

Nephrotic Syndrome as the Initial Presentation of IgA Nephropathy: A Case Report

Tânia Pereira da Silva ¹, Joana Rego ¹, Diane Pimenta ¹, Rosa Margarida Cardoso ¹, Glória Alves ¹

¹. Internal Medicine, Unidade Local de Saúde Alto Ave, Guimarães, PRT

Corresponding author: Tânia Pereira da Silva, tania.silvamed@gmail.com

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Abstract

IgA nephropathy (IgAN) is the most common primary glomerulonephritis worldwide and is characterized by mesangial deposition of IgA, leading to glomerular inflammation and progressive renal injury. Although it most commonly presents with hematuria, nephrotic syndrome is an uncommon manifestation and may indicate more severe disease.

We report the case of a 20-year-old woman who presented with hypertension and nephrotic syndrome. Initial renal biopsy demonstrated focal segmental glomerulosclerosis, while subsequent comprehensive histopathological evaluation, including immunofluorescence and electron microscopy, confirmed the diagnosis of IgAN. Despite optimized supportive management, the patient progressed to end-stage kidney disease requiring peritoneal dialysis.

This case underscores the importance of comprehensive histopathological evaluation in patients with nephrotic syndrome and atypical biopsy findings to avoid diagnostic delay, guide appropriate therapeutic decisions, and improve prognostic assessment.

Categories: Preventive Medicine, Internal Medicine, Nephrology

Keywords: focal segmental glomerulosclerosis, glomerulonephritis, iga nephropathy, nephrotic syndrome, proteinuria

Introduction

IgA nephropathy (IgAN), also known as Berger disease, is the most common primary glomerulonephritis worldwide and an important cause of chronic kidney disease. It is characterized by deposition of IgA-containing immune complexes in the glomerular mesangium, with subsequent inflammation, complement activation, and progressive glomerular and tubulointerstitial injury [1-3]. Nephrotic syndrome is an uncommon clinical presentation of IgAN, reported in approximately 5-15% of patients, and has been associated with more severe pathological findings and poorer renal outcomes [4,5]. Current management emphasizes optimized supportive therapy, including blood pressure control and renin-angiotensin system blockade, while immunosuppressive or targeted therapies are reserved for selected patients at risk of progression [3,6].

In some cases, IgAN may present with extensive podocyte injury and nephrotic syndrome, creating important diagnostic challenges, particularly when segmental sclerosis is identified on kidney biopsy [7]. Distinguishing primary focal segmental glomerulosclerosis (FSGS) from segmental sclerosis occurring as a histopathological lesion of IgAN is clinically relevant, as the underlying pathophysiology, prognosis, and therapeutic implications may differ [8-10]. Furthermore, diffuse podocyte foot-process effacement has been described in a subset of patients with IgAN and nephrotic syndrome, suggesting an associated podocytopathy that may contribute to the clinical presentation [8,10]. This case highlights the importance of integrating light microscopy, immunofluorescence, and electron microscopy findings when evaluating atypical glomerular disease presentations in order to establish an accurate diagnosis and guide appropriate management.

Case Presentation

A 20-year-old Brazilian woman with no significant past medical history was referred for evaluation of arterial hypertension. She reported severe occipital headache with holocranial radiation, photophobia, and episodes of vomiting.

Laboratory evaluation confirmed nephrotic syndrome, with 24-hour urinary protein excretion of 14 g, marked hypoalbuminemia with a serum albumin level of 2.1 g/dL, generalized edema, and severe dyslipidemia, including a total cholesterol level of 825 mg/dL, a low-density lipoprotein (LDL) cholesterol level of 706 mg/dL, and a triglyceride level of 349 mg/dL.

She was admitted for further investigation. Table 1 summarizes the laboratory findings at presentation,

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consistent with nephrotic syndrome.

