Nephrology Case Presentation for PCKD

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With update 2018

Case Presentation

- 48 y/o WM presents with back pain
  - Sharp, over L side/ribs
  - Intermittent but severe 8/10
  - No radiation
  - No recent injury, lifting, straining etc
  - Nothing like this ever happened before

Case Presentation

- PMH – chronic renal failure, obesity, HTN
- PSH – none
- All – NKDA
- Meds –
  - Diltiazem cd 240mg qd
  - Lasix 80 mg bid
- Fam – father and sister had kidney failure, but two brothers do not
- Soc – smoker x 20 years, occ EtoH

Case Presentation

- PE: afebrile, P 96, R16, BP 150/90
  - Mod distress, obese (wt=240), ht 72”
  - Back – no tender points, exam reveals no specific findings
  - H regular
  - L clear bilaterally
  - Abd – round, soft, nontender, bowel sounds present, ? masses/HSM/fullness
  - Ext – pulses normal, trace edema ankle

Case Presentation

- Na-138, K-4.2, Cl-104, HCO3-25
- BUN-48, Cr-6.1
- WBC-7.0, HGB-11, HCT-33, PLT-240
- CPK-70
- UA: SG-1.020, clear, BLO-1+, PRO-neg, KET-neg, LEU-neg

Case Presentation

- Differential diagnosis
  - Musculoskeletal/trauma
  - Infection: Pyelonephritis, cyst
  - Neoplasm: renal cell carcinoma
  - Congenital: ADPKD
  - Degenerative: arthritis
  - Inflammatory: Vasculitis
  - Nephrolithiasis
  - Loin pain – hematuria syndrome

Autosomal Dominant Polycystic Kidney Disease

- Multisystem disorder with multiple, bilateral renal cysts
- Associated with cysts in liver, pancreas, and arachnoid membranes
- Extrarenal manifestations: mitral valve prolapse, intracranial aneurysms, hernias

Autosomal Dominant Polycystic Kidney Disease

- Genetics:
  - Autosomal dominant
  - 100% penetrance but variable expression
- PKD1 short arm chromosome 16, responsible for 85-90%
- PKD2 long arm chromosome 4
- Polycystin 1 and 2 are the gene product proteins identified

Autosomal Dominant Polycystic Kidney Disease

- Only a small percent of nephrons develop cysts
- Cysts arise from focal dilatation of existing renal tubules, and can arise from any segment of the nephron
- Epithelial cells lining cysts have unique phenotype suggesting intermediate state of cell differentiation

Autosomal Dominant Polycystic Kidney Disease

- Epidemiology
  - 1:400 to 1:1000 in the general population
  - Prevalence 400,000 in USA
  - 1800/year progress to ESRD/Hemodialysis
  - Equal in gender distribution, but may manifest more severely in males

ADPKD
Renal Manifestations

- Pain and size
  - Size increases with age
  - Severity of structural abnormality correlates with pain, hematuria, renal insufficiency
  - Massive enlargement can lead to IVC obstruction, compression of local structures
  - DDx: cyst hemorrhage, infection, stones

ADPKD
Renal Manifestations

- Hematuria and cyst hemorrhage
  - 42% of patients will manifest
  - Communicating: with collecting duct = gross hematuria
  - Non communicating: can present with fever, and possibly cyst infection
    - Occasionally a retroperitoneal bleed can occur

