Case of IgG4-related Disease with Crescentic Glomerulonephritis: An Unusual Presentation of the Disease

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IgG4-related disease (IgG4-RD) is a chronic systemic inflammatory disease, characterized by tissue infiltration of lymphocytes and IgG4-secreting plasma cells, presenting by fibrosis of different tissues, which is usually responsive only to oral steroids therapy. Kidneys are one of the involved organs, exhibiting renal insufficiency, tubulointerstitial nephritis, and glomerulonephritis. Here, we describe a patient with acute renal insufficiency who was presented with edema, weakness, anemia and multiple lymphadenopathies. Kidney and lymph node biopsy showed crescentic glomerulonephritis in kidneys and lymphoplasmacytic infiltration in lymph nodes. After a course of treatment with an intravenous pulse of corticosteroid and cyclophosphamide, the patient's symptoms subsided, and kidney function improved.

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Case Report

INTRODUCTION

IgG4-related disease (IgG4-RD) is categorized as a systemic inflammatory and fibrotic condition that involves multiple organs.[1,2,3] Increased serum IgG4 level, tissue edema, fibrosis, and marked inflammatory infiltration of IgG4-positive plasma cells are essential diagnostic hallmarks.[1]Renal lesions include tubulointerstitial nephritis (TIN) or glomerular involvement such as membranous or IgA nephropathy and membranoproliferative glomerulonephritis (GN).[4]Although TIN is the predominant type of kidney involvement, a rare case of IgG4-RD is reported here with the coexistence of acute crescentic GN and TIN.[5]

The most common symptoms include abdominal pain, sicca syndrome, respiratory symptoms, pruritus, diarrhea, and lymphadenopathy.[6] Diffuse kidney enlargement in non-contrast computed tomographic (CT) scan and several low-density lesions on enhanced CT scan are the most important findings that help to distinguish the lesions from malignant tumors.[3]

The biopsy is performed from the affected organs. Although a mean IgG4 level that is four to six times greater than the upper limit of normal laboratory range is useful for the diagnosis, some studies propose measuring the IgG4/total IgG ratio.[6] Hypocomplementemia may also be detected.[7]Immediate response to corticosteroids is a significant feature of IgG4-RD, which is administered as the primary treatment to induce remission in all patients with active disease. Glucocorticoids plus cyclophosphamide is another effective regimen, with a lower relapse rate than monotherapy.[8]

CASE REPORT

A 52-year-old Iranian man was admitted to Hasheminejad Kidney Center (HKC) due to lower limbs edema, fatigue, decreased urine volume, and serum creatinine (SCr) of 4.3 mg/dL. Physical examination revealed bilateral pitting edema of the lower limbs and multiple lymphadenopathies up to 40 mm in the axillary regions. He was admitted with the diagnosis of acute kidney injury (AKI). He had a history of recent admission due to COVID-19 and melena, for which he received five units of blood. An upper gastrointestinal endoscopy revealed the presence of acute gastritis and a duodenal ulcer. In abdominopelvic sonography,

both kidneys were enlarged measuring 134 mm and chest spiral computed tomographic (CT) scan showed multiple para-tracheal, hilar, subcarinal (~24 mm), and mediastinal lymph nodes (~12 mm) along with mild cardiomegaly, bilateral pleural effusion, and foci of patchy ground glass opacities, due to SARS CoV-2 pneumonia, in his previous admission (Figure 1). SCr was 2 mg/dL in last hospitalization. After two months, in HKC, SCr and proteinuria were 4.3 mg/dL and 4627 mg/d, respectively; with the absence of monoclonality in serum, and urine protein electrophoresis.

Lymph node biopsy indicated focal replacement of lymphoid tissue by a mixture of reactive fibroblast, plasma cells and histiocytes, (A) many scattered eosinophils, (B) (Figure 2).

The kidney biopsy revealed the presence of 14 glomeruli, 10 of which displayed crescents. Additionally, there was evidence of tubular atrophy and interstitial fibrosis, affecting 40% of the tissue. Dense infiltration of lympho-plasma cells, eosinophils in the fibrotic stroma, and dominant IgG4 in 45% of plasma cells were reported. Immunofluorescence study revealed 2+ granular deposition of C3 and IgG, especially along the glomerular basement membrane. Kappa and lambda were also positive in the basement membrane Therefore, an immune complex-mediated type of diffuse crescentic glomerulonephritis was diagnosed (Figure 3).

