Postpartum Hemolytic Uremic Syndrome

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Clinical Scenario:

These are representative images of a kidney biopsy from a 20-year-old female patient, primigravida, who presented with acute kidney injury following childbirth. Prenatal and past history were unremarkable.

The biopsy sample was adequate with both cortex and medulla. Upto 28 glomeruli were included. The majority of glomeruli were abnormal. Only a few unremarkable glomeruli were found. Some of the representative glomeruli with pathologic lesions are shown in the following images.

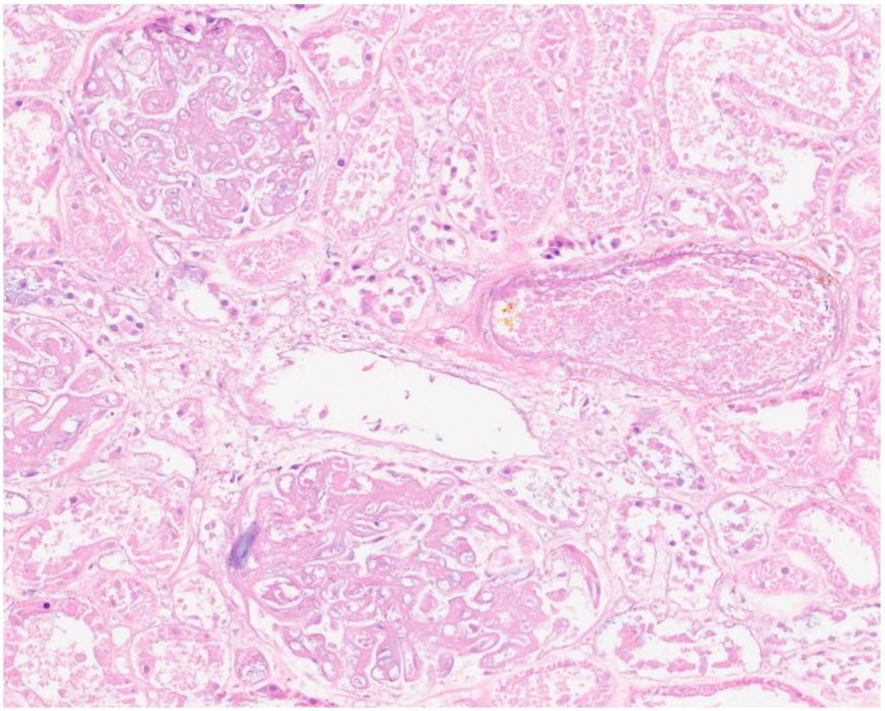

Figure 1. A medium-power view of kidney biopsy from the above case shows two glomeruli, one small artery, vein and many tubules. The lumen of the artery is filled with pink, granular to fibrillary material. All components of the kidney parenchyma are necrotic and devoid of nuclei, consistent with cortical necrosis. (H&E stain, × 200).

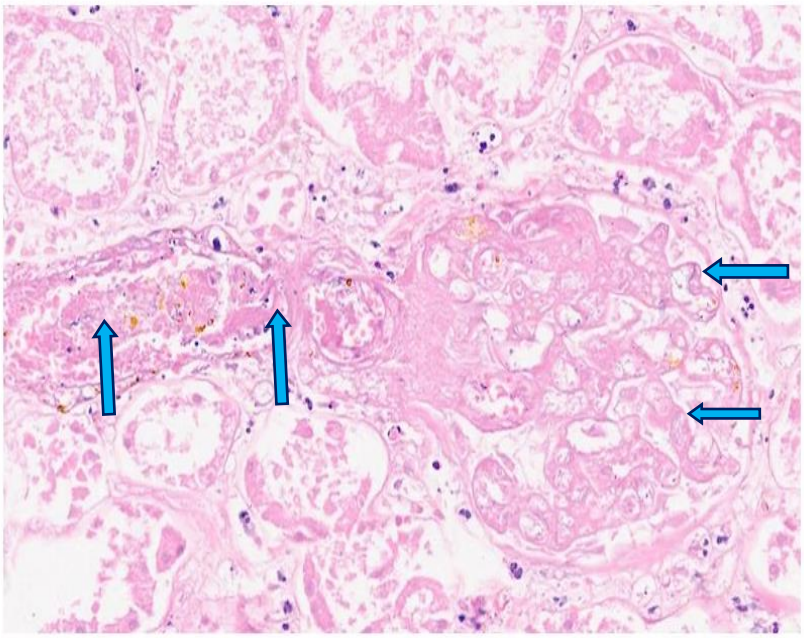

Figure 2. A high-power view of another glomerulus from the same biopsy. The glomerulus is completely necrotic and anucleate. Some capillary walls are thickened and appear double-contoured (horizontal arrows). IN addition, an arteriole can be seen at 9' O clock position filled with fibrin thrombus in the lumen (vertical arrows) (H&E stain, × 200).

