IgG4-Related Retroperitoneal Fibrosis – A Rare Cause of Obstructive Uropathy: Case Report

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Abstract

Immunoglobulin G4-related retroperitoneal fibrosis (IgG4-RPF) is a rare fibroinflammatory condition characterized by the infiltration of IgG4+ plasma cells and fibrosis, affecting the retroperitoneum and causing obstructive uropathy. We report a rare case of a 32-year-old male who experienced persistent left lumbar pain for 1.5 years. Imaging revealed a para-aortic soft tissue mass encasing the proximal ureter, causing mild hydronephrosis. Histological examination confirmed IgG4-RPF, indicated by marked fibrosis and plasma cell-rich inflammatory infiltrates. The patient received corticosteroid therapy followed by rituximab, resulting in significant clinical improvement and mass regression. This case highlights the need for awareness and understanding of IgG4-RPF as a distinct entity to ensure timely and accurate diagnosis. Early intervention with targeted therapy can effectively manage the condition, prevent severe complications, and improve patient outcomes. Long-term follow-up and monitoring of disease activity are essential to prevent recurrence and manage potential complications associated with IgG4-RPF.

Keywords: IgG4, Retroperitoneal Fibrosis, Obstructive Uropathy.

Introduction

The disease associated with immunoglobulin G4 (IgG4) was first identified as a novel entity in 2003 and given an official name in 2010. Elevated serum IgG4 levels, infiltration of IgG4+ plasma cells and lymphocytes, and related fibrosis are the hallmarks of this condition. Nearly all major organ systems, including the pancreas, hepatobiliary, salivary gland, lungs, and retroperitoneum, are susceptible to IgG4-related illness.[1] It is rather uncommon for IgG4-related diseases to manifest in the retroperitoneum. We report a case of retroperitoneal disease associated with IgG4 that results in obstructive uropathy.

Case Notes

A 32-year-old male presented with a history of pain in the left lumbar region for 1.5 years. There was no associated fever, vomiting, or urinary complaints. Prior to this pain, he did not report any history of symptoms associated with abdominal disturbance. His previous history was notable for diabetes mellitus (DM), hypertension (HTN) as well as a thyroidectomy in 2013 for a thyroid nodule. His mother had long-standing Rheumatoid Arthritis.

An ultrasound was done, followed by a CT KUB one month back when the pain intensified. Imaging reported as paraaortic soft tissue focus: 24 x 24 mm at L2, L3 level encasing the proximal ureter, causing left-sided mild hydronephrosis with no calcification and intact corticomedullary junction.

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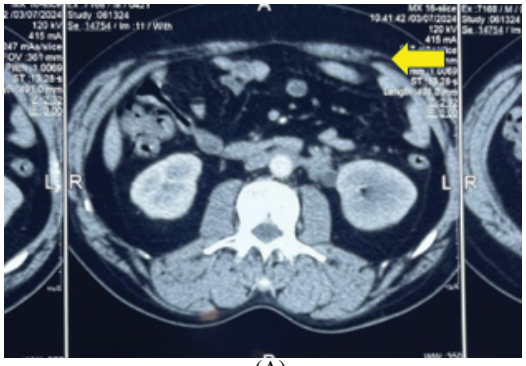
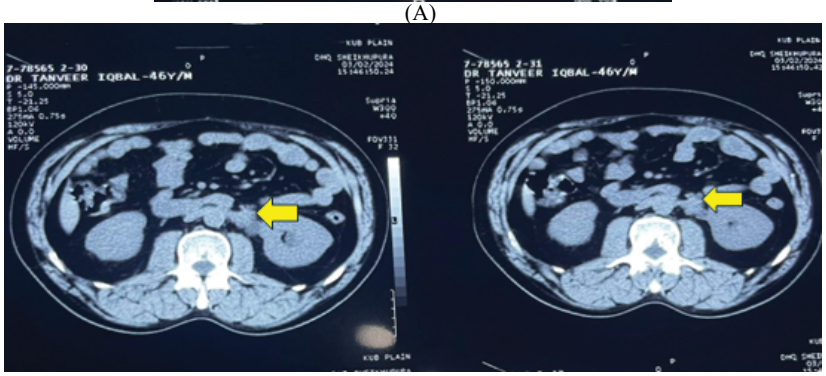


(A)



(B)

Figures 1: (a) & (b) Show Soft Tissue Para-aortic Mass Encasing Left Sided Ureter (yellow arrows).

