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IgG4-Related Nephritis Misdiagnosed as a Malignant Tumor Based on 18 F-Fluorodeoxyglucose Positron Emission Tomography/Computed Tomography: A Case Report

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Case report

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Abstract

Introduction: IgG4-related diseases is an autoimmune disease newly recognized in recent years, it is rarely seen in clinical practice, the main clinical features of IgG4-RKD include acute or chronic renal insufficiency, proteinuria, elevated serum Ig G4, histopathological manifestations were tubulointerstitial nephritis, mainly characterized by a large amount of IgG4 positive plasma cell infiltration in the tubulointerstitial, it responded well to glucocorticoid therapy. Renal parenchymal damage could be seen on imaging. However, PET/CT imaging has been less reported, here we reported a case of IgG4-related kidney disease with PET/CT imaging.

Case presentation: A 50-year-old female presented with chills and fever for more than 2 months, she came to the urology department of our hospital for further diagnosis and treatment due to the right kidney occupation revealed by CT examination in local hospital. MRI plain scan plus diffusion imaging suggested multiple lesions in the right kidney, multiple nodular abnormally hypermetabolism foci in the right kidney were seen on PET/CT imaging, and the negative findings in the other parts of the body, therefore, a primary malignant tumor of the kidney was considered. Laboratory tests revealed elevated Levels of C-reactive protein, erythrocyte sedimentation rate, and IgG4 of immunoglobulin, histological pathology of right kidney puncture indicated inflammation and infection with surgical indications, she underwent radical right nephrectomy with laparoscopic under general anesthesia and was discharged 1 week after the right kidney operation, her clinical symptom disappeared and kept in good health during follow-up.

Conclusions: IgG4-related nephritis could manifest multiple or solitary hypermetabolism foci in unilateral kidney on PET/CT imaging, while the rest of the systemic PET/CT imaging manifestation was negative, which may be related to the infiltration of lymphocytes, plasma cells and inflammatory cells at the lesion site. The cause of abnormal accumulation of FDG in lesion site was unclear, and the true mechanism needs to be further clarified.

Introduction

Immunoglobulin G4-related disease (IgG4-RD) is an immune-mediated inflammatory fibrotic disease in which a large number of IgG4-positive plasma cells infiltrate the involved tissue. This disease is characterized by storiform fibrosis with or without elevated serum concentrations of IgG4 and is considered a systemic disease that can involve the pancreas, bile duct, salivary glands, lacrimal glands, lungs, liver, and kidneys. Involvement of the kidneys is classified as IgG4-related kidney disease (IgG4-RKD), which includes IgG4-related tubulointerstitial nephritis and membranous renal disease secondary to IgG4-RD (membranous glomerulonephropathy). Cases of IgG4-RKD are very rare, first described in 2004 by Takeda et al[1], and generally involve elevated serum IgG4 concentrations with infiltration of IgG4-positive cells into the renal interstitium. Given that IgG4-RKD has no specific manifestations that can be detected during imaging, it can be easily misdiagnosed as a malignant renal tumor. Imaging using ^{18}F-fluorodeoxyglucose positron emission tomography/computed tomography (FDG PET/CT) is not

commonly used and the final diagnosis of IgG4-RKD is made via pathological examination of a puncture or surgical specimen. This report describes our experience with a 50-year-old woman who was initially diagnosed with a right renal malignancy based on ^{18}F-FDG PET/CT before surgery, although the postoperative pathological findings indicated that she had IgG4-RKD.

Case Presentation

A 50-year-old woman presented with a > 2-month history of fever and chills. An examination at her local hospital suggested that she had a space-occupying lesion in the right kidney, and she was referred to our hospital for diagnosis and treatment. A physical examination revealed no palpable enlargement of the superficial lymph nodes or clear signs of hepatosplenomegaly. The patient did not have any remarkable personal, genetic, or family history. Laboratory testing revealed high serum concentrations of IgG4 (20.74 g/L, reference range: 7.00–16.00 g/L) and C-reactive protein (113.00 mg/L, reference range: 0.00–8.00 mg/L).

