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Recognition and Management of kidney disease in vasculitis

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Outline

• Basic kidney facts

• How do you recognize kidney disease?
The Kidney: One of the most important organs

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Ca, PO₄, H⁺
1-25 (OH)₂ vitD
erythropoietin
RBC

Heart
Beat regulation
K, Ca

Blood pressure control
Renin
Parts of the Nephron

- Nephron
- Glomerulus
- Tubule
- Urine Out

Filtered Blood Out
Unfiltered Blood In
Filtered Blood Out
Unfiltered Blood In
Drawing of a cross section of a GLOMERULUS with arrows showing the flow of blood (red) and urine (yellow). The small vessel (arteriole) entering the glomerulus divides into even smaller vessels (capillaries).

Microscopic photograph of a cross section of a normal GLOMERULUS in a kidney biopsy specimen.

Three dimensional microscopic photograph of a normal GLOMERULUS with the small blood vessels (arterioles) sticking out. The glomerulus is a ball of capillaries (GLOMUS means ball in Greek).
Glomerular Capillaries

Drawing of a cross section of a GLOMERULUS with arrows showing the flow of blood (red) and urine (yellow)

Drawing of a cross section of one very small blood vessel called a CAPILLARY in a glomerulus showing the filtration of blood (red) into urine (yellow)
Normal Glomerular Capillary

- epithelial foot process
- basement membrane
- lumen
- endothelial cell
- mesangial cell
- mesangial matrix
Molecular Anatomy of the Foot Process

Proteinuria and Hematuria

A normal capillary in a glomerulus keeps red blood cells, white blood cells and most proteins in the blood and only lets watery fluid into the urine.

A capillary in a diseased glomerulus lets protein into the urine (proteinuria) and red blood cells into the urine (hematuria).
Proteinuria

- The degree of proteinuria may vary with the degree of glomerular disease activity
- In patients with glomerular disease, day-to-day variation in proteinuria with fever, exercise, protein intake…
- Residual proteinuria may persist as a result of glomerular scarring, even in the absence of active disease
Hematuria

- Normal to excrete up to ~ 1.2 million RBC/day.
- Normal is less than 3 RBC/high power field.
- Dipstick can detect as few as 3-4 RBC/hpf.
- Blood in the urine may originate anywhere in the urinary tract (kidney, ureters, bladder, prostate, urethra, or female genital tract)
- The presence of significant proteinuria is a clue that there is an injury to the glomeruli
Rapidly Progressive Glomerulonephritis

- Anti-GBM Antibody mediated
- Immune complex mediated
- Pauci-immune (ANCA)
Necrotizing and crescentic GN

Silver stain
Serologic Clues

Rapidly Progressive Glomerulonephritis

- Anti-GBM Antibodies
  - ANA, anti-dsDNA
  - Cryoglobulins
  - Hepatitis tests
- Immune complex mediated
- Pauci-immune
  - ANCA
ANCA
Anti-Neutrophil Cytoplasmic Autoantibodies (ANCA)

C-ANCA: Cytoplasmic Pattern
Anti-proteinase 3
PR3-ANCA

P-ANCA: Perinuclear Pattern
Anti-myeloperoxidase
MPO-ANCA
Measuring kidney function

- Measuring Creatinine Clearance
  - Obtaining a 24 hour collection of urine
  - Measuring the urine and blood concentration of creatinine.
  - Allows to measure how much creatinine was filtered in that period of time.

- Other, more accurate tests of kidney function, are seldom used in routine clinical practice because they are cumbersome and expensive.
When the serum creatinine is low, large changes in GFR, may “hide” within very small changes in creatinine.
Serum Creatinine (SCr) Alone Is a Poor Indicator of Kidney Function

2 patients with SCr levels of 1.5 mg/dL (0.133 mmol/L)

- Male
  - Age = 25 years
  - Estimated GFR*: 73 mL/min

- Female
  - Age = 65 years
  - Estimated GFR*: 37 mL/min

*Calculated with the MDRD equation.
MDRD Equation

GFR in mL/min per 1.73 m² = 175 × \( \text{Cr}^{[-1.154]} \) × \( \text{Age}^{[-0.203]} \) × (0.742 if female) × (1.21 if black)

not valid in the setting of a rising serum creatinine in acute kidney injury

Less accurate in populations with normal or near normal GFR, extremes of age and weight, amputees, in pregnancy and cirrhosis

www.kidney.org/professionals/KLS/gfr_calculator.cfm
www.nephron.com/mdrd/default.htm
Vasculitis and Kidneys: Basic facts

- 20-50% have kidney involvement at presentation and 70-80% during disease course

- Onset can be sudden and severe or smoldering
Vasculitis and Kidneys: Basic facts

- Kidney involvement in most common in small vessel vasculitides
  - GPA
  - MPA
  - Henoch-Schonlein purpura
  - Cryoglobulinemia
  - EGPA

- Some medications cause kidney disease while others may need to be avoided or need dose reduction when kidneys are not working normally
Vasculitis and kidney: Kidney involvement in all small vessel vasculitis is the same

- Elevated levels of blood urea nitrogen and creatinine
- Blood and/or protein in urine
- High blood pressure
- Low urine output
Vasculitis and Kidney: Disease course

