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CLINICAL CASE

IgA nephropathy associated with superimposed acute kidney injury. A report of an unusual case

Nefropatía por IgA asociada a Lesión renal aguda por sobreposición. A propósito de un caso inusual

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Abstract

IgA nephropathy is the most common glomerulopathy, characterized by immune complex deposits in the glomeruli causing renal damage. It is associated with genetic predisposition and abnormal immune responses. We present the case of a 15-year-old adolescent with glomerular hematuria and acute renal deterioration following a viral illness and exposure to NSAIDs and iodinated contrast. Renal biopsy revealed IgA nephropathy and acute tubulointerstitial nephritis (ATIN) with eosinophilia. She received methylprednisolone pulses, achieving renal recovery. This case highlights the importance of distinguishing acute complications in patients with IgA nephropathy to ensure timely and appropriate management. IgA nephropathy and interstitial nephritis are connected through inflammatory mechanisms in the kidney. Although IgA nephropathy primarily affects the glomeruli with different histologic patterns, in this case we found interstitial inflammation exacerbating damage and accelerating the deterioration of renal function. This highlights the importance of addressing all the mechanism of acute kidney injury to prevent progression to end-stage renal disease.

Keywords: *IgA nephropathy. Tubulointerstitial nephritis. Renal biopsy. Hematuria.*

Resumen

La nefropatía por IgA es la glomerulopatía más común, caracterizada por depósitos de complejos inmunes en los glomérulos que causan daño renal. Se asocia con predisposición genética y respuestas inmunológicas anormales. Se presenta el caso de una adolescente de 15 años con hematuria glomerular y deterioro renal agudo tras un cuadro viral y exposición a AINEs y contraste iodado. La biopsia reveló nefropatía por IgA y nefritis túbulo-intersticial aguda (NTIA) con eosinofilia. Recibió pulsos de metilprednisolona, logrando recuperación renal. Este caso subraya la importancia de diferenciar complicaciones agudas en pacientes con nefropatía por IgA para un manejo oportuno. La nefropatía por IgA y la NTIA están interconectadas a través de mecanismos inflamatorios a nivel renal. Aunque la nefropatía por IgA afecta principalmente a

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los glomérulos con diferentes patrones histológicos, en este caso encontramos una inflamación intersticial aguda y severa que exacerba el daño y acelera el deterioro de la función renal. Esto pone de manifiesto la importancia de abordar todos los mecanismos de la lesión renal aguda para prevenir la progresión a la enfermedad renal crónica avanzada.

Palabras claves: *Nefropatía por IgA. Nefritis túbulo intersticial. Biopsia renal. Hematuria.*

Introduction

As the most common glomerular disease, immunoglobulin A nephropathy (IgA) has become better understood over the years. This condition is characterized by the accumulation of immune complexes in the mesangium, which leads to inflammation and progressive renal damage. The pathophysiology of this disease is related to a combination of genetic predisposition and abnormal immune responses.

In genetically predisposed individuals, exposure to specific stimuli, such as bacterial infections, may trigger an exaggerated immune response in the mucosa. This hyperreactivity results in the production of an abnormal form of IgA known as galactose-deficient IgA (GD-IgA). This abnormality in the O-galactosylation of IgA causes these molecules to be less readily recognized and therefore less efficiently cleared by the immune system.[1]

The defect in O-galactosylation alters the structure of O-glycans in the hinge region of IgA, creating a form that is recognized as foreign by the immune system. In response, the body produces autoantibodies, predominantly of the IgG or IgA type, directed against these GD-IgA molecules[1,2].

Autoantibodies bind to GD-IgA to form circulating immune complexes. These complexes may deposit in the mesangial areas of the glomeruli, which are the filtering structures of the kidney. The deposition of these immune complexes in the mesangium triggers a series of inflammatory responses that include mesangial cell proliferation and excessive production of extracellular matrix, as well as the release of cytokines and chemokines.

These processes ultimately result in glomerular damage characterized by impaired renal function and progressive loss of the kidney's filtration capacity. Thus, the interaction between autoantibodies and GD-IgA, together with immune complex deposition, plays a central role in the pathogenesis of IgA nephropathy (IgAN)[1-3].

