1/ Hello #Medtwitter #NephTwitter.

Kidney tumors are often diagnosed incidentally, with parents noticing an abdominal mass in young children. Here we will discuss kidney tumors from genetic background to management and prognosis.

#ASPNFOAM group @ASPNeph #pedneph #kidneytumor

2/Poll: Before we begin, let's brainstorm with a quick poll on kidney tumors

What is the percentage of kidney tumors among childhood malignancies?

- 6%
- 3%
- 18%
- 12%

3/ Yes, A

Kidney tumors comprise 6% of all childhood malignancies.

Wilms tumor (WT) or nephroblastoma is the most common among them.

The other kidney tumors seen in children are:

- Clear cell sarcoma of the kidney
- Malignant rhabdoid tumor of the kidney
- Congenital mesoblastic nephroma
- Renal cell carcinoma

PMID: 16919774

4/ Majority of pediatric kidney tumors present in the first decade:

WT which comprises 90% of them.

RadioGraphics

Table 1: Pediatric Renal Tumors: The 1st Decade

Wilms tumor	Accounts for 90% of pediatric renal tumors Peak age, 2–3 y Solid, but often contains necrosis or old hemorrhage Calcification, 15% May invade renal vein Bilateral masses suggest nephroblastomatosis and genetic predisposition
Cystic nephroma and CPDN	Young boys Cystic with septa Herniates into collecting system No nodularity or solid enhancing components
Mesoblastic nephroma	Congenital; most common tumor under age 5 mo Solid, but cellular type may contain cystic components "Ring" sign at US (classic type)
Clear cell sarcoma	Mean age, 36 mo; rare at <6 mo Solid, but cystic components common Calcification uncommon Metastasizes to bone
Rhabdoid tumor	Rare Peak age, 11 mo Central; arises from medulla Calcification, 70% Subcapsular fluid collection Lobulated architecture Synchronous brain tumor
ORTI	Very rare Calcification typical; resembles staghorn calculus Attached to papilla and grows into collecting system
RCC	May occur in younger children with von Hippel–Lindau disease Resembles Wilms tumor and RCC in adults
Angiomylolipoma	May occur in younger children with tuberous sclerosis complex Contains fat and intensely enhancing areas
Metanephric stromal tumor	Mean age, 2 y Solid, but may contain large cystic component

Note.—RCC = renal cell carcinoma, US = ultrasonography.

PMID: 26963460

5/ Genetics of kidney tumors:

Wilms: *WT1, CTNNB1, WTX*

Metanephric tumors: *BRAFV600E*

Neuroblastoma: *MYCN*

PMID: 16919774

Table 5. The most common genetic aberrations useful in the differential diagnoses of pediatric renal tumors.

Tumor Type	Subtype	Genetic Aberrations Useful in Diagnostics	Techniques
WT		~35% *WT1, CTNNB1, WTX*	NGS
		~10% *SIX1/2*	NGS
		~15% microRNA processing genes (*DROSHA, DGCR8, DICER1*)	NGS
		~2.5% *TRIM28* mutations (up to 90% in pure epithelial WT)	NGS
		~5% *TP53* mutations (Anaplastic WT)	IHC, NGS
		Less common mutations: *FXBW7, MYCN, BCOR, MLLT1*	NGS
CCSK		Somatic *BCOR*-ITD (85-100%)	IHC, FISH
		t(10;17) (~10%)	FISH
		Rare: *BCOR-CCNB3* translocation	FISH, NGS
MRTK		~95% biallelic inactivation *INI1* (*SMARCB1*)	IHC, NGS, NGS
		~5% *SMARCA4* mutations	
CMN	Classic	~57% *EGFR*-ITD	NGS
	Cellular	70–80% t(12;15)(p13;q25)	FISH
		12% *EGFR*-ITD	NGS
		Few cases reported with *BRAF*-ID rearrangements	NGS
	Mixed	t(12;15)(p13;q25)	FISH, NGS
		82% *EGFR*-ITD	NGS
RCC	t(6;11) tRCC	Translocations involving *TFEB*	IHC (TFEB), FISH
	Xp11.2 tRCC	Translocations involving *TFE3*	IHC (TFE3), FISH
	PRCC	Type 1: 81% *MET* alterations	NGS
		Type 2: 25% *CDKN2A* alterations	NGS
	ALK-RCC	Translocations involving *ALK*	FISH
	HLRCC-RCC	*FH* mutations	IHC, NGS
	SDH-related RCC	*SDHB* mutations	IHC, NGS
Metanephric tumors	MA	~90% *BRAFV600E* mutation	IHC, NGS
	MST	~65% *BRAFV600E* mutation	IHC, NGS
	MAF	~50% *BRAFV600E* mutation	IHC, NGS
Neuroblastoma		Mainly in high risk: *MYCN* amplification (18–38%)	FISH, NGS
		Mutations in a variety of genes (e.g., *MYCN*)	NGS
EWS		Translocations involving *EWS*	FISH
DSRCT		>95% t(11;22)(p13;q11.2 or q12)	FISH

