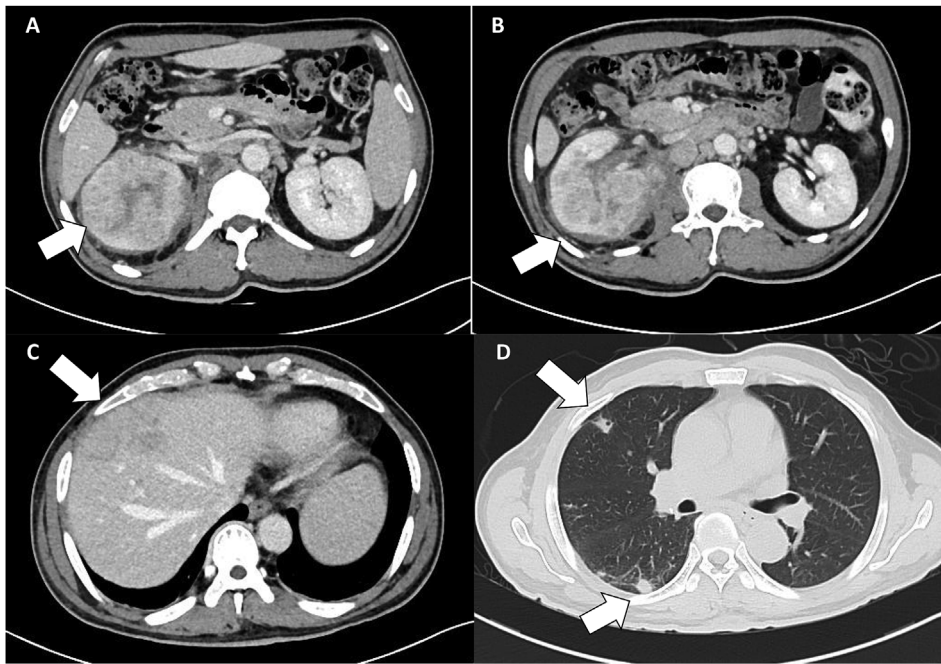


Fig. 1. (A and B) Contrast-enhanced axial CT of the abdomen showed a 7.5 × 7.9 × 8.5 cm infiltrative heterogeneous hypo-enhancing lesion involved upper to mid pole of right kidney (white arrow). (C) Contrast-enhanced axial CT of the abdomen showed a 6.8 × 3.8 cm partially-defined lobulate contour of heterogeneous hypo-enhancing lesion in hepatic segment IVa/VIII (white arrow). (D) Contrast-enhanced axial CT of the chest showed multiple various sized nodules scattered in both lungs, up to 0.9 cm. (white arrow).

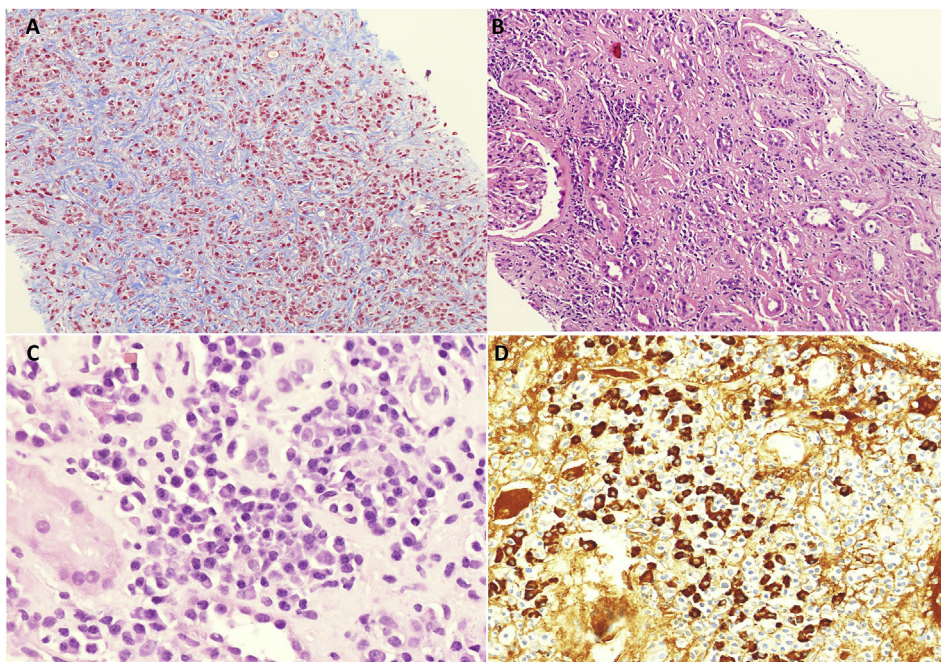


Fig. 2. (A) Histopathology of the liver biopsy includes plasma cell rich infiltrates and storiform fibrosis, which is easily apparent with Masson's trichrome stain. (B and C) Histopathology of kidney biopsy shows patchy foci of interstitial fibrosis and tubular atrophy and prominent interstitial plasma cell infiltration. (D) Immunoperoxidase staining shows numerous IgG- and IgG4-positive plasma cells with an IgG4+ /IgG + plasma cell ratio of 54%. Of note, the classic storiform fibrosis and obliterative phlebitis are not identified in the kidney biopsy. [Masson's trichrome stain, original magnification x100 (A); Hematoxylin & Eosin, original magnification x100 (B), x400 (C); immunohistochemistry for IgG4, original magnification x400 (D)].

