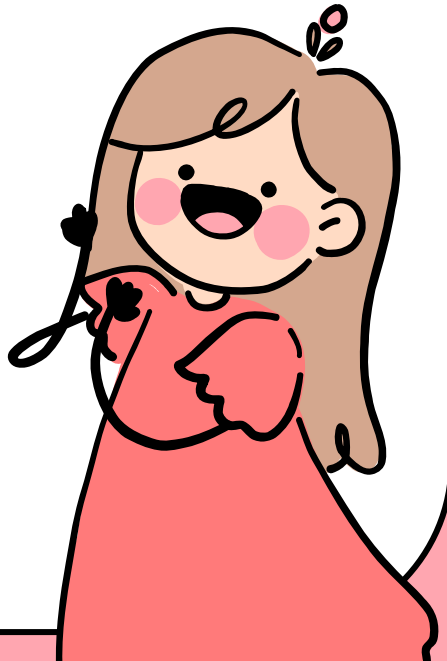
Grandround Nephrology

R2 Kotchapan/R3 Kanokporn
Aj.Chantida



Patient profile

Patient profile	เด็กชายไทย อายุ 1 ปี 6 เดือน ภูมิลำเนา จังหวัด สุรินทร์
Information source	ผู้ป่วย เวชระเบียนผู้ป่วยนอก ผู้ป่วยใน มีความน่าเชื่อถือสูง

Chief complaint : ท้องโต 1 ปี 4 เดือนก่อนมา รพ.

Present illness

- 1 ปี 4 เดือนก่อนมาโรงพยาบาล (ขณะอายุ 2เดือน) มารดาสังเกตว่าท้องโตมากขึ้น รับประทานนมได้น้อย ไม่มีอาเจียนเป็นเลือด น้ำหนักขึ้นไม่ดี อุจจาระปกติดี ปัสสาวะปริมาณปกติ ไม่มีปัสสาวะเป็นฟองหรือปัสสาวะเป็นเลือด ไม่มีไข้ ไม่มีอาการซึม ไปพบแพทย์ที่คลินิกวินิจฉัยท้องอืดได้การรักษาตามอาการ หลังจากนั้นอาการไม่ดีขึ้น จึงไปรักษาที่โรงพยาบาลสุรินทร์

- 1 ปี ก่อนมาโรงพยาบาล (ขณะอายุ 7 เดือน) Ultrasound abdomen ที่โรงพยาบาลสุรินทร์พบถุงน้ำในไตทั้ง 2 ข้าง

Past medical history

- เกิดก่อนครบกำหนด 36 สัปดาห์ น้ำหนักแรกเกิด 2,550 กรัม มีปัญหาตัวเหลืองแรกคลอดส่องไฟ 2 วัน กลับบ้านได้ ไม่มีภาวะแทรกซ้อนอื่น
- ประวัติฝากครรภ์ปกติที่คลินิก ไม่มีปัญหา
- ปฏิเสธประวัติการแพ้ยา แพ้อาหาร
- ได้รับวัคซีนครบตามเกณฑ์
- ประวัติ UTI ที่อายุ 11 เดือน urine culture : *Klebsiella sp.* >10^5 ได้ยาปฏิชีวนะ 7 วัน อาการดีขึ้น
  (รักษา รพ.แห่งหนึ่ง ไม่มีประวัติการตรวจวินิจฉัยเพิ่มเติม)

Past medical history (at 1 year 7 months)

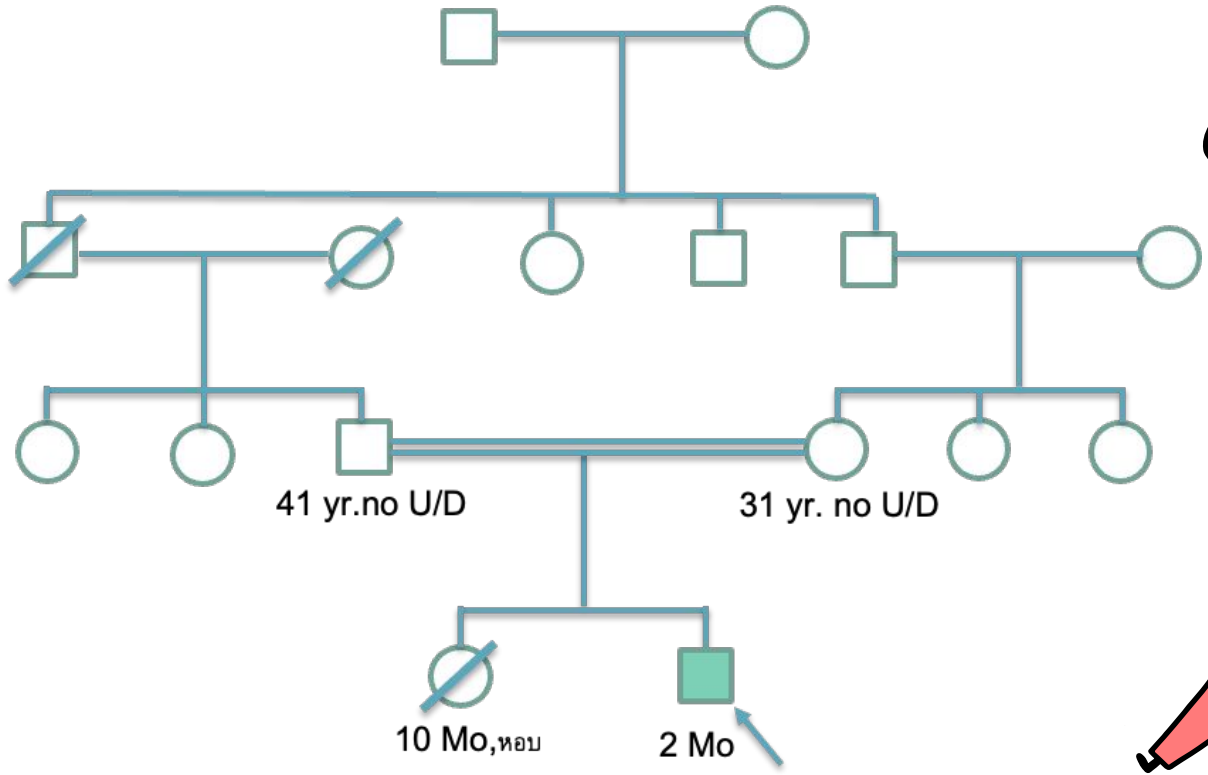
- **Nutrition** :
  - รับประทานข้าวเพียง 1-2 คำต่อมื้อ ดื่มนม NAN สูตร 2 จำนวน 6 oz 10 รอบ

- **Development** :
  - Gross motor: pull to stand (9 months)
  - Fine motor: towel and cubes (16 months)
  - Language: single slakable (6 months)
  - Social: play ball with examiner (12 months)