- 25% can require dialysis at disease onset
- With treatment, 25 to 75% recover renal function to discontinue dialysis
Vasculitis: Treatment

- Good news: Vasculitis is treatable
- Bad news:
  - Treatment has side effects
  - Damage that has happened can be irreversible
  - Difficult to predict disease course
Vasculitis: Treatment

• Better understanding of these diseases has led to better therapeutic approaches

• Newer drugs more effective and less toxic

• Scientific evidence for making treatment decisions
ANCA vasculitis treatment phases

- **Induction phase**: get the vasculitis under control : 3 to 6 months

- **Maintenance phase**: maintain the vasculitis under control : 18 to 24 months
Treatment: Induction Phase

- Steroids
- Cyclophosphamide
- Rituximab
- Plasmapheresis
Treatment: Maintenance Phase

- Steroids
- Azathioprine
- Rituximab
- Mycophenolate mofetil
- Methotrexate
Preserving kidney function

• Early detection is crucial. Always ask your doctor how your kidneys are doing. Home based urine dipstick monitoring can help detect early disease in vasculitis

• Control of BP around 125-130/75-80 : extremely important

• The blood pressure lowering medications, angiotensin converting enzyme inhibitors (ACE-I) and angiotensin receptor blockers (ARB), are the best way to lower BP and preserve kidney function if there is protein in the urine
Preserving kidney function

• Diet has to be individualized: dietary consult preferred

• Avoiding repetitive kidney injury (relapses, kidney toxic drugs)

• Control of blood sugar and cholesterol

• Smoking cessation
End stage renal disease and vasculitis

- 20 to 25% of ANCA vasculitis patients reach end stage renal disease
Uremia

- Typically seen with an eGFR < 10 mL/min/1.73 m²
  - Nausea/Vomiting
  - Fatigue
  - Anorexia
  - Weight Loss
  - Pruritus
  - <> Mental Status
  - Dysgeusia
  - Myoclonus
  - Sleep Disturbance
  - Other: bleeding, neuropathy, “odor”

SUBTLE
What are the options when kidneys have failed

- Hemodialysis
- Peritoneal dialysis
- Transplantation
Dialysis

What Dialysis Is?

- Life support for the kidneys
  Replacement ± Supportive
- Takes the place of what the kidneys are NOT able to do
- Difficult
  Removes independence
- Complicated
  High mortality
  Access issues
  High cost(s), not just financial

What Dialysis Isn’t?

- Magic
- Does NOT improve renal function
- Easy
- Isn’t for everyone
  Cognitive and Functional Status are important
PD Technique

Principle of Peritoneal Dialysis

- Bag containing dialysis solution
- Internal organs
- Peritoneal catheter
- Peritoneal cavity
- Disconnect tubing
- Drain line

Solution bag
PD-System
Connector
Catheter
Peritoneal dialysis solution
Peritoneum
Drainage bag
Types of Peritoneal Dialysis

- **CAPD**: Continuous Ambulatory PD
  - Several daily dwells (4-5/day)
  - Long *overnight* dwell

- **CCPD**: Continuous Cycler PD
  - Long *daily* dwell
Dialysis Access

Diagram showing blood flow in the arm with labels for
- Arterial line
  Blood flow from patient to dialyzer
- Venous line
  Blood return from dialyzer to patient
- Cephalic vein
- Radial artery
- Brachial artery
- Basilic vein

Connection: Needle
Blood from machine to Vein
Blood to machine
Vasculitis and dialysis: Survival

- Comparable to patients with other causes of kidney failure
- Median survival:
  - 5.2 years (MPA)
  - 6.1 years (GPA),
  - 5.8 years (others)
- 1 year survival:
  - 91-92% (compared to 89% for other causes)
- 5 year survival:
  - 46-47% (compared to 50% for other causes)
Vasculitis and dialysis: Relapse rates

- Relapses occur in dialysis patients, the relapse rate is lower compared to those who are not on dialysis.

- Infection due to immunosuppressive medications is common on dialysis patients and over immunosuppression needs to be avoided.
Kidney transplantation
Vasculitis and transplantation: Contraindications

- Active vasculitis
- Active infection
- Recent malignancy
- Bone marrow failure
Vasculitis and kidney transplant: **Results**

- **Patient survival:**
  5 year 85%

- **Graft survival:**
  1 year: 86%, 5 year: 69%
  Modern immunosuppressive drugs 5 year 93%

- **Vasculitis relapse:** 0.02 per patient per year
Update on clinical trials
Vasculitis clinical trials with results awaited

- **PEXIVAS**: plasma exchange and 2 different steroid dosing regimen

- **RITAZAREM**: comparing rituximab versus azathioprine for remission maintenance (induction: rituximab)

- **MAINRITSAN 2**: scheduled rituximab versus based on B cell repopulation and ANCA
New clinical trials enrolling patients

- ADVOCATE: oral complement inhibitor trial for ANCA vasculitis (steroid sparing)
- MAINRITSAN 3
- ABROGATE: Abatacept for non severe GPA: relapse prevention
New clinical trials enrolling patients

- **BREVAS**: Belimumab plus azathioprine for remission maintenance

- **TAPIR**: GPA in remission: evaluating 5mg prednisone vs. no prednisone for relapse prevention

- **LoVAS**: Low dose versus standard dose steroids for remission induction
Questions