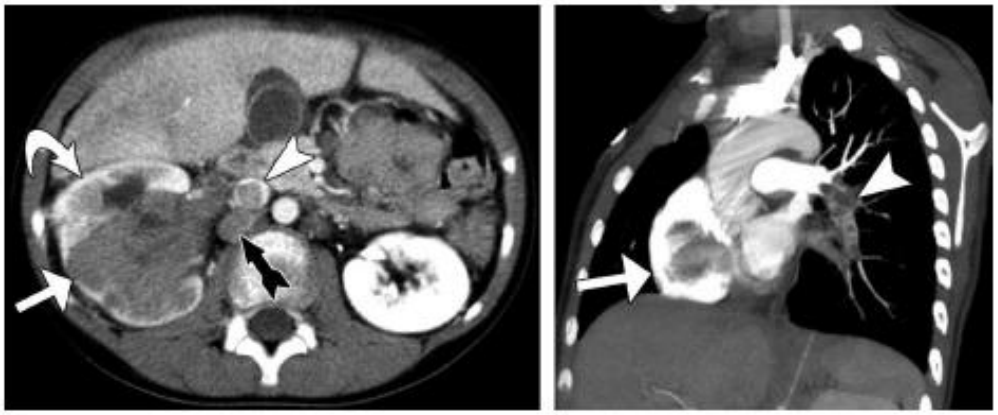
WT = Wilms tumor; CCSK = clear cell sarcoma of the kidney; MRTK = malignant rhabdoid tumor of the kidney; CMN = congenital mesoblastic nephroma; RCC = renal cell carcinoma; tRCC = translocation associated renal cell carcinoma; ALK-RCC = anaplastic lymphoma kinase-rearranged RCC; HLRCC-RCC = hereditary leiomyomatosis renal cell carcinoma - RCC; SDH-related -RCC = succinate dehydrogenase related renal cell carcinoma; MA = metanephric adenoma; MST = metanephric stromal tumor; MAF = metanephric adenofibroma; EWS = Ewing sarcoma; DSRCT = desmoplastic small blue round cell tumor; IHC = immunohistochemistry; FISH = fluorescence in situ hybridization; NGS = next generation sequencing; ITD = internal tandem duplication; ID = internal deletion.

6/ Wilms tumor

- Most common among the pediatric kidney tumors
- 75-80% of cases occur in children < than 5 yrs
- Parents often discover an asymptomatic abdominal mass
- Pain, malaise, hypertension (renovascular), and haematuria (microscopic or gross) are presenting features.

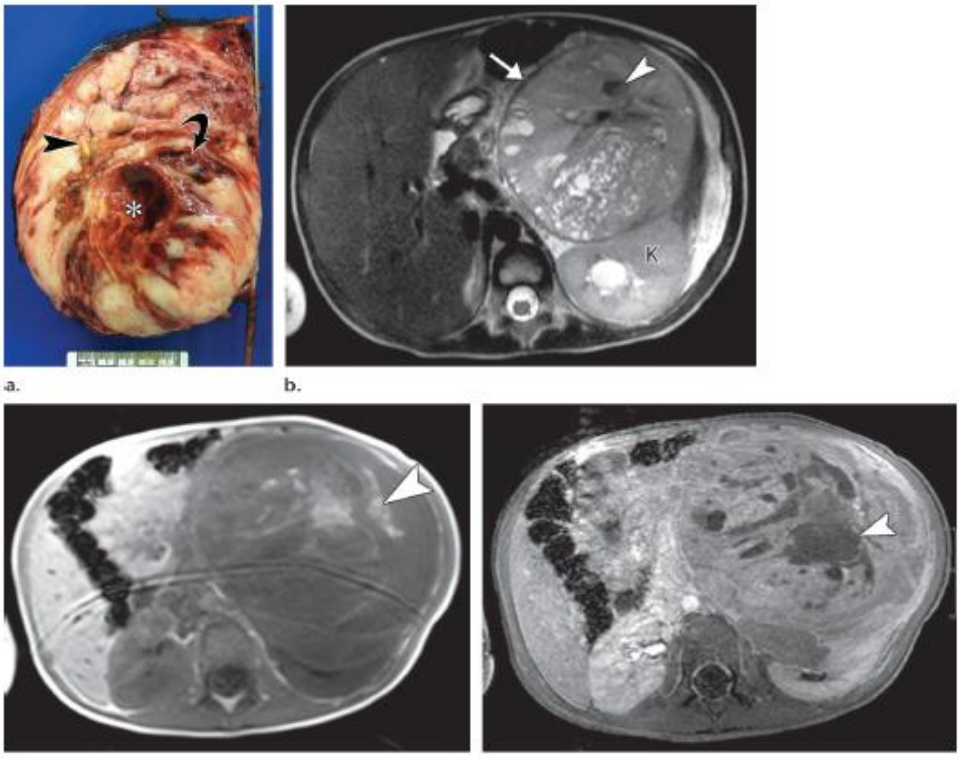
7/ Diagnosis of Wilms tumor

- US: Heterogeneous tumor hypoechoic & anechoic areas (Hemorrhage, necrosis & cyst). Color Doppler to see tumor spread →inf vena cava.
- CT scan: Large heterogeneous intrarenal mass; calcification in 15% case
- MRI: Heterogeneous lobulated & hypointense tumor
- Pathology: Well circumscribed/ microlobulated tumor ē central necrosis & hemorrhage



a. b.

