

Congress Abstract

IgA Nephropathy with a Clinical-Hematological Phenotype of Thrombotic Microangiopathy in a Patient with a Solitary Kidney: A Case Report

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ABSTRACT

Background: IgA nephropathy (IgAN) is an immune complex-mediated glomerular disease characterized by marked clinical and histopathological heterogeneity and a variable risk of progression. The coexistence of IgAN with features of TMA poses a particular diagnostic challenge, as a microangiopathic phenotype may emerge in the setting of severe glomerular injury, endothelial dysfunction, complement activation, and additional external triggers. The clinical consequences of such an interaction may be particularly significant in patients with a solitary functioning kidney.

Objective: To characterize the clinicopathological features of severe IgAN presenting with a clinical-hematological TMA phenotype in a young woman with a solitary functioning kidney and to explore the potential contribution of local complement activation and recurrent drug exposures as a putative "second hit" to endothelial injury and rapid deterioration of kidney function.

Case presentation: A 22-year-old woman had a solitary functioning right kidney following neonatal left nephrectomy. Kidney function remained preserved for years; however, persistent microscopic hematuria had been documented since 2022, retrospectively suggesting clinically silent glomerular disease. Between 2022 and 2026, she had substantial cumulative exposure to medications and supplements, including recurrent antiviral, antibacterial, and anti-inflammatory therapies, acne-directed treatments, vitamin/mineral preparations, and dietary supplements. These exposures preceded clinical deterioration and were considered potential external triggers in a susceptible renal background rather than evidence of definite drug-induced TMA. In June–July 2026, she developed recurrent massive edema followed by rapidly progressive kidney dysfunction with azotemia, hyperkalemia, active urinary sediment, and proteinuria, ultimately requiring hemodialysis. During hospitalization, microangiopathic hemolytic anemia, severe thrombocytopenia, schistocytosis, reticulocytosis, and elevated lactate dehydrogenase established a clinical-hematological TMA phenotype (Table 1). Preserved ADAMTS13 activity argued against immune-mediated thrombotic thrombocytopenic purpura (TTP), while autoimmune, anti-GBM, antiphospholipid, and infectious investigations were unrevealing. Given rapidly progressive dysfunction of the solitary kidney and an active nephritic syndrome, methylprednisolone and cyclophosphamide were administered before histopathological confirmation. Two sessions of therapeutic plasma exchange were subsequently performed in the setting of the pronounced TMA phenotype. Hematological parameters improved, whereas kidney function did not recover and dialysis dependence persisted. Kidney biopsy demonstrated advanced IgAN with severe chronic kidney damage (Oxford Classification M0E1S1T2C1) and intense mesangial IgA/C3 codeposition despite normal circulating C3. No definitive histopathological evidence of active TMA was identified.

Conclusion: This case demonstrates previously oligosymptomatic IgAN presenting with rapidly progressive kidney dysfunction, dialysis-dependent kidney failure, and a compelling clinical–hematological TMA phenotype. Preserved ADAMTS13 activity and an unrevealing investigation for major secondary causes supported a microangiopathic process distinct from immune-mediated TTP. Marked mesangial IgA/C3 codeposition despite normal circulating C3 raises the possibility that local complement activation may have amplified glomerular inflammation and endothelial injury. However, these findings are insufficient to establish complement-mediated TMA. The absence of active TMA lesions in a biopsy obtained later in the disease course likewise does not establish renal TMA, but cannot exclude a preceding transient or partially resolved microangiopathic process. A distinctive feature was the substantial cumulative medication and supplement exposure preceding clinical deterioration. In the setting of pre-existing IgAN and a solitary functioning kidney, recurrent drug exposures may have constituted an external “second hit,” potentially promoting immune activation, endothelial stress, and clinical decompensation. The absence of a clear temporal relationship with a single agent, however, precludes attribution to definite drug-induced TMA. Collectively, this case supports a multifactorial, hypothesis-generating model: pre-existing IgAN in a solitary kidney → recurrent external/drug exposures as a potential “second hit” → possible local complement activation and endothelial injury → clinical–hematological TMA phenotype → rapid kidney function deterioration. This proposed sequence should not be interpreted as evidence of direct causality.

Clinical lesson: in patients with IgAN and rapidly deteriorating kidney function, particularly when anemia and thrombocytopenia develop, targeted evaluation for TMA and potential secondary triggers should be considered even when circulating C3 levels are normal.

Keywords: IgA Nephropathy; Thrombotic Microangiopathy; Solitary Kidney; Complement Activation; Kidney Failure; Case Report

Table 1. Key Clinical, Laboratory, Therapeutic, and Histopathological Findings

Domain	Domain Key findings
Renal background	Solitary functioning right kidney; persistent microscopic hematuria since 2022
Potential drug-related “second hit” (2022–2026)	Recurrent antiviral, antibacterial, and anti-inflammatory therapies; acne-directed treatments; vitamin/mineral preparations and dietary supplements. Cumulative exposure preceded clinical deterioration and was considered a potential external “second hit,” not proven drug-induced TMA
Acute kidney deterioration (Jun–Jul 2026)	Recurrent massive edema; rapidly progressive azotemia; hyperkalemia; active urinary sediment; proteinuria 2.18 g/day; serum creatinine 609–700 $\mu\text{mol/L}$ → hemodialysis
Clinical–hematological TMA phenotype	Hb 85→63 g/L; platelets 201→37 $\times 10^9/\text{L}$; schistocytes 1–3%; reticulocytes 16%; $\uparrow\text{LDH}$; DAT negative → microangiopathic hemolysis with platelet consumption
TMA differential work-up	ADAMTS13 activity 82.55%, arguing against severe ADAMTS13 deficiency/immune-mediated TTP; autoimmune, anti-GBM, antiphospholipid, and infectious work-up unrevealing; circulating C3 normal
Treatment and hematological response	Methylprednisolone + cyclophosphamide; therapeutic plasma exchange on 11 and 13 Aug 2026. Platelets recovered 37→96→120 $\times 10^9/\text{L}$ and Hb improved 63→101 g/L following treatment; kidney function did not recover and dialysis dependence persisted
Kidney histopathology	Advanced IgAN; ~90% global/subtotal glomerulosclerosis; IFTA >50%; Oxford Classification M0E1S1T2C1

Complement-related findings	Intense mesangial IgA 3+/C3 3+ codeposition despite normal circulating C3, raising the possibility of local complement activation; insufficient to establish complement-mediated TMA
TMA morphology	No definitive active TMA lesions in the later biopsy; does not establish renal TMA but cannot exclude a preceding transient or partially resolved microangiopathic process

Abbreviations: ADAMTS13, a disintegrin and metalloproteinase with a thrombospondin type 1 motif, member 13; DAT, direct antiglobulin test; Hb, hemoglobin; IFTA, interstitial fibrosis and tubular atrophy; IgAN, IgA nephropathy; LDH, lactate dehydrogenase; TMA, thrombotic microangiopathy; TTP, thrombotic thrombocytopenic purpura.