Conventional ultrasonography revealed hypoechoic lesions in the upper pole and middle part of the right kidney. The largest lesion had an approximate size of 30 mm × 29 mm, with no clear rim and no obvious blood flow signal during color Doppler flow imaging. After injection of a contrast agent, we observed synchronous filling of the lesions in the upper pole and middle of the right kidney (vs. the normal renal parenchyma). Furthermore, wash-out in the two lesions occurred earlier than in the normal renal parenchyma, and malignant tumors were suspected based on the lack of clear lesion rims. Plain and diffusion-weighted magnetic resonance imaging revealed multiple lesions in the right kidney and contrast-enhanced magnetic resonance imaging was recommended. An abdominal scan revealed two hypointense lesions on the T2-weighted images (Fig. 1A, B) with moderate signal intensity on the T1-weighted images (Fig. 1C,D). We also performed ^{18}F-FDG PET/CT to determine whether the lesions were benign or malignant, which revealed that both lesions were FDG-avid (SUVmax values of 10.9 for the upper pole lesion and 11.8 for the middle lesion) (Fig. 2). No other lesions were observed and the suspected diagnosis was a primary malignant renal tumor.

Ultrasound-guided percutaneous biopsy of the right kidney was performed and the histopathological examination identified acute and chronic suppurative inflammation. Thus, laparoscopic radical right nephrectomy was performed under general anesthesia. A postoperative histopathological examination of the hematoxylin and eosin-stained surgical specimens revealed local atrophy in the right kidney cortex and medulla (Fig. 3A, 200), collagenous and fibrous hyperplasia, and infiltration of the renal interstitium by plasma cells, neutrophils, and lymphocytes (Fig. 3B, × 400). In addition, immunohistochemical staining revealed positive results for CD38 (Fig. 3C, × 200), CD138 (Fig. 3D, × 200), IgG (Fig. 3E, × 200), and IgG4 (Fig. 3F, × 200). Thus, the final diagnosis was IgG4-related nephritis. The patient was discharged 7 days later and has remained healthy during a 6-month follow-up.

Discussion

As a type of systemic disease, IgG4-RD is characterized by elevated serum concentrations of IgG4 and infiltration of IgG4-positive plasma cells in the involved tissues. This disease can involve the pancreas, bile duct, gallbladder, portal vein area of the liver, gastric mucosa, intestinal mucosa, salivary glands, lymph nodes, and bone marrow [2–8]. Cases that involve the kidneys are classified as IgG4-RKD, which generally involves secondary tubulointerstitial nephritis (IgG4-related tubulointerstitial nephritis), although a minority of lesions can be localized to the kidney. Given its rarity, it is easy to miss IgG4-RKD or misdiagnose it as a renal tumor if the physician does not have a comprehensive understanding of IgG4-RD.

The pathogenesis of IgG4-RKD is still being debated, and it may be related to allergies or autoimmune disorders, although it is unclear whether it is an autoimmune disease. Furthermore, it is unclear whether high concentrations of IgG4 are the cause of the disease or a pathological marker, and their antigenicity is also unclear. First-line glucocorticoid therapy is generally effective and provides a good prognosis, which highlights the importance of an early and accurate diagnosis. However, rituximab and other biological agents may be more promising treatments [9, 10]. Nevertheless, the lack of clear data regarding the pathogenesis of IgG4-RKD has hindered the development of specific therapeutic drugs.

Bilateral kidney involvement is more common and involvement of a single kidney is less common. Plain computed tomography typically reveals small, round, wedge-shaped, or irregular low-density nodules in the renal cortex. Furthermore, T1-weighted imaging will reveal a hypointense signal, T2-weighted imaging will reveal an isointense signal, and diffusion-weighted imaging will reveal a hyperintense signal, with slight enhancement during contrast-enhanced computed tomography or magnetic resonance imaging [11–13]. Multiple hypointense lesions are the most common findings during contrast-enhanced computed tomography in cases of IgG4-RKD [14, 15].