Figure 3. Wilms tumor with rhabdomyomatous differentiation in a 12-year-old boy. **(a)** Axial postcontrast CT image shows a partially circumscribed slightly heterogeneous tumor (straight white arrow), which is hypoattenuating compared with enhancing renal cortex (curved arrow). Hypoattenuating tumor thrombus surrounded by contrast material is seen in the IVC (arrowhead). Also note the enlarged regional lymph node (black arrow). **(b)** Oblique sagittal image from pulmonary embolism CT shows hypoattenuating tumor thrombus in the right ventricle (arrow) and left lower lobe pulmonary artery (arrowhead).



a. b.

c. d.

Figure 2. Wilms tumor with unfavorable histology in a 2-year-old girl. **(a)** Sectioned nephrectomy specimen shows a white-tan soft fleshy tumor with small foci of hemorrhage (arrow), necrosis (arrowhead), and cyst formation (•). **(b)** Axial T2-weighted image shows the tumor surrounded by a dark capsule (arrow). The internal signal is heterogeneous with areas that are isointense to adjacent parenchyma *(K)*, hypointense areas corresponding to hemorrhage (arrowhead), and fluid-signal-intensity cysts. **(c)** Axial T1-weighted image shows that the tumor is isointense to renal parenchyma with hyperintense areas representing hemorrhage (arrowhead). **(d)** Axial T1-weighted image with fat saturation after intravenous administration of gadolinium contrast material shows diffuse enhancement of the mass with nonenhancing areas of hemorrhagic necrosis (arrowhead).

8/ Management & prognosis WT

- Complete nephrectomy for unilateral WT
- According to NWTSG, primary surgery is followed by chemotherapy & radiation
- SIOP (International Society of Paediatric Oncology) recommends preoperative chemotherapy & then surgery
- Management of HTN (RAASi preferred)

PMID: 23331787

9/ Here is another quick poll about the prognosis of WT

What is the 5 years survival for WT?

- >90%
- >86%
- >35%
- >55%

10/ Yes, A

- 5 years of survival for disease localized to the abdomen is > 90%
- Overall survival is 70% for stage IV disease
- Long term WT survivors are at risk of
    - Secondary malignancy, congestive heart failure related to doxorubicin
    - Respiratory compromise due to radiation therapy,
    - CKD, Hypertension or renal failure PMID: 25156758

11/ Long term follow up of WT5

- Abdominal ultrasonography every 3 months for the first 2 years for surveillance of recurrence
- Children with the bilateral disease are at increased risk of renal impairment and ESKD compared to those with U/L disease
    - Need long term follow up for renal insufficiency

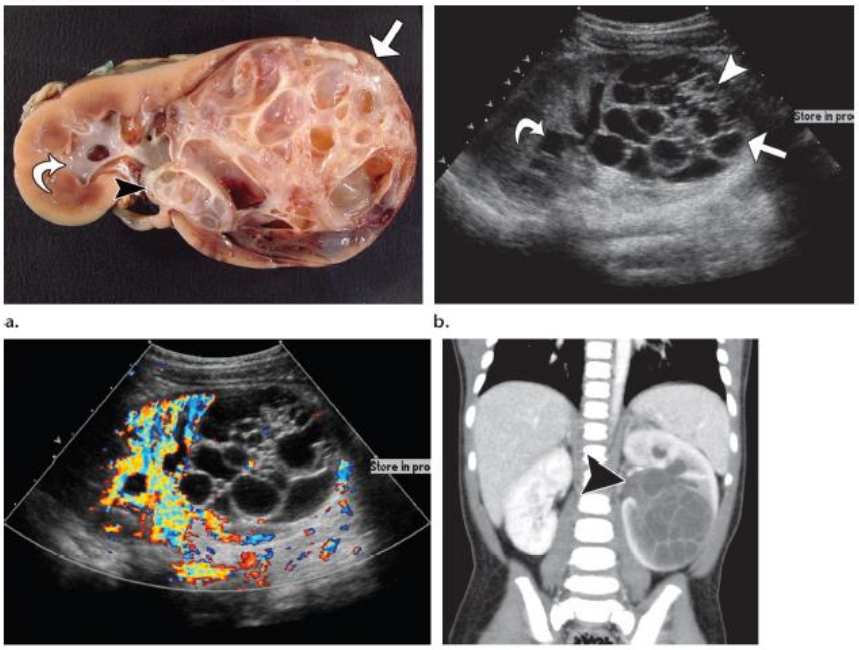
12/ Cystic Nephroma (CN) & CPDN (Cystic partially differentiated nephroblastoma)

