Kidney Medicine

Postpartum Renal Cortical Necrosis: A Case Series

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Rationale & Objective: Postpartum renal cortical necrosis (postpartum RCN) is a severe form of obstetric acute kidney injury. This study aimed to identify clinicopathologic features in Chinese postpartum RCN cases to determine how pathologic findings may contribute to the treatment and prognosis.

Study Design: Single-center, case series.

Setting & Participants: Twelve patients with postpartum RCN had kidney biopsies at Peking University First Hospital between 2014 and 2021. The diagnosis of postpartum RCN was made according to typical magnetic resonance imaging or pathologic features. Clinical, laboratory, and pathologic data were compared between patients with estimated glomerular filtration rate <30 (poor outcome) and ≥30 mL/min/1.73 m^2 after 6 months.

Observations: All patients with postpartum RCN presented with stage 3 acute kidney injury attributed to a probable atypical hemolytic uremic syndrome. Pregnancy terminations occurred at a median gestational age of 35.5 weeks. Kidney biopsy was performed from 18 days to 4 months from delivery. On biopsy, hemoglobin, platelet count, and lactate dehydrogenase levels had been restored to 137 g/L, 214 × 10^9/L, and 231.50 ± 65.01 U/L, respectively. Four patients exhibited poor outcome, demonstrating higher schistocyte count, serum creatinine, and mean arterial pressure at onset. Pathologically, glomerular segmental sclerosis was prevalent. The "not otherwise specified" variant was the most common type, followed by collapsing variant, cellular variant, and tip variant. Patients with poor kidney outcome had more glomerular coagulative necrosis, capillary thrombosis, extensive cortical coagulative necrosis, and pronounced arteriole/artery lesions including increased interlobular arteriole intimal edema and fibrin thrombosis, but a lower occurrence of segmental sclerosis.

Limitations: Limited sample size and retrospective design.

Conclusions: We identified key pathologic features in patients with postpartum RCN and atypical hemolytic uremic syndrome, highlighting the necessity for more effective therapeutic options. There is a clear demand for noninvasive biomarkers that can accurately track disease progression and inform treatment duration for long-term outcomes improvement.

Postpartum renal cortical necrosis (postpartum RCN) is a severe form of acute kidney injury (AKI) that occurs during pregnancy. The incidence of RCN in obstetric AKI varies greatly, from 7.8%-23.5% in high-income countries and developing countries.[1-4] This condition used to be considered in association with massive postpartum hemorrhage caused by conditions such as placenta previa and abruption placentae or septic abortion.[3] Sudden and prolonged decrease in blood flow to the kidneys can result in damage to the kidney cortex. Accumulating evidence indicates that the spectrum of postpartum RCN has changed and atypical hemolytic uremic syndrome (aHUS), as a specific form of thrombotic microangiopathy that primarily affects the kidneys during pregnancy is the frequent underlying cause in developing countries.[5,6] There is also evidence indicating that uncontrolled activation of the complement system contributes to aHUS, aggravating ischemia and ultimately leading to RCN.[5,7]

Previous studies revealed the characteristic pathologic finding of RCN is varying degrees of ischemic necrosis in all the components of the kidney cortex,[5,8] with unfavorable kidney outcomes and a high mortality rate.[9,10] To effectively manage this condition, prompt initiation of plasmapheresis, which may be beneficial to reduce mortality rate and improve long-term outcomes, is typically warranted based on clinical signs of hemolysis, thrombocytopenia, elevated levels of lactate dehydrogenase (LDH), and decreased complement levels. However, the diagnosis of kidney thrombotic microangiopathy can be challenging, particularly when the condition does not always elicit a systemic response. In such cases, conducting a biopsy may not be feasible due to severe thrombocytopenia. Although unenhanced magnetic resonance imaging (MRI) can provide a noninvasive imaging technique in detecting postpartum RCN during the early stages of the disease,[9,10] it should be noted that MRI alone may not be able to differentiate the specific causes. Kidney biopsy remains a valuable method for obtaining conclusive evidence in these cases despite its invasive nature.[11]

This study was conducted to investigate the detailed pathologic characteristics of postpartum RCN and explore its relationship with clinical presentations in a Chinese case series. The objective was to determine how pathologic findings may contribute to the treatment and prognosis.

METHODS

Patients and Definitions

This study was conducted retrospectively. A total of 12 patients diagnosed with postpartum RCN, who underwent

PLAIN-LANGUAGE SUMMARY

Our study investigated postpartum renal cortical necrosis (RCN) in 12 Chinese women, a severe form of kidney injury that occurs after childbirth, often linked to atypical hemolytic uremic syndrome (aHUS). We aimed to identify clinical and pathologic features to improve treatment and predict patient outcomes. The women experienced stage 3 acute kidney injury, with kidney biopsies revealing various degrees of glomerular and vascular damage. Key findings included segmental glomerular sclerosis and arteriole lesions, which were more pronounced in patients with poor outcomes. The study, though limited by its small and retrospective design, underscores the importance of recognizing aHUS in postpartum RCN for better management and highlights the urgent need for noninvasive biomarkers to monitor disease progression and improve long-term prognosis.

kidney biopsy at Peking University First Hospital between 2014 and 2021, were included in the study. The diagnosis of RCN was made based on characteristic findings in unenhanced MRI and/or kidney pathology. The severity was categorized based on T2-weighted imaging, which can distinguish between severe and mild cases according to whether the cortical lesion area exceeds 50% or remains within 50%.

The decision regarding the choice of terminating pregnancy, conducting plasmapheresis, plasma infusion, and kidney replacement therapy was made at the discretion of the clinicians based on the diagnosis of aHUS. The clinicians primarily referred to platelet level (aiming for >100 × 10^9/L) and LDH concentration (aiming for <220 IU/L) to comprehensively determine whether the cessation of plasmapheresis was appropriate for the patients with aHUS. Patient follow-up was conducted either through our specialty clinic or via telephone interviews. The long-term kidney outcome was assessed based on the estimated glomerular filtration rate-based staging of chronic kidney disease (CKD) during follow-up, specifically at the last follow-up beyond 6 months.