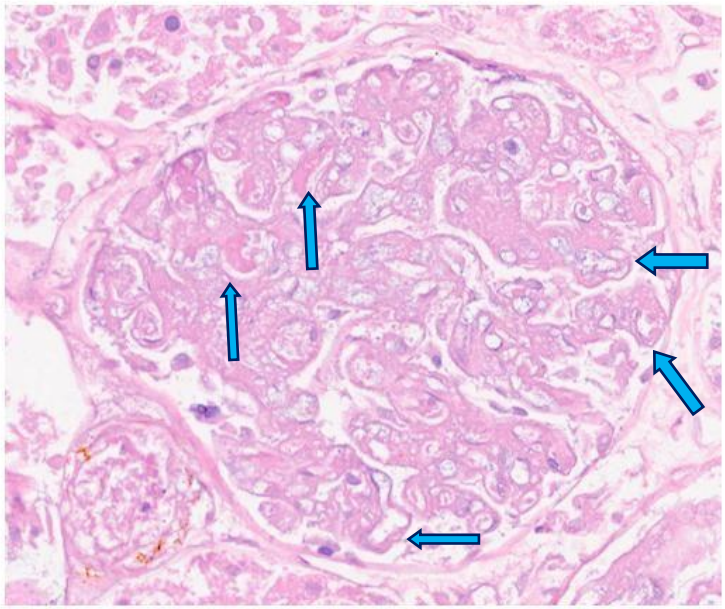

Figure 3. A high-power view of another glomerulus from the same kidney biopsy from the above case shows loss of cell nuclei signifying necrosis. Many of the capillary walls are thickened and double-contoured (horizontal arrows). In addition, two capillaries show fibrin thrombi in their lumena (vertical arrows). (H&E, × 400).

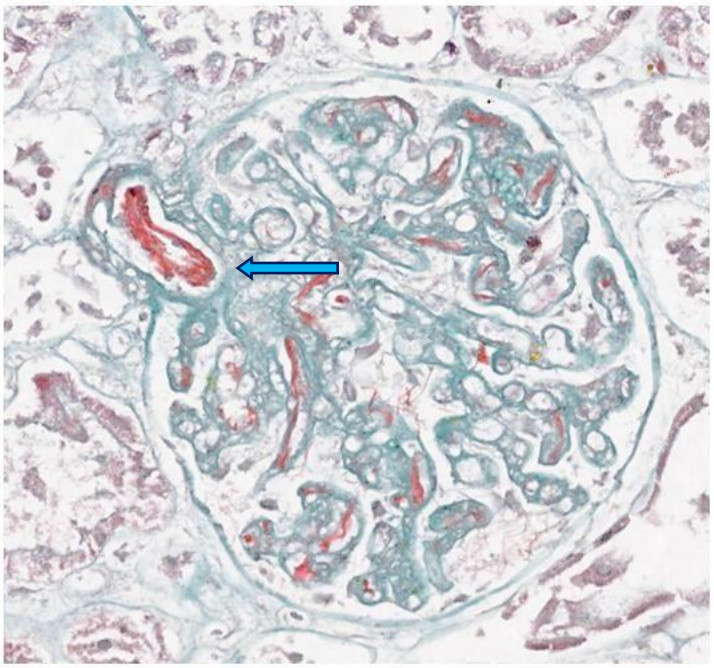

Figure 4. A high-power view of another glomerulus from the same kidney biopsy from the above case, showing complete necrosis, widespread thickening and reduplication of glomerular basement membranes, and fibrin thrombi (staining red in colour) in arteriole at the vascular pole of the glomerulus (arrow), and in glomerular capillaries. (Trichrome stain, × 400).