Parameter	Result	Reference Range	Interpretation
Proteinuria (24h)	14 g/24h	<0.15 g/24h	Nephrotic-range proteinuria
Serum albumin	2.1 g/dL	3.5-5.0 g/dL	Hypoalbuminemia
Total cholesterol	825 mg/dL	<200 mg/dL	Severe hypercholesterolemia
LDL cholesterol	706 mg/dL	<130 mg/dL	Marked elevation
Triglycerides	349 mg/dL	<150 mg/dL	Hypertriglyceridemia
HDL cholesterol	49 mg/dL	>40 mg/dL	Normal
Edema	Present	Absent	Consistent with nephrotic syndrome
Blood pressure	Elevated	<120/80 mmHg	Hypertension

TABLE 1: Baseline clinical and laboratory findings at presentation

HDL: high-density lipoprotein; LDL: low-density lipoprotein

The patient denied macroscopic hematuria, and urinary sediment examination was unremarkable. An extensive etiological workup for secondary causes of glomerular disease, including autoimmune and infectious investigations, was negative. Ambulatory blood pressure monitoring performed at presentation demonstrated adequate blood pressure control, with a 24-hour average blood pressure of 115/72 mmHg, a daytime average of 121/78 mmHg, and a nighttime average of 102/60 mmHg.

Renal biopsy initially demonstrated FSGS with marked chronic damage. Of the 33 glomeruli identified, 13 were globally sclerosed and six showed segmental sclerosis. Focal mesangial hypercellularity was present, whereas endocapillary hypercellularity and crescents were absent. Interstitial fibrosis and tubular atrophy involved approximately 60% of the sampled renal cortex. Based on these initial histopathological findings, corticosteroid therapy with prednisolone at a dose of 1 mg/kg/day (60 mg/day) was initiated, resulting in a reduction in proteinuria and improvement in serum albumin levels, although nephrotic-range proteinuria persisted. Subsequent ultrastructural analysis of the same biopsy specimen demonstrated diffuse podocyte foot-process effacement, mesangial expansion and sclerosis, and mesangial and mesangiocapillary immune-type electron-dense deposits, raising the possibility of a podocytopathy associated with IgAN. Due to the incomplete response to corticosteroid therapy, additional immunosuppressive treatment with cyclosporine (100 mg twice daily; approximately 3 mg/kg/day for a body weight of 60 kg) was initiated. Table 2 summarizes the evolution of key laboratory parameters during treatment and follow-up.

Timepoint	Proteinuria (g/24 h)	Serum Albumin (g/dL)	Total Cholesterol (mg/dL)	Treatment/Clinical Status
Baseline	14.0	2.1	825	Corticosteroid therapy initiated (initial working diagnosis: FSGS)
4 weeks (high-dose corticosteroids)	4.5	4.1	346	Partial response to corticosteroid therapy, with persistent nephrotic-range proteinuria
16 weeks (completion of high-dose corticosteroids)	3.3	3.6	283	Partial response; corticosteroid taper initiated
Follow-up	-	-	-	Subsequent biopsy review and electron microscopy supported the diagnosis of IgA nephropathy with marked chronic damage. Progressive renal function decline ultimately led to end-stage kidney disease requiring renal replacement therapy.

TABLE 2: Evolution of key laboratory parameters during treatment and long-term follow-up.

FSGS: focal segmental glomerulosclerosis

This table summarizes the temporal evolution of the major biochemical parameters associated with nephrotic syndrome. Initial management was based on a working diagnosis of FSGS, with a partial response to corticosteroids and cyclosporine.

Subsequent comprehensive histopathological review, integrating the original light microscopy findings with electron microscopy, demonstrated mesangioproliferative glomerulonephritis with mesangial and mesangiocapillary immune-type electron-dense deposits, supporting the diagnosis of IgAN with associated chronic histopathological changes. Immunofluorescence evaluation was non-contributory because no glomeruli were present in the submitted specimen.

Following biopsy re-evaluation, which demonstrated marked chronic kidney damage without evidence of potentially reversible active lesions, immunosuppressive therapy was eventually discontinued and a conservative management strategy was adopted, including optimization of antihypertensive therapy and dietary sodium restriction.

The patient was referred to nephrology for long-term follow-up. Intensive conservative management was pursued, including optimization and titration of antihypertensive therapy, dietary sodium restriction, and close monitoring of renal function and proteinuria. However, the patient was lost to follow-up for several months, resulting in suboptimal clinical and laboratory monitoring during a critical period of disease evolution. Despite these interventions, renal function continued to decline, ultimately necessitating renal replacement therapy.

Histological findings are shown in Figures 1-3.