Family history

- บิดา อายุ 41 ปี อาชีพ รับจ้าง ปฏิเสธโรคประจำตัว
- มารดา อายุ 31 ปี อาชีพ แม่บ้าน ปฏิเสธโรคประจำตัว
- พี่สาว อายุ 10 เดือน เสียชีวิตด้วยโรคหอบเหนื่อย
- ปฏิเสธโรคไตในครอบครัว
- ปฏิเสธโรคอื่นๆในครอบครัวและโรคทางพันธุกรรม
- มีการแต่งงานในเครือญาติ

Pedigree



Physical examination(at 1 year 7 months)

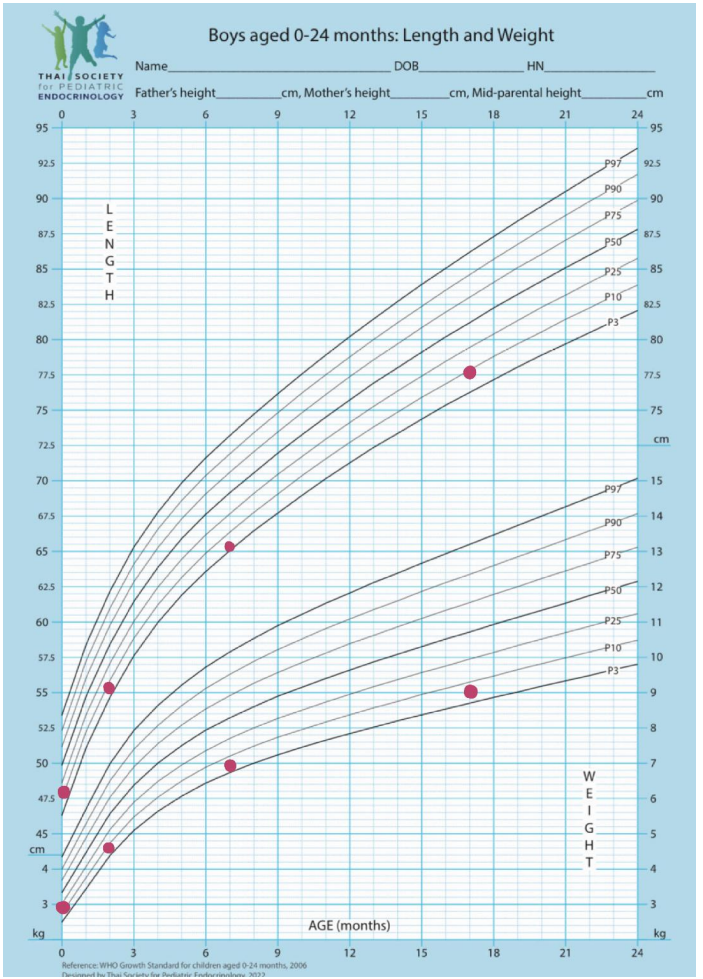
Vital signs	BT 37 C, BP 116/75 mmHg (>P95+12), PR102 bpm , RR 26 /min
Measurement	BW 9 kg (P3-10), Height 78 cm(P10)
GA	A Thai boy, Active, Alert
HEENT	Anicteric sclerae, mild pallor, no puffy eyelids
CVS	Pulse full,regular,normal s1s2,no murmur
RS	Symmetrical chest move , normal breath sound, No adventitious sound, no retraction

Physical examination(at 1 year 7 months)

ABDOMEN	Marked distension, superficial vein dilatation,no gynecomastia, no spider nervi, soft, not tender, palpable liver 3 cm BRCM and 2 cm at epigastrium, firm consistency, spleen 2 cm BLCM, bimanual palpable positive
Genitalia	Phimosis
EXT	No deformities, no edema
LN	No palpable LN at axillary , groin and epitrochlear node

Growth curve

- BW 9 kg (P3-10)
- Height 78 cm (P10)



Pertinent finding

Positive finding

- Failure to thrive
- Abdominal distension
- Feeding intolerance
- Bimanual palpable positive both side
- Anemia
- Superficial vein dilatation
- Splenomegaly
- Hypertension
- History of consanguinity
- History of preterm labour
- Delayed development
- Complete vaccination

Negative finding

- No polyuria
- No nocturia
- No antenatal history problems
- No underlying
- No history of kidney disease in family

Problem list

A Thai boy 1 years and 6 month of age presented with bilateral enlarged kidney with sign of portal hypertension.

Differential diagnosis

1. ARPKD
2. ADPKD
3.Nephronophthisis
4. Glycogen storage disease

WBC	7200	Cell/mm^3
Hb	7.8	d/dl
Hct	25.7	%
MCV	62.4	fl
MCH	24.3	peg
MCHC	33.6	g/dl
RDW	15	%
Platelet	154,000	Cells/mm^3
PMN	64	%
Lymphocyte	32	%
Monocyte	3	%
Eosinophil	1	%
Basophil	0	%

Anemia

WBC	7200
Hb	7.8
Hct	25.7
MCV	62.4
MCH	24.3
MCHC	33.6
RDW	15
Platelet	154,000
PMN	64
Lymphocyte	32
Monocyte	3
Eosinophil	1
Basophil	0

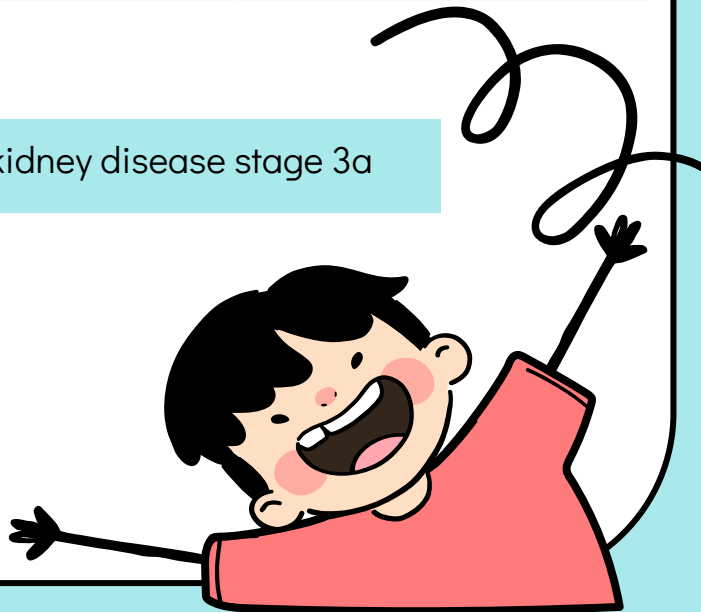
PBS : anisocytosis 2+, fragmented RBC 1+,target cell 1+

Hb tying : Suspected Hb E trait with Hb CS

BUN	**39.52**	**mg/dL**
Creatinine	0.60	mg/dL
GFR (Schwartz formula)	53.69	ml/min/1.73m2
Total protein	139	mg/dL
Albumin	4.77	mg/dL
Total bilirubin	105.1	mg/dL
Direct bilirubin	23	mg/dL
AST	43	U/L
ALT	43	U/L
ALP	145	U/L

