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Postpartum complement-mediated thrombotic microangiopathy/atypical hemolytic uremic syndrome with active IgA nephropathy and acute tubular injury: a case report

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Case Report

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Abstract

Background

Postpartum anemia, thrombocytopenia, and acute kidney injury (AKI) should raise concern for thrombotic microangiopathy (TMA). However, thrombotic thrombocytopenic purpura, complement-mediated TMA/atypical hemolytic uremic syndrome (CM-TMA/aHUS), obstetric TMA, and other secondary causes may overlap early in the course.

Case presentation:

A 35-year-old woman developed oliguria 5 h after cesarean delivery complicated by an estimated blood loss of approximately 1200 mL. On admission, hemoglobin was 54 g/L, platelet count 32 × 10^9/L, serum creatinine 235.2 μmol/L, and lactate dehydrogenase 1411.3 U/L. Plasma exchange and continuous kidney replacement therapy were started while TTP was being assessed. ADAMTS13 activity was 94% with a negative inhibitor test, and complement testing showed low C3 and elevated soluble C5b-9. Eculizumab was initiated for clinically suspected postpartum CM-TMA/aHUS. Kidney biopsy showed TMA-related vascular lesions, active IgA nephropathy (Oxford M1E1S1T0-C2), and acute tubular injury. Recurrent microscopic hematuria from early pregnancy suggested that IgA nephropathy probably preceded the postpartum TMA event. The patient recovered hematologically, discontinued dialysis, and showed short-term improvement in kidney function and proteinuria after complement-directed and IgA nephropathy-directed treatment.

Conclusions

This case highlights the need for parallel diagnosis and treatment in postpartum TMA. Pre-existing IgA nephropathy may provide a complement-active renal background, whereas delivery, hemorrhage, infection, and coagulation disturbance may trigger or amplify CM-TMA/aHUS and tubular injury.

Background

Thrombotic microangiopathy (TMA) during pregnancy or the puerperium requires rapid differentiation among thrombotic thrombocytopenic purpura (TTP), complement-mediated TMA/atypical hemolytic uremic syndrome (CM-TMA/aHUS), preeclampsia or HELLP syndrome, obstetric disseminated intravascular coagulation (DIC), and other secondary forms of TMA. These conditions may share anemia, thrombocytopenia, and organ injury, but their management differs substantially. Early ADAMTS13 testing is therefore central to identifying patients who need urgent TTP-directed treatment; after severe ADAMTS13 deficiency is not supported, the timing of disease onset, obstetric context, organ involvement, complement assessment, pathology, and subsequent clinical course guide the differential diagnosis [1–4].

CM-TMA/aHUS often presents with prominent renal involvement. In severe or diagnostically complex AKI, kidney biopsy may show TMA-related lesions and may also uncover coexisting glomerular or tubular injury. IgA nephropathy can be accompanied by complement activation and, in some patients, microangiopathic lesions [5, 6]. Postpartum hemorrhage, renal hypoperfusion, and TMA-related microcirculatory injury may also contribute to acute tubular injury (ATI) [7].

We report a postpartum patient who was initially treated with plasma exchange while TTP was being excluded. After ADAMTS13 testing did not support TTP and complement activation was documented, eculizumab was initiated for clinically suspected CM-TMA/aHUS. Kidney biopsy performed after platelet recovery demonstrated TMA-related vascular injury, active IgA nephropathy, and ATI, which directly shaped subsequent treatment.

Case presentation

A 35-year-old woman at 39 weeks and 4 days of gestation underwent cesarean delivery at an outside hospital. The estimated intraoperative blood loss was approximately 1200 mL, and she received 2 units of packed red blood cells and 400 mL of fresh frozen plasma. Five hours after surgery, she developed oliguria; hemoglobin was 58 g/L, platelet count was 32 × 10^9/L, and serum creatinine was 158 μmol/L. She was transferred to our hospital for further management.

She had no known previous kidney disease, chronic hypertension, gestational hypertension, preeclampsia, or family history of hereditary kidney disease. Prenatal urinalysis at 11 weeks of gestation had shown microscopic hematuria, with urinary red blood cells (++) and 50/μL by dipstick and 10–12/HPF by microscopy, while urine protein was negative. Subsequent prenatal urine tests also repeatedly showed microscopic hematuria. These findings indicated that hematuria had been present before the postpartum TMA episode and, in light of the later biopsy, suggested that IgA nephropathy likely predated the acute postpartum event.

