Kidney Biopsy in Hypertension-Induced Thrombotic Microangiopathy (HTN-TMA)

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Clinical scenario:

A 52-year-old man with a 15-year history of poorly controlled hypertension presents to the emergency department with a sudden onset of severe headache, blurring of vision, and shortness of breath. On examination, his blood pressure is 240/135 mmHg, and he appears acutely ill. Fundus examination reveals bilateral papilledema with flame-shaped hemorrhages and cotton-wool spots, consistent with hypertensive retinopathy grade IV.

Laboratory investigations show serum creatinine of 3.5 mg/dL (baseline 1.2 mg/dL six months prior), elevated urea, and microscopic hematuria with mild proteinuria. Hematology demonstrates microangiopathic hemolytic anemia with schistocytes and thrombocytopenia. Urinalysis reveals red blood cell casts.

A renal biopsy is performed. Representative images of the renal biopsy stained by a number of stains are provided below:

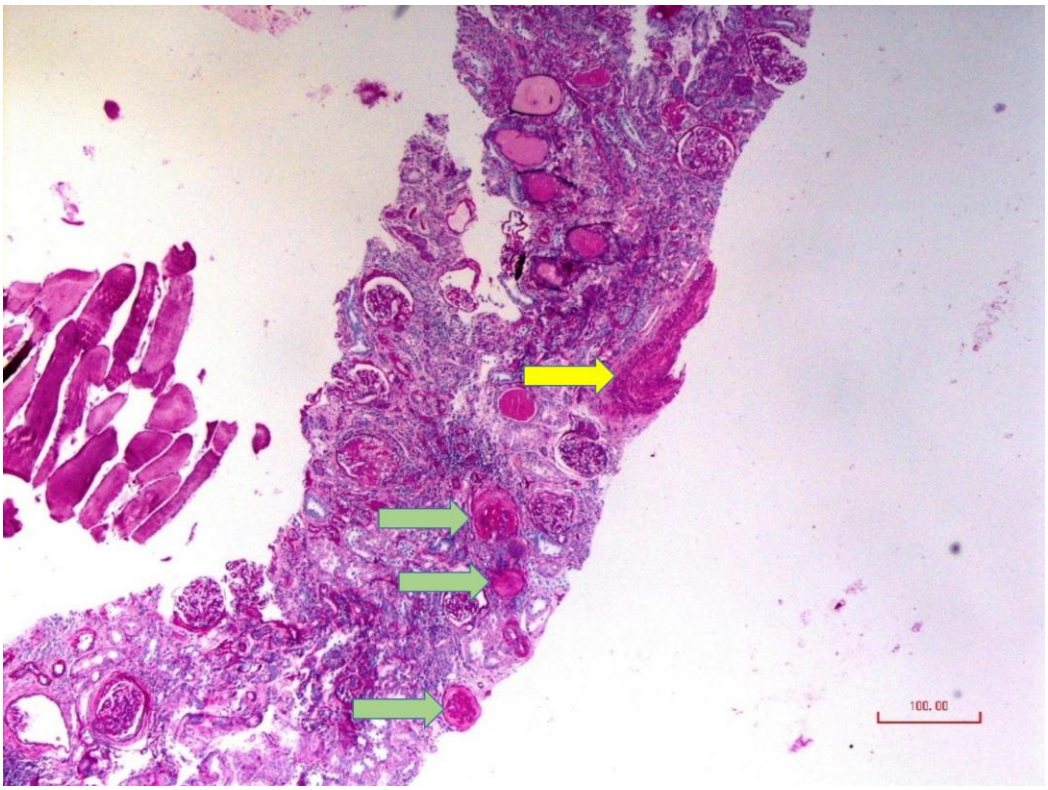

Figure 1. Low-power view showing renal cortex with many glomeruli and an interlobular-sized artery. The background parenchyma shows moderate chronic changes (PAS, ×40).