- Also known as *multilocular cystic renal tumor*
- CN originates from metanephric tissue & represents part of the spectrum of neuroblastoma, ganglioneuroblastoma & ganglioneuroma
- Children aged 3 months to 4 years are affected; M>F 2:1 (PMID: 21807169)

13/ Diagnosis & Management of CN & CPDN

- Imaging: A well-circumscribed, encapsulated, multiseptated cystic masses ē no nodular solid components
- For unifocal cyst, Bosniak criteria for is suggested for monitoring (PMID: 25910795)
- Multilocular cystic renal tumor: Surgical resection
- CPDN is more aggressive & local recurrence is rare

Figure 7. Cystic nephroma in an 11-month-old girl. **(a)** Photograph of sectioned nephrectomy specimen shows a large cystic tumor in the lower pole (straight arrow). The tumor is seen to herniate into the renal pelvis (arrowhead), causing dilatation of the collecting system (curved arrow). **(b)** Longitudinal US image shows the mass composed of many anechoic cysts in the lower pole of the left kidney (straight arrow). The mass is causing caliectasis (curved arrow). Areas with small cysts appear echogenic and solid (arrowhead). **(c)** Longitudinal color Doppler image shows some flow within the septa. **(d)** Coronal CT image after intravenous administration of iodinated contrast material shows enhancement of only the septa and herniation of the tumor into the renal pelvis (arrowhead).



a. b.

14/ Congenital mesoblastic nephroma (CMN)

- 3-6% of pediatric renal tumors & most common in neonates ē M:F is 1.5:1
- Mostly diagnosed in the first 3 months; Prenatal diagnosis can be as early as mid-second trimester
- 71% associated ē perinatal complications (Polyhydramnios, hydrops fetalis & preterm delivery)

15/ Tumor types & managements

- Types: Classic & cellular; 10-20% are of both patterns.
- Cellular CMN: Larger & occur in slightly older patients (>3 months of age); relatively aggressive growth
- Imaging: Homogeneous solid mass & involvement of renal hilum without vessel invasion.
- Treatment:
    - Nephrectomy
    - Chemotherapy & multimodal therapy (Unresectable or residual tumor)
- Survival > 90% & prognosis is best if the tumor resected <6 months