At admission, her temperature was 36.9°C, pulse rate 65 beats/min, respiratory rate 20 breaths/min, and blood pressure 117/67 mmHg. She was alert and appeared pale. There was no dyspnea, the lungs were clear, cardiac rhythm was regular without murmurs, the abdomen was soft, and there was no peripheral edema. Laboratory tests showed hemoglobin 54 g/L, platelet count 32 × 10^9/L, blood urea nitrogen 12.92 mmol/L, serum creatinine 235.2 μmol/L, alanine aminotransferase 40.1 U/L, aspartate aminotransferase 115.5 U/L, lactate dehydrogenase (LDH) 1411.3 U/L, C3 0.46 g/L, and C4 0.13 g/L. Fibrin/fibrinogen degradation products were > 120 mg/L and D-dimer was > 35.2 mg/L. The direct antiglobulin test was negative.

A peripheral blood smear showed fragmented red cells < 1%, and plasma free hemoglobin was 8.2 mg/L (reference range < 40.0 mg/L). Both tests, however, were obtained after plasma exchange had already begun and therefore could not reliably reflect the degree of intravascular hemolysis before treatment. Haptoglobin was not immediately available. Although pretreatment hemolysis testing was incomplete,

the abrupt perioperative fall in platelet count from 100 × 10^9/L to 32 × 10^9/L, marked LDH elevation, oliguria, and progressive kidney dysfunction made TMA the leading initial consideration.

Because TTP could not be excluded at presentation, ADAMTS13 and complement samples were obtained before plasma exchange, and plasma exchange, continuous kidney replacement therapy, transfusion, and supportive care were started. On hospital day 2, a multidisciplinary team including nephrology, hematology, transfusion medicine, obstetrics, and critical care recommended continuing daily plasma exchange. Four sessions of plasma exchange were completed early in the admission.

On hospital day 4, ADAMTS13 activity returned at 94% (reference range, 40–130%) and the inhibitor test was negative, which did not support immune TTP. Soluble C5b-9 was elevated at 353.79 ng/mL (reference range, 72.0-244.0 ng/mL). Complement factor H (CFH) concentration was 173.769 ng/mL (reference range, 46.5-417.69 ng/mL), indicating no quantitative CFH deficiency; this result did not assess CFH function or anti-CFH antibodies. Given postpartum onset, prominent renal involvement, disease progression after delivery, and evidence of terminal complement activation, postpartum CM-TMA/aHUS was clinically suspected. Plasma exchange was stopped, and eculizumab was started on hospital day 5 at 900 mg intravenously once weekly. The planned induction regimen was 900 mg weekly for 4 weeks, followed by maintenance dosing of 1200 mg every 2 weeks. Pulmonary infection was treated with meropenem for 2 weeks followed by cefazoxime for 1 week.

Because eculizumab had to be started urgently, meningococcal vaccination could not be completed before complement inhibition. Meningococcal vaccination was administered on hospital day 23 after clinical stabilization. After infectious diseases consultation, cefdinir was given as prophylactic coverage until at least 2 weeks after vaccination, and pneumococcal vaccination was arranged after a subsequent eculizumab dose.

Urine output was 85–365 mL/day on hospital days 4–6. On hospital day 7, urine output increased to 1780–2540 mL/day, but predialysis serum creatinine peaked at 785 μmol/L. At the same time, the platelet count increased to 121 × 10^9/L and LDH decreased to 527 U/L. After continuous kidney replacement therapy, she received intermittent hemodialysis three times weekly from hospital days 4 to 14.