Worldwide prevalence remains uncertain due to the large number of asymptomatic cases that do not undergo renal biopsy for definitive diagnosis, as many patients opt for a more conservative management approach[4].

Of note, acute deterioration of renal function in patients with IgA nephropathy is not always exclusively due to the activity of the underlying disease. In some situations, acute kidney injury (AKI) may be related to other etiologies. In this context, a detailed clinical history, appropriate complementary studies, and, when necessary, renal biopsy are essential.

We present a case in which acute tubulointerstitial nephritis (ATIN) was identified as the underlying cause of the associated AKI, highlighting the importance of comprehensive evaluation for accurate diagnosis and appropriate treatment.

Case summary

This is a 15-year-old female patient, born and residing in Ecuador, with a medical history of asthma diagnosed at the age of 6 years and atopic dermatitis. The patient sought medical attention due to macroscopic hematuria.

One month prior to admission, she presented an episode of hematuria associated with an upper respiratory viral infection, which was managed on an outpatient basis with second-generation antihistamines. Due to the persistence of hematuria, she was evaluated by urology, where cystoscopy revealed bleeding originating from the left ureter. Management with nonsteroidal anti-inflammatory drugs (NSAIDs) was indicated, and a contrast-enhanced computed tomography (CT) scan of the abdomen and pelvis was requested.

Following administration of iodinated contrast and the use of NSAIDs, an increase in nitrogenous waste markers and the development of oliguria (200 mL/day) were observed. Nephrology consultation was therefore requested due to the rapid deterioration of renal function.

During the nephrology evaluation, the first urinary sediment report showed isomorphic erythrocytes; however, in a repeat sediment reviewed directly by the nephrology team, dysmorphic erythrocytes and hematic casts were identified, consistent with glomerular hematuria. In light of these findings and the progressive renal deterioration, it was decided to administer pulses of methylprednisolone at a dose of 250 mg intravenously

every 24 hours for 3 days, with the aim of controlling the underlying inflammatory process contributing to renal injury.

Complementary examinations: Laboratory tests (Table 1) and imaging modalities (Table 2) were performed to evaluate renal status and rule out other possible causes of hematuria and renal deterioration. The patient remains under close monitoring by a multidisciplinary team, including nephrology, urology, and pediatrics.

A percutaneous ultrasound-guided renal biopsy was performed, with the following results:

In hematoxylin-eosin (HE), PAS, Masson trichrome, and Jones silver methenamine stains, 12 glomeruli were identified, without global or segmental sclerosis. All glomeruli showed mesangial matrix expansion with preserved cellularity, without endocapillary or extracapillary hypercellularity. The tubules showed focal tubulitis without atrophy. The interstitium showed no fibrosis but demonstrated a focus of lymphocytic inflammatory infiltrate with some eosinophils. The vessels showed normal histology (Fig. 1).

Direct immunofluorescence showed: IgG negative, IgA positive ++/+++ with fine granular diffuse mesangial deposition, IgM traces, C3 negative, and C1q negative, establishing a diagnosis of IgA nephropathy with an Oxford MEST-C score of M0, E0, S0, T0, C0, associated with tubulointerstitial nephritis with eosinophils (Fig. 2).

After initiation of treatment with intravenous corticosteroid pulses (methylprednisolone) at a dose of 250 mg every 24 hours for 3 days, the patient—who presented with overt hematuria and progressive deterioration of renal function—showed significant improvement in renal parameters (Table 3). Renal biopsy revealed acute tubulointerstitial nephritis (ATIN) associated with IgA nephropathy. This finding highlights the effectiveness of corticosteroid therapy in reducing the inflammatory process and promoting recovery of impaired renal function.