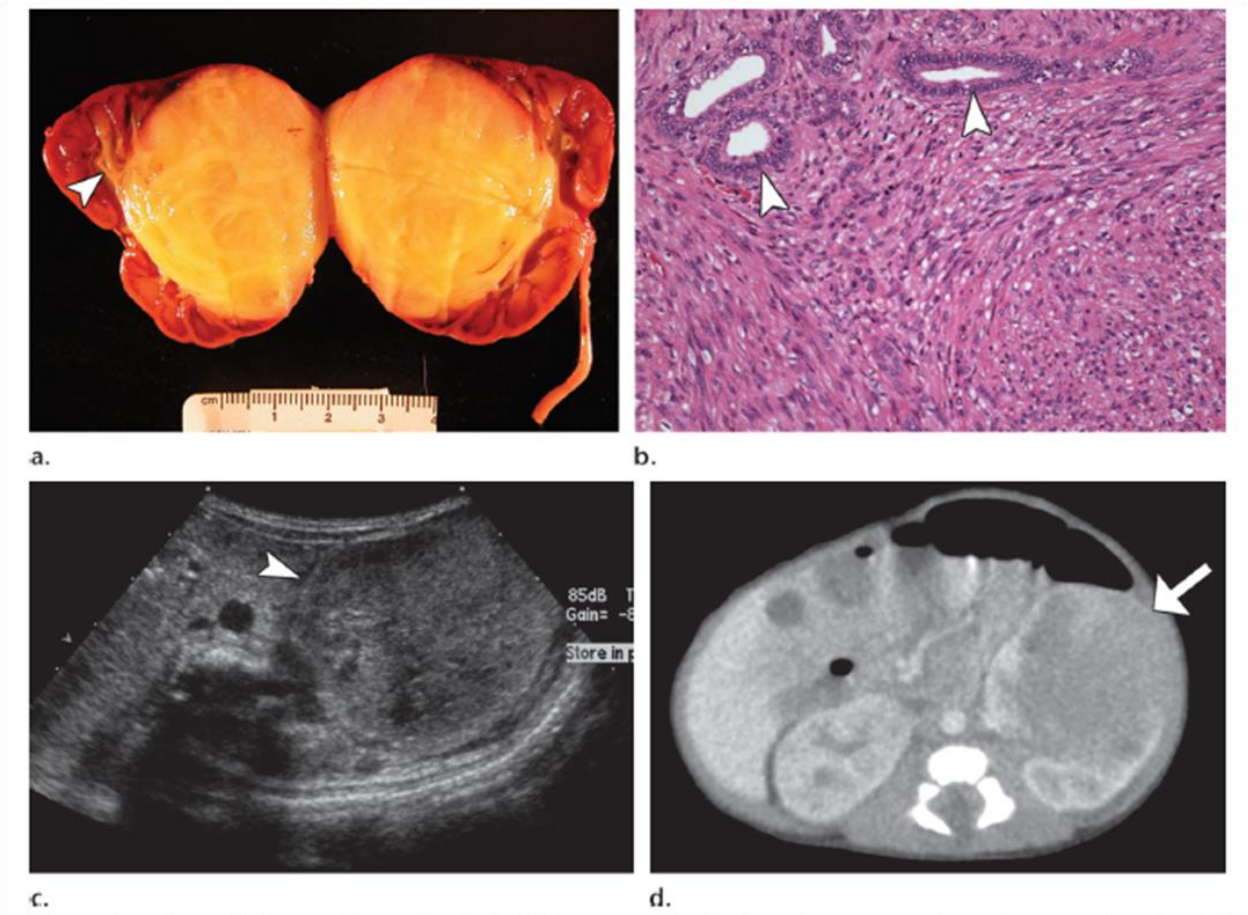


Figure 10. Classic CMN in a 14-day-old girl. **(a)** Photograph of bivalved nephrectomy specimen shows a yellow whorled cut surface and portions of tumor extending into the collecting system (arrowhead). **(b)** Photomicrograph shows interlaced fascicles of spindle cells surrounding entrapped tubules (arrowheads). (H-E stain; original magnification, ×40.) **(c)** Transverse US image of the left kidney shows a fairly homogeneous tumor of the upper pole with a surrounding rim of alternating hypo- and hyperechogenicity (arrowhead). **(d)** Axial contrast-enhanced CT image shows that the mass is homogeneous and hypoattenuating compared to adjacent kidney with thin peripheral enhancement (arrow).

16/ Clear Cell Sarcoma (CCS)

- 4-5% of renal tumors; mean age- 36m & M:F is 2:1
- CCS is noted for its propensity to metastasize to bone
- Unilateral, well-circumscribed, large, solid mass replacing most of the kidney or centered in the renal medulla

17/ Diagnosis & Management of CCS

- Imaging: US- solid heterogeneous renal mass ē cystic areas. Cysts and mucoid material are seen & the cysts are anechoic. The tumor often crosses the midline
- Radical nephrectomy with lymph node dissection is the mainstay of therapy
- CCSK has a relapse rate of 20-40%. Intense chemotherapy & sometimes radiotherapy 5-year survival has increase from 25% to 86%