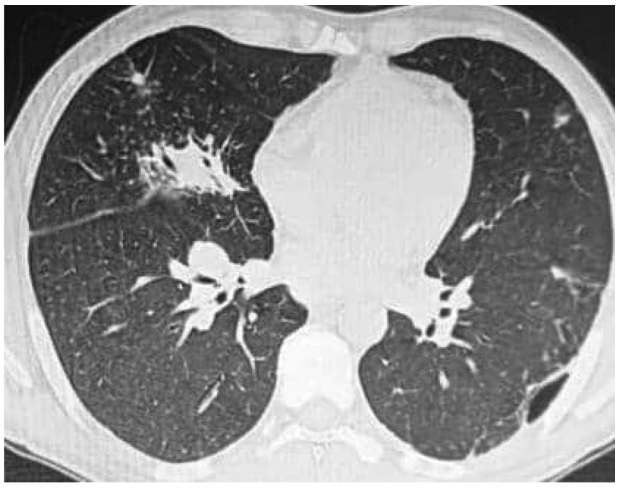


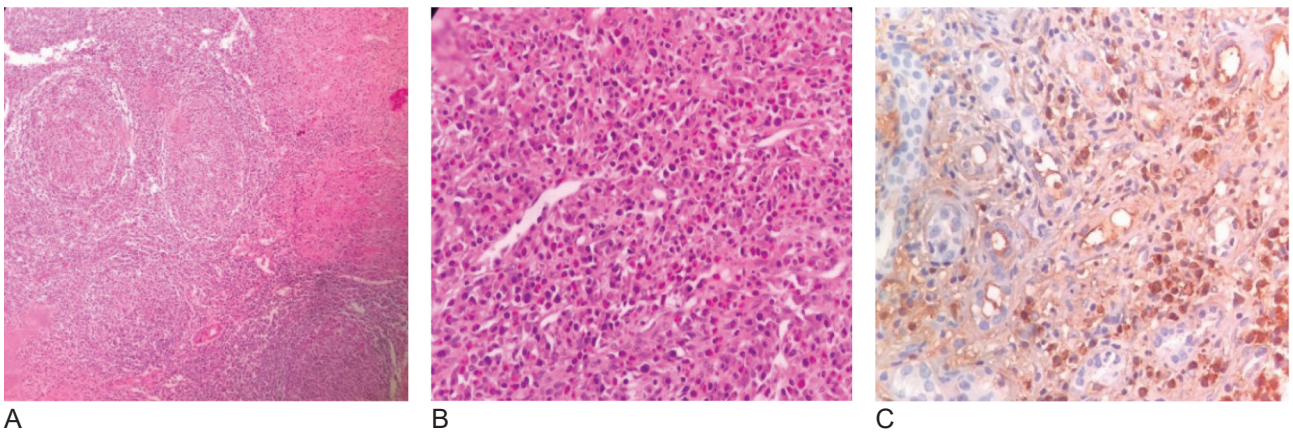
Figure 1. Spiral Chest CT Without Contrast (Multiple lymph node in both hilum, consolidation and focal fibrotic change in right middle lobe, subpleural bulla in left lower lobe)

Based on the clinical, laboratory, and biopsy findings, IgG4-RD with crescentic glomerulonephritis was confirmed. The patient received three daily intravenous (IV) pulses of 500 mg methyl-prednisolone continued by 50 mg prednisolone/day which was subsequently tapered to 15 mg/d, and two monthly courses of one gram IV cyclophosphamide. One month later, SCr dropped from 4.3 to 2.5 mg/dL. After four months of receiving 15 mg/day prednisolone, the symptoms subsided, SCr reduced to 1.5 mg/dL, and proteinuria to 550 mg/d. He reported good general condition with no symptoms on a phone call 12 months later.

DISCUSSION

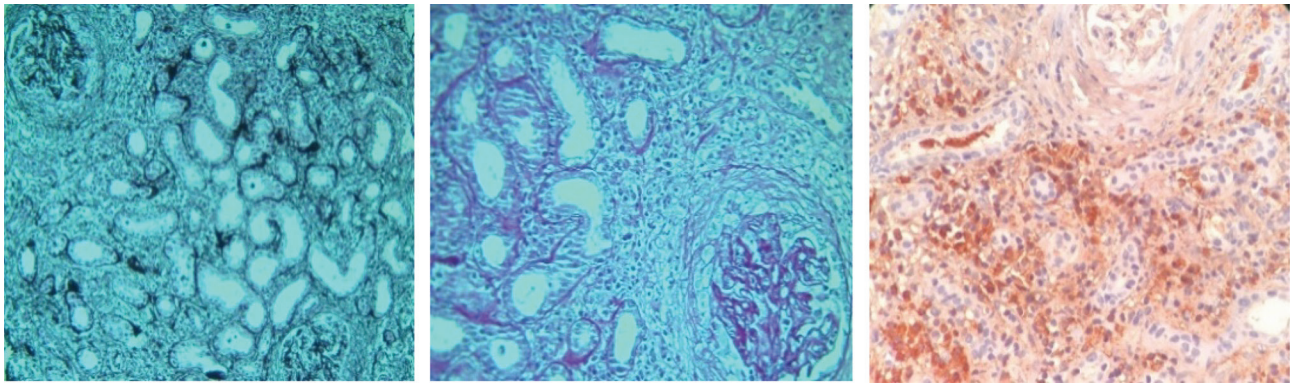
Here we present a middle-aged man with AKI and generalized lymphadenopathy, who was diagnosed with IgG4-RD, and showed a good response to immunosuppressive therapy.

IgG4-RD typically presents as TIN in the kidneys, which may be accompanied by a gradual or rapid deterioration of kidney function. [3] Involvement of the glomeruli has been reported in a few patients



A B C

Figure 2. Lymph Node Biopsy [(A) dense infiltration of plasma cells and (B) eosinophils (C) many of them being positive for IgG4 in immunohistochemistry (× 400)]



A B C

Figure 3. Kidney Biopsy Showing Diffuse Crescentic Glomerulonephritis [(A) fibro-cellular crescent and acute tubulointerstitial nephritis with lymphocyte and plasma cell infiltration in PAS stain and (B) atrophic changes in Jones stain (C) presence of many IgG4 positive cells in immunohistochemical staining (× 400)]

who present with nephrotic syndrome.[9] Lymphoplasmocytic infiltration rich in IgG4 positive plasma cells, are the typical histological findings.[10] There are few reports of IgG4-myeloma, [11] which was ruled out in our case. In IgG4-RD with nephrotic range proteinuria, steroids as the first-line therapy ameliorate kidney dysfunction and radiological and serological abnormalities. Other immunosuppressive agents should be considered in cases of rapid and progressive decline in kidney function.

CONCLUSION

In conclusion, IgG4-RD can rarely present as crescentic glomerulonephritis and nephrotic range proteinuria which is favorably responsive to a combination of steroid and short-course of cyclophosphamide.

ACKNOWLEDGEMENTS

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CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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