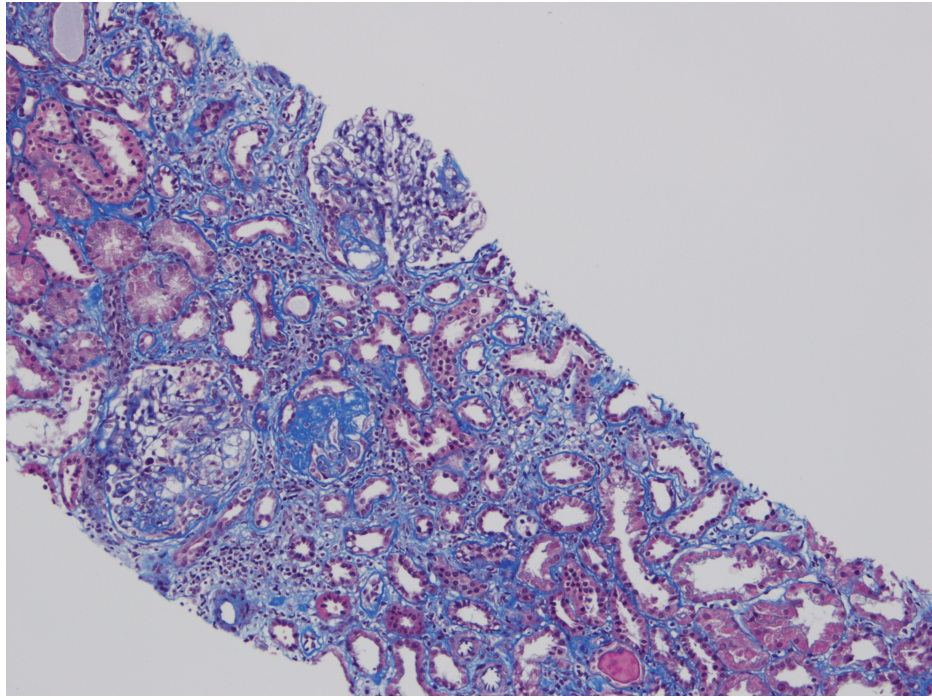


FIGURE 1: Light photomicrograph of the renal biopsy showing mesangioproliferative glomerulonephritis with increased mesangial cellularity and mesangial matrix expansion (Masson's trichrome stain, 100× magnification).

Image kindly provided by Dr. Roberto Silva, Department of Pathology, Hospital de São João, Porto, Portugal.

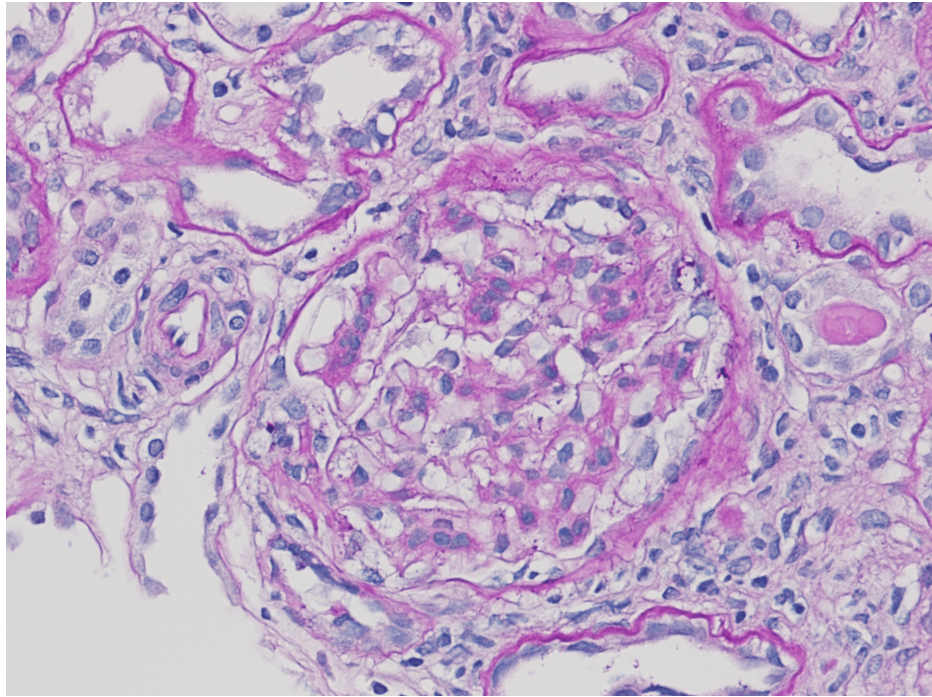


FIGURE 2: Renal biopsy showing marked chronic kidney damage, including global and segmental glomerulosclerosis, extensive interstitial fibrosis, and tubular atrophy (periodic acid–Schiff [PAS] stain, 400× magnification).