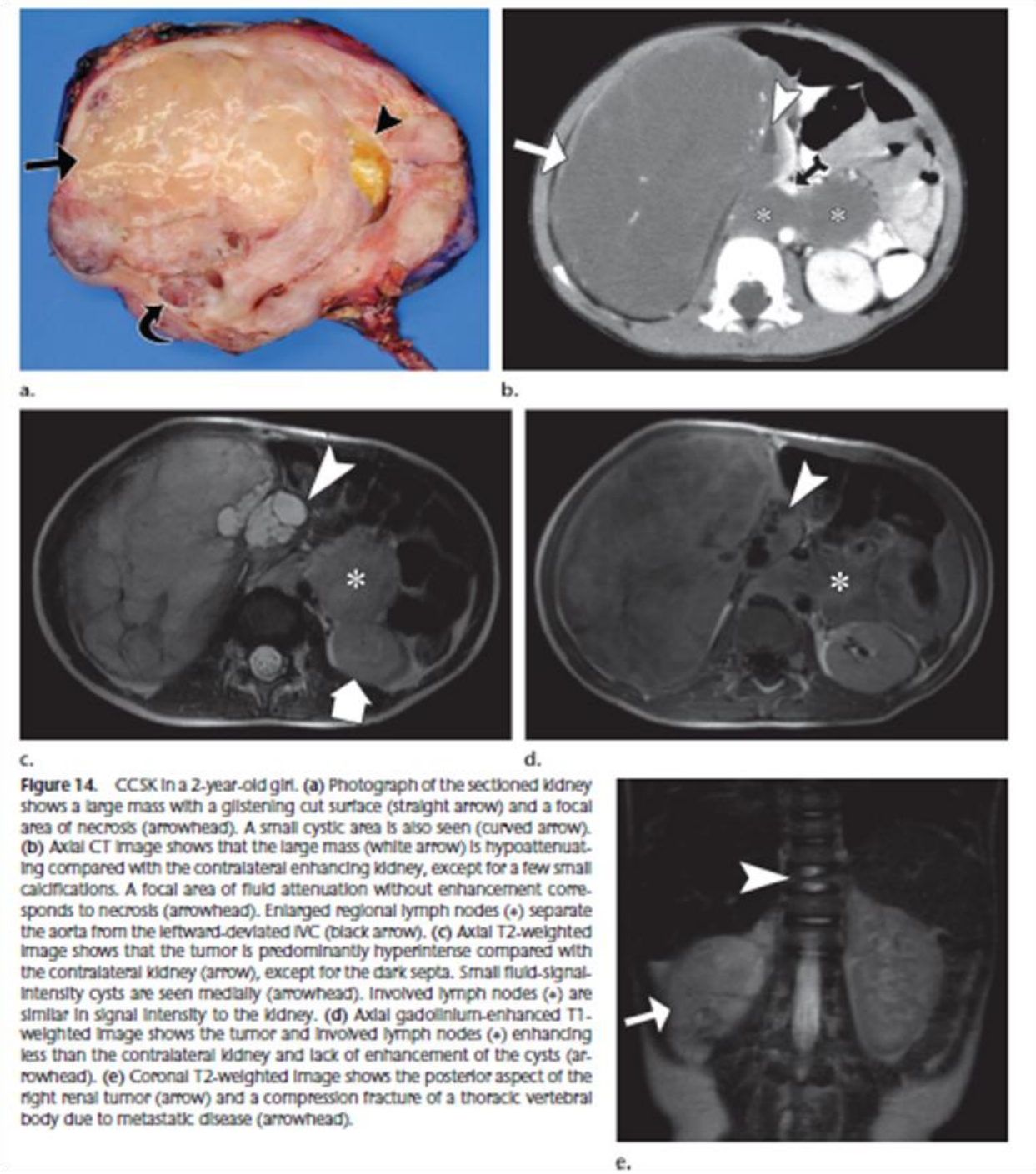


Figure 14. CCSK in a 2-year-old girl. **(a)** Photograph of the sectioned kidney shows a large mass with a glistening cut surface (straight arrow) and a focal area of necrosis (arrowhead). A small cystic area is also seen (curved arrow). **(b)** Axial CT image shows that the large mass (white arrow) is hypoattenuating compared with the contralateral enhancing kidney, except for a few small calcifications. A focal area of fluid attenuation without enhancement corresponds to necrosis (arrowhead). Enlarged regional lymph nodes (•) separate the aorta from the leftward-deviated IVC (black arrow). **(c)** Axial T2-weighted image shows that the tumor is predominantly hyperintense compared with the contralateral kidney (arrow), except for the dark septa. Small fluid-signal-intensity cysts are seen medially (arrowhead). Involved lymph nodes (•) are similar in signal intensity to the kidney. **(d)** Axial gadolinium-enhanced T1-weighted image shows the tumor and involved lymph nodes (•) enhancing less than the contralateral kidney and lack of enhancement of the cysts (arrowhead). **(e)** Coronal T2-weighted image shows the posterior aspect of the right renal tumor (arrow) and a compression fracture of a thoracic vertebral body due to metastatic disease (arrowhead).

14/ Rhabdoid tumor

- < 2% of pediatric renal tumors, 80% are diagnosed <2 years ē M:F 1.5:1
- Association ē intracranial neoplasm (commonly posterior fossa- primitive neuroectodermal tumor, rhabdoid tumor of the brain, medulloblastoma, ependymoma & cerebellar or brainstem astrocytoma) in 15% cases
- Hypercalcemia (↑PTH). 80% present with advanced disease & symptoms referable to metastases (lung, brain & bone)

18/ Diagnosis & treatment of Rhabdoid tumor

- Imaging: Tumor appears similar to Wilms tumor & more likely to contain calcifications. There is subcapsular fluid collection (Hemorrhage or area of necrosis)
- Radical nephrectomy & resection of adjacent lymph node followed by chemotherapy

