CLINICAL CASE

IGA NEPHROPATHY IN PATIENTS WITH CIRRHOSIS: DIAGNOSTIC AND THERAPEUTIC IMPLICATIONS. A CASE SERIES.

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Abstract

Renal dysfunction in patients with liver cirrhosis represents a diagnostic challenge due to the coexistence of multiple etiologies and the overlap between functional and structural mechanisms. In this setting, errors in etiological attribution may lead to inappropriate therapeutic decisions. We report two cases of IgA nephropathy in cirrhotic patients illustrating opposite diagnostic pitfalls. The first case involved a patient with liver cirrhosis in whom renal dysfunction was initially attributed to hepatorenal syndrome despite abnormal urinary sediment findings, delaying the diagnosis of IgA nephropathy until kidney biopsy was performed. The second case concerned a patient with IgA nephropathy initially considered primary and treated with immunosuppressive therapy until decompensated liver cirrhosis was subsequently identified, leading to reclassification as secondary IgA nephropathy. These cases highlight how a simplified interpretation of renal dysfunction in cirrhotic patients may result in diagnostic errors with relevant therapeutic implications. Dynamic clinical reassessment, integration of clinical and laboratory findings, and consideration of kidney biopsy in selected cases are essential to establish an accurate etiological diagnosis.

Keywords: IgA nephropathy, cirrhosis, hepatorenal syndrome, renal biopsy.

Introduction

The deterioration of renal function in patients with liver cirrhosis poses a complex diagnostic challenge due to the coexistence of multiple etiologies and the overlap of functional and structural mechanisms. In this context, diagnostic biases can lead to incorrect etiological attribution, with significant therapeutic implications. We present two clinical cases that illustrate contrasting scenarios of IgA nephropathy in patients with cirrhosis and highlight the need for diagnostic reevaluation in the face of clinical discordance or lack of response to treatment.

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Lorente Martínez MÁ, González Peregrina SM, Martín Navas MÁ, Ruiz Escolano E. IgA nephropathy in patients with cirrhosis: diagnostic and therapeutic implications. A case series. RAPD 2026;49(5):178-182. DOI: 10.37352/2026495.5

Clinical Case 1

A 56-year-old man with a history of chronic hepatitis B virus (HBV) infection without antiviral treatment and long-standing harmful alcohol use presented to the emergency department with progressive abdominal distension and deterioration of his general condition.

Physical examination revealed painless hepatomegaly and dullness in the flanks. Initial laboratory tests showed acute renal dysfunction, with a serum creatinine level of 1.82 mg/dL (previous levels were within the normal range). Urinalysis revealed mild proteinuria and microscopic hematuria. Abdominal ultrasound revealed findings consistent with advanced chronic liver disease and moderate ascites, with no structural renal abnormalities. Liver function at admission was classified as Child-Pugh Class C (11 points), with a MELD score of 18 and a MELD-Na score of 21.

HBV infection was confirmed, and antiviral treatment with entecavir was initiated. Infectious precipitating factors were ruled out through diagnostic paracentesis, blood cultures, urine culture, and chest X-ray, as well as recent alcohol consumption. Immunological testing was negative, except for IgA hypergammaglobulinemia (674 mg/dL) and mild hypocomplementemia (C3: 72 mg/dL; C4: 11 mg/dL).

The progressive worsening of renal function (from 1.82 to 3.7 mg/dL), despite volume expansion therapy with albumin, reinforced the initial clinical suspicion of hepatorenal syndrome, and treatment with terlipressin was initiated. Despite reaching maximum doses, no improvement in renal function was observed, prompting a reconsideration of the initial diagnosis and an evaluation of structural causes of renal damage.

It was decided to perform a renal biopsy, the histological findings of which were consistent with IgA nephropathy (Figure 1). Terlipressin treatment was discontinued, and antiviral therapy was continued; partial recovery and stabilization of renal function were observed in the following months. Given the progressive deterioration of liver function (Child-Pugh C [10 points] and MELD and MELD-Na scores of 26 points), the patient was evaluated for a liver transplant, which was performed successfully, resulting in a significant improvement in renal function (Cr 1.77 mg/dL).