Ethical approval for this study was obtained from the Ethics Committee of Peking University First Hospital (MR-11-23-021020). The Committee also waived the requirement for informed consent due to the retrospective design of the study and the use of anonymized patient data. This decision aligns with the regulations of Peking University First Hospital, which adhere to or surpass the ethical standards established by the Declaration of Helsinki.

Clinical and Laboratory Investigations

Clinical information was collected, including age, blood pressure, gestational weeks, past history of kidney or rheumatologic diseases, and obstetric complications (during pregnancy and postpartum). The pathologic pregnancies included pregnancy-induced stillborn, spontaneous abortion, HELLP (hemolysis, elevated liver enzymes and low platelets) syndrome, and preeclampsia. Laboratory data included hemoglobin level, platelet count, schistocyte count, serum levels of creatinine, LDH, complement 3 and complement 4, complement factor H, ADAMTS13 (A Disintegrin and Metalloproteinase with a Thrombospondin Type 1 Motif, Member 13) activity, and urinary protein. These data were collected both at the onset of the disease and the last follow-up. The characteristic MRI features of RCN included a lack of enhancement in the renal cortex accompanied by well-enhanced kidney medulla, as well as a complete absence of contrast excretion.[6,12]

Pathologic Evaluation

All biopsied kidney samples underwent standard processing techniques for immunofluorescence, light microscopy, and electron microscopy. Immunofluorescence staining of the kidney was conducted on frozen sections. The intensity of the staining signals for immunoglobulin (Ig) G, IgA, IgM, complement 3, complement 1q, albumin, and fibrinogen were semiquantitatively scored from 0-3. Formalin-fixed, paraffin-embedded samples were sectioned at 2-3 μm thickness and subjected to the following staining techniques for light microscopy observation: hematoxylin–eosin, periodic acid–silver methenamine, Masson's trichrome, and methenamine silver–Masson's trichrome. Two experienced pathologists independently reviewed and scored all slides. The findings are summarized in detail in Table S1. Electron microscopy was used to examine the ultramicroscopic structure, including the presence of glomerular basement membrane double contours, glomerular endothelial swelling, subendothelial expansion, and intracapillary cell infiltration in glomeruli.

Statistical Analyses

Statistical analyses were performed using SPSS version 16.0. Continuous data are expressed as mean ± standard deviation or median (25th, 75th percentiles) as appropriate. Categorical data are described as frequencies and percentages. Differences in quantitative parameters between groups were assessed using the t test, paired sample t test, Mann–Whitney U test, or Wilcoxon matched-pairs signed rank test. Differences in qualitative results were compared using the χ^2 test. A 2-sided P value < 0.05 was considered significant.

RESULTS

Clinical Characteristics

From 2014-2021, a total of 19 patients who underwent kidney biopsies at Peking University First Hospital were diagnosed with RCN, based on findings from MRI or

Table 1. Clinical Characteristics of Patients With Postpartum Renal Cortical Necrosis Classified According to Different Kidney Outcome

Clinical Parameters	Total	CKD 2-3 (n = 8)	CKD 4-5 (n = 4)	P
Age (y)	31.00 (3.64)	31.13 (3.80)	30.75 (3.86)	0.9
Course of disease[a] (mo)	1 (0.78, 1.75)	1 (0.78, 1.75)	1 (0.78, 2.50)	0.9[b]
Gestational week (wk)	35.5 (31.50, 39.50)	37.5 (31.75, 39.50)	33.5 (31.5, 40.00)	0.81[b]
Multiparous	5 (41.66%)	4 (50%)	1 (25%)	0.40[c]
Twin pregnancy	4 (33.33%)	4 (50%)	0	0.04[c,d]
Pathological pregnancy	9 (75%)	6 (75%)	3 (75%)	>0.99[c]
Stillborn	2 (16.67%)	2 (25%)	0	
Spontaneous abortion	1 (8.33%)	1 (12.5%)	0	
HELLP syndrome	2 (16.67%)	1 (12.5%)	1 (25%)	0.59[c]
Preeclampsia	6 (50%)	3 (37.5%)	3 (75%)	0.21[c]
Cesarean section	7(58.33%)	5 (62.5%)	2 (50%)	0.68[c]
Postpartum hemorrhage	8 (66.67%)	5 (62.5%)	3 (75%)	0.61[c]
Blood pressure (mm Hg)				
SBP	150.5 (26.01)	143.00 (22.11)	165.50 (29.83)	0.17
DBP	98.42 (26.06)	86.38 (10.11)	122.50 (33.03)	0.11
MAP	115.78 (25.08)	105.25 (13.64)	136.83 (31.39)	0.03[d]
Hypertension	8 (66.67%)	5 (62.5%)	3 (75%)	0.66[c]
Hemoglobin[e] (g/dL)	69.58 (17.95)	72.75 (17.68)	63.25 (19.28)	0.41
Hemoglobin[f] (g/dL)	87.33 (17.75)	88.74 (22.07)	84.50 (1.73)	0.24
Platelet count[e] (×10⁹/L)	67 (34.75, 116.25)	87.50 (36.25, 174.00)	50.50 (31.75, 92.5)	0.46[b]
Platelet count[f] (×10⁹/L)	214 (195.00, 288.75)	222 (155.00, 288.00)	199 (130.75, 216.25)	0.11[b]
Thrombocytopenia (n)	8 (66.67%)	5 (62.5%)	3 (75%)	0.66[c]
LDH[e] (U/L)	1,615.62 (772.07)	1,624.18 (862.91)	1,598.50 (669.07)	0.96
LDH[f] (U/L)	231.50 (65.01)	215.38 (70.54)	263.75 (42.52)	0.24
Schistocyte count[g] (%)	0.5 (0.10, 1.95)	0.2 (0, 0.45)	1.95 (1.05, 2.55)	0.02[b,d]
Serum creatinine (µmol/L)	408.15 (146.05)	342.56 (136.35)	539.32 (20.53)	0.02[d]
SUN (mmol/L)	14.12 (4.37)	12.69 (4.27)	16.98 (3.34)	0.11
Albumin (g/L)	39.18 (4.94)	40.36 (5.01)	36.80 (4.42)	0.26
C3[h] (g/L)	0.83 (0.28)	0.90 (0.28)	0.70 (0.26)	0.29
Low C3, n (%)	3 (25%)	1 (12.5%)	2 (50%)	0.17[c]
C4[h] (g/L)	0.25 (0.13)	0.26 (0.12)	0.22 (0.15)	0.60
Low C4, n (%)	3 (25%)	1 (12.5%)	2 (50%)	0.17[c]
Complement factor H[h] (µg/mL)	511.13 (106.32)	543.90 (93.22)	453.78 (115.79)	0.19
ADAMTS13 activity[h] (%)	78.45 (9.85)	81.43 (7.93)	73.25 (11.87)	0.20
Proteinuria (g/d)	1.74 (0.79)	1.97 (0.82)	1.29 (0.57)	0.17
ACR[h] (mg/g)	1,915.25 (1,041.60)	1,908.71 (875.01)	1,932.69 (1,656.57)	0.9
Anuria	9 (75%)			
Oliguria	3 (25%)			
Treatment				
Glucocorticoid	5 (41.67%)	2 (25%)	3 (75%)	0.09[c]
Plasmapheresis	10 (83.33%)	6 (75%)	4 (100%)	0.28[c]
Not done	2 (16.67%)	2 (25%)	0	
3-5 times	3 (25%)	2 (25%)	1 (25%)	
6-10 times	6 (50%)	4 (50%)	2 (50%)	
>10 times	1 (8.33%)	0	1 (25%)	
After kidney biopsy	6 (50%)	3 (37.5%)	3 (75%)	0.21[c]
Plasma infusion	5 (41.66%)	2 (25%)	3 (75%)	0.094
Kidney outcome				
Stage 2	4 (33.33%)			
Stage 3	4 (33.33%)			