Table 1. Patient paraclinical profile at admission

Paraclinical test	Patient value
Blood analysis	
Hemoglobin	13.1 g/dL
MCV	83 fL
MCH	29 pg
RDW	9 fL
Platelets	343000 mm^3
Leukocytes	5270 mm^3
Eosinophils	321.47 mm^3
Basophils	21.08 mm^3
Monocytes	368.90 mm^3
Lymphocytes	1707.48 mm^3
Neutrophils	2851.07 mm^3
Serum urea	21 mg/dL
GOT	15 IU/L
GPT	6 IU/L
Serum creatinine	4.85 mg/dL
Serum glucose	83 mg/dL
ANCA	Negative
AntiDNA	Negative
Lupus anticoagulant	Negative
ANA	Negative
Urinalysis	
Appearance	Slightly turbid
Color	Dark yellow
Density	1.009
pH	6.0
Leukocyte esterase	Negative
Nitrites	Negative
Urine proteins	25 mg/dL
Glucose	Negative
Ketone bodies	Negative
Bilirubin	Negative
Blood	150/µL
Red blood cells	224/HPF
Leukocytes	5/HPF
Dysmorphic erythrocytes	4.00%
Isomorphic erythrocytes	96.00%

MCV: mean corpuscular volume; MCH: mean corpuscular hemoglobin; RDW: red cell distribution width; GOT: aspartate aminotransferase; GPT: alanine aminotransferase; ANCA: antineutrophil cytoplasmic antibodies; AntiDNA: anti-DNA antibodies; ANA: antinuclear antibodies.

Discussion

The present case showed a combination of IgA nephropathy with ATIN following exposure to NSAIDs and contrast material. ATIN is an inflammation of the renal interstitium, which corresponds to the region surrounding the tubules. It is often caused by allergic reactions to medications, infections, or autoimmune diseases. This inflammation can lead to tubular dysfunction, reduced urine-concentrating capacity, and, in severe cases, acute or chronic kidney failure.

IgA nephropathy is a renal disease with a variable clinical course characterized by IgA deposition in the mesangium, which triggers several pathogenic processes. This cascade is divided into three main phases: (1) the synthesis of pathogenic IgA; (2) its mesangial deposition and the resulting inflammatory injury; and (3) the development of tubulointerstitial damage[5].

Although abnormal IgA glycosylation and its interaction with mesangial receptors are recognized as playing an important role, the exact mechanisms remain incompletely understood. What has been established is that deposited IgA induces the release of inflammatory mediators that damage renal tissue. A less explored aspect is how this mesangial deposition can lead to tubulointerstitial injury[6].

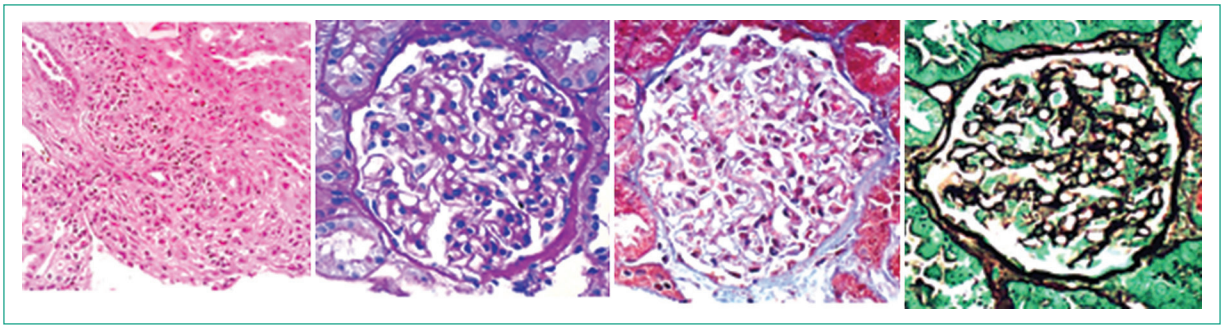

Figure 1. HE, PAS, trichrome, and methenamine silver stains. A total of 12 glomeruli were present. There was no global sclerosis or segmental sclerosis; all glomeruli showed expansion of the mesangial matrix (preserved cellularity), with no endo- or extracapillary hypercellularity. The tubules showed focal tubulitis, but no atrophy. The interstitium, without fibrosis, showed a focus of lymphocytic inflammatory infiltrate with some eosinophils. The vessels were of normal histology.