Given that the decision was taken by the Urologist to implant a double J ureteral stent on the left side, as shown in Figure 2., after stenting, a core biopsy was performed; portions of the para-aortic mass were subjected to histological and immunocyto-histochemistry examination, which revealed large areas of fibrosis and foci of moderate lymphoplasmacytic inflammation and perivascular accentuation of inflammation. On presentation, his vitals were normal. His labs reported as ESR 71mm/hr, Hb 12.1g/dl, TLC 9.8 x 10^9, PLT 320 x 10^9, Creatinine 0.8mg/dl, Urine R/E was unremarkable.

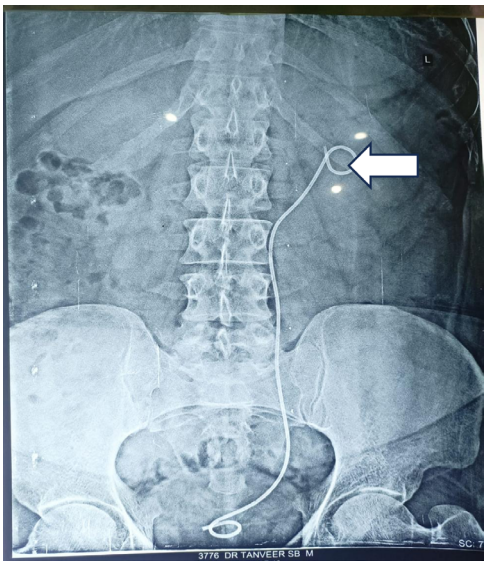


Figure 2: DJ Stent in Situ Following Left-sided Ureter (white arrow).

Re-reporting for soft tissue mass biopsy with IgG-4 staining was requested which came out to be positive, and re-reporting was in concordance with previous reporting showing marked fibrosis with plasma cell-rich inflammatory infiltrates, which raised the likelihood of IgG4-related fibrosing lesion. These immunological and histological results ultimately led to the patient's diagnosis of IgG4-related retroperitoneal fibrosis. (IgG4-RPF).

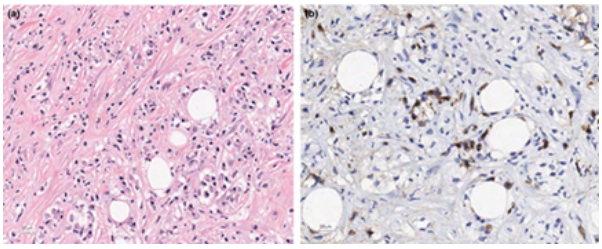


Figure: 3 Storiform Fibrosis.

He was started on Pulse Solumedrol 500mg IV for 3 days, and a plan was made to administer Rituximab after preliminary biological screening if the patient presented to be normal. He was switched to oral Prednisone 40mg/day after Pulse Solumedrol and was gradually tapered off to 10mg/day in the subsequent 3 months. Meanwhile, the patient became asymptomatic. A follow-up CT KUB was done which showed regression of retroperitoneal mass in anteroposterior, transverse, and craniocaudal dimensions. Every month, standard laboratory tests such the total blood count, serum creatinine, ESR, and CRP were performed and found to be within normal limits.

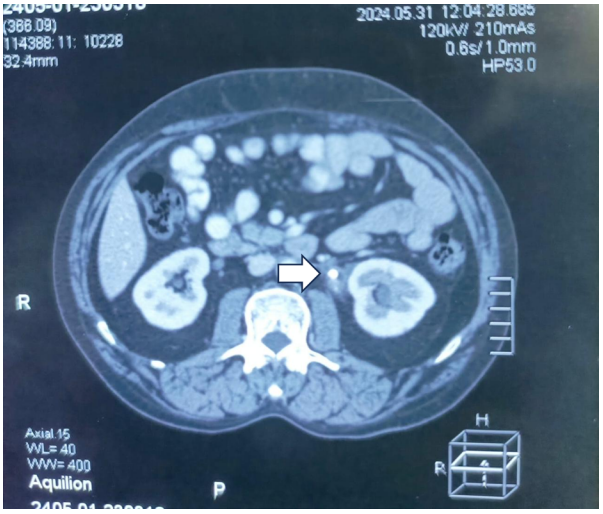


Figure 4: Follow-up CT, after 3 Months Showing the DJ Stent In Situ with Mild Peri-ureteral Strandings (white arrow).