On hospital day 13, the platelet count had increased to 234 × 10^9/L and hemoglobin was stable at approximately 80 g/L. Ultrasound-guided kidney biopsy was therefore performed. Light microscopy showed 17 glomeruli, including 2 globally sclerotic glomeruli, 7 segmentally sclerotic glomeruli, and 7 glomeruli with cellular crescents. There was diffuse segmental mesangial hypercellularity and matrix expansion, with narrowing or occlusion of some capillary loops. Tubular epithelial swelling, vacuolar change, brush-border loss, epithelial flattening and detachment, exposed tubular basement membrane, and regenerative repair were consistent with ATI. Some intrarenal small vessels showed intimal edema and mucoid change, endothelial swelling, and subintimal fragmented red cells, supporting TMA-related vascular injury. Immunofluorescence showed mesangial IgA (+ + to +++) and C3 (++) deposition. Electron microscopy demonstrated mesangial electron-dense deposits and segmental foot process

effacement. The integrated diagnosis was IgA nephropathy, Oxford M1E1S1T0-C2, with TMA-related vascular lesions and ATI (Fig. 1).

On hospital day 14, urine output was approximately 2000 mL/day and serum creatinine had decreased to 294 μmol/L; dialysis was discontinued. On hospital day 17, because the biopsy demonstrated IgA nephropathy with cellular crescents in addition to TMA and ATI, methylprednisolone 500 mg/day was given intravenously for 3 days, followed by oral prednisone 0.5 mg/kg/day and hydroxychloroquine 200 mg twice daily. On hospital day 23, serum creatinine was 110.5 μmol/L, hemoglobin 101 g/L, platelet count 178 × 10^9/L, LDH 249 U/L, C3 0.79 g/L, and repeat sC5b-9 had decreased to 256.5 ng/mL, close to the upper reference range.

After discharge, eculizumab 1200 mg intravenously every 2 weeks was continued. Because active IgA nephropathy and proteinuria persisted, prednisone tapering began 2 weeks after discharge after pneumococcal vaccination had been completed. Four weeks after discharge, telitacicept 80 mg was started subcutaneously once weekly and hydroxychloroquine was discontinued. Six weeks after discharge, telitacicept was increased to 160 mg once weekly, and eculizumab was individualized to 1200 mg once monthly with close monitoring. At that visit, hemoglobin was 126 g/L, platelet count 220 × 10^9/L, LDH 210 U/L, serum creatinine 100.66 μmol/L, estimated glomerular filtration rate 62.53 mL/min/1.73 m^2, and 24-h urine protein 1.02 g. Microscopic hematuria persisted, with urinary red blood cells 332/μL and 50–60/HPF on microscopy.

Complement-related genetic testing did not identify any clearly pathogenic or likely pathogenic variants. Three heterozygous variants of uncertain significance were reported: TERT NM_198253.3:c.746C > T (p.Thr249Met), ANKRD26 NM_014915.3:c.4732G > C (p.Glu1578Gln), and COPA NM_004371.4:c.1915C > A (p.Leu639Met). These genes are not established core complement-regulatory genes for CM-TMA/aHUS.

1. Intrarenal small-vessel intimal edema and mucoid change with endothelial swelling and subintimal fragmented red blood cells are indicated by the red arrow, supporting thrombotic microangiopathy-related vascular injury (hematoxylin and eosin staining, ×200).B. Mesangial proliferation, narrowing of capillary loops, and cellular crescent formation are shown; the red arrow indicates the cellular crescent. Adjacent tubular injury is also present (periodic acid–silver methenamine staining, ×100).C. IgA immunofluorescence shows clumped and granular mesangial deposits indicated by the red arrow (+ + to +++).D. Electron microscopy shows mesangial electron-dense deposits indicated by the red arrow, accompanied by segmental foot process effacement (original magnification approximately ×3000; scale bar, 1 μm).