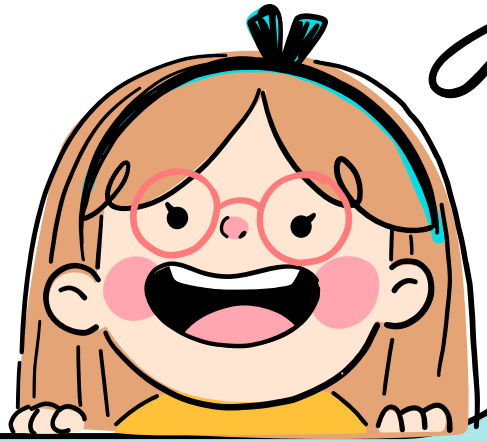
Sodium	**135**	mg/dL
Potassium	5.15	mg/dL
Chloride	105	mg/dL
Bicarbonate	16.6	mg/dL

>>Chronic kidney disease stage 3a

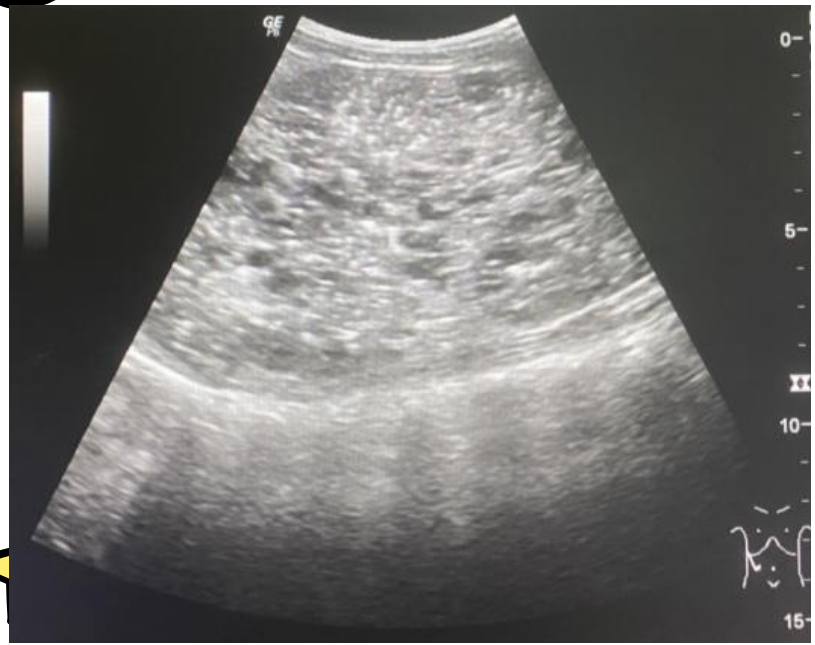


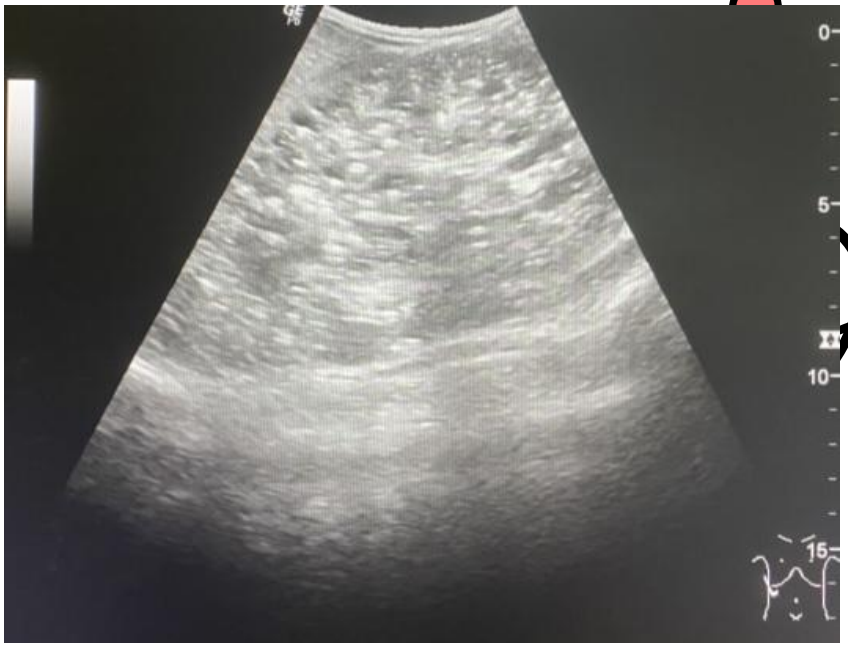
Urinary analysis (at 1 year 6 months)

Color/Appearance	Yellow/Clear
Specific gravity	1.015
pH	6
Protein	1+
Sugar	Negative
Ketone	Negative
Nitrite	Negative
WBC(/HPF)	5-10
RBC(/HPF)	10-20
Epithelium	1-2