Clinical Case 2

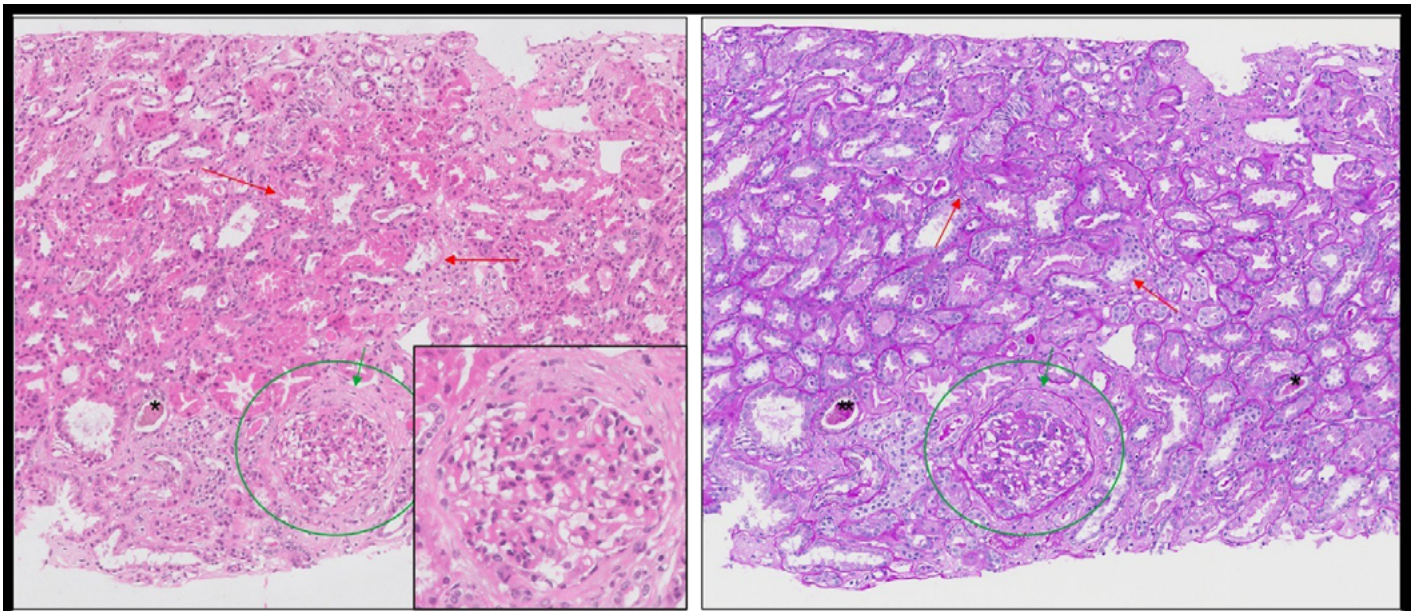
A 49-year-old man with active harmful alcohol use, under evaluation for nephrotic-range proteinuria. The physical examination revealed pitting edema extending to the pretibial region. Tests for autoimmunity (ANA, anti-PLAR2, ANCA, ENA, anti-MBG), complement, light chains, and protein profile were within normal limits. No structural abnormalities of the kidneys or liver were detected on ultrasound. Consequently, a renal biopsy was performed; the histopathological findings were consistent with IgA nephropathy, which—in the absence of initial evidence of liver disease or other triggering conditions—was attributed to a primary etiology.

During follow-up, the patient developed progressive deterioration of renal function (creatinine from 1.05 to 2.23 mg/dL) associated with a sustained increase in proteinuria (from 2 to 8 g/24 h). Given the suspicion of progression of primary IgA nephropathy, immunosuppressive therapy with mycophenolate mofetil and prednisone was initiated.