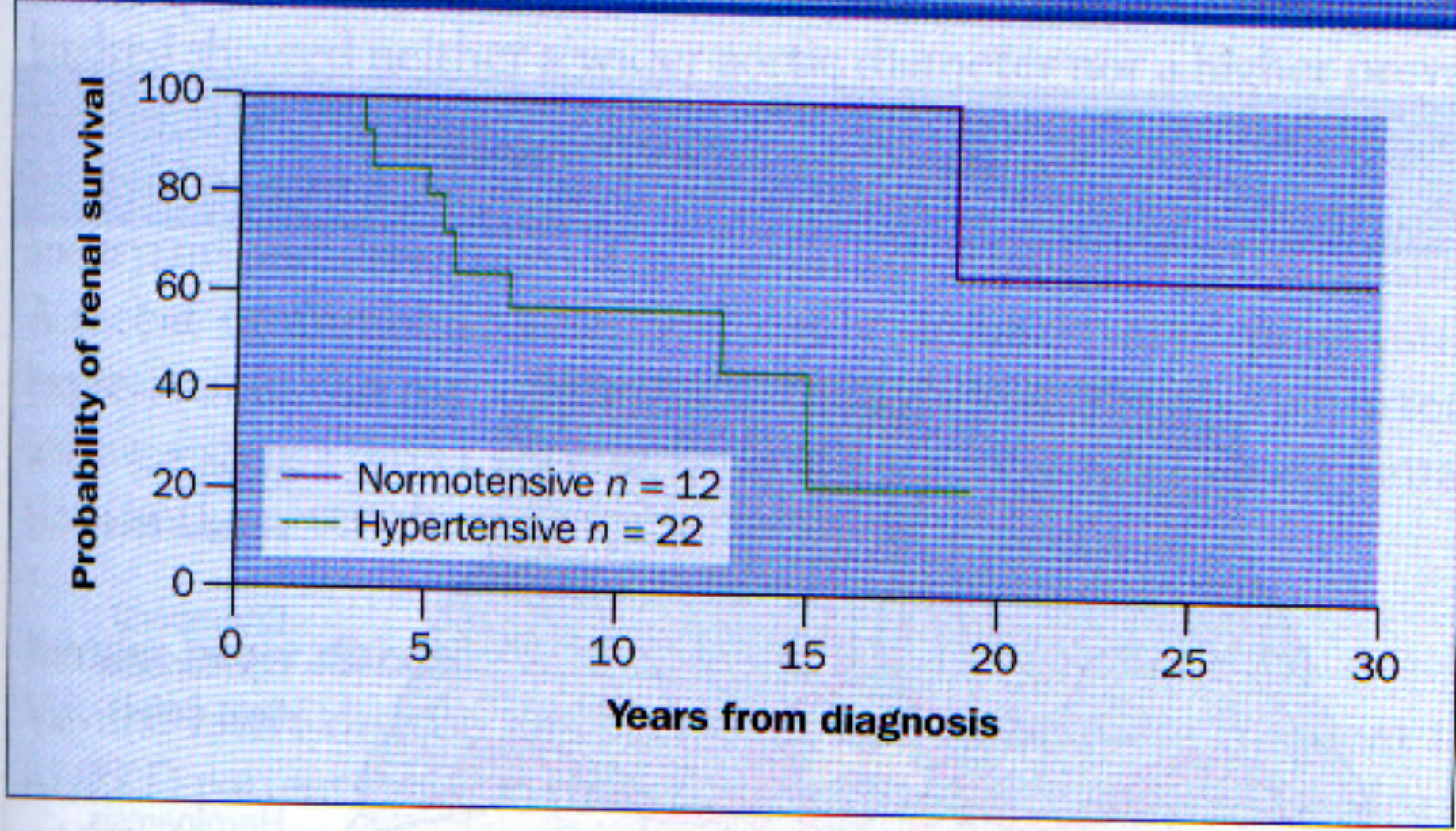
ADPKD
Renal Manifestations

- Infection: cystitis, pyelonephritis, cyst infection and perinephric infection
  - Women > men
  - E. coli, Klebsiella, Proteus, Enterobacter
- Nephrolithiasis
  - 20% of ADPKD
  - Uric acid /calcium oxalate
  - Risk factors: decreased NH3 excretion, low urine ph, low urine citrate

ADPKD
Renal Manifestations

- HTN
  - In ADPKD, HTN present in 75% before onset of renal failure
  - Statistical correlation between size and HTN
  - HTN correlates with progression of failure
  - Proteinuria/albuminuria correlate with MAP
  - LVH occurs early in the course
  - Risk factor for intracranial aneurysms

Effect of blood pressure on renal survival in autosomal dominant polycystic kidney disease



ADPKD
Renal Manifestations

- Renal Failure
  - 50% by age 57-73
  - Linear decline in GFR of 5-6.4 mL/min/yr
  - Risk factors:
    - Male
    - Dx before age 30
    - First hematuria before age 30
    - HTN before age 35
    - Hyperlipidemia
    - DD ACE gene polymorphism
    - Sickle cell trait

