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.

PMID: 26963460
5/ Genetics of kidney tumors:
Wilms: WT1, CTNNB1, WTX
Metanephric tumors: BRAFV600E
Neuroblastoma: MYCN
PMID: 16919774

<table>
<thead>
<tr>
<th>Tumor Type</th>
<th>Subtype</th>
<th>Genetic Aberrations Useful in Diagnostics</th>
<th>Techniques</th>
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</thead>
<tbody>
<tr>
<td>WT</td>
<td></td>
<td>− 35% WT1, CTNNB1, WTX</td>
<td>NGS</td>
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<td></td>
<td></td>
<td>−10% SDHX1</td>
<td>NGS</td>
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<td>−15% microRNA processing genes (DROSHA, DGCR, DICER1)</td>
<td>NGS</td>
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<td></td>
<td></td>
<td>− 2.5% TRIM3 mutations (up to 90% in pure epithelial WT)</td>
<td>NGS</td>
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<td></td>
<td></td>
<td>−5% TP53 mutations (Anaplastic WT)</td>
<td>IHC, NGS</td>
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<td>Late-onset mutations: FUS, MYCN, RCC, MT2J</td>
<td>NGS</td>
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<td>CCSK</td>
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<td>Semi-autosomal RCC (85–100%)</td>
<td>IHC, FISH</td>
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<td>t(10;17) (~10%)</td>
<td>FISH</td>
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<td></td>
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<td>Rare: BCOR-CCNB3 translocation</td>
<td>FISH, NGS</td>
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<td>MTKT</td>
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<td>−95% bilateral inactivation INI 1 (SMARCD1)</td>
<td>IHC, NGS, NGS</td>
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<td>−5% SMARCA4 mutations</td>
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<tr>
<td>CMN</td>
<td>Cellular</td>
<td>75–89% (t(12;15)(p13;p15.2))</td>
<td>FISH</td>
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<td>15% EGFR-ITD</td>
<td>NGS</td>
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<td></td>
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<td>Few cases reported with BRAF-ITD</td>
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<td></td>
<td></td>
<td>rearrangements</td>
<td></td>
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<tr>
<td></td>
<td>Mixed</td>
<td>t(12;15)(p13;p15.2)</td>
<td>FISH, NGS</td>
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<tr>
<td></td>
<td></td>
<td>87% EGFR-ITD</td>
<td>NGS</td>
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<tr>
<td>RCC</td>
<td></td>
<td>hTERT+ RCC: Translocations involving hTERT</td>
<td>IHC (TFE3, FISH</td>
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<td>t(p12.1;11q13)</td>
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<td>Rearranged: Translocations involving hTERT</td>
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<td>PRCC: Type 1: 81% MET alterations</td>
<td>NGS</td>
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<td>Type 2: 26% CDKN2A alterations</td>
<td>NGS</td>
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<td>A1K-RCC: Translocations involving A1K</td>
<td>FISH</td>
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<td>HLRCC-RCC: FISH mutations</td>
<td>IHC, NGS</td>
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<td>SDH-related RCC: SDH mutations</td>
<td>IHC, NGS</td>
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<tr>
<td>Metanephric tumors</td>
<td>MA</td>
<td>−90% BRAFV600E mutation</td>
<td>IHC, NGS</td>
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<tr>
<td></td>
<td>MST</td>
<td>−65% BRAFV600E mutation</td>
<td>IHC, NGS</td>
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<tr>
<td></td>
<td>MAF</td>
<td>−50% BRAFV600E mutation</td>
<td>IHC, NGS</td>
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<tr>
<td>Neuroblastoma</td>
<td></td>
<td>Mostly in high risk: MYCN amplification</td>
<td>IHC, NGS</td>
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<td></td>
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<td>(16–20%)</td>
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<td>Multifocality in a variety of organs (e.g., MYCN)</td>
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<tr>
<td>IWS</td>
<td></td>
<td>Translocations involving IWS</td>
<td>FISH</td>
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<tr>
<td>DSRCT</td>
<td></td>
<td>&gt;95% (t(11;12)(p13;q11.2) or q12)</td>
<td>FISH</td>
</tr>
</tbody>
</table>