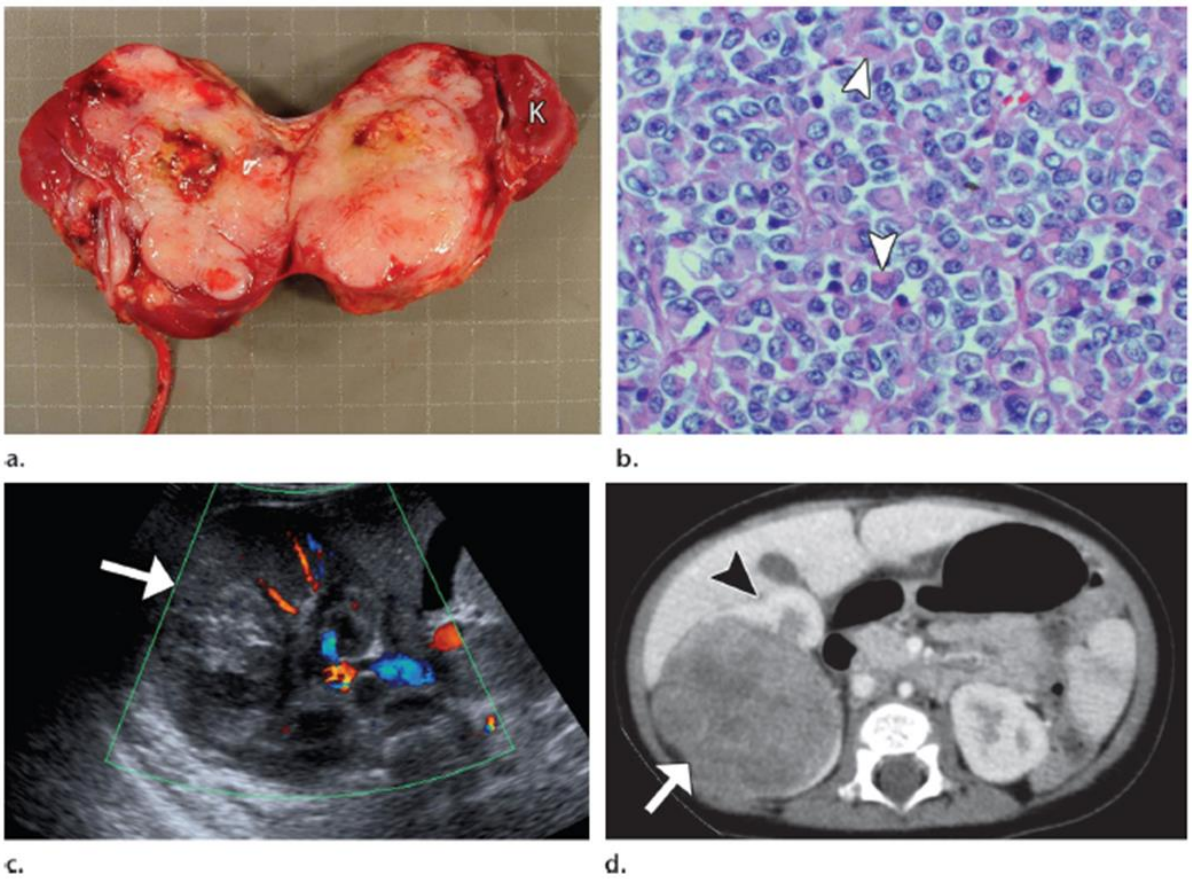


Figure 16. Renal rhabdoid tumor in a 6-month-old boy. **(a)** Photograph of the bivalved kidney shows a gray-white, lobulated, well-demarcated tumor within the kidney *(K)*. **(b)** Photomicrograph shows discohesive cells with vesicular nuclei. A few rhabdoid cells show eosinophilic cytoplasm displacing the nuclei to one side (arrowheads). (H-E stain; original magnification, ×100.) **(c)** Transverse color Doppler image shows a tumor of heterogeneous echogenicity (arrow) with some internal flow. **(d)** Axial CT image shows a slightly heterogeneous mass (arrow) enhancing less than the adjacent kidney (arrowhead).

19/Renal cell carcinoma (RCC):

- 2-4% of pediatric kidney tumors
- Usually in older children (>50% among children >12years)
- Associated with von Hippel-Lindau disease, tuberous sclerosis
- Papillary RCC is more common in children

20/Other tumors

- Ossifying Renal Tumor of Infancy (ORTI): Accounts for <1% of pediatric tumors. Usually calcified and presents as a staghorn calculus at radiography. Benign tumor & resection is the main treatment
- Others: Lymphoma (Burkitt lymphoma is the most common), angiomyolipoma associated ē tuberous sclerosis & metanephric tumors

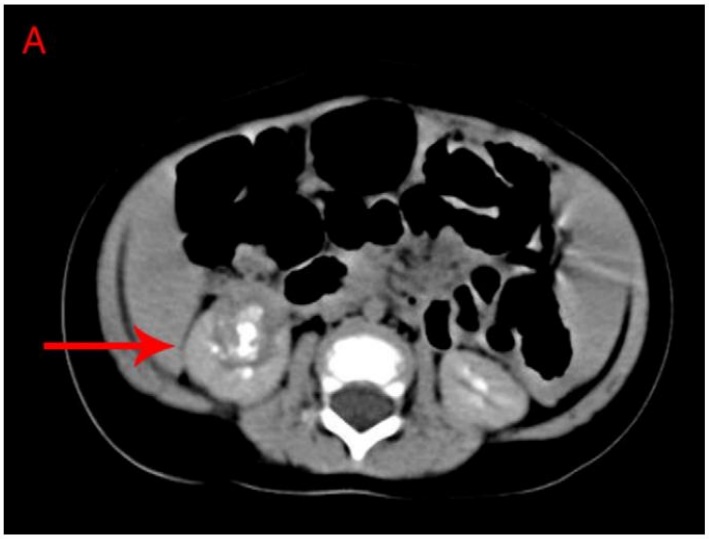


Fig. 1 Unenhanced Computed tomography (CT) illustrated a calcified renal hamartomatous soft tissue mass in the lower pole of right kidney.