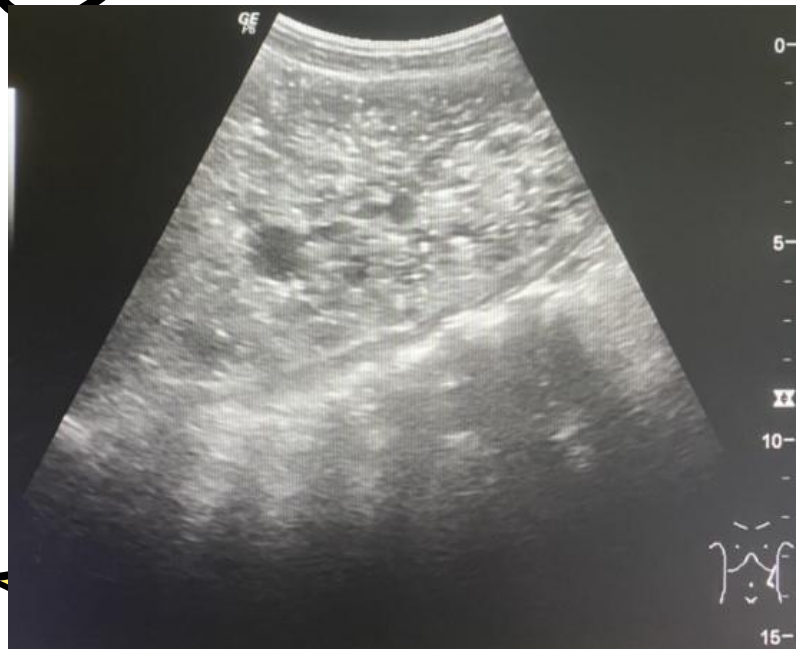


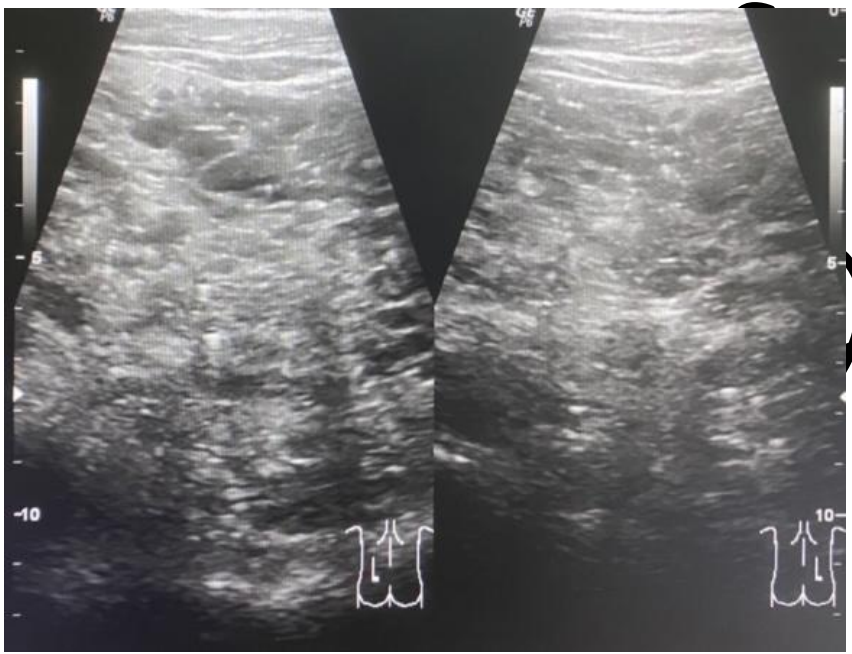
Ultrasound abdomen





Ultrasound abdomen





Ultrasound abdomen

- Marked enlargement of both kidneys with innumerable microcytic lesion scatter at both kidneys. Loss of corticomedullary differentiation is seen.All of these finding are suggestive of ARPKD
- Heterogeneous parenchymal echogenicity of liver with diffuse fibrosis. Suggestive of liver fibrosis.

- **Esophagogastroduodenoscopy**
  - No esophageal varice
- **Liver biopsy**
  - Hepatic fibrosis

Hepatic fibrosis with portal hypertension

Cystic kidney disease

Cystic kidney disease

" clinically and genetically heterogeneous group of disorder that have renal cysts or cystic dysplasia"

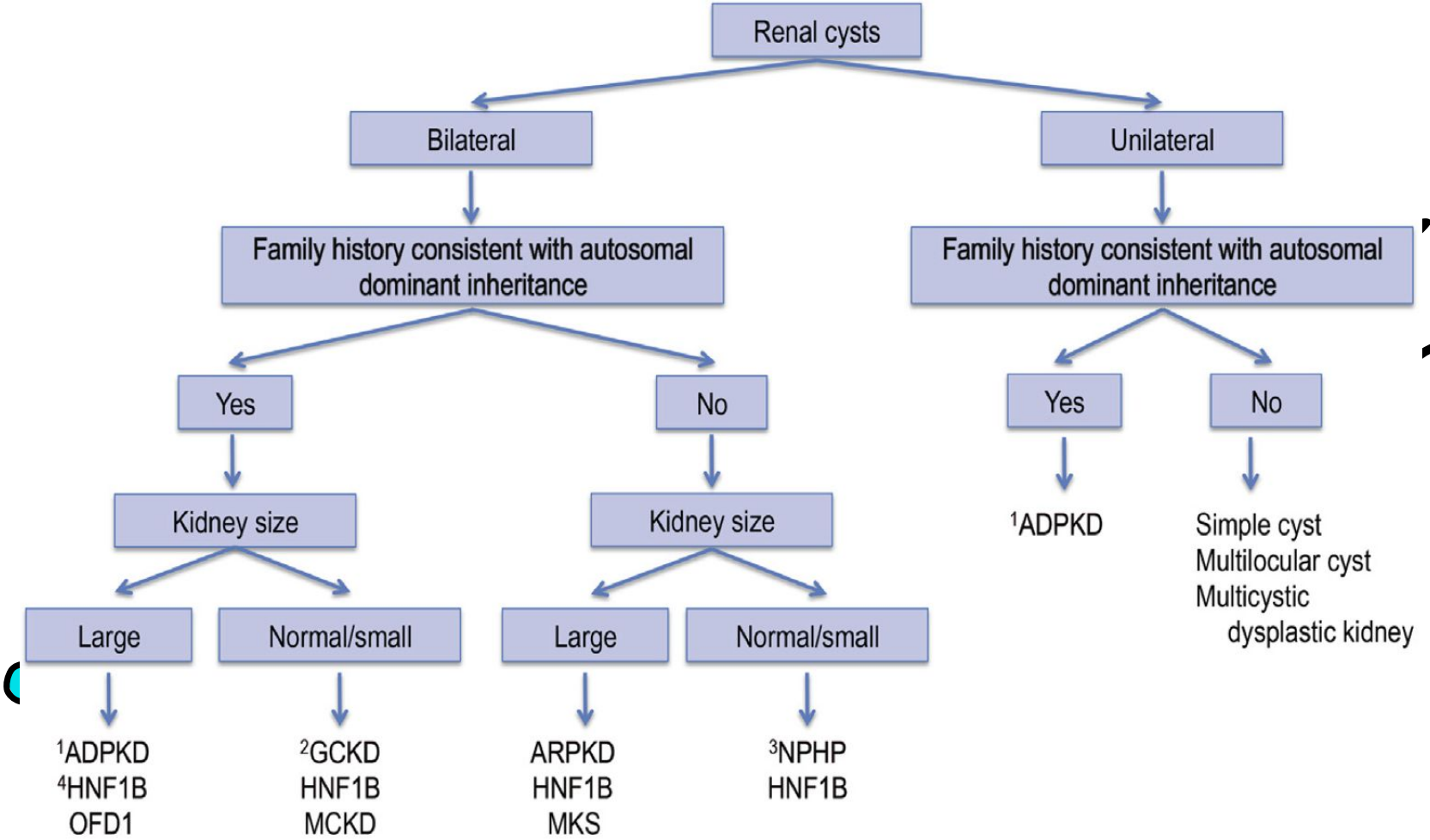
Ellis D. Avner et al., Pediatric Nephrology 7th edition.

01	Non-Hereditary	• Multicystic dysplastic kidney (MCDK) • Segmental multicystic dysplasia
02	Genetic disorder	• Polycystic kidney disease (ARPKD, ADPKD) • Glomerular renal cyst • Tubular cysts
03	Isolated renal cyst	• Simple renal cyst • Complex renal cyst
04	Acquired renal cyst	• ESRD • Liver transplantation

History taking

- Age of onset
- Location
- Size and Characteristic of kidney or cyst
- Clinical symptom
- Associated symptoms
  - Abdominal mass
  - Hypertension
  - Proteinuria
  - Urinary tract abnormality
  - Intracranial aneurysm
  - Hepatic fibrosis
- Family history of Polycystic kidney disease

Kliegman R Stanton B St Geme JW Schor NF Behrman RE Nelson WE. *Nelson Textbook of Pediatrics*. Edition 21 ed. Philadelphia PA: Elsevier; 2020.



