Some renal vascular disorders

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Introduction

• Nearly all diseases of the kidney involve the renal blood vessels secondarily

• We will discuss:
  - Hypertension (arterionephrosclerosis in benign HTN & hyperplastic arteriolosclerosis in malignant HTN)
  - Thrombotic microangiopathies
Benign HTN, arterioneuphrosclerosis

- Arterioneuphrosclerosis = thickening and sclerosis of arterial walls and the renal changes associated with benign hypertension

- It mainly affects small arterioles and appears morphologically as: hyaline arteriolosclerosis

- Some mild degree present at autopsy in many persons older than 60 years of age

- Because many renal diseases cause hypertension, this change can superimpose other primary kidney diseases

- Recent studies: apolipoprotein L1 gene mutations (like FSGS)...more in African Americans
Benign HTN, arterionephrosclerosis...morphology

• Grossly, the kidneys are symmetrically atrophic, each weighing 110 to 130 g

• Renal surface shows diffuse, fine granularity that resembles grain leather

• Microscopically: hyaline thickening of the walls of the small arteries and arterioles, known as hyaline arteriolosclerosis

In advanced cases of arterionephrosclerosis, the glomerular tufts may become sclerosed, in addition to tubular atrophy & interstitial fibrosis

All structures of the kidney can show ischemic atrophy due to this narrowing
What about larger vessels here?

• The larger blood vessels (interlobar and arcuate arteries) show reduplication of internal elastic lamina along with fibrous thickening of the media and the subintima = fibroelastic hyperplasia
Benign HTN, arterionephrosclerosis... clinical notes

• All patients with this lesion usually show:
  - some functional impairment, such as loss of concentrating ability or a variably diminished GFR
  - mild degree of proteinuria

• More severe in African Americans... may lead to uremia & death
Malignant HTN

• Defined as blood pressure usually greater than 200/120 mm Hg

• It may arise de novo (i.e., without preexisting hypertension), or it may appear suddenly in a person who had mild hypertension

• The prevalence of malignant hypertension is higher in less developed countries

• The lesion morphologically is called here: hyperplastic arteriolar sclerosis
Malignant HTN, hyperplastic arteriolsclerosis

- Injury of arteriolar wall
- Permeability to fibrinogen, plasma proteins and platelet deposition
- Fibrinoid necrosis & intravascular thrombosis
- Intimal hyperplasia due to mitogenic factors from platelets (e.g., PDGF)
- Narrowing of lumen
- The kidneys become markedly ischemic
- With severe involvement of the renal afferent arterioles, renin-angiotensin system activation...vicious cycle
Malignant HTN, hyperplastic arteriolosclerosis...morphology

*Gross features:
- The kidney may be essentially normal in size or slightly shrunken, depending on the duration and severity of the hypertensive disease
- Small, pinpoint petechial hemorrhages may appear on the cortical surface from rupture of arterioles or glomerular capillaries, giving the kidney a peculiar, flea-bitten appearance

*Microscopic features:
- Fibrinoid necrosis of the arterioles
- Onion-skin appearance
- Necrosis also may involve glomeruli, with microthrombi within the glomeruli as well as necrotic arterioles

Similar changes can be seen in: acute thrombotic microangiopathies (described next), and in patients with scleroderma in renal crisis
Malignant HTN, clinical course

• Papilledema

• Encephalopathy

• Cardiovascular abnormalities

• Renal failure

• Increased intracranial pressure

*Renal manifestations:
Early: marked proteinuria and microscopic, or sometimes macroscopic, hematuria but no significant alteration in renal function. Soon, however, acute kidney injury develops

90% of deaths are caused by uremia and the other 10% by cerebral hemorrhage or cardiac failure
**Characterized in general by:**
- Widespread thrombosis in the microcirculation
- Microangiopathic hemolytic anemia
- Thrombocytopenia
- In certain instances, renal failure

**Common causes**
- Childhood hemolytic uremic syndrome (HUS)
- Various forms of adult HUS
- Thrombotic thrombocytopenic purpura (TTP)
- Various drugs
- Malignant hypertension or scleroderma
Thrombotic microangiopathies, childhood HUS

• 75% of cases follow intestinal infection with Shiga toxin–producing E. coli and infections with Shigella dysenteriae type I

• Renal glomerular endothelial cells are targets because the cells express the membrane receptor for the toxin
Thrombotic microangiopathies, childhood HUS...cont’d

• The toxin also gains entry to the cells and directly causes cell death

• The resultant endothelial damage leads to:
  - thrombosis, which is most prominent in glomerular capillaries, afferent arterioles, and interlobular arteries
  - vasoconstriction

Approximately 10% of the cases of HUS in children are not preceded by diarrhea caused by Shiga toxin–producing bacteria. In a subset of these patients, mutational inactivation of complement regulatory proteins (e.g., factor H) allows uncontrolled complement activation after minor vascular injuries. These conditions promote the formation of thrombi.
Thrombotic microangiopathies, childhood HUS...clinical notes

• Sudden onset, usually after a gastrointestinal or flulike prodromal episode

• Bleeding manifestations (especially hematemesis and melena)

• Severe oliguria

• Hematuria

• Microangiopathic hemolytic anemia

• (in some persons) prominent neurologic changes

• 25% of these children, renal insufficiency...due to secondary scarring

TTP more often has dominant involvement of the central nervous system than HUS and the kidneys are less commonly involved compared to HUS

This disease is one of the main causes of acute kidney injury in children
Thrombotic microangiopathies, TTP

• TTP often is caused by an acquired defect in proteolytic cleavage of von Willebrand factor (vWF) multimers due to autoantibodies
  ...or more rarely, an inherited defect as seen in familial TTP

• These antibodies are directed against ADAMTS 13 (a metalloprotease) that cleaves vWF multimers into smaller sizes
  ...increased levels of large vWF multimers in the circulation can activate platelets spontaneously, leading to platelet aggregation and thrombosis
  ...genetic defects in ADAMTS 13 lead to a similar pattern of disease
Chronic kidney disease (CKD)
(a brief note)

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CKD morphology

• The kidneys are symmetrically contracted

• Their surfaces are red-brown and diffusely granular when the underlying disorder affects blood vessels or glomeruli

• Kidneys damaged by chronic pyelonephritis are typically unevenly involved and have deep scars

• Microscopically, the feature common to all cases is advanced scarring of the glomeruli, sometimes to the point of complete sclerosis
  ...interstitial fibrosis
  ...tubular atrophy
  ...small and medium-sized arteries frequently are thick-walled, with narrowed lumina, secondary to hypertension
  ...Lymphocytic (and, rarely, plasma cell) infiltrates
  ...may become difficult to ascertain whether the primary lesion was glomerular, vascular, tubular, or interstitial

(Courtesy of Dr. M.A. Venkatachalam, Department of Pathology, University of Texas Health Sciences Center, San Antonio, Texas.)
CKD clinical manifestations

• Insidious, and the renal insufficiency may be discovered late

• In the case of nephrotic syndrome, proteinuria diminishes with the progressive sclerosis of glomeruli (the way is closed to filtrate)

• Some degree of proteinuria is present in almost all cases

• Hypertension is very common, and its effects may dominate the clinical picture

• Although microscopic hematuria is usually present, grossly bloody urine is infrequent at the late stage
Thank You