Renal Disease

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03

Vascular Diseases

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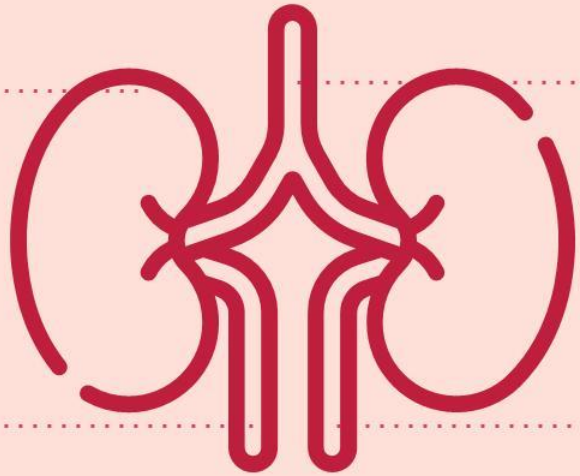
Nephrosclerosis

01 Sclerosis of small renal arteries & arterioles that is strongly ass/wi hypertension.

02 Affected vessels have thickened walls & consequently narrowed lumens → focal parenchymal ischemia.



03 Ischemia leads combinations of interstitial fibrosis, tubular atrophy, & focal global glomerulosclerosis.

04 Ass/ w aging. HTN & DM increase the incidence & severity of the lesions.

Nephrosclerosis - Pathogenesis

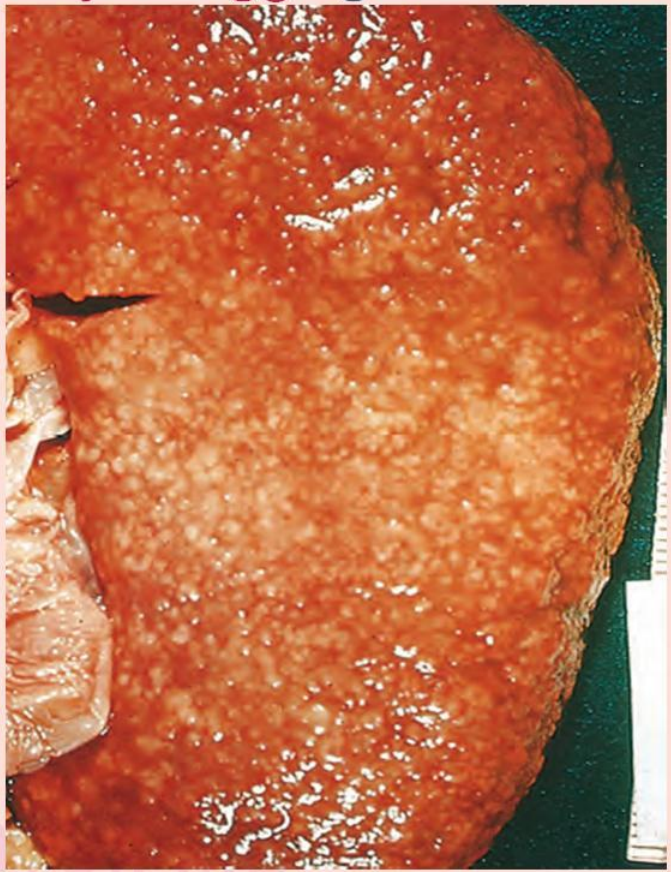
- Two processes participate in the arterial lesions:

I. Medial and intimal thickening, as a response to hemodynamic changes, aging, genetic defects, or some combination of these
II. Hyalinization of arteriolar walls, caused by extravasation of plasma proteins through injured endothelium & by increased deposition of basement membrane matrix

- known as benign nephrosclerosis → "benign" because renal function is minimally affected or proceeds to chronic kidney injury slowly.