(Continued)

Table 1 (Cont'd). Clinical Characteristics of Patients With Postpartum Renal Cortical Necrosis Classified According to Different Kidney Outcome

Clinical Parameters	Total	CKD 2-3 (n = 8)	CKD 4-5 (n = 4)	P
Stage 4	1 (8.33%)			
Stage 5	3 (25%)			

Note: Continuous data are expressed as mean (SD) or median (25th, 75th percentiles) as appropriate. Categorical data are expressed as n (%). CKD stage was evaluated beyond 6 months of follow-up.

Abbreviations: ACR, albumin-creatinine ratio; ADAMTS13, a disintegrin and metalloproteinase with thrombospondin type 1 repeats, member 13; C3, complement 3; C4, complement 4; CKD, chronic kidney disease; DBP, diastolic blood pressure; HELLP, hemolysis, elevated liver enzymes and low platelets; LDH, lactate dehydrogenase; MAP, mean arterial pressure; SBP, systolic blood pressure; SUN, serum urea nitrogen.

[a]Course from onset of anuria/oliguria to kidney biopsy.
[b]Mann–Whitney *U* test.
[c]χ^2 test.
[d]Statistically significant.
[e]Tested at the onset of the disease.
[f]Tested on kidney biopsy.
[g]Based on 7 patients having results of schistocyte count.
[h]Missing data in 1 patient.

kidney pathology. The incidence of RCN among inpatients at the kidney pathology center during this period was 1.96% of 9,697 patients. Of the total RCN cases, 14 (73.68%) patients with postpartum RCN. However, only 12 patients with satisfactory kidney biopsy slides suitable for further investigation were included in this study. These patients were women with an average age of 31.00 ± 3.64 years and no history of kidney, rheumatic, or other systemic diseases.

High-risk factors during pregnancy included having twins (4 [33.33%] patients), preeclampsia (6 [50%]), HELLP syndrome (2 [16.7%]), and a history of abortions (1 [8.33%]). The pregnancies were terminated at various gestation weeks, with a median of 35.5 weeks. The gestational week of 6 patients was >37 weeks (37-41 weeks). With the exception of 1 patient who experienced the onset of AKI during the seventh week of pregnancy, the remaining 5 patients delivered at a median gestational age of 31 weeks. In patients who exhibited preeclampsia or HELLP syndrome before delivery, the pregnancies were terminated on diagnosis. During delivery, 8 (66.67%) patients experienced postpartum hemorrhage, with blood loss ranging from 600 to 6,000 mL. Clinically, all patients presented with symptoms indicative of a probable diagnosis of aHUS[13] and stage 3 AKI necessitating kidney replacement therapy. The median time between delivery and referral to our hospital was 11.63 days, with a range from 1-60 days. The time between delivery and kidney biopsy varied widely, from 18 days to 4 months. Further clinical data can be found in Table S2.

Thrombocytopenia was observed in 8 (66.67%) patients, while 3 (25%) patients showed schistocyte levels of >1.5%. Among the patients, 3 experienced oliguria (patients 2, 8, and 11), while others had anuria throughout the course. The mean daily proteinuria was 1.74 ± 0.79 g (range, 0.5-2.94 g). Three (25%) patients exhibited decreased serum complement 3 and/or complement 4 levels. However, the levels of complement factor H and ADAMTS13 activity were within normal ranges for all patients. Unenhanced MRI examinations

were conducted for all patients, with 6 (50%) patients showing focal RCN based on typical MRI findings of diffuse RCN. Further clinical data can be found in Table S2, and a summary is provided in Table 1.

The patients were treated with supportive strategies, including 5 (41.66%) plasma infusion, 10 (83.33%) plasmapheresis (from 3-17 times, totaling 14,000-34,500 mL in 9 patients with detailed information; Table S2), and kidney replacement therapy. Some of these patients were initially treated at local hospitals where plasmapheresis was unavailable, and they received plasma infusion. Glucocorticoid was prescribed for 5 (41.66%) patients based on the clinician's recommendation based on pathologic findings. The duration from the onset of oliguria or anuria to kidney biopsy varied from 18 days to 4 months, depending on when their condition stabilized. At the time of biopsy, both hemoglobin and platelet count had significantly increased to 87.33 ± 17.75 g/L (range, 69-137; P = 0.02) and 214×10^9/L (range, 111-409; P = 0.002), respectively. There was a significant decrease in LDH levels to 231.50 ± 65.01 U/L (P < 0.001) (Table 1).