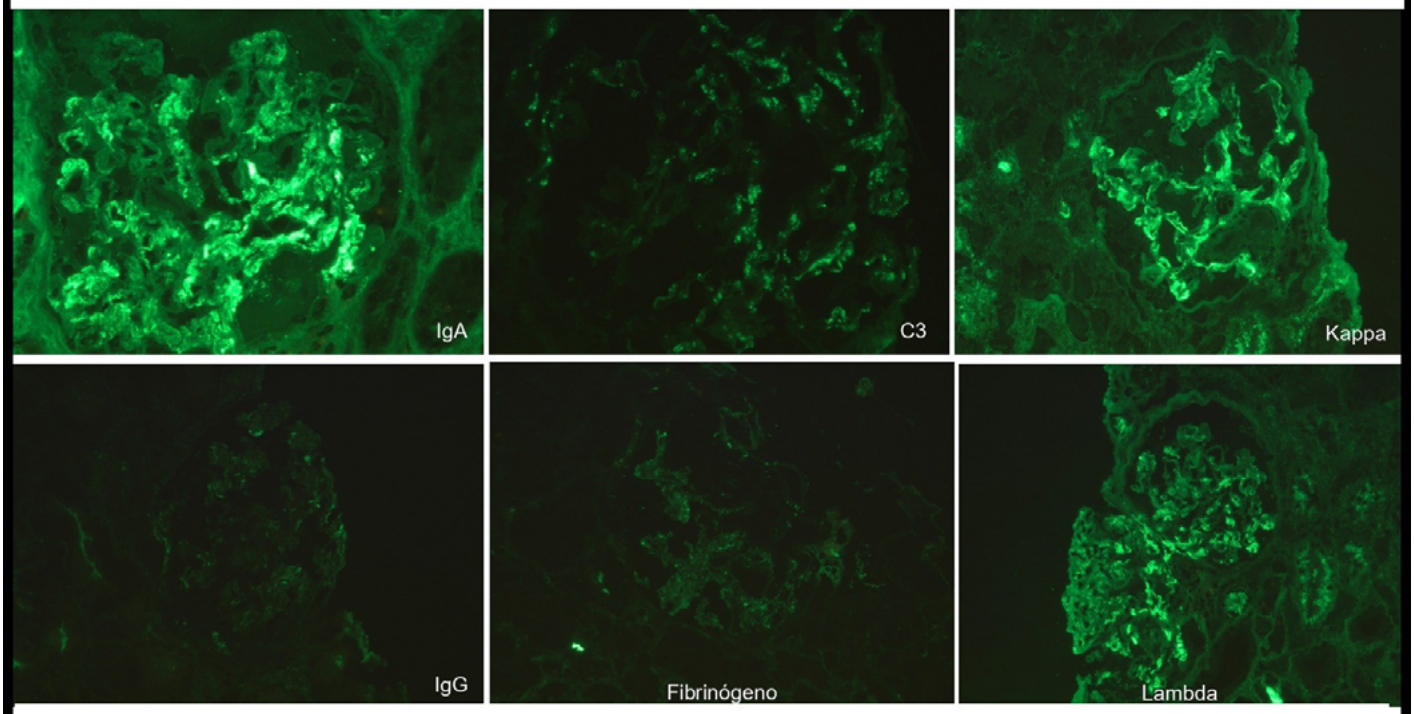
Despite treatment, renal function continued to deteriorate, with worsening edema in the lower extremities and the development of tension ascites. Analysis of the ascitic fluid confirmed a secondary cause related to portal hypertension, and abdominal ultrasound revealed findings consistent with advanced chronic liver disease, which had not been diagnosed previously. At the onset of liver disease, the Child-Pugh stage was B (9 points), with a MELD and MELD-Na score of 15 points.

The lack of response to immunosuppressive therapy, along with the incidental diagnosis of decompensated liver cirrhosis, led to a reevaluation of the cause of the nephropathy and the gradual discontinuation of the immunosuppressive regimen. The initiation of intravenous albumin therapy contributed to the resolution of the first episode of ascites decompensation and an improvement in renal function (1.5 mg/dL). Furthermore, cessation of alcohol consumption was accompanied by an improvement in liver function, contributing to further recovery of renal function. The lack of response to immunosuppressive therapy and the improvement in renal function parallel to the improvement in liver function led to a reconsideration of advanced chronic liver disease as the most likely cause of IgA nephropathy.

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H&E (left) and PAS (right) images of a renal core biopsy showing a glomerulus (green circle) with increased mesangial cellularity, mild segmental endocapillary hypercellularity, and an extracapillary component in the form of a predominantly fibrous crescent (green arrow). Mild interstitial fibrosis and tubular atrophy. A proportion of tubules display cytoplasmic microvesiculation, loss of the brush border (red arrow), and nuclear pyknosis, as well as intratubular red blood cell casts (asterisk). These features are accompanied by a sparse lymphocytic infiltrate.



Most relevant direct immunofluorescence findings, demonstrating granular, predominantly mesangial, diffuse, and global positivity for IgA (++/+++), C3 (++), kappa light chains (++), lambda light chains (++), fibrinogen (+), and IgG (+/-).

Figure 1. ***Anatomopathological examination of the renal biopsy, consistent with IgA nephropathy.***

Currently, the patient maintains stable renal function (creatinine 1.8 mg/dL; proteinuria 4 g/24 h) without an immunosuppressive regimen and while receiving weekly albumin infusions, although he has developed refractory ascites and is awaiting evaluation for a liver transplant (Child-Pugh C [11 points] with current MELD and MELD-Na scores of 22 and 24, respectively).

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Discussion

Chronic liver disease is the most common cause of secondary IgA nephropathy, although it can also occur in association with inflammatory bowel disease, celiac disease, neoplasms, or rheumatologic diseases.[1]. Distinguishing between primary and secondary IgA nephropathy is a clinical diagnosis of exclusion, since the histologic findings are indistinguishable between the two forms.[1,2].

IgA nephropathy secondary to chronic liver disease is an underdiagnosed condition, primarily because renal biopsy is not routinely performed in patients with cirrhosis who present with renal dysfunction; rather, it is reserved for cases of treatment failure, unfavorable clinical course, or suspicion of underlying nephropathy[1]. Consequently, it is very difficult to establish a specific prevalence, as reflected in the wide variability (9–64%) observed across different patient cohorts[1,2].