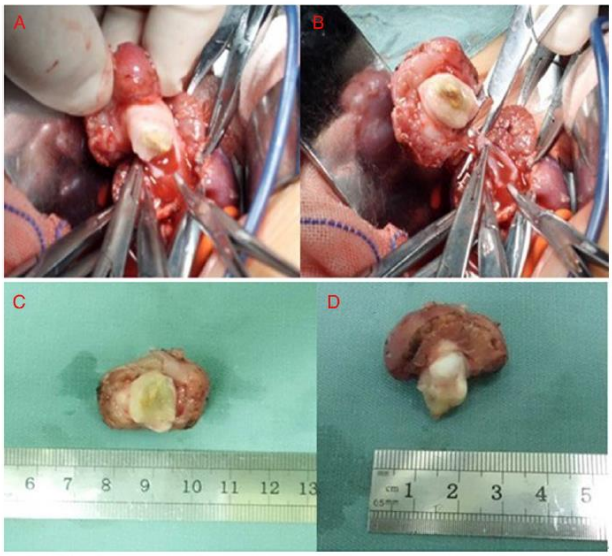


Fig. 2 During the operation (A, B), we found 3 cm × 2 cm × 1.5 cm rock-hard mass located in the lower pole of right kidney. Resected specimen (C, D) revealed an ossifying-like appearance that occupied the right renal pelvis.

- PMID: 23414900

21/ To summarize,

- Kidney tumors comprise 6% of childhood malignancies
- Wilms tumor is the most common kidney tumor with a 5 years survival is >90%

Kidney tumors in children

Types of tumor	Salient features	Imaging	Treatment & prognosis
Wilms tumor	Most common kidney tumor (90%) Pain, malaise, HTN & haematuria are presenting features	Heterogeneous tumor ē hypoechoic & anechoic areas Calcification in 15% cases	Nephrectomy followed by chemotherapy & radiation 5 years survival (localized disease) >90%
Cystic Nephroma (CN) & CPDN (Cystic partially differentiated nephroblastoma)	Originate from metanephric tissue. Children aged 3m to 4 years are affected with M>F 2:1	Well circumscribed, encapsulated, multiseptated cystic mass.	Unifocal cyst: Bosniak criteria for monitoring Multilocular tumors: Can be cured by surgical resection
Congenital mesoblastic nephroma (CMN)	Most common in neonates 2 types: Cellular & Classic Cellular CMN: Larger & occurs in an older patient (>3m age)	Homogeneous solid mass Involve renal hilum without vessel invasion	Nephrectomy Chemotherapy & multimodal therapy (unresectable residual tumor) Prognosis Is better if resected before 6m age
Clear cell sarcoma (CCS)	Mean age 36m & M:F 2:1 Unilateral and noted for its propensity to metastasize bone	Solid, heterogeneous renal mass with cystic areas. The tumor often crosses midline	Radical nephrectomy with lymph node dissection. Overall survival has improved to 86% with intense chemotherapy & radiotherapy
Rhabdoid tumor	80% are diagnosed before 2years 15% has an association with intracranial neoplasm	Tumor appears similar to Wilms tumor & more likely to contain calcification	Radical nephrectomy & resection of adjacent lymph node followed by chemotherapy Highly aggressive tumor with worst prognosis
Renal cell carcinoma (RCC)	Usually in older children (>50% among children >12years) Abdominal pain and gross haematuria is the main presentation	Tumor Classification: T1: Tumor is <7cm & limited to the kidney T2: Tumor is >7cm & limited to the kidney T3: Tumor extends outside the kidney but not past Gerota's fascia T4: Tumor extends past Gerota's and/or metastasized.	Nephrectomy or cytoreductive nephrectomy followed by immunotherapy in advanced RCC 5 years survival of a localized tumor is up to 93% but for a tumor with distant metastasis is 14%
Ossifying renal tumor of infancy (ORTI)	ORTI is a benign tumor comprises <1% of the pediatric kidney tumor	Usually calcified and presents as a staghorn calculus	Resection is the main treatment @md_abdulqader83

22/That's all folks!
For a case-based clinical discussion with a radiology expert login to @ASPNeph website. Special thanks to @drM_sudha, @SwastiThinks, @nefron1310, and #ASPNFOAM group
Here's a tweetorial on kidney mass by @nailetpek
https://twitter.com/nailetpek/status/1337577646797049863?s=20&t=VIVU6_jCeqU3ACI_MWEi6g

Until next time…

#ASPNFOAM Group
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