While PET/CT is used for diagnosing and staging tumors [16], it is rarely used for diagnosing inflammatory diseases. In this context, IgG4-RD can manifest as multi-organ FDG-avid lesions on PET/CT, and whole-body PET/CT can reveal disease activity [17]. However, IgG4-related nephritis is rarely observed via PET/CT, and in our case the FDG-avid lesions that were detected during PET/CT were misdiagnosed as primary or metastatic renal malignancy. Therefore, we conclude that IgG4-RKD should be considered in cases with elevated IgG4 concentrations and multiple hypermetabolic lesions in a single kidney. A histopathological examination of the biopsy or surgical specimens is needed to confirm the diagnosis.

Abbreviations

PET-CT: positron emission tomography/computed tomography; MRI: Magnetic resonance imaging; IgG4-RD: IgG4-related disease; IgG4-RKD: IgG4-related kidney disease; FDG: fluorodeoxyglucose

Declarations

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Authors' contributions

All authors participated in manuscript preparation. ZKC provided pathological images and described in this report. CS constructed the conception and design of this report. BP prepared the draft of the manuscript. All authors read and approved the final manuscript.

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Availability of data and materials

Data will be available upon request to the first author Bo Pan.

Ethics approval and consent to participate

Not applicable.

Consent for publication

Written informed consent for publication of their clinical details and clinical

images were obtained from the patient.

Competing interests

The authors declare that they have no conflicts of interest.