Discussion

Immunoglobulin G4-related disease (IgG4-RD) was described as a new entity in 2003 and was officially named in 2010.[2] It is a rare progressive fibroinflammatory disease that often affects middle-aged to older males and is thought to be caused by dysregulation of CD4 T-lymphocytes and plasmablasts.[3] Exclusive histological features such lymphoplasmacytic infiltration, storiform fibrosis, obliterative phlebitis, and a high number of plasmablasts or plasma cells expressing IgG4 in the afflicted tissues help identify the condition.[2,4-7]

IgG4-related retroperitoneal fibrosis is part of the broader spectrum of IgG4-RD, which can affect multiple organs including kidneys, ureters, pancreas, and mesenteries. Lower extremity edema and back or stomach pain are among the initial symptoms, while mesenteric ischemia, intestinal obstruction, acute renal damage, hypertension, uremia, anuria and deep vein thrombosis are examples of late symptoms. Another way that IgG4-RPF varies from other autoimmune illnesses is that it is rarely accompanied by joint pain or fever.[3]

It is essential to distinguish IgG4-RPF from non-IgG4-RPF (usually idiopathic) and rule out cancer in order to make an appropriate diagnosis. As ultrasound is easily operated and is non-invasive, it is preferred in the beginning. The lesion appears hypo- to iso-echoic through ultrasonography. Although it is useful in determining whether a patient has hydronephrosis, it is not as sensitive when a mass is enclosed. Abdominal CT and MRI are the most often utilized diagnostic radiological technologies. CT can reveal the damaged area as well as the location, size, and range of the pathology. Lesions on a CT non-contrast-enhanced scan have a density similar to that of a muscle, which is why they are often referred to as soft-tissue masses. When monitoring IgG4-related RPF, CT is useful in determining the impact of glucocorticoid therapy and the level of disease activity. However, it is unable to differentiate fibrosis from active lesions. Under magnetic resonance imaging (MRI), lesions typically appear hyperintense on T2 weighted images (WI) and hypointense on T1 WI, and the retroperitoneal soft tissue is easily identified. For patients with impaired kidney function or renal insufficiency who are not good candidates for contrast-enhanced CT, MRI is a safe option. Fluorine-18-labelled fluorodeoxyglucose (18FDG)-PET may also be used for identifying lesions in the retroperitoneum as well as other organs because it can identify active inflammation.

Nevertheless, imaging methods are unable to differentiate between IgG4-RPF and non-IgG4-RPF.. The primary diagnostic test is the histopathological examination, which is capable of ruling out benign and malignant lesions and is especially sensitive to the presence of inflammatory infiltrates in IgG4-RPF. Multicenter lymphoid follicles, an excess of IgG4-positive plasma cells (more than 10 IgG4+ cells/HPF), and lymphocyte and plasmacyte infiltrations linked to fibrosis are common histological markers of this illness.[3]

Glucocorticoids are generally considered the first-line medication for inducing remission in all individuals with active IgG4-RD.[8] Following therapy, approximately half of the patients report little or no bulk, as well as a drop in blood IgG4 content.[9] The length of treatment varies based on the organs involved and the degree of impairment because of the heterogeneous character of the disease and the way it affects numerous organs with differing degrees of aggression. For patients who are resistant or refractory, immunosuppressive drugs such as azathioprine, methotrexate, rituximab, and cyclophosphamide are utilized as second-line therapies.[10]

Monitoring the clinical characteristics, serum IgG4 levels, and inflammatory indicators closely is necessary to determine how well a medication is working. After these indicators have dropped, the immunosuppressive medication should be gradually stopped while being closely monitored.

As an alternative to glucocorticoids, Almeqdadi *et al.*[11] discussed the possible therapeutic function of rituximab in the treatment of IgG4-RD. Corticosteroids frequently result in a reduction in the size of the retroperitoneal lesions and the cure of obstructive problems, and they frequently produce a rapid improvement in symptoms. Corticosteroids, however, have the potential to have serious adverse effects and morbidity over time. Because uncontrolled sickness in several major organs can cause irreversible harm, some patients will need immediate intervention as in our patient, DJ stenting was done for hydronephrosis.

Conclusion

In conclusion, early and accurate diagnosis, supported by imaging and histopathological confirmation, is crucial for effective management of the disease. Treatment with corticosteroids and immunosuppressive agents, such as rituximab, can lead to significant clinical improvement and mass regression, highlighting the need for a tailored

therapeutic approach. In order to control potential consequences and prevent recurrence, it is imperative to conduct ongoing monitoring of disease activity and therapy response. This case contributes to the growing recognition of IgG4-RD as a distinct clinical entity and underscores the importance of targeted treatment strategies in improving patient outcomes.

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