Nephrosclerosis -Morphology -gross

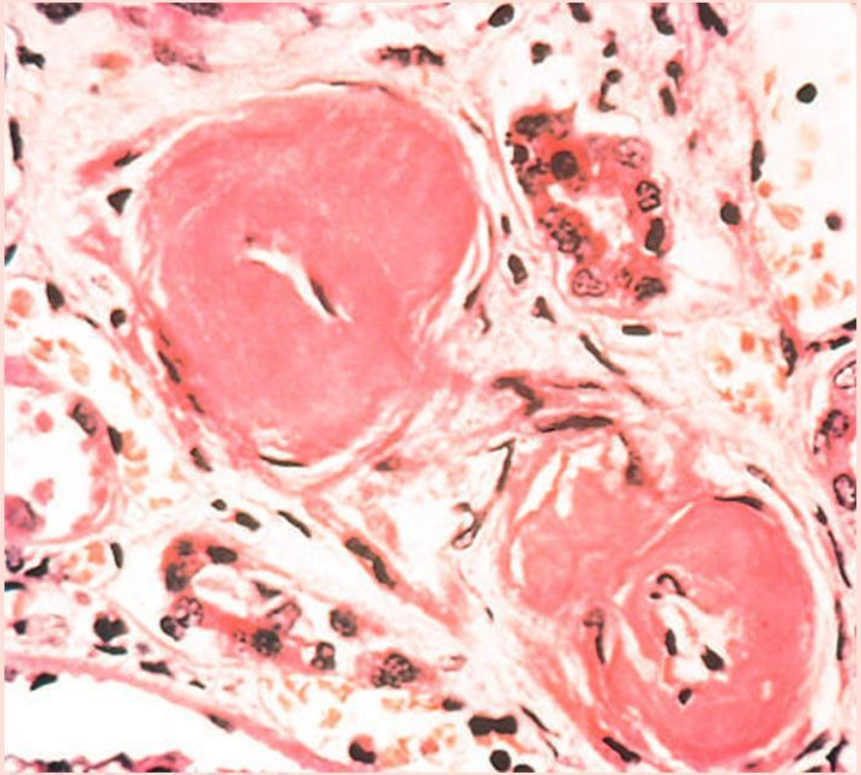
There is patchy ischemic atrophy with focal loss of renal parenchyma that gives the surface of the kidney the characteristic granular appearance, resembles grain leather.



Nephrosclerosis -Morphology -LM

The most prominent change is hyaline thickening of the walls of the arterioles → **hyaline arteriolosclerosis.**

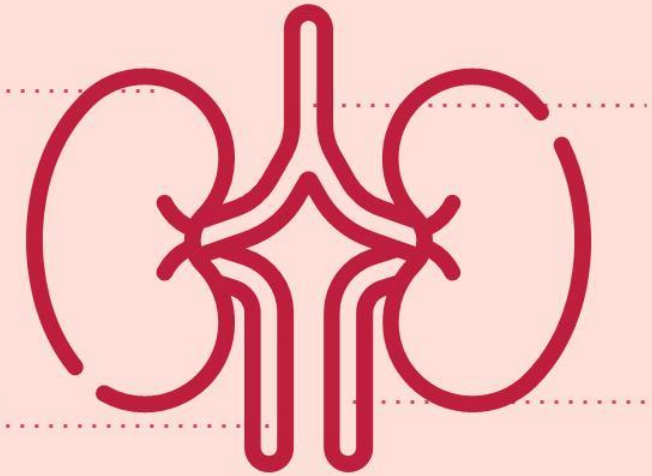
A homogeneous, pink hyaline thickening, at the expense of the vessel lumina, with loss of underlying cellular details



Malignant Hypertension

01 A blood pressure usually greater than 200/120 mm Hg,

02 Far less common than essential hypertension, occurs in only about 5% of hypertensive individuals



03 May arise de novo (w/o preexisting HTN), or appear suddenly in an individual with mild HTN

04 It may present with severe acute kidney injury and renal failure

Malignant Nephrosclerosis- Pathogenesis

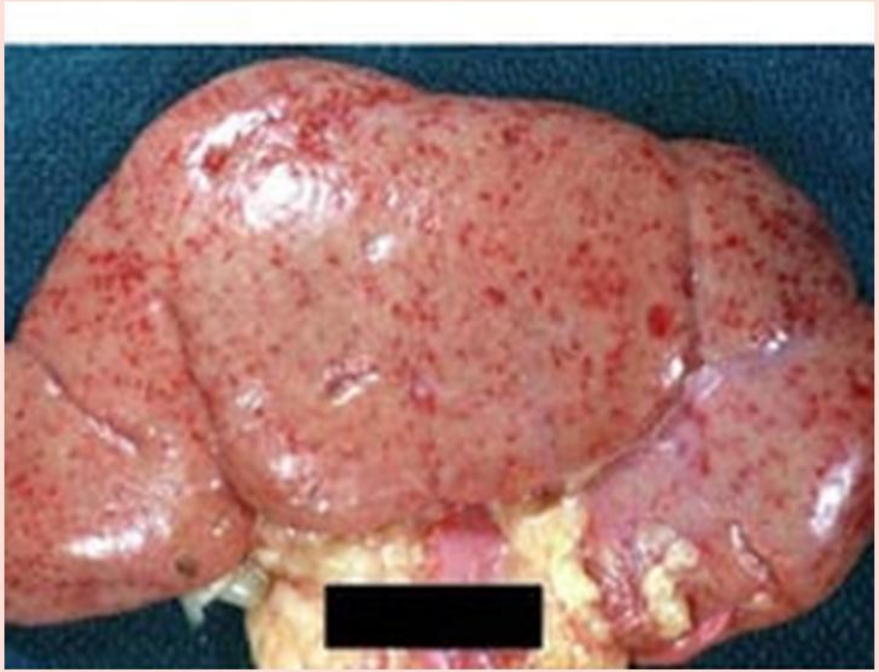
- The fundamental lesion in malignant nephrosclerosis is vascular injury:

I. Long-standing hypertension → increased permeability of the vessels to fibrinogen & other plasma proteins, endothelial injury, & platelet deposition → can leads to the fibrinoid necrosis of arterioles & small arteries & intravascular thrombosis.

II. Mitogenic factors from platelets (e.g., platelet-derived growth factor), plasma, & other cell cause hyperplasia of the intimal smooth muscles of vessels → hyperplastic arteriosclerosis.
Luminal narrowing → kidneys are markedly ischemic → further elevation of blood pressure via the renin-angiotensin system.

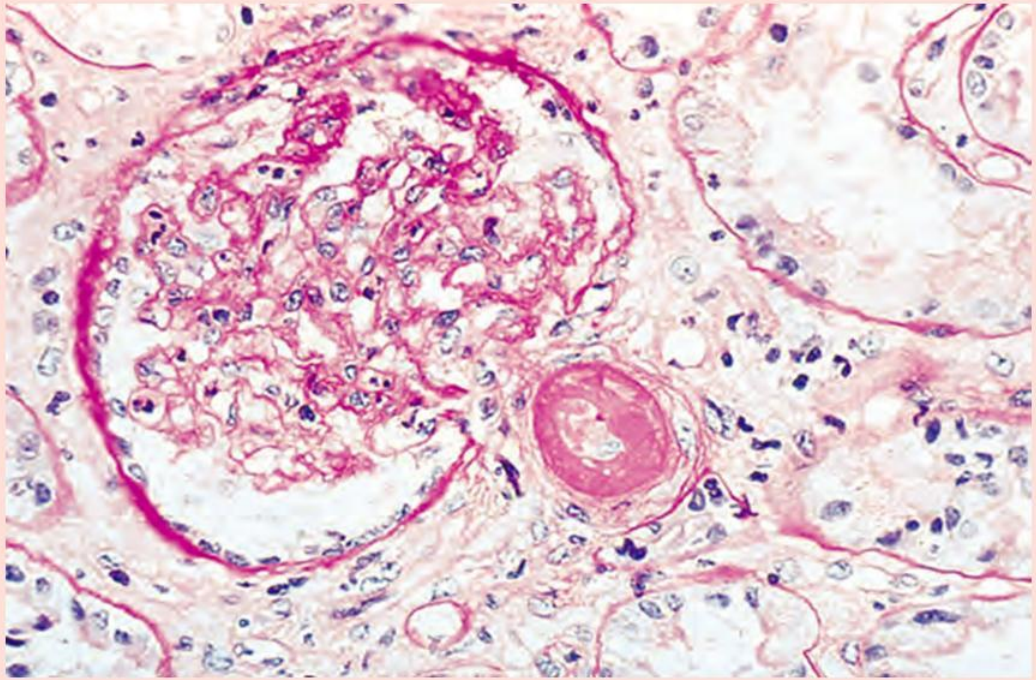
Malignant Nephrosclerosis- Morphology -gross

Small, pinpoint petechial hemorrhages may appear on the cortical surface→ rupture of arterioles or glomerular capillaries, giving the kidney a peculiar "flea-bitten" appearance.