Pathologic Findings

Nine (75%) patients exhibited some degree of coagulative necrosis in their glomeruli and/or tubules. In 3 (25%) patients, the coagulative necrosis was extensive, involving >50% of the cortical area. In the remaining 6 patients, the damaged lesion was localized, affecting <25% of the area (Fig 1A and B). Three cases did not display typical coagulative necrosis and were diagnosed with focal RCN based on MRI findings. In addition to the pathologic findings of coagulative necrosis, all patients had ischemic tubular necrosis (Fig 1C).

On average, approximately 15.71% of glomeruli displayed global ischemia (Fig 1D). Segmental sclerosis was also prevalent, affecting 2.86%-25.58% of the total glomeruli, with a median of 11.81%. Among these, 7 (58.33%) cases exhibited multilayer podocyte hypercellularity around the sclerotic segments (Fig 2A and B). In the remaining 5 cases, the sclerotic segments were capped with monolayer podocytes (Fig 2D). At the glomerular
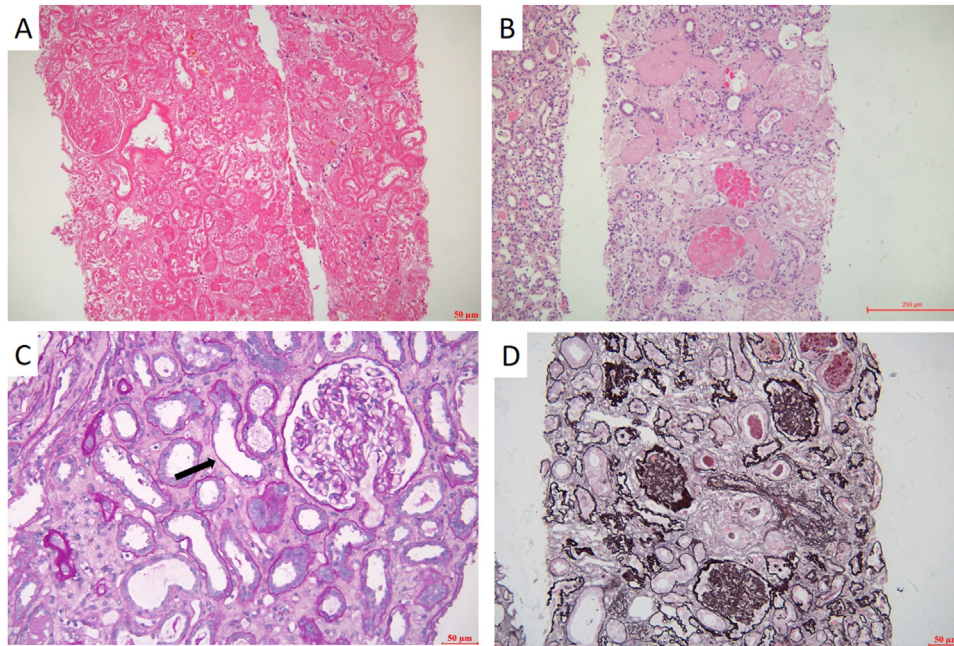
Figure 1. Ischemic lesions of postpartum renal cortical necrosis. (A-B) Diffuse (A) and patchy (B) coagulative necrosis of kidney cortex (HE, ×100, scale bar = 50 μm and 250 μm). (C) Tubular epithelial cell simplification and naked basement membrane (arrow) (PAS, ×200, scale bar = 50 μm). (D) Ischemic glomerular sclerosis (PASM, ×100, scale bar = 50 μm). HE, hematoxylin–eosin; PAS, periodic acid–silver methenamine; PASM, methenamine silver–Masson's trichrome.

level, 52 (12%) of the total glomeruli displayed segmental sclerotic lesions: 10 (2.30%) had collapsing lesions, 10 (2.30%) had cellular lesions, 5 (1.15%) had tip lesions (Fig 2A-C), and the other 27 (6.21%) lesions were classified as not otherwise specified (Fig 2D). No perihilar lesions were identified in any of these cases. Using the Columbia classification system of focal segmental glomerulosclerosis (FSGS), the not otherwise specified variant was found in 5 (41.67%) patients, the collapsing variant in 4 (33.33%), the cellular variant in 2 (16.67%), and the tip variant in 1 (8.33%) patient. Compared to patients with non-collapsing variants, those with the collapsing variant had significantly more segmental sclerosis (19.17 ± 5.35% vs 7.47 ± 4.98%; P = 0.004), but the difference in the extent of necrotic glomeruli was not statistically significant (4.07 ± 8.14% vs 31.70 ± 35.63%; P = 0.07) (Table 2). Segmental glomerular basement membrane double contours were found in 4 (33.33%) cases (Fig 2E), while arteriole occlusion was detected in 10 (83.33%) cases (Fig 3F). In contrast to the necrosis and chronic injuries, active lesions were commonly present. These included segmental endocapillary hypercellularity in 6 (50%) cases (Fig 2B), mesangiolysis in 6 (50%) cases (Fig 2B and F), thrombosis of glomerular capillaries in 5 (41.67%) cases (Fig 3A and B), arteriole endothelial proliferation in 10 (83.33%) cases (Fig 3C and D), and intimal edema in 8 (66.67%) cases (Fig 3E). Additionally, arteriole fibrin thrombosis was seen in 3 (25%) patients (Fig 3B).