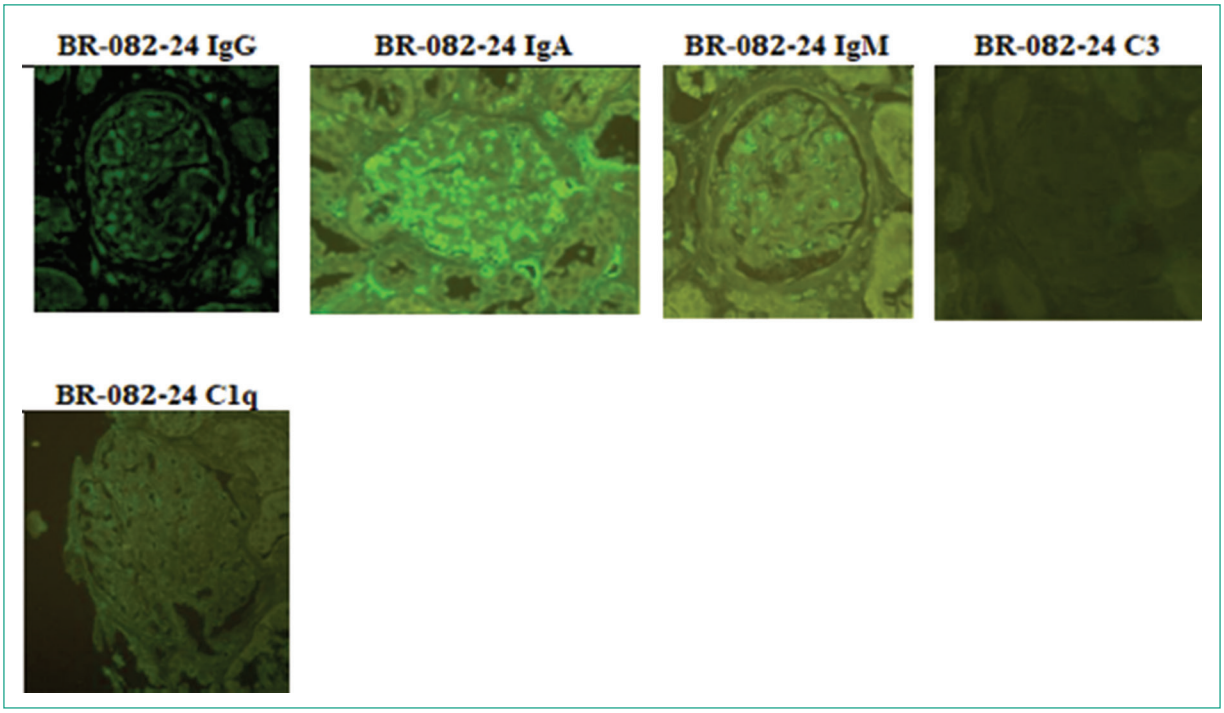

Figure 2. Direct immunofluorescence results: IgG: negative, IgA: positive ++/+++ fine granular diffuse mesangial, IgM: traces, C3: negative, C1q: negative, with a diagnosis of IgA nephropathy. Oxford MEST-C scale: M0, E0, S0, T0, C0, and associated with tubulointerstitial nephritis with eosinophils.

There are four main pathogenic mechanisms that may contribute to tubulointerstitial injury in IgAN, acting independently or jointly: infiltration of monocytes and macrophages, proteinuria, direct inflammatory effects of IgA, and glomerulotubular communication. The infiltration of inflammatory cells is a key mechanism mediating tubular injury and renal fibrosis. This process may activate resident cells, particularly proximal tubular epithelial cells (PTEC), which amplify the inflammatory response by producing chemotactic mediators that attract additional inflammatory cells, generating a feedback cycle that over time may lead to fibrosis and loss of renal function[7,8].