Cramer, M. T., & Guay-Woodford, L. M. (2015). Cystic kidney Disease: a primer. Advances in Chronic Kidney Disease, 22(4), 297–305. https://doi.org/10.1053/j.ackd.2015.04.001

omparison of Clinical Features of Cystic Kidney Diseases

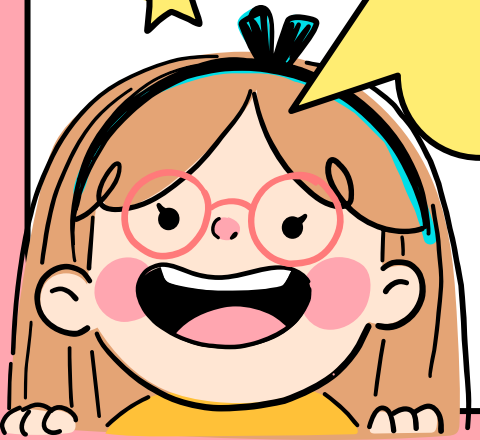
INHERITANCE	FREQUENCY	GENE PRODUCT	AGE OF ONSET	CYST ORIGIN	RENOMEGALY	CAUSE OF ESRD	OTHER MANIFESTATI
AD	1:400-1,000	*PKD1* *PKD2*	20s and 30s; <2% before age 15 Occasional perinatal onset	Anywhere (including the Bowman capsule)	Yes	Yes	Liver cysts Cerebral aneurysms Hypertension Mitral valve prolapse Kidney stones UTIs
AR	1:6,000-10,000	*PKHD1*	First year of life; perinatal onset	Distal nephron, CD	Yes	Yes	Hepatic fibrosis Pulmonary hypoplasia Hypertension
No	90% of ESRD patients at 8 yr	None	Years after onset of ESRD	Proximal and distal tubules	Rarely	No	None
No	50% in those older than 40 yr	None	Adulthood	Anywhere (usually cortical)	No	No	None
AR	1:80,000	Nephrocystins (NPHP1-9)	Childhood or adolescence	Medullary DCT	No	Yes	Retinal degeneration; neurologic, skeletal, hep cardiac malformations
AD	Rare	Uromodulin, others	Adulthood	Medullary DCT	No	Yes	Hyperuricemia, gout
No	1:5,000-20,000	None	30s	Medullary CD	No	No	Kidney stones Hypercalciuria
AD	1:10,000	Hamartin (TSC1) Tuberin (TSC2)	Childhood	Loop of Henle, DCT	Rarely	Rarely	Renal cell carcinoma Tubers, seizures Angiomyolipoma Hypertension
AD	1:40,000	VHL protein	20s	Cortical nephrons	Rarely	Rarely	Retinal angioma, CNS hemangioblastoma, rena carcinoma, pheochromo
XD	1:250,000	OFD1 protein	Childhood or adulthood	Renal glomeruli	Rarely	Yes	Malformation of the face, cavity, and digits; liver cy mental retardation
AR	1:65,000-160,000	BBS 14	Adulthood	Renal calyces	Rarely	Yes	Syndactyly and polydactyly obesity, retinal dystrophy hypogenitalism, hyperter intellectual disability

idney disease; AD, autosomal dominant; ADPKD, autosomal dominant polycystic kidney disease; AR, autosomal recessive; ARPKD, autosomal recessive polycystic kidney disease; CD, coll ous system; DCT, distal convoluted tubule; ESRD, end-stage renal disease; MCKD, medullary cystic kidney disease; MSK, medullary sponge kidney; UTI, urinary tract infection; VHL, von Hi minant.

ystic kidney disease. In Goldman L, Schafer AI (eds): Goldman's Cecil medicine, 24/e, Philadelphia, 2012, Saunders, Table 129-1.

Diagnosis

" Autosomal recessive polycystic kidney disease (ARPKD)"



ARPKD

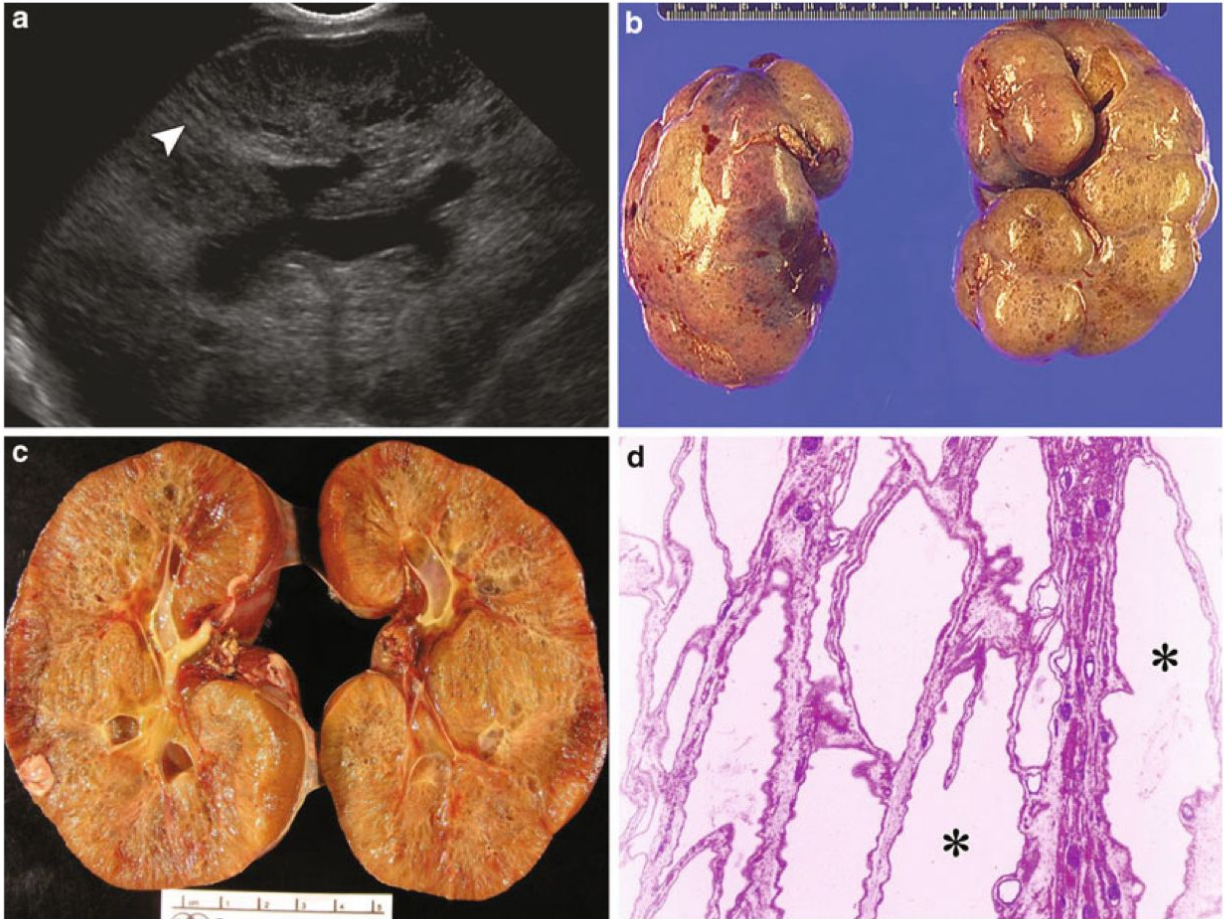
- ➔ “ ARPKD-congenital hepatic fibrosis”
- ➔ Autosomal recessive disorder
- ➔ Incidence 1:1,000 to 1:40,000
- ➔ Gene : PKHD1 (encodes fibrocystin)