Immunofluorescence examination revealed that 3 (25%) patients exhibited moderate to strong IgA staining, while 8 (66.67%) patients displayed nonspecific weak IgM staining in the mesangial area of the glomeruli. Under electron microscopy observation, no glomeruli were found in the specimens of 2 patients (patients 4 and 5), and ischemic glomeruli were the only findings in 1 patient (patient 1). In the other 9 specimens, subendothelial expansion was evident (Fig 4A and B). Diffuse foot process effacement was seen in 2 patients. Furthermore, foot process deletion was identified in 3 patients in the CKD 4-5 subgroup (Fig 4C).

Based on the observations from light microscopy of the kidney pathology, only 3 patients were identified as belonging to the severe group. This finding was in contrast to the results based on T2-weighted imaging, which assigned 6 patients to the severe group.

Follow-up and Factors Influencing Kidney Outcomes

All 12 patients had available clinical follow-up data. During the follow-up period, 4 patients exhibited advanced kidney dysfunction, progressing to CKD stages 4-5. Compared to the remaining 8 who experienced better kidney recovery, reaching CKD stages 2-3, the 4 patients with advanced dysfunction demonstrated significantly higher schistocyte counts (P = 0.02), baseline serum creatinine (P = 0.02), and mean arterial pressure (P = 0.03), but there were fewer cases of twin pregnancy among them (P = 0.04) (Table 1, Table S2).

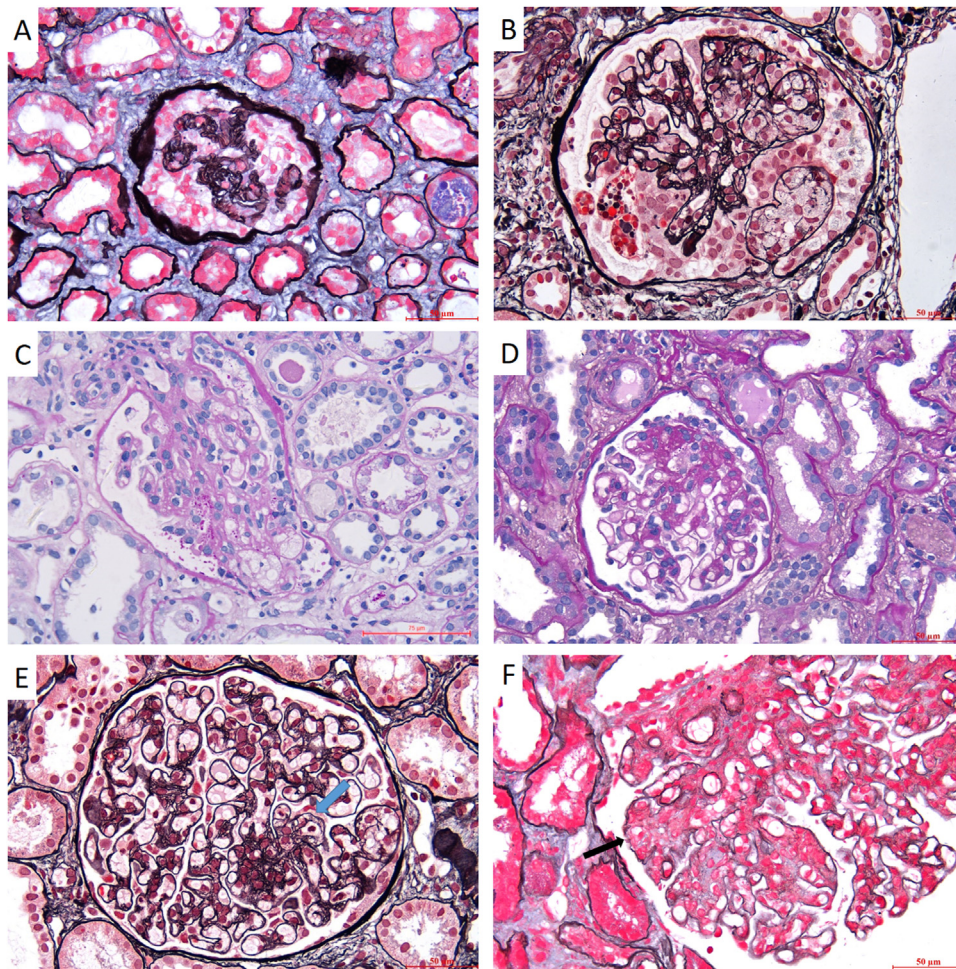Notably, the group with more severe kidney dysfunction had a higher incidence of glomerular coagulative

Figure 2. Examples of non-necrotic glomerular histopathology of postpartum renal cortical necrosis. (A) Multilayer podocyte hypercellularity with collapsed capillary loops (PASM, ×400, scale bar = 50 μm). (B) Multilayer podocyte hypercellularity, segmental endothelial proliferation, and swelling. Segmental mesangiolysis can be seen (PASM, ×400, scale bar = 50 μm). (C) Segmental sclerosis containing endocapillary foam cells and forming an adhesion to Bowman's capsule at the origin of the tubular pole (PAS, ×400, scale bar = 75 μm). (D) Segmental obliteration of the glomerular tuft by increased matrix and with capped podocytes at a non-determined location (PAS, ×400, scale bar = 50 μm). (E) Segmental duplication of glomerular basement membranes (blue arrow) and segmental endocapillary hypercellularity (PASM, ×400, scale bar = 50 μm). (F) Mesangial cell proliferation and segmental mesangiolysis (black arrow) (PASM, ×400, scale bar = 50 μm). PAS, periodic acid–silver methenamine; PASM, methenamine silver–Masson's trichrome.

necrosis (P = 0.004), thrombosis of glomerular capillaries (P = 0.001), and a more extensive area of diffuse total cortical coagulative necrosis (P = 0.007). Their pathology also revealed more severe arteriole/artery damage, characterized by increased interlobular arteriole intimal edema (P = 0.04) and fibrin thrombosis (P = 0.003). Furthermore, they showed a greater prevalence of the cellular variant of FSGS (P = 0.04). In contrast, this group had a lower number of structurally normal glomeruli (P = 0.047), a reduced occurrence of segmental sclerosis (P = 0.001), and less pronounced podocyte hypercellularity (P = 0.001). On the other hand, patients presenting with the collapsing variant of FSGS tended to have improved kidney function, recovering to CKD stages 2-3 (P = 0.125).