Image kindly provided by Dr. Roberto Silva, Department of Pathology, Hospital de São João, Porto, Portugal.

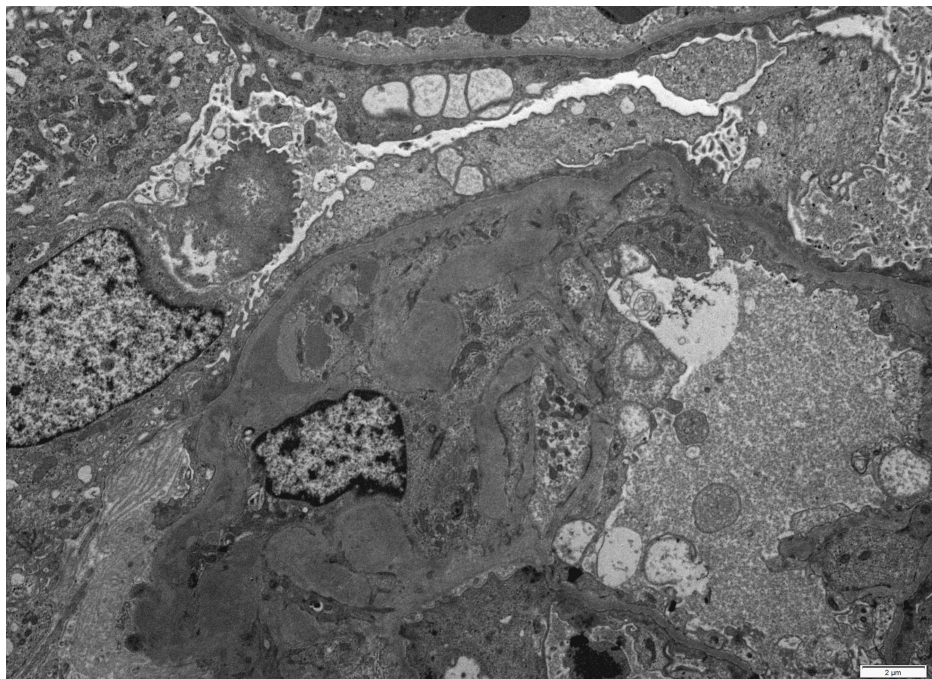


FIGURE 3: Electron microscopy demonstrating mesangial electron-dense deposits consistent with IgA nephropathy.

Image kindly provided by Dr. Roberto Silva, Department of Pathology, Hospital de São João, Porto, Portugal.

Despite an initial partial response to corticosteroid therapy, the patient's kidney function progressively deteriorated throughout follow-up (Table 3). At presentation in July 2023, serum creatinine was 1.33 mg/dL, corresponding to an estimated glomerular filtration rate (eGFR) of 51.4 mL/min/1.73 m², with nephrotic-range proteinuria of 14 g/24 h. The patient remained on irbesartan 300 mg daily throughout follow-up for blood pressure control and renin-angiotensin system blockade. Although proteinuria initially improved with corticosteroids and later with cyclosporine, kidney function continued to decline. After initiation of cyclosporine, proteinuria decreased from 5.9 to 3.27 g/24 h; however, renal function worsened despite therapeutic cyclosporine levels. Cyclosporine trough levels were regularly monitored throughout treatment and consistently remained within the therapeutic range. In August 2024, following a prolonged period of loss to follow-up despite repeated attempts at contact, the patient returned with recurrent nephrotic-range proteinuria, worsening renal function, and uncontrolled hypertension (150/93-166/97 mmHg), requiring intensification of antihypertensive therapy with diltiazem and referral to Nephrology. While calcineurin inhibitor nephrotoxicity cannot be entirely excluded, the progressive decline in kidney function was more likely related to the underlying glomerular disease and the marked chronic kidney damage identified on biopsy review. Reevaluation of the kidney biopsy in January 2025 confirmed these advanced chronic changes and did not support further immunosuppressive therapy. The patient ultimately progressed to end-stage kidney disease, requiring hemodialysis in September 2025 and peritoneal dialysis in October 2025, approximately 26 months after the initial presentation.