Kliegman R Stanton B St Geme JW Schor NF Behrman RE Nelson WE. *Nelson Textbook of Pediatrics*. Edition 21 ed. Philadelphia PA: Elsevier; 2020.

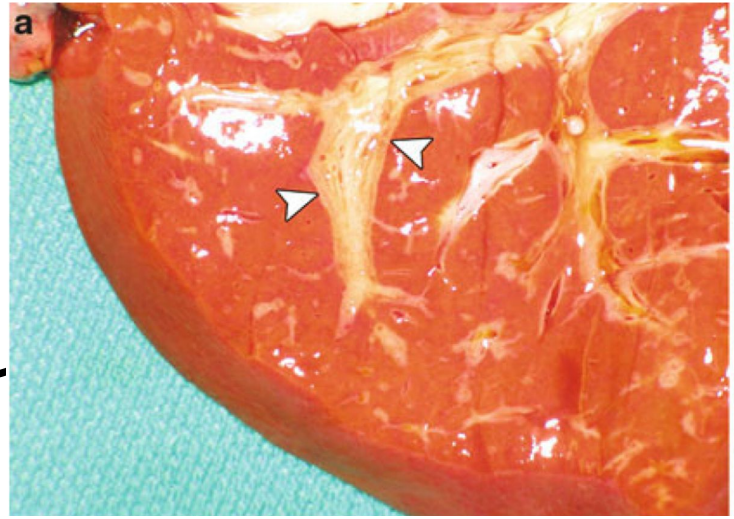
Pathology

- ➔ Markedly enlarged both kidneys
- ➔ Gross : innumerable small cyst throughout the cortex and medulla
- ➔ Microscopic : dilated, ectatic collecting ducts radiating from medulla to cortex
- ➔ Advance stage : interstitial fibrosis and tubular atrophy
- ➔ Liver involvement : ductal plate abnormality , bile duct proliferation and ectasia >> progressive hepatic fibrosis

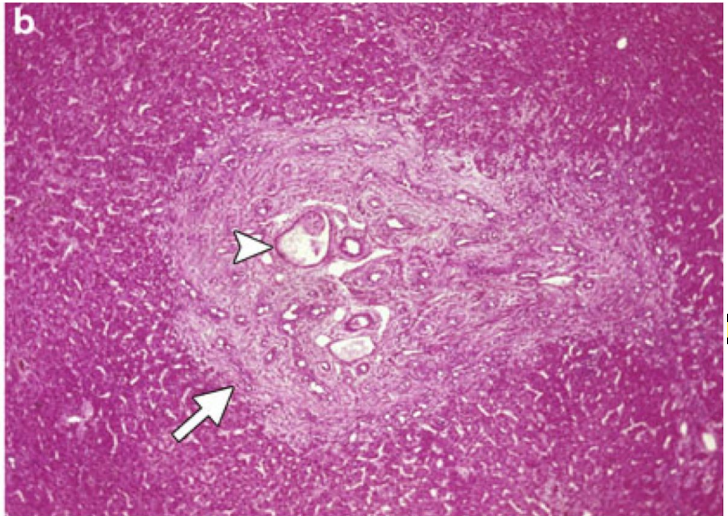
Kliegman R Stanton B St Geme JW Schor NF Behrman RE Nelson WE. *Nelson Textbook of Pediatrics*. Edition 21 ed. Philadelphia PA: Elsevier; 2020.



Ellis D. Avner et al., Pediatric Nephrology 7th edition.

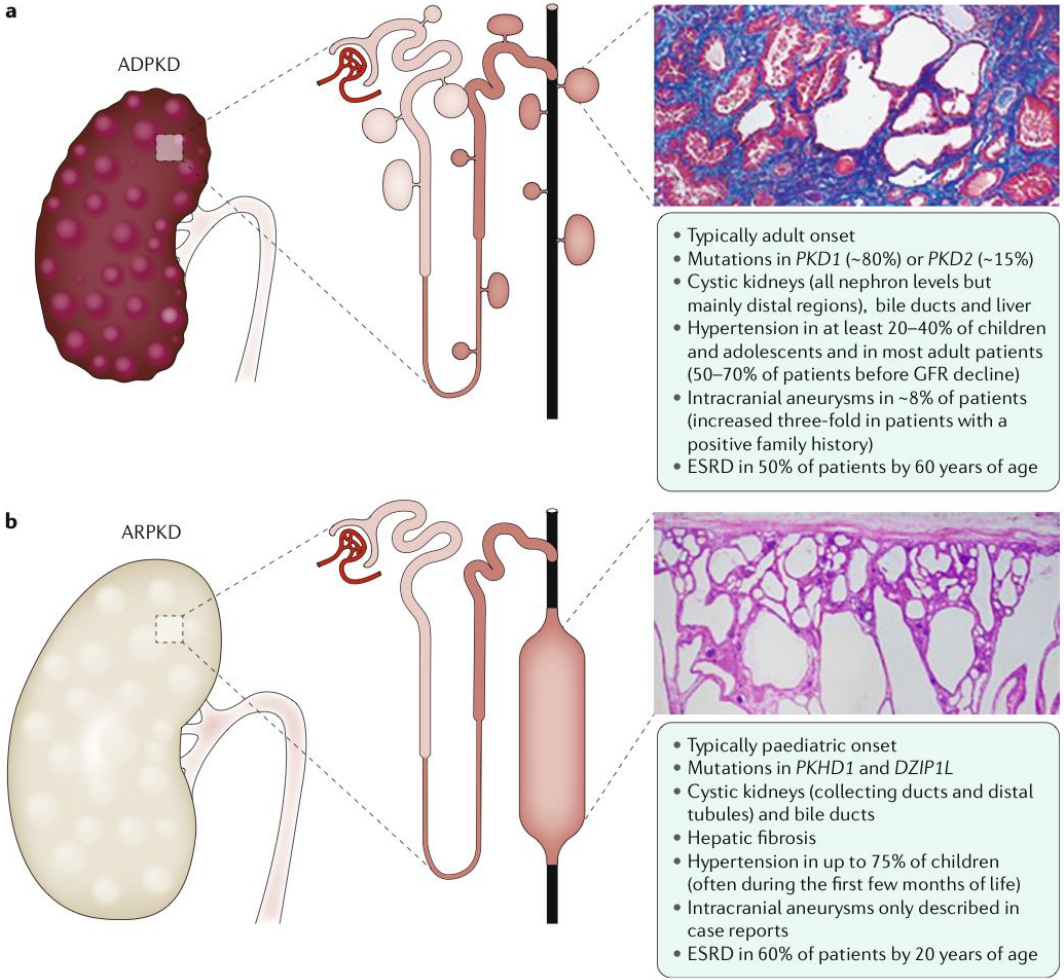


Liver section shows periportal fibrosis (arrowheads).