DISCUSSION

Postpartum RCN is a rare but underrecognized condition that is currently being reported as an identifiable cause of postpartum AKI, which is still an important cause for maternal new-onset CKD. Previously, RCN was commonly found in early pregnancy associated with septic abortion; however, RCN occurring in late pregnancy now accounts for the majority of reported RCN cases.[8,14] Based on the literature, aHUS is frequently considered the cause of non-obstetric RCN, whereas all pregnant women in our case series were clinically diagnosed with aHUS, which distinguishes them from previously reported cases.[1]

Histological examination of postpartum RCN may typically reveal patchy or diffuse coagulative necrosis involving tubular segments and glomeruli and ischemic

Table 2. Pathological Findings of Patients With Postpartum Renal Cortical Necrosis Classified According to Different Kidney Outcome (CKD Stage Evaluated at the Last Follow-up Beyond 6 Months)

Pathological Parameters	Total (n = 12)	CKD 2-3 (n = 8)	CKD 4-5 (n = 4)	P
Light microscopy				
Number of total glomeruli	29 (20, 44.8)	23 (18.5, 43.8)	45 (23.8, 63)	0.37[a]
Glomeruli with ischemic sclerosis (%)	15.7 (2.5, 50.3)	13.6 (2.5, 50.3)	17.8 (4.4, 65)	0.9[a]
Glomeruli with segmental sclerosis (%)	11.8 (4.6, 16.8)	14.5 (11.5, 20.0)	3.7 (2.9, 4.9)	0.004[a,b]
Number of cases with FSGS subtypes				0.04[b,c]
NOS	5	3	2	
Collapsing variant	4	4	0	
Cellular variant	2	0	2	
Tip variant	1	1	0	
Total number of glomeruli with FSGS lesions of the group (total number of glomeruli of the group)	52 (435)	46 (266)	6 (169)	
NOS lesions	27	23	4	
Collapsing lesions	10	10	0	
Tip lesions	5	5	0	
Cellular lesions	10	8	2	
Podocyte hypercellularity				0.001[b,c]
Monolayer (capping)	5 (41.7%)	1 (12.5%)	4 (100%)	
Multilayer	7 (58.3%)	7 (87.5%)	0	
Glomerular coagulative necrosis (%)	3.6 (0, 56.0)	0 (0, 4.3)	73.9 (36.4, 78.5)	0.004[a,b]
Non-sclerotic non-necrosis glomeruli (%)	45.3 (25.2, 69.5)	68.2 (35.4, 79.6)	23.2 (12.3, 44.1)	0.048[a,b]
Segmental endocapillary hypercellularity	6 (50%)	4 (50%)	2 (50%)	0.9[c]
Double contour of GBM	4 (33.3%)	3 (37.5%)	1 (25%)	0.66[c]
Mesangial cell proliferation (>3 cells)	6 (50%)	5 (62.5%)	1 (25%)	0.21[c]
Mesangiolysis	6 (50%)	3 (42.9%)	3 (75%)	0.21[c]
Thrombosis of glomerular capillaries	5 (41.7%)	1 (12.5%)	4 (100%)	0.001[b,c]
Scores of coagulative necrosis based on total cortical area involved				0.02[a,b] 0.01[b,c]
0	3 (25%)	3 (37.5%)	0	
1 (<25%)	6 (50%)	5 (62.5%)	1 (25%)	
2 (25-50%)	0	0	0	
3 (>50%)	3 (25%)	0	3 (75%)	
Scores of tubular atrophy based on area involved				0.12[c]
0	4 (33.3%)	2 (25%)	2 (50%)	
1 (<25%)	4 (33.3%)	4 (50%)	0	
2 (25-50%)	4 (33.3%)	2 (25%)	2 (50%)	
3 (>50%)	0	0	0	
Scores of interstitial inflammation based on area involved				0.9[c]
0	0	0	0	
1 (<25%)	9 (75%)	6 (75%)	3 (75%)	
2 (25-50%)	3 (25%)	2 (25%)	1 (25%)	
3 (>50%)	0	0	0	
Scores of interstitial fibrosis based on area involved				0.9[c]
0	3 (25%)	2 (25%)	1 (25%)	
1 (<25%)	6 (50%)	4 (50%)	2 (50%)	
2 (25-50%)	3 (25%)	2 (25%)	1 (25%)	
3 (>50%)	0	0	0	
Interlobular arteriole				
Media thickening	11 (91.7%)	7 (87.5%)	4 (100%)	0.36[c]
Endothelial proliferation	10 (83.3%)	6 (75%)	4 (100%)	0.18[c]
Intimal edema	8 (66.7%)	4 (50%)	4 (100%)	0.04[b,c]
Onion skin lesions	2 (16.7%)	1 (12.5%)	1 (25%)	0.59[c]
Fibrin thrombosis	3 (25%)	0	3 (75%)	0.003[b,c]
Arteriosclerosis	4 (33.3%)	2 (25%)	2 (50%)	0.39[c]

(Continued)

Table 2 (Cont'd). Pathological Findings of Patients With Postpartum Renal Cortical Necrosis Classified According to Different Kidney Outcome (CKD Stage Evaluated at the Last Follow-up Beyond 6 Months)

Pathological Parameters	Total (n = 12)	CKD 2-3 (n = 8)	CKD 4-5 (n = 4)	P
Hyalinosis	1 (8.3%)	1 (12.5%)	0	0.36[c]
Occlusion	10 (83.3%)	6 (75%)	4 (100%)	0.18[c]
Arcuate artery (n = 6)				
Media thickening	5 (41.7%)	2 (25%)	3 (75%)	0.17[c]
Endothelial proliferation	5 (71.4%)	3 (75%)	2 (66.7%)	0.81[c]
Intimal edema	6 (50%)	3 (37.5%)	3 (75%)	0.38[c]
Arteriosclerosis	3 (42.9%)	2 (50%)	1 (33.3%)	0.66[c]
Electron microscopy				
Number of glomeruli (range)	1.5 (0-5)	1 (0-5)	3 (0-5)	0.67[a]
Subendothelial expansion (n = 10)	9 (90%)	7 (100%)	2 (66.7%)	0.10[c]
Foot process (n = 10)				0.002[b,c]
Segmental effacement (n = 10)	5 (50%)	5 (71.4%)	0	
Diffuse effacement (n = 10)	2 (20%)	2 (28.6%)	0	
Deletion (n = 10)	3 (30%)	0	3 (100%)	

Note: Continuous data are expressed as median (25th, 75th percentiles). Categorical data are expressed as n (%).
Abbreviations: CKD, chronic kidney disease; FSGS, focal segmental sclerosis; GBM, glomerular basement membrane; NOS, not otherwise specified.
[a]Mann–Whitney *U* test.
[b]Statistically significant.
[c]χ² test.