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Figures

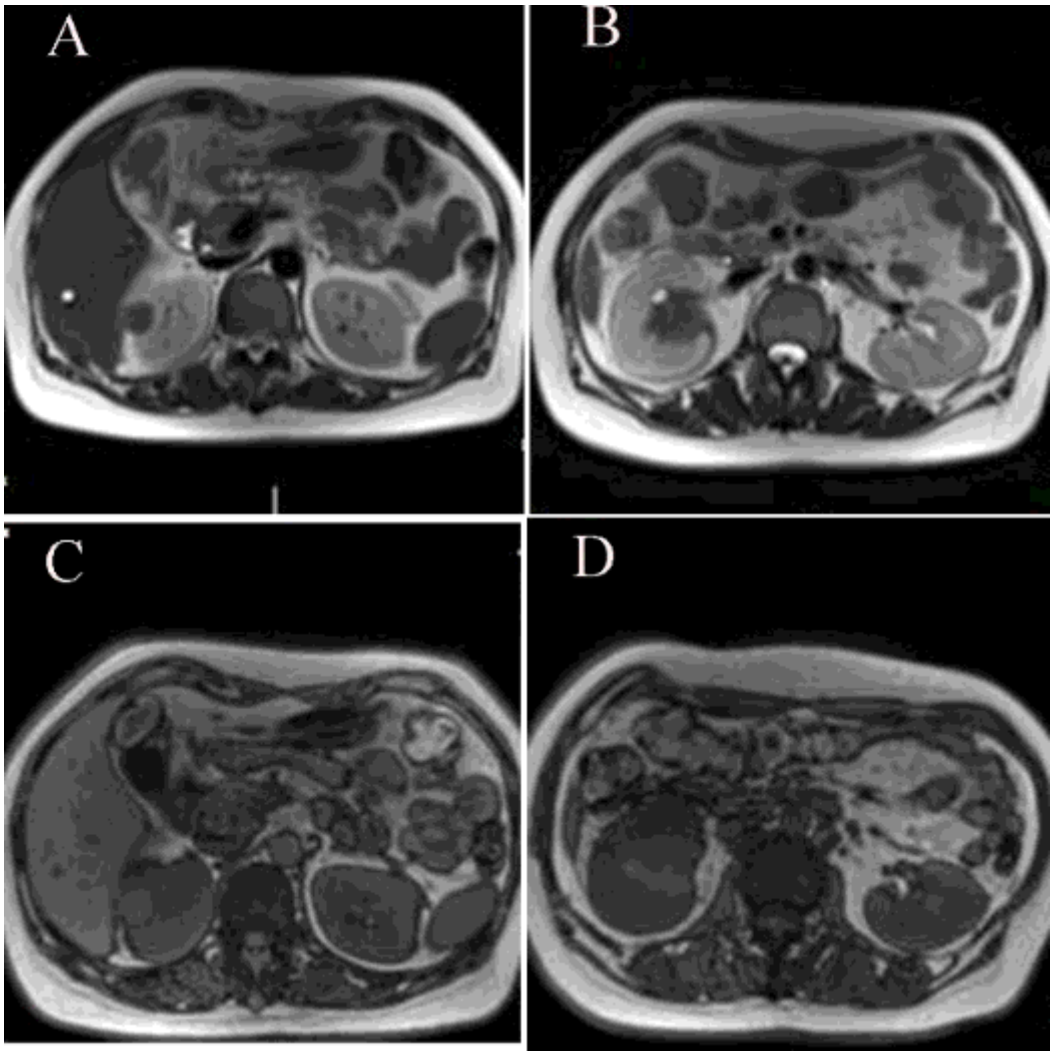

Figure 1

A homogenous low signal with clear boundary 19mm×19mm in size was seen in the upper pole of right kidney on transverse T2 weighted image, B. A homogenous hypo-signal 29mm×30mm in size was observed in the level of the right renal pelvis on transverse T2 weighted image, C. the lesion of upper pole of right kidney revealed moderate signal intensity on the transverse T1-weighted images, D. the lesion located the level of the right renal pelvis showed moderate signal intensity on the transverse T1-weighted images.

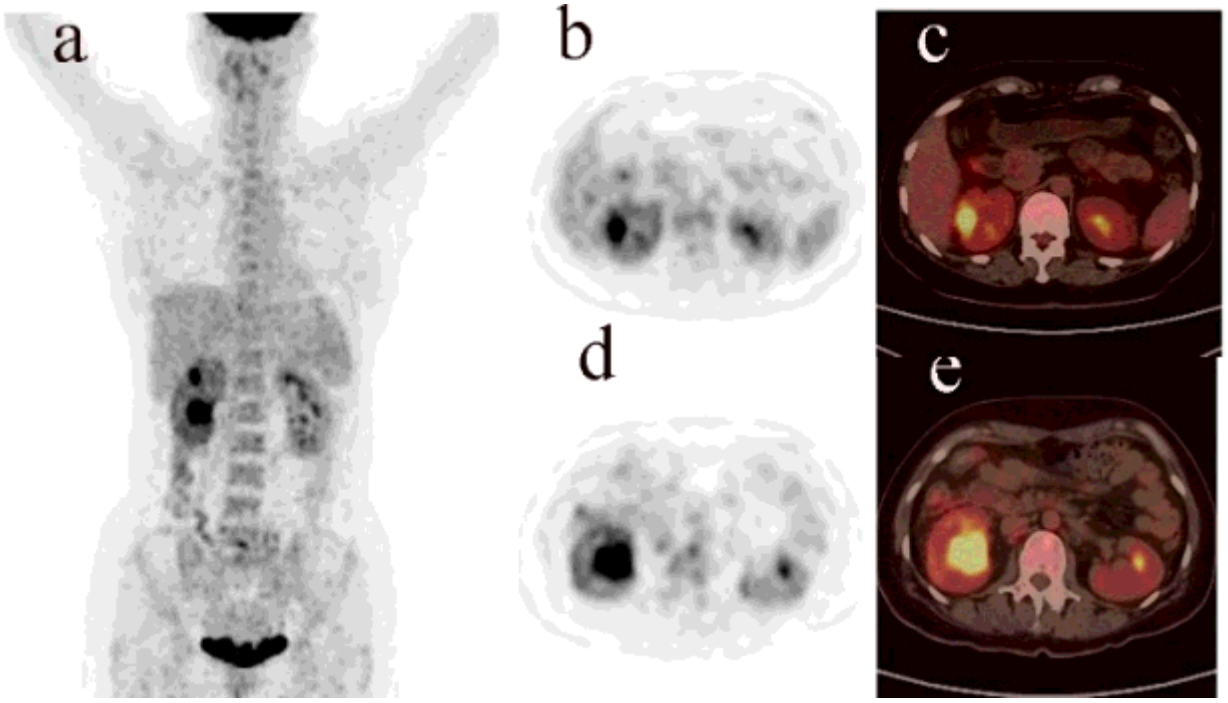

Figure 2

A. Two nodular FDG increased foci were observed in the right kidney, and the rest of whole body were negative on the PET MIP (maximum intensity projection) image. B/C, A nodular hypermetabolic foci in the upper pole of the right kidney (SUVmax:10.9) was observed on transverse PET/fusion PET/CT images. D/E, A nodular hypermetabolic lesion located in the level of the right renal pelvis (SUVmax:11.8) was seen on transverse PET/fusion PET/CT images.