Table 1
Clinical timeline

Time	Main findings	Treatment/outcome
Postpartum 5 h / hospital day 1	Oliguria; Hb 54 g/L; PLT 32 × 10^9/L; Scr 235.2 μmol/L; LDH 1411.3 U/L; low C3.	TMA recognized; ADAMTS13 and complement samples obtained; plasma exchange, continuous kidney replacement therapy, transfusion, and supportive care started.
Hospital day 2	Multidisciplinary consultation; 24-h urine output reached a minimum of approximately 125 mL; PLT 39 × 10^9/L; LDH 1870 U/L.	Four early sessions of plasma exchange were completed; continuous kidney replacement therapy continued.
Hospital day 4	ADAMTS13 activity 94%, inhibitor negative; CFH 173.769 ng/mL within reference range; sC5b-9 353.79 ng/mL elevated.	TTP was not supported; plasma exchange was stopped.
Hospital day 5	Postpartum CM-TMA/aHUS clinically suspected after integration of the obstetric course, renal involvement, and complement results.	First eculizumab dose, 900 mg intravenously.
Hospital day 7	Scr peaked at 785 μmol/L; urine output increased to 1780–2540 mL/day; PLT 121 × 10^9/L; LDH 527 U/L.	Intermittent hemodialysis continued.
Hospital day 13	PLT 234 × 10^9/L; Hb stable at approximately 80 g/L.	Ultrasound-guided kidney biopsy performed.
Hospital day 14	Urine output approximately 2000 mL/day; Scr 294 μmol/L.	Dialysis discontinued.
Hospital day 17	Kidney biopsy showed TMA-related vascular lesions, IgA nephropathy with cellular crescents, and ATI.	Methylprednisolone pulse therapy, followed by oral prednisone and hydroxychloroquine.
Hospital day 23 / before discharge	Scr 110.5 μmol/L; Hb 101 g/L; PLT 178 × 10^9/L; LDH 249 U/L; C3 recovered; sC5b-9 decreased to near the upper reference range.	Meningococcal vaccination completed; eculizumab and glucocorticoid therapy continued; pneumococcal vaccination planned.
4 weeks after discharge	Scr 117.7 μmol/L; 24-h urine protein 1.49 g.	The sixth eculizumab dose had been given (four 900-mg induction doses followed by two 1200-mg maintenance doses every 2 weeks); telitacicept 80 mg once weekly was added for persistent proteinuria.
6 weeks after discharge	Hb 126 g/L; PLT 220 × 10^9/L; LDH 210 U/L; Scr 100.66 μmol/L; eGFR 62.53 mL/min/1.73 m^2; 24-h urine protein 1.02 g; microscopic hematuria persisted.	Telitacicept increased to 160 mg once weekly; eculizumab individualized to 1200 mg once monthly with close monitoring.

Discussion

The key diagnostic issue in this case was the development, within hours after delivery, of severe anemia, thrombocytopenia, LDH elevation, and rapidly progressive AKI. This combination first required an approach to TMA rather than attribution to postpartum hemorrhage alone. International recommendations for pregnancy-associated TMA support obtaining ADAMTS13 samples early and starting plasma exchange when TTP cannot be rapidly excluded in a high-risk clinical setting [2, 3]. In this patient, four plasma exchange sessions were completed before ADAMTS13 results became available. Once ADAMTS13 activity returned at 94% with a negative inhibitor test, immune TTP was not supported.

Other obstetric and infectious causes of TMA were considered. The absence of gestational hypertension, preeclampsia, or eclampsia, together with relatively limited liver enzyme elevation and disproportionate renal involvement, made preeclampsia-related TMA or HELLP syndrome insufficient to explain the full course. Postpartum hemorrhage of approximately 1200 mL and markedly elevated fibrin/fibrinogen degradation products and D-dimer suggested that bleeding-related coagulation activation and hypoperfusion likely aggravated kidney injury. However, these factors did not fully account for the persistent thrombocytopenia, LDH elevation, worsening renal function, low C3, elevated sC5b-9, and biopsy-confirmed TMA-related vascular injury. STEC-HUS was not clinically supported because there was no diarrheal or gastrointestinal infectious prodrome, although the absence of Shiga toxin testing remains a limitation.

Clinically suspected aHUS is now commonly discussed within the broader concept of CM-TMA. Complement testing in suspected cases may include C3, C4, CFH, complement factor I, complement factor B, sC5b-9, CH50, AH50, and anti-CFH antibodies. In this patient, low C3 and elevated sC5b-9 supported complement activation. The CFH concentration was within the reference range, but this finding only excluded a quantitative CFH deficiency and did not evaluate CFH function or anti-CFH antibodies. No pathogenic complement gene variant was identified. Even so, the combination of postpartum onset, dominant renal involvement, biopsy-proven TMA lesions, complement activation, and clinical improvement after C5 inhibition supported the clinical diagnosis of postpartum CM-TMA/aHUS [2, 4, 8].