ADPKD ExtraRenal Manifestations

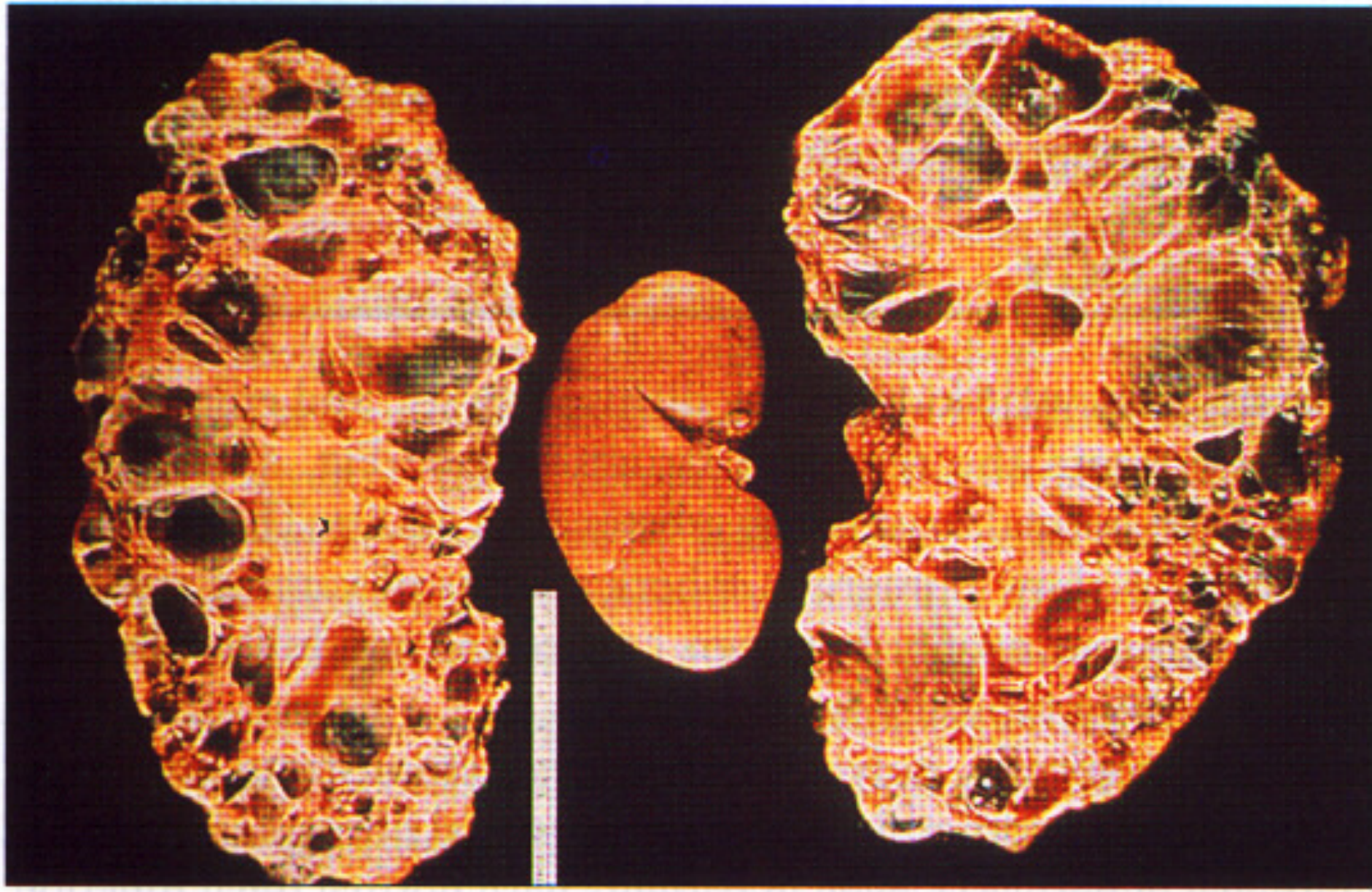
- Polycystic liver disease
  - Suspected with 4 or more cysts in hepatic parenchyma
  - Typically asymptomatic
  - Typically hepatic synthetic function is preserved
  - If fibrosis is extensive, will develop thrombocytopenia from hypersplenism
- Mitral Regurgitation with murmur