Proteinuria is an important stimulus for PTEC activation and immune cell chemotaxis in multiple nephropathies; however, in IgAN—where massive proteinuria is

Table 2. Patient imaging modalities

Imaging study	Patient result
Renal ultrasound	The right kidney measures 85 × 37 × 41 mm and the left kidney 88 × 38 × 41 mm. Both show normal morphology, preserved cortex, and adequate corticomedullary relationship without cysts, lithiasis, or tumors. Mild bilateral pyelocaliceal ectasia is observed with no identifiable cause and persists after voiding. The bladder is normal with a thin wall, a pre-void volume of 319 cc, and a post-void residual of 53 cc.
Renal doppler	Native kidneys with preserved parenchymal-cortical relationship. No significant vascular or hemodynamic alterations are observed bilaterally at the intrarenal level. The left renal vein shows increased diameter with an SMA axis angle of 18° and PSV of 8 cm/s.

Table 3. Patient paraclinical profile after corticosteroid use

Paraclinical test	Patient value	Paraclinical test	Patient value
Blood analysis			
Hemoglobin	9.10 g/dL	Serum urea	31 mg/dL
MCV	74 fL	Serum creatinine	0.74 mg/dL
MCH	24 pg		
RDW	16 fL		
Platelets	434000 mm^3		
Leukocytes	14280 mm^3		
Eosinophils	185.68 mm^3		
Basophils	14.28 mm^3		
Monocytes	828.24 mm^3		
Lymphocytes	4184.04 mm^3		
Neutrophils	9067.80 mm^3		

uncommon—other factors, such as the direct toxic effect of IgA on the tubules, may be relevant[8].

In the management of patients with IgA nephropathy, it is essential to recognize that although tubulointerstitial involvement may be secondary to the primary disease, atypical presentations exist in which other etiologies must be considered. One such example is ATIN, an entity that may be associated with the use of certain drugs, such as NSAIDs, which are widely recognized for their nephrotoxic potential[9].

In the present case, the patient with IgA nephropathy developed acute kidney injury whose clinical course and histological findings did not fully align with tubulointerstitial involvement attributable solely to IgAN. Although electron microscopy was not performed, in this context such analysis would only have confirmed the presence of electron-dense deposits in the mesangium and paramesangium.

The renal biopsy findings were more consistent with ATIN, which led to the consideration of recent NSAID use as a key factor in the acute renal injury. This reasoning is supported by the atypical clinical course, the relevant medical history, and the fact that the entire clinical picture could not be explained by a single entity. Although IgA nephropathy and ATIN are usually considered separate diseases, in this case their coexistence suggests a multifactorial phenomenon requiring consideration of multiple hypotheses.

One such hypothesis is tubular obstruction by red blood cells, particularly in the context of macroscopic hematuria. This obstruction may occur when erythrocytes present in the urine accumulate within the tubules, reducing urinary flow, increasing intratubular pressure, and causing tubular damage. This form of tubulitis may contribute to renal dysfunction and mimic the findings of ATIN[10].

In such scenarios, precise identification of the etiology allows discontinuation of the causative agent and facilitates renal recovery, especially when intervention occurs early. Therefore, differentiating between tubulointerstitial involvement secondary to IgA nephropathy and drug-induced ATIN, such as that associated with NSAIDs, is essential to guide treatment and improve prognosis. Likewise, this highlights the importance of a detailed clinical history and careful review of medications recently used by the patient.

Conclusions

Our clinical case involves a patient with IgA nephropathy associated with acute kidney injury due to overlap with ATIN. It is important to keep in mind that acute kidney injury in patients with IgA nephropathy is not always explained solely by decompensation of the underlying disease. When atypical clinical features are present, the possibility of overlapping renal diseases should be considered. Renal biopsy is an important diagnostic tool that can be highly useful in establishing an accurate diagnosis and guiding appropriate management.

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The authors declare that this work was conducted with the authors' own resources.

Conflicts of interest

The authors declare that they have no conflicts of interest.

Ethical considerations

Protection of human subjects and animals. The authors declare that no experiments on humans or animals were performed for this research.

Confidentiality, informed consent, and ethical approval. This study does not involve personal patient data, medical records, or biological samples, and does not require ethical approval. SAGER guidelines do not apply.

Declaration on the use of artificial intelligence (AI). The authors declare that no generative artificial intelligence was used in the writing or creation of the content of this manuscript.

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