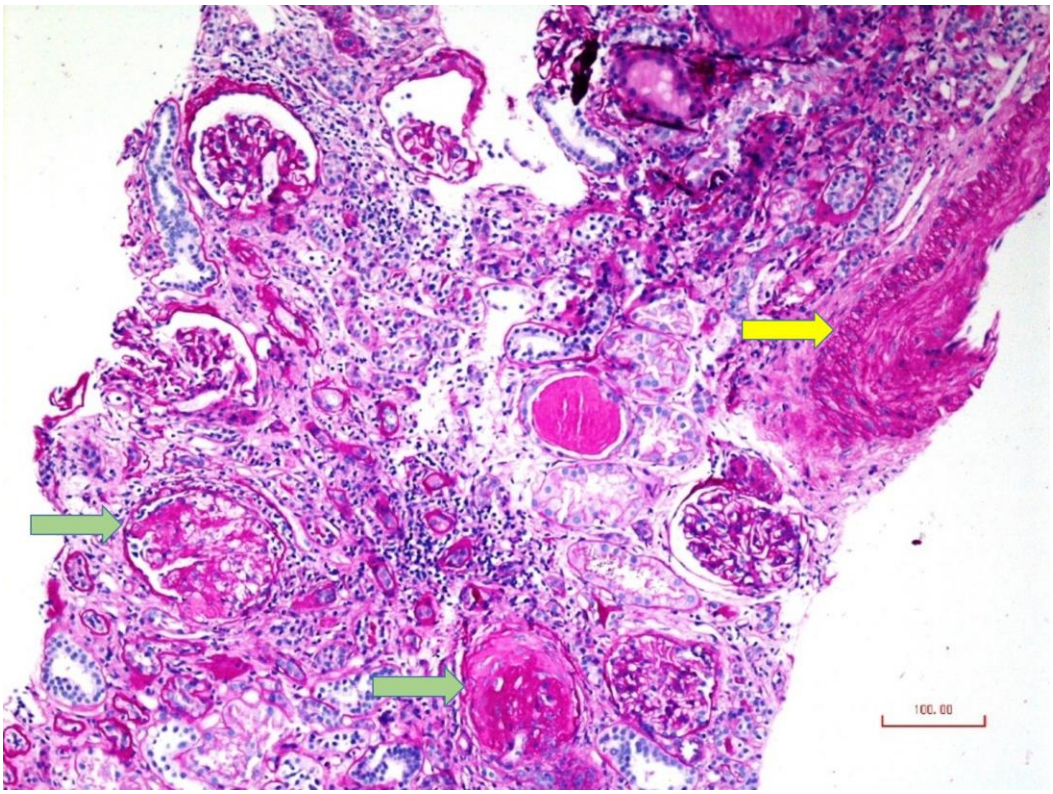

Figure 2. Medium-power view showing renal cortex with a number of glomeruli displaying a range of sclerosing changes and an interlobular artery with moderate fibrointimal thickening. (PAS, ×100).