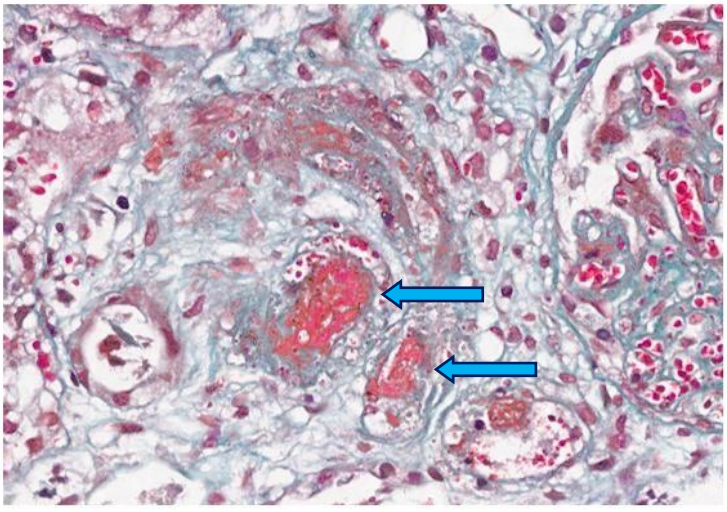

Figure 5. A high-power view of the same kidney biopsy from the above case showing part of a glomerulus with congested capillaries and three adjacent arterioles. The lumena of two arterioles are filled with fibrin thrombi (staining red in colour). (Trichrome stain, × 400).

Questions

Q1. Given the clinical scenario and the morphologic lesions shown in above images, what is the pathologic diagnosis?
Q2. What is the pathogenesis of this particular form of vasculopathy?
Q3. What are the main pathological features of pHUS on kidney biopsy?

Answers:

Answer 1. The pathological diagnosis in this case is that of extensive cortical infarction, most probably secondary to postpartum hemolytic uremic syndrome (pHUS). pHUS is defined as a thrombotic microangiopathy (TMA) typically following a normal delivery after a variable symptom-free interval (mean 26.6±35 days). It usually occurs in primigravida with a mean age of 27.0±6 years, and preeclampsia is historically associated with the disease. The involvement of extrarenal vascular beds in PHUS is typically rare in this condition.

Answer 2. The exact pathogenesis of pHUS is still not completely understood. The currently available evidence suggests that the condition is predominantly driven by the dysregulation of the alternative complement pathway (the first hit), where the physiological stress of pregnancy and the postpartum state act as a "second hit" in genetically susceptible individuals.

Answer 3. The pathologic hallmark of pHUS is TMA predominantly affecting the renal microvasculature. The morphological changes can be categorized into acute and chronic types, or a mixture of both (as in this case), depending on the duration and severity of the disease prior to biopsy. In the acute stage, the glomeruli exhibit characteristic features of endothelial injury. The glomerular capillary walls are thickened due to endothelial cell swelling (endotheliosis) and the subendothelial accumulation of fluffy, acellular material. Mesangiolysis, the dissolution of the mesangial matrix, is frequently observed, leading to capillary microaneurysm formation. Fibrin thrombi are present within the glomerular capillary lumens and the afferent arterioles, often entrapping fragmented red blood cells (schistocytes). Arterioles may demonstrate fibrinoid necrosis and severe intimal edema, which can completely occlude the vascular lumen. In severe cases, extensive microvascular thrombosis can lead to ischemic changes, tubular necrosis, and even irreversible renal cortical necrosis, as seen in this case, which is a known poor prognostic factor.

In the chronic stage, the glomeruli show remodeling secondary to protracted endothelial injury. This is characterized by the duplication of the glomerular basement membranes (GBMs), creating a "double contour" or tram-track appearance on silver or PAS stains. The arterioles and small arteries develop concentric myointimal hyperplasia and fibrosis, resulting in a classic "onion-skin" appearance that narrows the vascular lumen and causes downstream ischemic tubular atrophy and interstitial fibrosis.

The histopathological pattern of TMA is not entirely specific to pHUS; it represents a morphological endpoint of severe endothelial injury. Therefore, the pathologist must interpret the biopsy in conjunction with the clinical history and laboratory data. The primary differential diagnoses in the postpartum period include thrombotic thrombocytopenic purpura (TTP), HELLP (Hemolysis, Elevated Liver enzymes, and Low Platelets) syndrome, and severe preeclampsia.

While TTP and pHUS share identical renal histological features of TMA, TTP is driven by a severe deficiency of ADAMTS13 (activity <10%) and typically presents with more profound thrombocytopenia and neurological symptoms, with less severe renal impairment. Conversely, pHUS is characterized by normal or slightly reduced ADAMTS13 activity and prominent, often anuric, acute kidney injury. HELLP syndrome and preeclampsia can also cause endothelial injury (glomerular endotheliosis); however, true occlusive microthrombi and severe arteriolar fibrinoid necrosis are less common in preeclampsia unless complicated by disseminated intravascular coagulation (DIC) or concurrent atypical HUS (aHUS). Furthermore, HELLP syndrome typically resolves rapidly following delivery, whereas pHUS progresses relentlessly in the postpartum period without specific complement-blocking therapy.

Further reading:

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