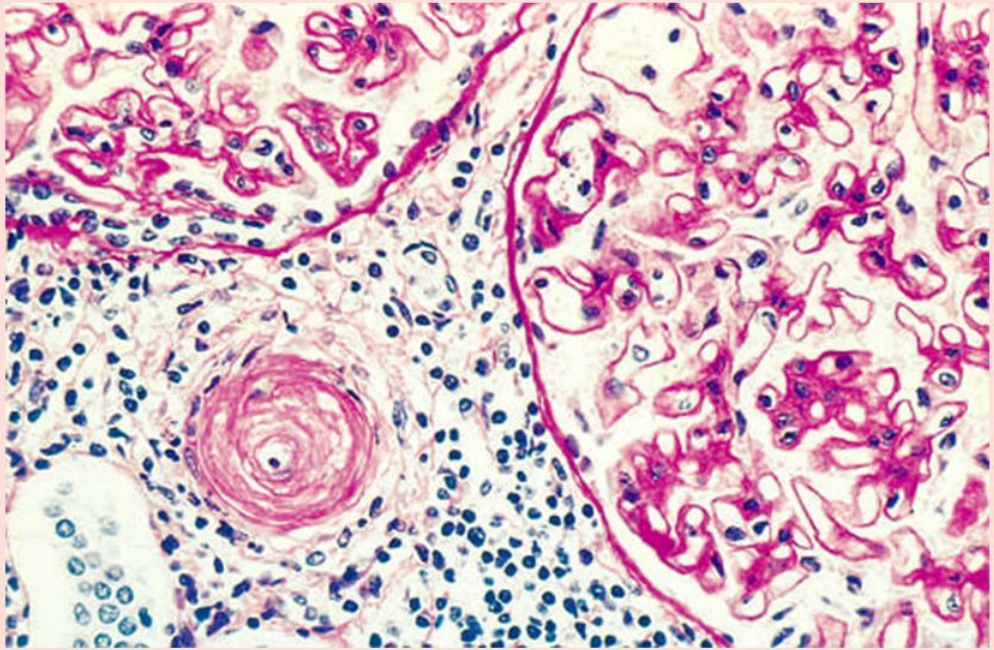
Malignant Nephrosclerosis- Morphology -LM

Damage to the small vessels is manifested as fibrinoid necrosis of the arterioles..



Malignant Nephrosclerosis- Morphology -LM

In interlobular arteries & larger arterioles, proliferation of intimal cells after acute injury produces an onion-skin appearance (derived from the concentric arrangement of cells). Hyperplastic arteriolosclerosis causes marked narrowing to the point of total obliteration.



Malignant Hypertension- Clinical

- Syndrome of malignant hypertension is characterized by papilledema, encephalopathy, cardiovascular abnormalities, & renal failure.
- Most often, the early symptoms are related to increased intracranial pressure ; headache, nausea, vomiting, & visual impairment.
- acute kidney injury develops
- A true medical emergency→ requires prompt & aggressive anti-hypertensive therapy before irreversible renal lesions develop.
- ~ 50% survive at least 5 years
- 90% of deaths are due to uremia, and the other 10% → cerebral hemorrhage or cardiac failure

04

CHRONIC KIDNEY DISEASE

CHRONIC KIDNEY DISEASE

- A broad term that describes the final common pathway of progressive nephron loss resulting from any type of kidney disease.
- Alterations in the function of remaining intact nephrons are ultimately maladaptive and cause further scarring.
- Eventually results in an end-stage kidney ; sclerosed glomeruli, tubules, interstitium and vessels, regardless of the anatomic site of the original injury.
- Unless the disorder is treated with dialysis or transplantation, death from uremia, electrolyte disturbances, or other complications of ends stage renal disease results.

Nephron Loss

01 Once renal disease, destroys sufficient nephrons → GFR to 30%-50% of normal

- symptoms appear
- progression to end-stage renal disease proceeds at varying rates.