ADPKD ExtraRenal Manifestations

- Intracranial aneurysms
  - 8% of ADPKD population
  - Familial clustering
  - Yearly rate of rupture
    - 0.5% if <5mm
    - 4% if >10mm
  - Screening: for Family history of rupture, previous rupture, pre-op evaluation, high anxiety

ADPKD Pathology

- Macro: cysts of varying size distributed evenly between cortex and medulla
- Micro: advanced sclerosis of preglomerular vessels, interstitial fibrosis, and tubular epithelial hyperplasia



ADPKD Diagnostics

- Ultrasound
  - <30 2 cysts unilateral or bilateral
  - 30-59 2 cysts both kidney
  - >60 4 cysts in each kidney
- Genetic analysis

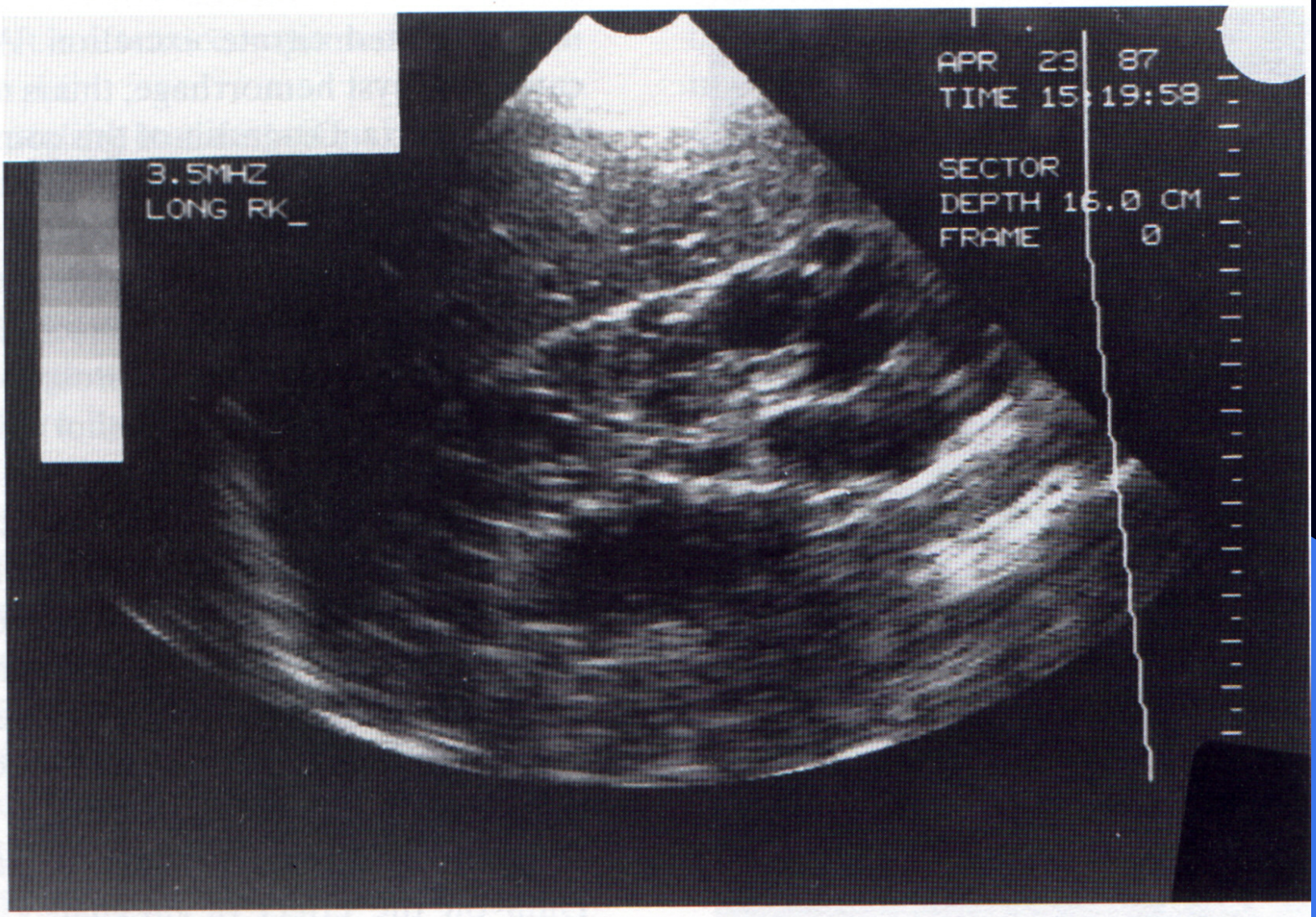


FIGURE 1 Renal ultrasonogram of a 44-year-old male with autosomal dominant polycystic kidney disease. The kidney is moderately enlarged and contains multiple cysts of variable size.

ADPKD
Natural History

- Risk factors for progression to renal failure:
  - PKD1 genotype
  - Male
  - Diagnosis before age 30
  - Hematuria before age 30
  - HTN before 35
  - High urine sodium excretion

ADPKD Transplantation

- Treatment of choice for ADPKD with ESRD
- No differences in graft/overall survival rates
- Complications no different from general population
- Native nephrectomy performed only if hx infected cysts, frequent bleeding, severe HTN, or massive enlargement with extension into pelvis

ADPKD Treatment

- Flank Pain
  - Must exclude infection, stone, tumor
  - Conservative therapy
  - Avoid nephrotoxins (NSAIDs)
  - Judicious use of narcotics
  - TCAs, Splanchnic nerve block
  - Decompression and sclerosis
    - Aspiration or open fenestration

ADPKD Treatment

- Cyst Hemorrhage
  - Bedrest, analgesics, fluids
  - Transfusion if necessary
  - Embolization of segmental artery if required
- Urinary Tract Infection/Cyst Infection
  - Prompt tx bacteruria/cystitis
  - Use lipophilic atbx agents for penetration into cysts and cyst fluid