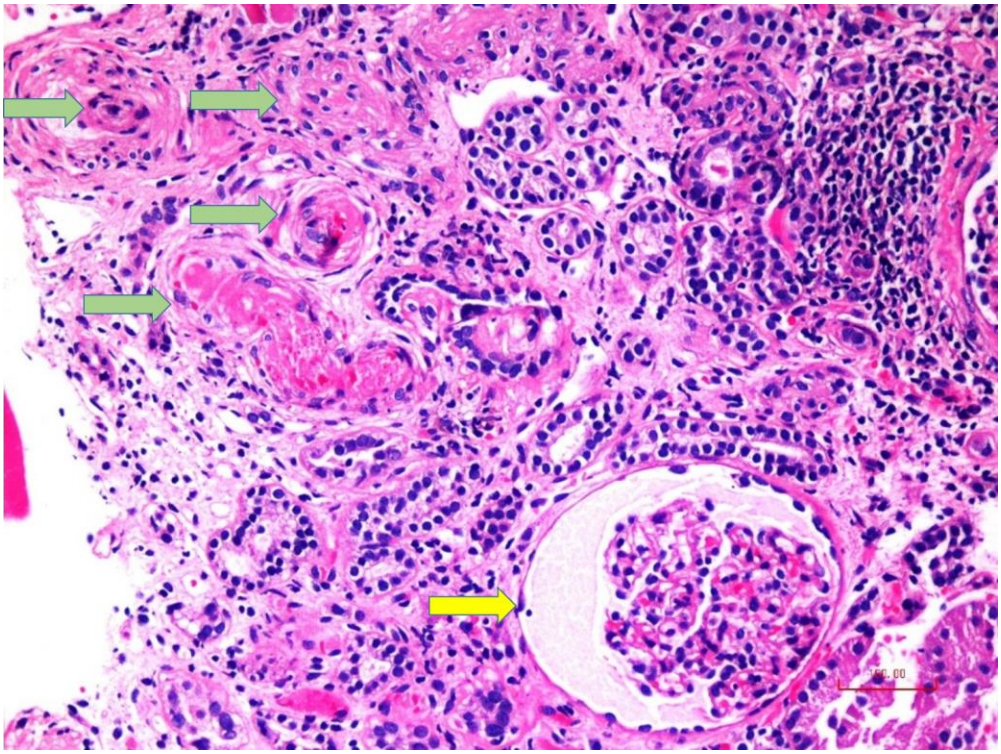

Figure 3. High-power view showing renal cortex with one glomerulus displaying retraction of the glomerular tuft and widening of Bowman's urinary space. A few arterioles exhibit significant pathological lesions (HE, ×200).

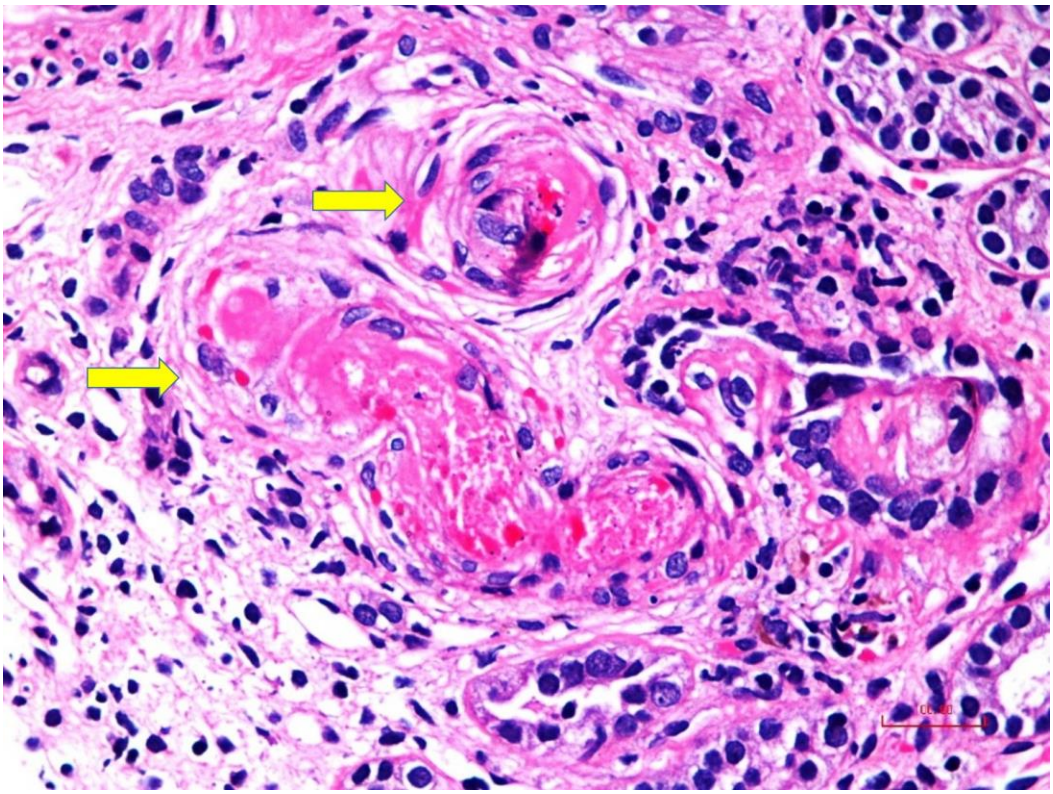

Figure 4. High-power view showing the arterioles with significant pathological lesions (HE, ×400).