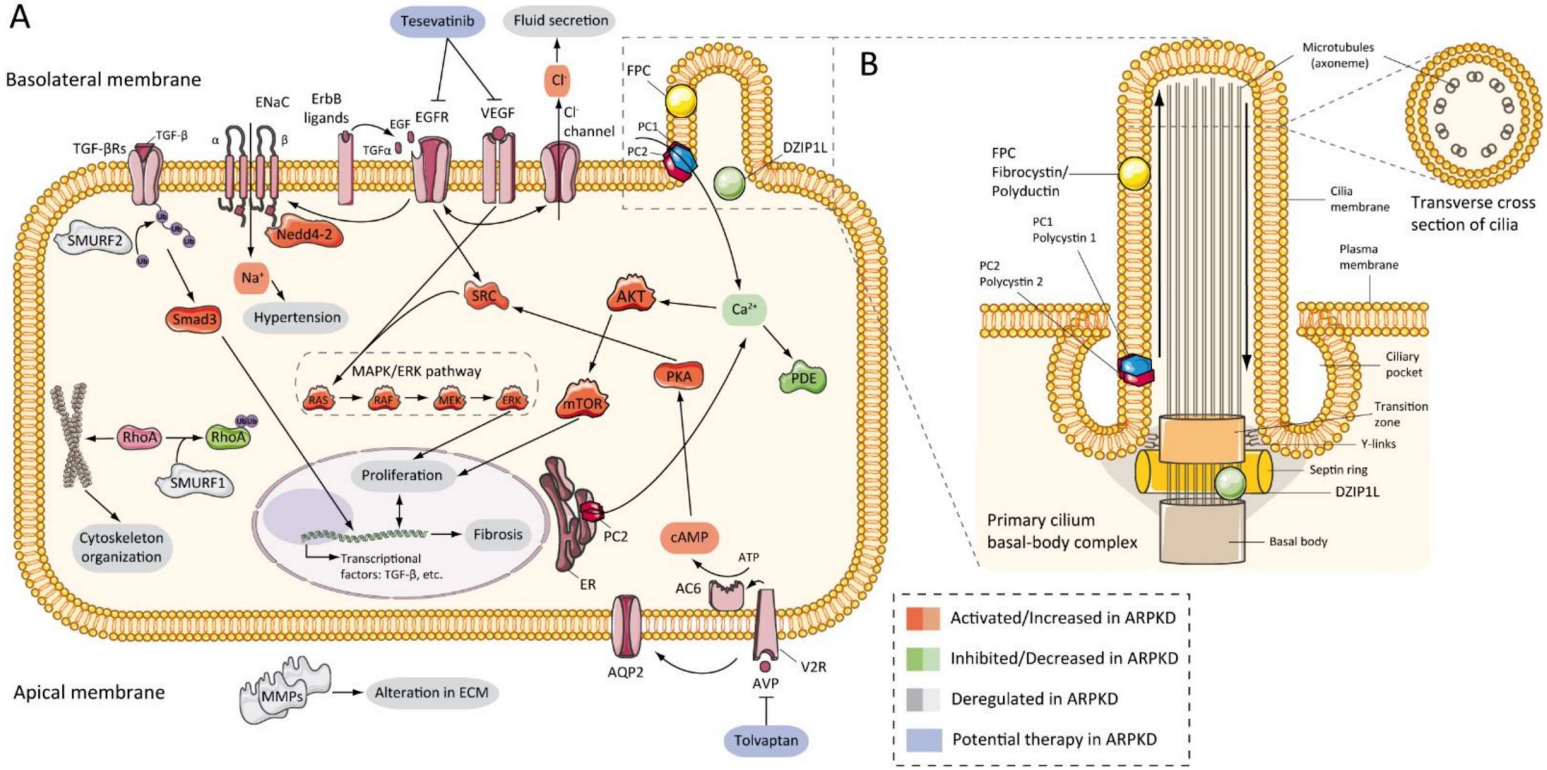
Hematoxylin–eosin stain of the liver shows the portal vein and hepatic artery (arrowhead) in a portal area expanded by fibroblastic proliferation (arrow)

Ellis D. Avner et al., Pediatric Nephrology 7th edition.



Carsten B, et al . Polycystic kidney disease :. Nature Reviews Disease Primers 2018

Pathogenesis



Cordido, A., Vizoso-González, M., & García-González, M. A. (2021). Molecular Pathophysiology of Autosomal Recessive Polycystic kidney Disease. International Journal of Molecular Sciences, 22(12), 6523. https://doi.org/10.3390/ijms22126523

Clinical

Fetal period

- ➔ Enlarged echogenic kidney with poor corticomedullary differentiation
- ➔ Oligohydramnios
- ➔ Pulmonary hypoplasia

Kliegman R Stanton B St Geme JW Schor NF Behrman RE Nelson WE. *Nelson Textbook of Pediatrics*. Edition 21 ed. Philadelphia PA: Elsevier; 2020.

Clinical

Older infant period

- ➔ Flank mass (enlarged kidney)
- ➔ Urine concentrating defect
- ➔ Hypertension
- ➔ Hepatosplenomegaly

Kliegman R Stanton B St Geme JW Schor NF Behrman RE Nelson WE. *Nelson Textbook of Pediatrics*. Edition 21 ed. Philadelphia PA: Elsevier; 2020.

Clinical

Older children period

- ➔ Hepatosplenomegaly
- ➔ Portal hypertension

Kliegman R Stanton B St Geme JW Schor NF Behrman RE Nelson WE. *Nelson Textbook of Pediatrics*. Edition 21 ed. Philadelphia PA: Elsevier; 2020.

Diagnosis

1. Ultrasound kidney

- Enlarge both kidney with increased echogenicity and poor corticomedullary differentiation.

2. One or more of following ;

2.1 Absence of renal cyst in both parents

2.2 Clinical, Laboratory, or radiographic evidence of hepatic fibrosis

2.3 Hepatic pathology ; ductal plate abnormalities

2.4 Previous affected sibling with pathologically or genetically confirmed disease

2.5 Parental consanguinity suggestive of autosomal recessive inheritance

Ellis D. Avner et al., Pediatric Nephrology 7th edition.