    - TMP-SMZ, floroquinilones
  - Persistent fevers>1-2 weeks require drainage

ADPKD Treatment

- Nephrolithiasis
  - ECSW lithotripsy
- Hypertension
  - Agent of choice ACE-I/ARB
  - CCB will also increase renal blood flow

ADPCKD Treatment

- Marker for progression is kidney size
- Attempts to unroof cysts or multiple cyst puncture studies were ineffective and came with high morbidity.

ADPKD Treatment

Rapimmune: reduced kidney volume but no impact on loss of GFR

Somatostatin: reduced kidney volume but no impact on loss of GFR

Tolvaptan Treatment 2018 …..

ADPKD Treatment

Tolvaptan Treatment 2018:

TEMPO3:4 trial
NEJM2012;367;2407-2418.

REPRISE trial
Replicating Evidence of Preserved Renal Function. NEJM 2017;6;377:1930-1942.

ADPKD Treatment

Tolvaptan Treatment 2018:

Best results in pts with eGFR 25-65 ml/min/1.7 M2

Rate of decline in GFR reduced from 3.6 ml/min/year to 2.34 ml/min/year.

Saves 1.27 ml/min/year and would delay need for dialysis by 6-9 years.

ADPKD Treatment

Tolvaptan Treatment 2018:

Risk of hepatitis requiring withdrawal from drug: 5%

Risk for withdrawal from drug due to polyuria 6.8%

Have to get monitored through a provider trained in treatment with Jynarque (Tolvaptan labeled for treatment of PCKD) J-REMS

ADPKD Treatment

- Renal Failure – general approach
  - Control HTN
  - Treat hyperlipidemia
  - Dietary protein restriction
  - Control of acidosis
  - Control of hyperphosphatemia

ADPKD Treatment

- Intracranial Aneurysm
- <5mm can be watched and followed yearly, if size increases perform surgery
- 6-9 mm definitive treatment is controversial
- >10 mm and unruptured requires surgery

References

- Comprehensive Clinical Nephrology, 2000. RJ Johnson
- The Kidney, 6th Ed. 2000. BM Brenner
- Autosomal dominant polycystic kidney disease: modification of disease progression, DJ Peters, The Lancet 2001;358:1439-1444.

References

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