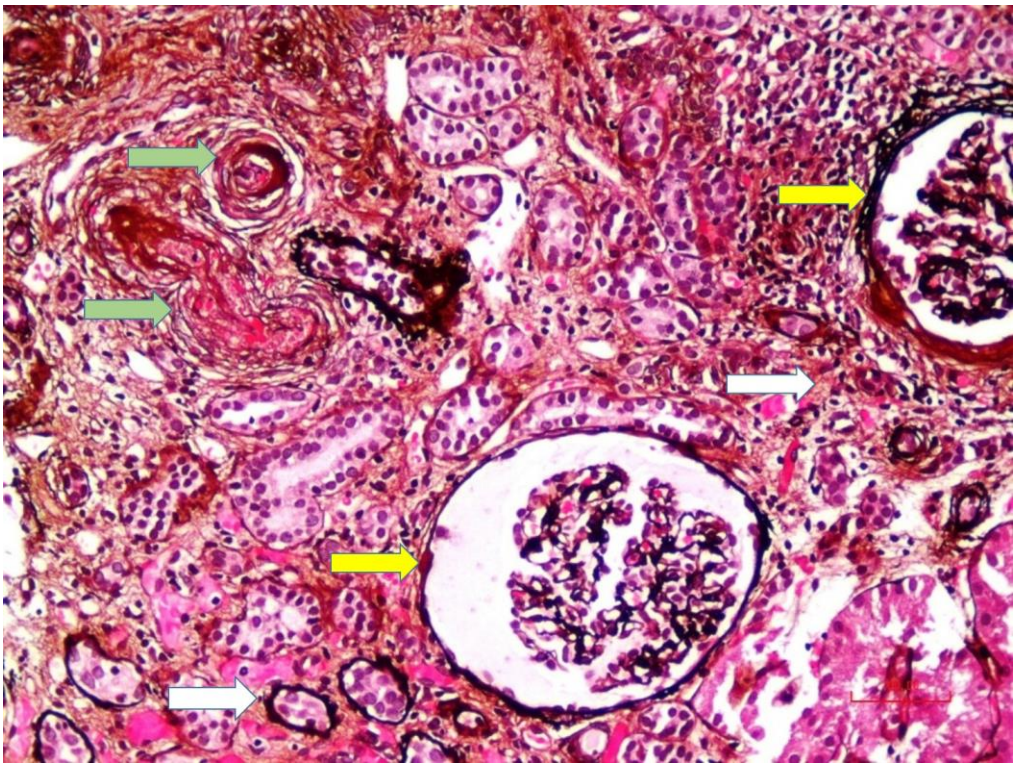

Figure 5. Medium-power view showing a spectrum of lesions involving the glomeruli, arterioles, and the background parenchyma. (JMS, ×100).

Questions:

Q1. Which clinical scenario best explains these biopsy changes?
Ans. Long-standing uncontrolled hypertension with acute malignant crisis.

Q2. What is the best possible biopsy diagnosis?
Ans. Hypertension-induced TMA.

Q3. What is the pathophysiological mechanism behind the arteriolar and glomerular findings in this condition?
Ans. Endothelial injury with subendothelial fibrin and matrix accumulation.