Date	Serum Creatinine (mg/dL)	eGFR (mL/min/1.73 m²)	Proteinuria (g/24 h)	Clinical course / Treatment
July 2023	1.33	51.4	14.0	Initial presentation with nephrotic syndrome
Nov 2023	1.57	41	3.3	Partial response after 16 weeks of high-dose corticosteroids
Jan 2024	1.45	45	5.9	Relapse during corticosteroid taper (prednisolone 40 mg/day). Prednisolone increased to 70 mg/day and cyclosporine 100 mg twice daily initiated.
Feb 2024	1.71	38.5	3.27	Partial proteinuria response after 1 month of cyclosporine. Renal function deteriorated despite therapeutic cyclosporine levels
Aug 2024	1.90	33	~6.0	Recurrent nephrotic-range proteinuria after loss to follow-up. Prednisolone was increased to 70 mg/day and cyclosporine increased to 150 mg twice daily.
Sep 2024	2.16	26	2.18	Progressive kidney dysfunction; nephrology referral.
Jan 2025	Progressive CKD	NR	NR	Biopsy review revealed advanced chronic changes; immunosuppression discontinued.
Sep 2025	ESKD	-	-	Hemodialysis initiated.
Oct 2025	ESKD	-	-	Peritoneal dialysis initiated.

TABLE 3: Evolution of kidney function and proteinuria during follow-up

eGFR: estimated glomerular filtration rate, CKD: chronic kidney disease, NR: not reported, ESKD: end-stage kidney disease

Discussion

This case illustrates an uncommon presentation of IgAN manifesting as nephrotic syndrome. Although IgAN most commonly presents with hematuria, nephrotic syndrome occurs in a minority of patients, with reported frequencies of approximately 5-15%, and is associated with distinct clinicopathological features and less favorable renal outcomes [4,5]. The 2025 Kidney Disease: Improving Global Outcomes (KDIGO) guideline recognizes nephrotic syndrome as a rare special presentation of IgAN and emphasizes that its pathological substrate may vary, ranging from mesangioproliferative IgAN to cases with features of a podocytopathy resembling minimal change disease [3].

The pathogenesis of IgAN is commonly described by a multi-hit model involving increased production of galactose-deficient IgA1, formation of circulating autoantibodies and immune complexes, deposition of these complexes in the glomerular mesangium, and subsequent activation of inflammatory and complement

pathways. This cascade promotes mesangial activation, glomerular injury, and progressive fibrosis [2,7].

In the present case, the identification of FSGS on the initial biopsy likely represented a secondary lesion associated with podocyte injury rather than a primary FSGS process. Segmental sclerosis is a recognized histopathological lesion in IgAN and has prognostic relevance within the Oxford classification, particularly when associated with evidence of podocyte injury [8,9]. This illustrates the potential for diagnostic misclassification when segmental sclerosis is interpreted in isolation. Comprehensive histopathological assessment was therefore essential. Although immunofluorescence was non-contributory because no glomeruli were present in the submitted specimen, electron microscopy demonstrated mesangial electron-dense deposits consistent with IgA nephropathy, thereby establishing the diagnosis in conjunction with the light microscopy findings [3,9,10].

Management of IgAN is primarily focused on reducing proteinuria, controlling blood pressure, and preserving kidney function. The current KDIGO 2025 guideline emphasizes optimized supportive therapy, including maximally tolerated renin-angiotensin system blockade, and incorporates sodium-glucose cotransporter-2 inhibitors and other disease-specific therapies according to individual risk and eligibility [3,11]. Corticosteroids and targeted-release budesonide may be considered in selected patients with persistent proteinuria and sufficient kidney function, while the potential benefits of systemic immunosuppression must be balanced against adverse effects [3,6]. In patients with advanced chronic histopathological lesions, the expected benefit of immunosuppression may be limited, reinforcing the importance of early recognition and optimized supportive treatment.

The occurrence of nephrotic syndrome in IgAN is associated with a more aggressive clinical course in several observational cohorts. In a propensity score-matched study, nephrotic syndrome was independently associated with a higher risk of a composite renal endpoint, while another cohort demonstrated poorer long-term outcomes in patients with nephrotic syndrome compared with those without this presentation [4,5]. In the present case, despite an initial partial response to corticosteroid and cyclosporine therapy, subsequent histopathological clarification led to discontinuation of immunosuppression and a shift toward conservative management. The subsequent progression to end-stage kidney disease highlights the importance of accurate diagnosis, recognition of chronic pathological damage, treatment adherence, and close nephrological follow-up.