The findings of the pathogenic study of IgA nephropathy secondary to chronic liver disease remain insufficient, but several mechanisms appear to be involved: impaired hepatic clearance of immune complexes, increased intestinal translocation of IgA, and elevated plasma IgA concentrations. All these factors promote mesangial deposition of IgA complexes and consequent glomerular damage[3]. Furthermore, as illustrated in Clinical Case 1, the coexistence of chronic HBV infection adds a possible additional pathogenic mechanism. There is evidence that viral antigens (HBsAg, HBcAg) can be deposited in the glomerular mesangium and contribute to the formation of immune complexes that cause IgA nephropathy in chronic carriers of the virus[4,5].

The cases presented illustrate two different clinical scenarios in which an error in etiological classification occurs, with significant therapeutic consequences. The first case demonstrates how the initial assumption of hepatorenal syndrome—despite the presence of abnormalities in the urine sediment—can mask structural kidney disease. Although secondary IgA nephropathy is a recognized cause of renal function impairment in patients with cirrhosis, its diagnosis is complicated by the coexistence of other common conditions, such as hepatorenal syndrome, prerenal renal failure, or drug-induced nephrotoxicity.[6]. In this context, determining the etiology of renal impairment is typically based on clinical criteria, which may be insufficient to distinguish between functional and structural causes. Therefore, the presence of discordant clinical findings, abnormalities in the urine sediment, or a lack of response to medical treatment should prompt a diagnostic reevaluation, with the renal biopsy playing a key role[6].

In the second case, the presence of an initially undiagnosed underlying liver disease acted as a confounding factor in the assessment of renal function and led to a treatment choice with limited effectiveness. Although immunosuppressive therapy has been shown to be effective in certain settings of primary IgA nephropathy[7], current evidence does not support its use in forms secondary to liver cirrhosis. Even the latest update to the KDIGO guidelines[8] moves away from the widespread use of systemic glucocorticoids in primary forms and prioritizes therapies aimed at reducing immune complex formation, blocking the renin-angiotensin-aldosterone system, or inhibiting the sodium-glucose cotransporter type 2. It is important to note that the management of the primary form cannot be fully extrapolated to secondary forms. In fact, there is currently no specific treatment for secondary IgA nephropathy, and its prognosis depends largely on the course of the underlying disease.[3]. In selected cases of IgA nephropathy secondary to chronic liver disease, liver transplantation has been associated with a significant improvement in renal function[9], reinforcing the importance of accurate etiological diagnosis in these patients.

Conclusion

Both cases highlight the need for dynamic assessment of renal impairment in patients with cirrhosis and reinforce the need to maintain a high index of suspicion to prevent underdiagnosis of secondary IgA nephropathy[10], based on the integration of clinical, laboratory, and follow-up findings.

Bibliography

1. *Saha MK, Julian BA, Novak J, Rizk DV. Secondary IgA nephropathy. Kidney Int. 2018;94(4):674-681.*

2. *Hemminger J, Arole V, Ayoub I, Brodsky SV, Nadasdy T, Satoskar AA. Acute glomerulonephritis with large confluent IgA-dominant deposits associated with liver cirrhosis. PLoS One. 2018;13(4):e0193274.*

3. *Kanduri SR, Peleg Y, Wadhwani S. Liver Disease-Associated Glomerulopathies. Adv Kidney Dis Health. 2024;31(2):147-156.*

4. *Gao MZ, Xu LL, Li Y, Wang X, Chen P, Shi SF, Liu LJ, Lv JC, Hong FY, Zhang H, Zhou XJ. Hepatitis B Virus Status and Clinical Outcomes in IgA Nephropathy. Kidney Int Rep. 2024;9(4):1057-1066.*

5. *Lai KN, Lai FM, Tam JS. IgA nephropathy associated with hepatitis B virus antigenemia. Am J Kidney Dis. 1989.*

DOI: 10.37352/2026495.5

6. European Association for the Study of the Liver (2018). EASL Clinical Practice Guidelines for the management of patients with decompensated cirrhosis. Journal of hepatology, 69(2), 406–460.

7. Wyatt RJ, Julian BA. IgA nephropathy. N Engl J Med. 2013;368(25):2402-2414.

8. Rovin BH, Barratt J, Cook HT, et al. KDIGO 2025 Clinical Practice Guideline for the Management of Immunoglobulin A Nephropathy (IgAN) and Immunoglobulin A Vasculitis (IgAV). Kidney Int. 2025;108(4S Suppl):S1-S71

9. Hommos MS, El-Zoghby ZM. Renal Outcomes in Patients With IgA Nephropathy Undergoing Liver Transplant: A Retrospective Cohort Study. Transplant Direct. 2017;3(8):e193.

10. Stoneman, S., Teh, J. W., & O'Shaughnessy, M. M. (2026). IgA Nephropathy in Adults: A Review. JAMA, 335(9), 799–813.

DOI: 10.37352/2026495.5