Q4. What key biopsy feature helps distinguish HTN-TMA from complement-mediated TMA?
Ans. Absence of immune deposits on immunofluorescence (IF) microscopy

Explanation of biopsy findings:

In Figure 1, the biopsy shows changes consistent with benign nephrosclerosis, characterized by moderate fibrointimal thickening of small artery (yellow arrow) and global glomerulosclerosis (green arrows) in a proportion of glomeruli. These findings are typically seen in the setting of long-standing hypertension and/or aging and represent chronic vascular injury. The degree of interstitial fibrosis and tubular atrophy is in keeping with the chronicity of the process. No features of active glomerulonephritis, vasculitis, or other specific renal pathology are identified in this field.

Figure 2 illustrates the renal cortex at medium power (PAS, ×100), where a number of glomeruli exhibit a spectrum of chronic sclerosing changes, ranging from segmental involvement to complete global sclerosis (green arrows). The presence of an interlobular-sized artery with intimal fibrosis highlights the associated vascular remodeling (yellow arrow). Together, these features reflect the chronic ischemic and hemodynamic injury typically encountered in benign nephrosclerosis, most often related to long-standing hypertension and aging.

Figure 3 shows a high-power view of the renal cortex (H&E, ×200). A glomerulus is seen with marked retraction of the glomerular tuft, resulting in an apparent widening of Bowman' s urinary space (yellow arrow), a feature reflecting ischemic injury secondary to vascular compromise. The surrounding interstitium shows a few arterioles with significant pathological alterations, including wall thickening and luminal narrowing, consistent with hypertensive vascular damage (green arrows). These vascular changes contribute to glomerular ischemia and progressive sclerosis, forming the histological substrate of hypertensive nephropathy.

Figure 4 shows a high-power view of an arteriole in the renal cortex (H&E, ×400). The vessel wall demonstrates fibrinoid necrosis, characterized by intensely eosinophilic, smudgy material replacing the normal wall architecture and associated inflammatory cell infiltration (yellow arrows). These vascular lesions are characteristic of malignant nephrosclerosis, reflecting the acute vascular injury and reparative response that occur during a hypertensive emergency or malignant hypertensive crisis. Such severe arteriolar damage underlies the ischemic glomerular changes and rapidly progressive renal impairment seen clinically.

Figure 5 demonstrates a medium-power view of the renal cortex stained with Jones' methenamine silver (JMS, ×100). A spectrum of lesions is evident, involving multiple components of the renal parenchyma. The glomeruli show variable changes, including ischemic wrinkling of capillary loops and segmental to global sclerosis (yellow arrow). The arterioles exhibit severe vascular pathology, with thickened walls and markedly narrowed lumina, some showing onion-skin concentric intimal hyperplasia and fibrinoid necrosis consistent with malignant hypertension – induced vascular injury (green arrows). The background parenchyma reveals interstitial fibrosis and tubular atrophy, reflecting chronicity of injury superimposed on acute vascular damage (white arrows). Together, these findings illustrate the combined glomerular, vascular, and interstitial lesions that characterize advanced hypertensive nephropathy with malignant transformation.

Discussion

HTN-TMA is a severe microvascular injury that arises in the setting of malignant or markedly uncontrolled hypertension. Extremely elevated blood pressure causes direct endothelial damage in arterioles and capillaries, leading to fibrinoid necrosis, plasma protein leakage, and platelet-rich microthrombi formation. These vascular changes result in ischemic collapse of glomerular capillary tufts, "onion-skin" concentric arteriolar thickening (hyperplastic arteriolosclerosis), and narrowing of the vascular lumen. Clinically, patients present with acute kidney injury, microangiopathic hemolytic anemia (with schistocytes on smear), and thrombocytopenia, often accompanied by retinopathy and neurological symptoms of hypertensive emergency. Unlike immune- or complement-mediated TMAs, immunofluorescence typically shows no immune complex or complement deposition, helping distinguish HTN-TMA from entities such as atypical HUS or lupus nephritis. Prompt recognition and aggressive blood pressure control are crucial, as kidney injury may be partially reversible if treated early.