Caroli disease

- A dilatation of intrahepatic bile ducts and/or dilatation of common bile duct
- Predisposition to ascending cholangitis
- Associated with portal hypertensive bleeding

Caroli syndrome

Caroli disease presented with congenital hepatic fibrosis or portal hypertension

Kliegman R Stanton B St Geme JW Schor NF Behrman RE Nelson WE. *Nelson Textbook of Pediatrics*. Edition 21 ed. Philadelphia PA: Elsevier; 2020.

Progression note

Ultrasound whole abdomen

- Enlarged size and heterogeneous parenchymal echogenicity of liver with diffuse fibrosis. Mild dilated IHD at porta hepatis is seen.
- The gallbladder shows partial distension with a few gallstones. No pericholecystic fluid is noted.

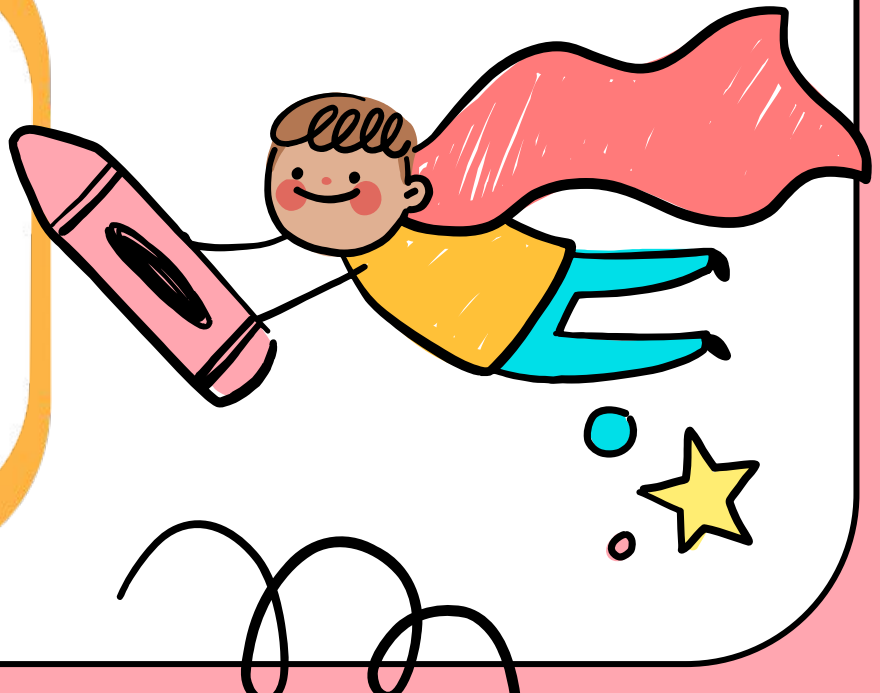
"Caroli syndrome"

Progression note

02/05/2023

- **Esophagogastroduodenoscopy**

  Multiple small EVs without sign of bleeding.



Management

- Supportive treatment
  - Control blood pressure (ACEI
  - Correct electrolyte abnormalities
  - Appropriate volume status
  - Nutritional support
- Nephrectomy (unilateral/bilateral) if Indicated
- Renal replacement therapy
- CKD management
- Kidney / Kidney-Liver transplantation
- Genetic counseling

"No specific treatment"

Kliegman R Stanton B St Geme JW Schor NF Behrman RE Nelson WE. *Nelson Textbook of Pediatrics*. Edition 21 ed. Philadelphia PA: Elsevier; 2020.

Prognosis

- ➔ Pulmonary hypoplasia in newborn period (high mortality rate)
- ➔ CKD within 10 years
- ➔ Survival rate 67% - 79% at age 15 years

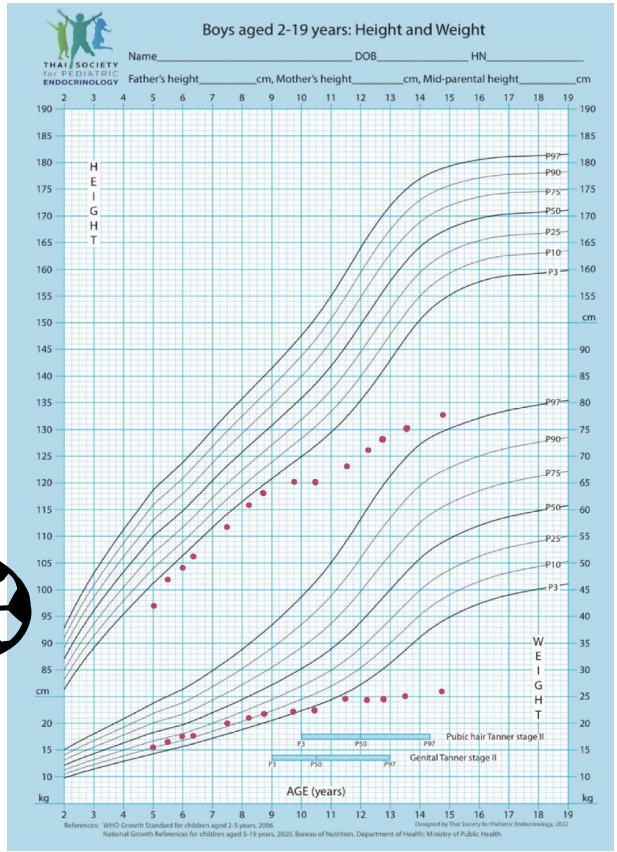
Kliegman R Stanton B St Geme JW Schor NF Behrman RE Nelson WE. *Nelson Textbook of Pediatrics*. Edition 21 ed. Philadelphia PA: Elsevier; 2020.

Diagnosis Summary

- Autosomal recessive polycystic kidney disease (ARPKD)
- Chronic kidney injury stage 4
- Hypertension
- Anemia due to chronic disease
- Hepatic fibrosis with portal hypertension
- History of recurrent UTI

Progression note

Last visit 31/10/2023
ARPKD with CKD stage 4
#Calori syndrome



WBC	3000
Hb	9.2
Hct	28.5
MCV	62.5
MCH	24.3
MCHC	33.5
RDW	15
Platelet	69,000
PMN	70.9
Lymphocyte	21.8
Monocyte	4
Eosinophil	2.3
Basophil	1

Progression note

Last visit 31/10/2023
ARPKD with CKD stage 4
#Calori syndrome

BUN	67.3
Creatinine	3.26(16.95)
Sodium	137.2
Potassium	4.81
Chloride	101.1
Bicarbonate	23.6

Calcium	9.7
Phosphorus	4.46
Vitamin D	38
Ferritin	464

Chronic kidney disease stage 4

Take home message

- ➔ Learn about clinical to determine cystic kidney disease.
- ➔ How to approach and selected investigation for diagnosis cystic kidney disease.
- ➔ Appropriate initial management and continuity care in patient with ARPKD.
- ➔ To learn about prognosis in ARPKD for initial counseling with their parents.

Thank You

Any question?