The treatment sequence followed the diagnostic evolution. Initial therapy covered TTP, a diagnosis that cannot be safely missed. After the ADAMTS13 result became available, plasma exchange was stopped and eculizumab was started. Once urine output and hematologic parameters improved and the platelet count normalized, kidney biopsy was performed. The biopsy clarified that different processes were contributing to kidney injury: eculizumab targeted the clinically suspected CM-TMA/aHUS; kidney replacement and supportive care addressed severe AKI; and glucocorticoids with hydroxychloroquine were used for active IgA nephropathy. The subsequent increase in platelet count, decrease in LDH, and discontinuation of dialysis were compatible with control of the TMA process, although the improvement

cannot be attributed to eculizumab alone because transfusion, kidney replacement therapy, corticosteroids, antimicrobial treatment, and supportive care were also used.

The biopsy also helped integrate the three renal lesions. Besides TMA-related vascular injury, the patient had IgA nephropathy with mesangial IgA and C3 deposition, cellular crescents, and Oxford M1E1S1T0-C2 classification. Repeated microscopic hematuria from early pregnancy, with little or no proteinuria at the earliest documented prenatal urinalysis, suggests that IgA nephropathy was likely present before the postpartum TMA event. Previous studies have shown that IgA nephropathy can involve activation of the alternative and lectin complement pathways and, in some patients, intrarenal microangiopathic lesions [5, 6]. In this setting, pre-existing IgA nephropathy may have provided an intrarenal inflammatory and complement-active background, while cesarean delivery, postpartum hemorrhage, infection, and coagulation disturbance amplified endothelial injury and complement activation, culminating in postpartum CM-TMA/aHUS. At the same time, hemorrhage-related hypoperfusion and TMA-related microcirculatory injury probably contributed to ATI. This interpretation is consistent with the clinical course: platelet count and LDH improved before full renal recovery, and proteinuria with microscopic hematuria persisted after control of the acute TMA process.

The biopsy showed cellular crescents in 7 of 17 glomeruli, meeting Oxford C2. C2, however, is not by itself equivalent to rapidly progressive IgA nephropathy. KDIGO emphasizes that a rapidly progressive course should be judged by sustained and marked eGFR decline after other causes have been excluded, rather than by the proportion of crescents alone [9]. In this patient, acute renal deterioration was also driven by TMA and ATI, so glucocorticoid therapy was an individualized decision directed at active glomerular disease in a complex setting.

Persistent proteinuria and microscopic hematuria after control of TMA activity were consistent with ongoing IgA nephropathy activity and possible risk of later progression. Telitacicept was added after pneumococcal vaccination and infection-risk assessment. Phase 2 data have shown that telitacicept can reduce proteinuria in patients with IgA nephropathy and persistent proteinuria [10]. In the present case, proteinuria decreased over the short follow-up interval, but the independent contribution of telitacicept cannot be established because follow-up was brief and complement inhibition, glucocorticoids, and supportive treatment were being used concurrently. Longer observation is needed to assess both renal response and the safety of combining telitacicept with eculizumab.

Genetic testing did not identify a clearly pathogenic or likely pathogenic variant in classical complement-regulatory genes. A negative genetic result does not exclude CM-TMA/aHUS, because acquired complement abnormalities, structural variants, variants outside the tested regions, and multifactorial triggers may still be relevant [4, 8]. The reported TERT, ANKRD26, and COPA variants were all variants of uncertain significance. Under ACMG/AMP principles, a variant of uncertain significance should not be used as evidence of causality, nor should it determine relapse-risk stratification or the duration of eculizumab therapy [11]. Their current value is mainly to guide future re-evaluation as the patient's phenotype, family studies, and genetic databases evolve.

Eculizumab increases susceptibility to Neisseria meningitidis and other encapsulated bacteria [12]. In this case, complement inhibition was initiated before vaccine protection could be established because of the severity and progression of disease. Antimicrobial therapy was administered for pulmonary infection, and meningococcal vaccination was completed after clinical stabilization, with cephalosporin coverage during the vaccination period and for at least 2 weeks afterward. Because the patient later received both complement inhibition and telitacicept, monitoring of immunoglobulin levels, infection education, and close follow-up were considered important during maintenance therapy.