02 Two major histologic characteristics of progressive renal damage

- Focal segmental glomerulosclerosis-FSGS
- Tubulointerstitial fibrosis

03 Sclerosis and fibrosis is exacerbated by adaptive changes that occur in response to the loss of nephrons.

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Nephron Loss

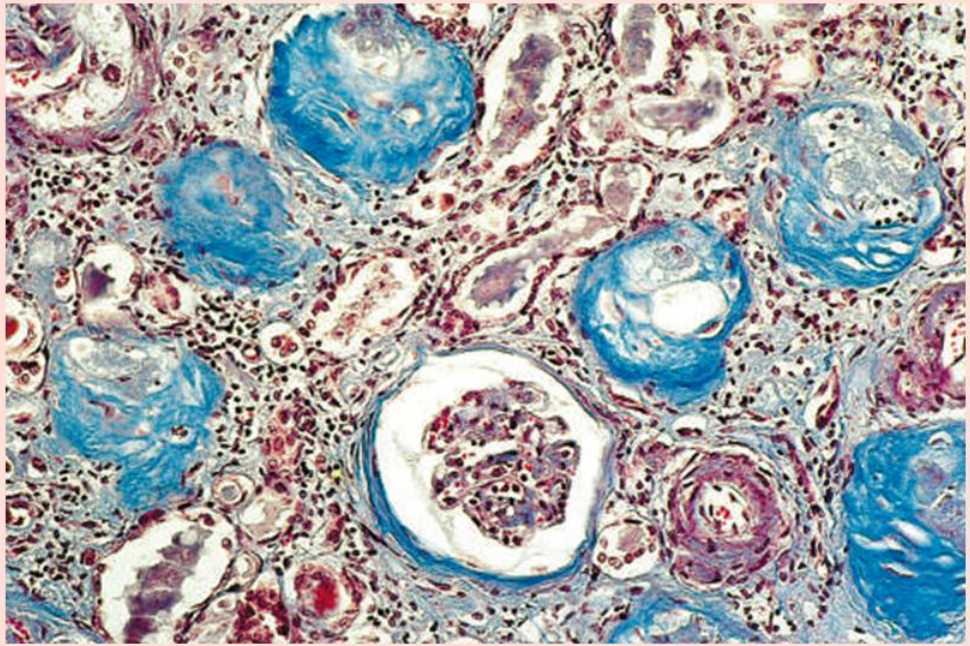
- Process is initiated by adaptive change in the relatively unaffected glomeruli .
- Compensatory hypertrophy of the these glomeruli to maintain renal function → ass/w hemodynamic changes; increases in single-nephron GFR, blood flow, & transcapillary pressure (capillary /glomerular hypertension) → often with systemic hypertension.
- Alterations → maladaptive → further endothelial & podocyte injury ;

1. Increased glomerular permeability to proteins
2. Accumulation of proteins & lipids in the mesangial matrix.
3. Capillary obliteration,
4. Increased deposition of mesangial matrix
5. Segmental or global sclerosis of glomeruli.
6. Further reduction of nephron mass

- Initiating a vicious cycle of progressive glomerulosclerosis.

Nephron loss-Morphology -LM

Advanced scarring to complete sclerosis of the glomeruli. Obliteration of the glomeruli is the end point→ impossible to ascertain from the nature of the initial lesion. Also marked interstitial fibrosis.



CHRONIC KIDNEY DISEASE-Clinical

- Often asymptomatic → develop insidiously and discovered late in course
- Frequently, first detected by the discovery of proteinuria, hypertension, or azotemia on routine medical examination.
- In patients with glomerular disease resulting in nephrotic syndrome, as the glomeruli undergo sclerotic changes & nephron loss, the avenue for protein loss is progressively lessened, & the nephrotic syndrome becomes less severe with advanced disease.
- Hypertension is very common.
- Without treatment, the prognosis is poor → progression to uremia and death is the rule. The rate is extremely variable.

Cases Discussion

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Case 1

A 7-year-old boy is recovering from impetigo. Physical examination shows five honey-colored crusts on his face. The crusts are removed, and a culture of the lesions grows *Streptococcus pyogenes.* He is treated with antibiotics. One week later, he develops malaise with nausea and a slight fever and passes dark brown urine. Laboratory studies show an elevated serum anti–streptolysin O titer Which of the following is the most likely outcome of his renal disease?

A Chronic renal failure
B Complete recovery
C Crescentic glomerulonephritis
D Rheumatic heart disease
E Streptococcal urinary tract infection

Case 2

A 53-year-old woman has had fever and flank pain for the past 2 days. On physical examination, her temperature is 38.2° C, pulse is 81/min, respirations are 16/min, and blood pressure is 130/80 mm Hg. Urinalysis shows no protein, glucose, or ketones. Microscopic examination of the urine shows numerous polymorphonuclear leukocytes and occasional WBC casts. Which of the following organisms is most likely to be found in the urine culture?

A *Cryptococcus neoformans*
B *Escherichia coli*
C Group A streptococcus
D *Mycobacterium tuberculosis*
E *Mycoplasma hominis*

Case 3

A 45-year-old man has had headaches, nausea, and vomiting that have worsened over the past 5 days. He has started "seeing spots" before his eyes and experienced periods of mental confusion. On physical examination, his blood pressure is 270/150 mm Hg. Urinalysis shows 1+ proteinuria; 2+ hematuria; and no glucose, ketones, or leukocytes. The serum urea nitrogen and creatinine levels are elevated. He dies 2 weeks later from a cerebral bleed. Which of the following histologic findings is most likely to be seen in this patient's kidneys at autopsy?

A Glomerular crescents
B Hyperplastic arteriolosclerosis
C Mesangial IgA deposition
D Nodular glomerulosclerosis
E Segmental tubular necrosis

Keep busy with survival. Imitate the trees.
Learn to lose in order to recover, and remember
that nothing stays the same for long, not even pain.
Sit it out. Let it all pass. Let it go.

THANX!

Questions?

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