completely excluded at this point, we obtained a kidney biopsy, which revealed patchy foci of interstitial fibrosis and tubular atrophy (Fig. 2B) and prominent interstitial plasma cell infiltration (Fig. 2C) without any evidence of malignancy. The similarity of the findings at both locations raised the possibility of IgG4-related disease. Nevertheless, lymphoma and plasma cell neoplasm remained in the differential diagnoses. In situ hybridization for kappa and lambda light chains were performed and showed no light chain restriction confirming that these plasma cells are polyclonal, and thus are not lymphoma or plasma cell neoplasm. Immunohistochemical study demonstrated that these plasma cells, both in the liver and the kidney (Fig. 2D), are positive for IgG and IgG4 with an IgG4+ /IgG + plasma cell ratio of 45% and 54%, respectively.

Subsequent laboratory studies revealed elevated serum IgG and IgG4 levels. The final diagnosis was IgG4-related inflammatory pseudotumor of the kidney with multi-organ involvement and the treatment

was initiated with the prednisolone at the dose of 1 mg/kg/day for 3 weeks and then tapered off. The serum IgG4 level was substantially decreased over time after treatment. The CT scan at 3 months after treatment revealed interval decreased size of the prior mentioned infiltrative renal mass as well as much decreased size and numbers of intraabdominal nodes are also seen. The gross hematuria disappeared and results of all laboratory studies were normal.

Discussion

IgG4-RD is a multi-organ immune-mediated condition that has been described in virtually every organ system in which the histopathological features are consistent across a wide range of organ systems, regardless of the site of disease.¹ The inflammatory lesion frequently forms a tumefactive mass that may destroy the involved organ. The

imaging features are generally nonspecific and do not permit reliable distinctions between IgG4-RD and cancer. Renal involvement of IgG4-RD is extremely rare, the most common finding is tubulointerstitial nephritis (TIN),² however, mass forming lesions mimicking malignancy may be seen. In IgG4-related renal disease has been mistaken for malignant mass and mostly the diagnosis is established after nephrectomy.^{3,4} Therefore, greater awareness of this disease should be needed to avoid unnecessary surgical procedure.

In our case, the clinical presentation and imaging finding were highly suggestive for malignancy and tissue biopsy is the key to diagnosis either malignancy or IgG4-RD in this patient. Fortunately, histopathological result was negative for malignancy and the characteristic storiform pattern as observed in our case, raised the possibility of IgG4-RD.⁵ The IgG4 immunostaining may help to distinguish IgG4-RD from other conditions and the ratio of IgG4 to IgG-bearing plasma cells that higher than 40% further assists in confirming the diagnosis of IgG4-RD.

However, the histopathological mimickers of IgG4-RD are lymphomas and the kidney are a common extranodal site of lymphoma involvement. Clonality studies are necessary to rule out these cancers. Another issue is the distinction between infiltrates caused by IgG4-RD and other inflammatory infiltrates, such as those adjacent to neoplastic lesions. IgG4-positive plasma cells are generally present diffusely throughout lesions of IgG4-RD, in contrast to the focal aggregates of IgG4-bearing cells that are detected in most other inflammatory mimickers of this condition. Correlation with specific histopathological findings is essential.

In conclusion, despite the rarity of this disease, IgG4-RD should be considered in the differential diagnosis of renal mass and establish the diagnosis of IgG4-RD should be done by tissue diagnosis. This could be preventing further unnecessary surgical intervention. Most of patients with IgG4-renal disease have other organs involvement at diagnosis. Evaluating the mass lesions in other organs might provide an important clue to the diagnosis of the IgG4-related disease. This case emphasizes the importance of considering that IgG4-related diseases can involve

the kidney and give rise to mass-like lesions and mimic renal malignancy.

Conflicts of interest

The authors declare no potential conflicts of interest.

Consent

Written informed consent was obtained from the patient for publication of this Case Report and any accompanying images.

Authors' contributions

P. Sitthideatphaiboon drafted the manuscript. Kewalee Sasiwimonphan provided imaging description and figures. Jerasit Surinrspanont and Anapat Sanpawata provided pathology description and figures. All authors have read and approved the final manuscript.

Appendix A. Supplementary data

Supplementary data to this article can be found online at <https://doi.org/10.1016/j.eucr.2019.100953>.

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