This case has several limitations. First, complete pretreatment hemolysis markers were not available; the fragmented red cell count and plasma free hemoglobin were obtained after plasma exchange had started and may have underestimated earlier hemolysis. Second, postpartum hemorrhage and abnormal coagulation markers were present, but serial prothrombin time, activated partial thromboplastin time, and fibrinogen data were not sufficient to fully assess the contribution of obstetric DIC. Third, Shiga toxin testing was not performed despite the lack of diarrheal prodrome. Fourth, specialized complement testing, family validation of the genetic findings, and follow-up after combined biologic therapy remain limited.

Conclusions

When postpartum patients develop thrombocytopenia, anemia with LDH elevation, and rapidly progressive AKI, evaluation and treatment for TMA should proceed in parallel. After severe ADAMTS13 deficiency is not supported, the obstetric context, renal involvement, complement testing, pathology, and disease course should be integrated to assess CM-TMA/aHUS.

In this patient, platelet count and LDH improved after switching from plasma exchange to eculizumab, and dialysis was discontinued. Kidney biopsy demonstrated TMA-related vascular injury, active IgA nephropathy, and ATI, indicating that renal dysfunction resulted from overlapping pathological processes. The case also suggests a clinically useful unifying model: pre-existing IgA nephropathy may have provided a complement-active renal background, while postpartum hemorrhage and related stressors triggered or amplified complement-mediated TMA.

Abbreviations

ADAMTS13
a disintegrin and metalloproteinase with thrombospondin type 1 motif, member 13
aHUS
atypical hemolytic uremic syndrome
AKI
acute kidney injury
ATI
acute tubular injury

CFH
complement factor H
CM-TMA
complement-mediated thrombotic microangiopathy
CRRT
continuous renal replacement therapy
DIC
disseminated intravascular coagulation
eGFR
estimated glomerular filtration rate
HELLP
hemolysis, elevated liver enzymes, and low platelet count
HPF
high-power field
IgAN
IgA nephropathy
LDH
lactate dehydrogenase
PLT
platelet count
Scr
serum creatinine
sC5b-9
soluble C5b-9
STEC-HUS
Shiga toxin-producing Escherichia coli-associated hemolytic uremic syndrome
TMA
thrombotic microangiopathy
TTP
thrombotic thrombocytopenic purpura
VUS
variant of uncertain significance.

Declarations

Ethics approval and consent to participate: Not applicable. This was a single case report and did not involve an interventional study.

Consent for publication: Written informed consent for publication of de-identified clinical data and accompanying pathological images was obtained from the patient.

Availability of data and materials: Data supporting the conclusions of this case report are included in the article. To protect patient privacy, original clinical records and pathology materials are not publicly available; reasonable requests may be addressed to the corresponding author, subject to institutional and ethical restrictions.

Competing interests: The authors declare that they have no competing interests.

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Authors' contributions

H. and M.Z. contributed equally to this work and share first authorship. Z.H. and M.Z. conceived and designed the report, collected and organized the clinical data, reviewed the literature, and drafted the initial manuscript. W.W. and W.Y. contributed to renal pathological evaluation, interpretation of the biopsy findings, and preparation of the pathological figures. Z.S. and L.W. contributed to clinical interpretation, treatment decision-making, supervision, and critical revision of the manuscript. All authors read and approved the final manuscript.

Ethics approval and consent to participate: Not applicable. This was a single case report and did not involve an interventional study.

Consent for publication: Written informed consent for publication of de-identified clinical data, images, and supplementary video was obtained from the patient's legal guardian.

Availability of data and materials: Data supporting the conclusions of this case report are included in the article. To protect patient privacy, original clinical records are not publicly available; reasonable requests may be addressed to the corresponding author, subject to institutional and ethical restrictions.

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Image integrity: All pathological images were obtained from de-identified original renal biopsy materials. No AI-generated, synthetic, or AI-modified clinical or pathological images were used in this manuscript.