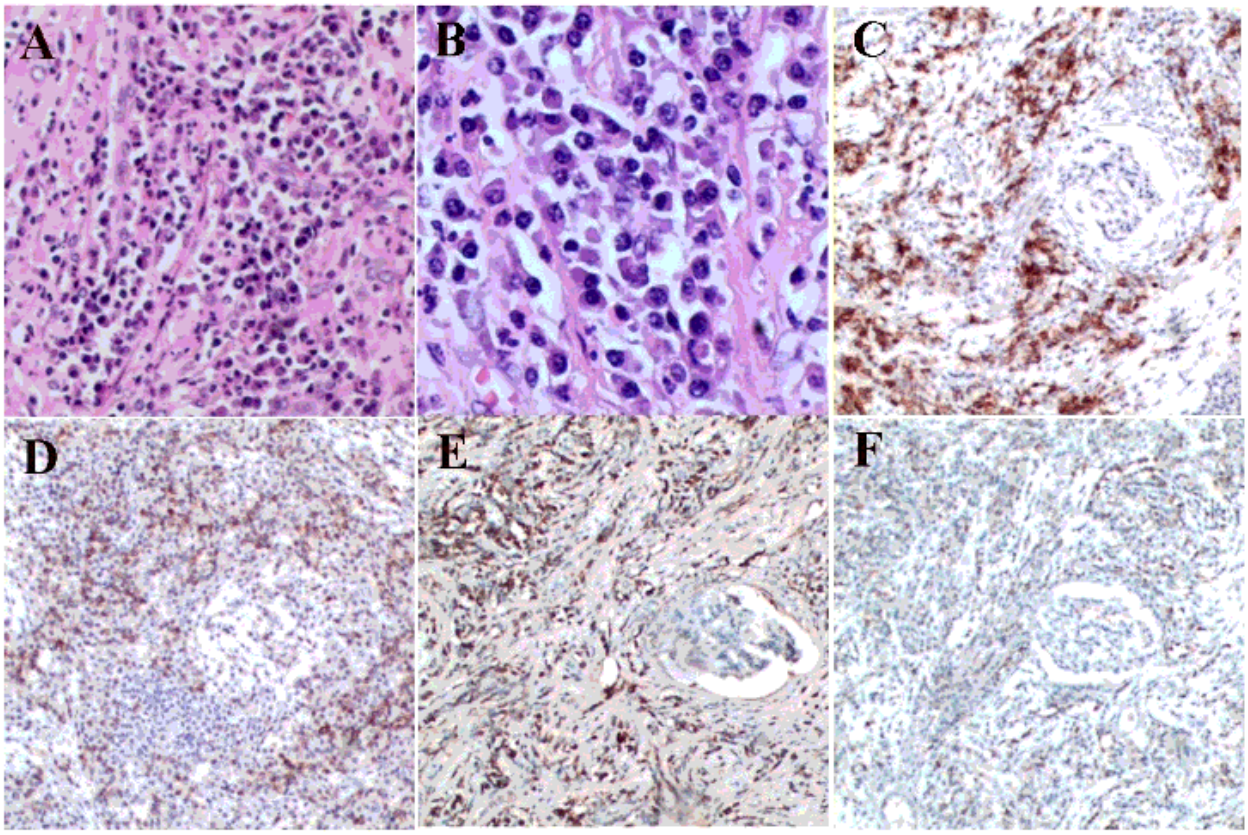

Figure 3

A×200/B×400HE staining of tissue specimens revealed local atrophy in the right kidney cortex and medulla, collagenous and fibrous hyperplasia, and infiltration of the renal interstitium by numerous plasma cells, neutrophils, and lymphocytes. C×200 CD38 expression was positive for plasma cell, D×200, CD138 expression was positive for plasma cell, E×200, plasma cells that are IgG positive, F×200, plasma cells that are IgG4 positive, and the ratio of IgG4 to IgG was greater than 40%, thus, IgG4-related diseases could be diagnosed.