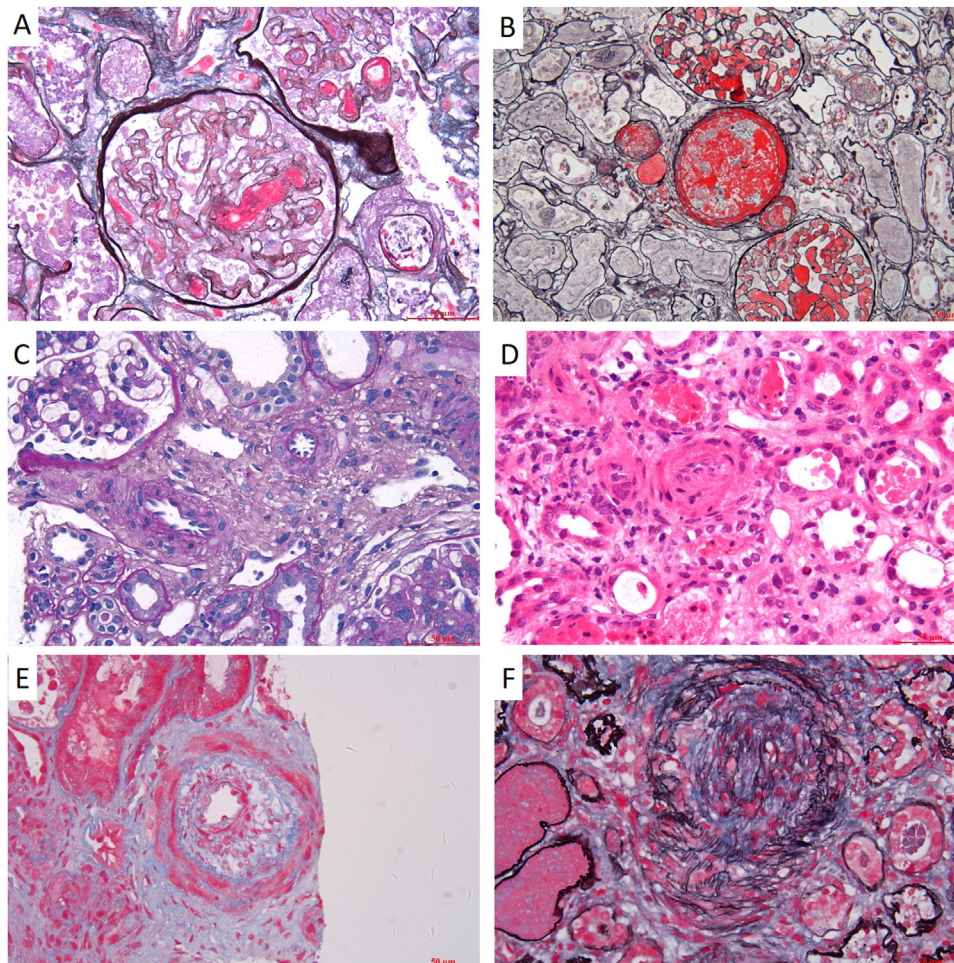**Figure 3.** Capillary and vascular lesions of postpartum renal cortical necrosis. (A, B) Glomerular and arteriolar fibrin thrombi (A: PASM, ×400; B: PASM, ×200; scale bar = 50 μm). (C, D) Arteriolar endothelial proliferation (C: PAS, ×400; D: HE, ×400; scale bar = 50 μm). (E) Arteriolar intimal edema (Masson, ×400; scale bar = 50 μm). (F) Arteriolar concentric thickening and myoendothelial cells proliferation, leading to occlusion of the lumen (PASM, ×400, scale bar = 50 μm). Masson, Masson's trichrome; PAS, periodic acid–silver methenamine; PASM, methenamine silver–Masson's trichrome.
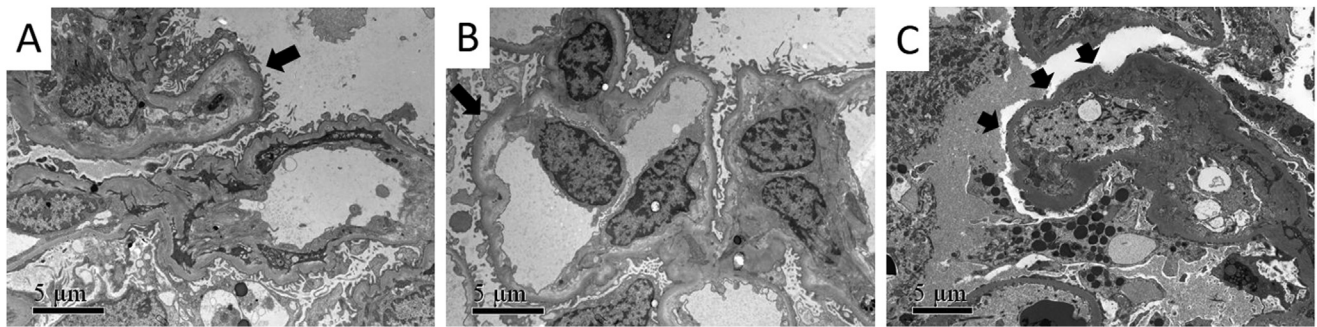
Figure 4. Ultrastructural features of postpartum renal cortical necrosis. (A-B) Subendothelial expansion (arrows) and endothelial proliferation with luminal narrowing (B) (×6000, scale bar = 5 μm). (C) Foot process deletion (arrows) (×5000, scale bar = 5 μm).