Conclusions

IgAN may rarely present as nephrotic syndrome, creating significant diagnostic challenges, particularly when initial histopathological findings suggest FSGS. This case highlights the importance of comprehensive histopathological evaluation, including the integration of light microscopy, immunofluorescence when available, and electron microscopy, to establish an accurate diagnosis in atypical presentations. It also illustrates the potential association between IgAN, podocyte injury, and nephrotic syndrome, as well as the adverse prognostic implications of advanced chronic kidney damage. Careful clinicopathological correlation remains essential for appropriate risk stratification and individualized management of patients with complex glomerular disease.

Additional Information

Author Contributions

All authors have reviewed the final version to be published and agreed to be accountable for all aspects of the work.

Concept and design: Tânia Pereira da Silva, Glória Alves, Joana Rego, Diane Pimenta, Rosa Margarida Cardoso

Acquisition, analysis, or interpretation of data: Tânia Pereira da Silva, Glória Alves, Joana Rego, Diane Pimenta, Rosa Margarida Cardoso

Drafting of the manuscript: Tânia Pereira da Silva, Glória Alves, Joana Rego, Diane Pimenta, Rosa Margarida Cardoso

Critical review of the manuscript for important intellectual content: Tânia Pereira da Silva, Glória Alves, Joana Rego, Diane Pimenta, Rosa Margarida Cardoso

Supervision: Tânia Pereira da Silva, Glória Alves, Joana Rego, Diane Pimenta, Rosa Margarida Cardoso

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References

1. Stoneman S, Teh JW, O'Shaughnessy MM: IgA nephropathy in adults: a review . JAMA. 2026, 335:799-813. [10.1001/jama.2025.25020](https://doi.org/10.1001/jama.2025.25020)
2. Cheung CK, Alexander S, Reich HN, Selvaskandan H, Zhang H, Barratt J: The pathogenesis of IgA nephropathy and implications for treatment. Nat Rev Nephrol. 2025, 21:9-23. [10.1038/s41581-024-00885-3](https://doi.org/10.1038/s41581-024-00885-3)
3. 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:S1-S71. [10.1016/j.kint.2025.04.004](https://doi.org/10.1016/j.kint.2025.04.004)
4. Tan L, Jin LH, Wang YQ, Chen W, Wen Q: Clinical features, pathological characteristics, and prognosis of patients with IgA nephropathy complicated with nephrotic syndrome. Sci Rep. 2025, 15:1804. [10.1038/s41598-025-86081-0](https://doi.org/10.1038/s41598-025-86081-0)
5. Jiang Y, Chen P, Zhao W, Liu L, Shi S, Lv J, Zhang H: Distinct characteristics and prognosis of IgA nephropathy patients with nephrotic syndrome: a propensity score-matched cohort study. Front Med (Lausanne). 2024, 11:1344219. [10.3389/fmed.2024.1344219](https://doi.org/10.3389/fmed.2024.1344219)
6. Caster DJ, Lafayette RA: The treatment of primary IgA nephropathy: change, change, change . Am J Kidney Dis. 2024, 83:229-40. [10.1053/j.ajkd.2023.08.007](https://doi.org/10.1053/j.ajkd.2023.08.007)
7. Novak J, Julian BA, Mestecky J, Renfrow MB: Glycosylation of IgA1 and pathogenesis of IgA nephropathy . Semin Immunopathol. 2012, 34:365-82. [10.1007/s00281-012-0306-z](https://doi.org/10.1007/s00281-012-0306-z)
8. Cook HT: Focal segmental glomerulosclerosis in IgA nephropathy: a result of primary podocyte injury? . Kidney Int. 2011, 79:581-3. [10.1038/ki.2010.521](https://doi.org/10.1038/ki.2010.521)
9. Trimarchi H, Barratt J, Cattran DC, et al.: Oxford classification of IgA nephropathy 2016: an update from the IgA Nephropathy Classification Working Group. Kidney Int. 2017, 91:1014-21. [10.1016/j.kint.2017.02.003](https://doi.org/10.1016/j.kint.2017.02.003)
10. Pattapornpisut P, Avila-Casado C, Reich HN: IgA nephropathy: core curriculum 2021. Am J Kidney Dis. 2021, 78:429-41. [10.1053/j.ajkd.2021.01.024](https://doi.org/10.1053/j.ajkd.2021.01.024)
11. KDIGO 2021 clinical practice guideline for the management of glomerular diseases . Kidney Int. 2021, 100:S1-S276. [10.1016/j.kint.2021.05.021](https://doi.org/10.1016/j.kint.2021.05.021)