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Figures

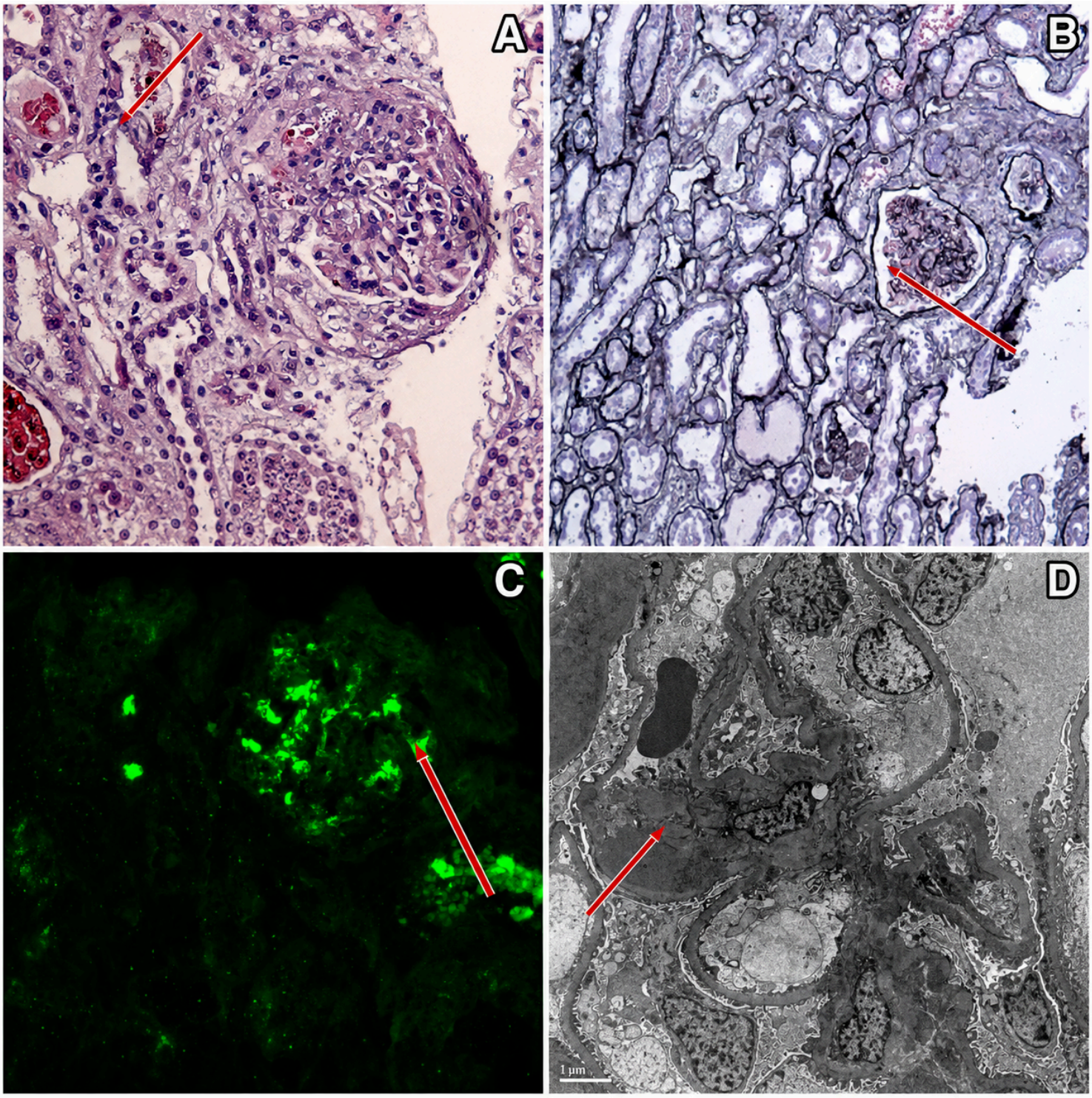


Figure 1

Kidney biopsy findings.

A. Intrarenal small-vessel intimal edema and mucoid change with endothelial swelling and subintimal fragmented red blood cells are indicated by the red arrow, supporting thrombotic microangiopathy-related vascular injury (hematoxylin and eosin staining, ×200).B. Mesangial proliferation, narrowing of capillary loops, and cellular crescent formation are shown; the red arrow indicates the cellular crescent. Adjacent tubular injury is also present (periodic acid–silver methenamine staining, ×100).C. IgA

immunofluorescence shows clumped and granular mesangial deposits indicated by the red arrow (++ to +++).D. Electron microscopy shows mesangial electron-dense deposits indicated by the red arrow, accompanied by segmental foot process effacement (original magnification approximately ×3000; scale bar, 1 μm).