changes in the kidney cortex, including glomerular ischemia, kidney tubular necrosis, and interstitial inflammation. Thrombi may sometimes be present in vessels at the edge of the infarct lesion.[9] The results of our study suggest that active lesions of aHUS, such as active arteriolar and vascular endothelial injuries (eg, segmental endocapillary hypercellularity, mesangiolysis, glomerular capillary thrombosis, arteriole endothelial proliferation, intimal edema, and arteriolar fibrin thrombosis), are easily observed. These pathological features might be detected even during the early remission phase of aHUS even though platelet count and LDH levels had returned to normal at the time of biopsy.

In our study, features such as ischemic sclerosis and FSGS were common. These pathological findings collectively point toward the role of persistent ischemia resulting from endothelial cell dysfunction in aHUS. There is known to be crosstalk between vascular endothelial cells and glomerular podocytes in the kidneys. Featured endothelial cell dysfunction can lead to alterations in the structure and function of podocytes and the glomerular filtration barrier,[15-17] aggravating kidney injury and contributing to the development of proteinuria in postpartum RCN[2,18-23]; however, unlike a thrombotic microangiopathy case series reported by Buob et al[24] in which the collapsing variant was the predominant subtype (35.8%), in our cases, the not otherwise specified variant was more prevalent. This difference in FSGS subtypes might be partly explained by the racial diversity between the White and Asian cohorts. The variations of FSGS were also determined by the stages of aHUS among these cases. This warrants further research exploring the underlying mechanism.

A comparison between patients with different kidney outcomes has provided valuable insights for making therapeutic decisions. Beyond clinical factors, such as schistocyte count, there were more pronounced pathological features that enabled the distinction of patients with poor kidney outcomes. These included easily identifiable glomerular/total cortical coagulative necrosis and glomerular capillary thrombosis, and more arteriole/artery lesion involvement such as interlobular arteriole intimal edema and fibrin thrombosis. Additionally, electron microscopy identified foot process effacement, which was significantly associated with poor kidney outcomes. This supports the notion that irreversible podocyte injury may ultimately lead to nephron loss and unfavorable outcomes, as suggested by previous studies.[14,25] However, contrary to the previous understanding, neither tubular atrophy nor interstitial fibrosis, recognized as influential factors in predicting CKD,[26,27] were found to be significantly different between the groups with CKD stage 2-3 and those with CKD stage 4-5 among our patients with postpartum RCN.

Over 20 years ago, postpartum RCN was considered a life-threatening condition occurring in approximately 20% of patients with pregnancy-related AKI.[25,28] However, recent reports have shown a significant reduction in hospitalization mortality, ranging from 0%-23.8%. This is a significant improvement compared to the mortality rates of 60%-80% observed in the early years.[1,4,5,8,14,24,25,28] Despite this decrease in mortality, kidney outcomes still appear to be poor. A previous study by Frimat et al[3] reported that 39% of patients progressed to kidney failure with replacement therapy within 12-55 months of follow-up. In the current study, 20% of the patients progressed to kidney failure with replacement therapy, while the others remained at CKD stage 3-4, and none of them fully recovered to their baseline kidney function before pregnancy. These findings indicate that postpartum RCN continues to pose a significant risk to the health of young women, despite advancements in diagnostic and treatment methods.

In our study, we did not find any difference in the plasmapheresis times and total plasma volume with kidney outcomes, which is consistent with the results of Bhaduria et al,[4] who found no significant difference between patients with and without plasmapheresis. However, the small sample size in this study limits the ability to fully explore the intricacies of plasmapheresis and its role in remission of aHUS. Considering the nature of postpartum RCN as a special type of aHUS, it suggests that terminating therapeutic strategies such as plasmapheresis or fresh frozen plasma infusion once normal platelet and LDH levels are reached may not ensure sufficient therapeutic

efficacy. Further research is necessary to elucidate these aspects. Both clinical and pathological indicators are crucial for guiding treatment decisions and evaluating their effectiveness. It is important to mention that none of the patients in our study received complement-specific biotherapies, such as eculizumab, which has been demonstrated to enhance outcomes in aHUS.[29,30] With the growing understanding of the role of complement activation in the pathogenesis of postpartum RCN, the potential benefits of complement inhibition therapy could lead to improved patient outcomes.

Some previous studies have investigated the role of noninvasive MRI, which can assist in early diagnosis and overall assessment of RCN.[31] In our study, the results based on MRI clearly provided a more accurate assessment of the severity of RCN lesions than those based on pathologic findings, consistent with previous research.[6] The discrepancy highlights the varying sensitivity and specificity of different diagnostic modalities in evaluating the severity of postpartum RCN. However, kidney pathology provides insight into detailed cellular and structural information in postpartum RCN. This underscores the importance of a multimodal diagnostic approach to achieve a more comprehensive understanding of the disease state. Nonetheless, our findings underscore the significance of kidney biopsy in the management of patients with postpartum RCN. However, it is essential to recognize the limitations inherent in this study. The small sample size in this study limits the ability to fully explore the intricacies of plasmapheresis and its role in the remission of aHUS. Further research is necessary to elucidate these aspects.

In conclusion, we identified key pathological features in postpartum RCN patients with aHUS, highlighting the necessity for more effective therapeutic options. There is a clear demand for noninvasive biomarkers that can accurately track disease progression and inform treatment duration. Future studies should concentrate on crafting treatment strategies aimed at improving patient prognosis and long-term health outcomes for those with postpartum RCN.

SUPPLEMENTARY MATERIALS

Supplementary File (PDF)

Table S1: Definition of Light Microscopic Pathological Findings.

Table S2: Clinical Characteristics of the 12 Patients with Postpartum Renal Cortical Necrosis.

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