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 ć central necrosis & hemorrhage
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 Æ 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
14/ Congenital mesoblastic nephroma (CMN)

- 3-6% of pediatric renal tumors & most common in neonates ě 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 ě 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
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 ê 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%
14/ Rhabdoid tumor

- < 2% of pediatric renal tumors, 80% are diagnosed <2 years M:F 1.5:1
- Association with 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
19/Renal cell carcinoma (RCC):
- 2-4% of pediatric kidney tumors
- Usually in older children (>50% among children >12 years)
- 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 with tuberous sclerosis & metanephric tumors
Kidney tumors comprise 6% of childhood malignancies. Wilms tumor is the most common kidney tumor with a 5 years survival rate >90%.

PMID: 23414900

To summarize,
- Kidney tumors comprise 6% of childhood malignancies
- Wilms tumor is the most common kidney tumor with a 5 years survival rate >90%
Kidney tumors in children

<table>
<thead>
<tr>
<th>Types of tumor</th>
<th>Salient features</th>
<th>Imaging</th>
<th>Treatment &amp; prognosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Wilms tumor</td>
<td>Most common kidney tumor (90%) Pain, malaise, HTN &amp; haematuria are presenting features</td>
<td>Heterogeneous tumor &amp; hypoechoic &amp; anechoic areas</td>
<td>Nephrectomy followed by chemotherapy &amp; radiation 5 years survival (localized disease) &gt; 90%</td>
</tr>
<tr>
<td>Cystic Nephroma (CN) &amp; CPDN (Cystic partially differentiated nephroblastoma)</td>
<td>Originate from metanephric tissue Children aged 3m to 4 years are affected with M:F 2:1</td>
<td>Well circumscribed, encapsulated, multifocal cystic mass.</td>
<td>Unilateral cyst. Bosniak criteria for monitoring Multilocular tumors: Can be cured by surgical resection</td>
</tr>
<tr>
<td>Congenital mesoblastic nephroma (CMN)</td>
<td>Most common in neonates 2 types: Cellular &amp; Classic Cellular CMN: LARGER &amp; occurs in an older patient (&gt;3m, age)</td>
<td>Homogeneous solid mass</td>
<td>Nephrectomy Chemotherapy &amp; multimodal therapy (unresectable residual tumor) Prognosis is better if resected before 6m age</td>
</tr>
<tr>
<td>Clear cell sarcoma (CCS)</td>
<td>Mean age 36m &amp; M:F 2:1 Unilateral and noted for its propensity to metastasize bone</td>
<td>Solid, heterogeneous renal mass with cystic areas. The tumor often crosses midline</td>
<td>Radical nephrectomy with lymph node dissection. Overall survival has improved to 80% with intense chemotherapy &amp; radiotherapy</td>
</tr>
<tr>
<td>Rhabdoid tumor</td>
<td>80% are diagnosed before 2 years 15% has an association with infranial neoplasm</td>
<td>Tumor appears similar to Wilms tumor &amp; more likely to contain calcification</td>
<td>Nephrectomy &amp; resection of adjacent lymph node followed by chemotherapy Highly aggressive tumor with worst prognosis</td>
</tr>
<tr>
<td>Renal cell carcinoma (RCC)</td>
<td>Usually in older children (&gt;50% among children &gt;12 years) Abnormal pain and gross haematuria is the main presentation</td>
<td>Tumor Classification: T1: Tumor is &lt;7cm &amp; limited to the kidney T2: Tumor is &gt;7cm &amp; limited to the kidney</td>
<td>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%</td>
</tr>
<tr>
<td>Ossifying renal tumor of infancy (ORTI)</td>
<td>ORTI is a benign tumor comprises &lt;1% of the pediatric kidney tumor Usually calcified and presents as a staghorn calculus</td>
<td>Resection is the main treatment</td>
<td>N/A</td>
</tr>
</tbody>
</table>

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_jCeqU3AC1_MWEi6g

Until next time…