Case 1
Clinical history

17-month-old boy with a kidney tumor found during routine childhood care program. CT scan showed a solid mass. Chemotherapy was given for 4 weeks using actinomycin D and vincrsitine followed by nephrectomy.
Microscopy

- Encapsulated tumor
- Mixture of small cells grown in nests, spindle cells and tubular structures
- Focally cells with broad eosinophilic cytoplasm
- Regressive changes
Nephroblastoma, mixed type intermediate risk (SIOP)
Nephroblastoma

- Synonymous: Wilms’ tumor
- Most common malignant kidney tumor in childhood
- Incidence (Germany):
  - 0.9 cases/100,000 children/year
Case 1

Nephroblastoma

• Epidemiology
  • Most common between the 2. and 3. year of life
  • Very rare in children below 6 months and in adolescents above 16 years of age
  • Almost equal sex distribution

• Site
  • About 95 percent unilateral
  • About 5 percent bilateral
Treatment protocols for pediatric renal tumors

- **Children's Oncology Group (COG)**
  
  *Operation first*, if possible
  
  -> followed by chemotherapy (and radiotherapy) depending on tumor type and stage

- **International Society of Paediatric Oncology (SIOP)**

  *Chemotherapy first* (in patients between 6 months and 16 years of age)
  
  -> followed by operation and a second chemotherapy (and radiotherapy) depending on tumor type and stage
Advantages of the SIOP strategy

- smaller tumors after pre-operative chemotherapy
  - lower incidence of intraoperative tumor rupture
  - lower incidence of radiotherapy
  - lower tumor stages → less chemotherapy necessary
  - response to chemotherapy can be measured

- Survival rate of COG and SIOP studies are similar!
Treatment of pediatric renal tumors in Africa

- **French African Pediatric Oncology Group**

  - **GFAOP NEPHRO**
    - 229 patients
    - treatment based on the SIOP 2001 protocol
    - 7.5 percent tumor rupture
    - Two-year and 5-year disease-free survival: 72.7 and 71.6 percent

Parameters necessary for treatment of pediatric renal tumors (SIOP)

- Risk group of tumor
- Tumor stage
Classification of pediatric renal tumors (SIOP)

Tumors primarily operated

I Low risk tumors
- *connatal mesoblastic Nephroma*
- cystic partial diff. Nephroblastoma

II Intermediate risk tumors
- Nephroblastoma - non-anaplastic
- Nephroblastoma - focal anaplasia

III High risk tumors
- Nephroblastoma - diffuse anaplasia
- *Clear cell sarcoma of kidney*
- *Mal. rhabdoid tumor of kidney*

Tumors after pre-operative Chemotherapy

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Nephroblastoma

• Three tumor components
  
  • Blastema
  • Epithelial structures (tubules, glomerular bodies)
  • Stromal cells (Spindle cells, myogenic cells, cartilage)

• Large variability in composition of the components
Classification is based on histological differentiation in nephroblastomas
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Anaplasia in Nephroblastoma

**focal anaplasia**

- not in LK
- not in metastases
- not extrarenal

Bloc guide neccessary!
# Classification of pediatric renal tumors (SIOP)

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complete embedding of at least one tumor slice
Histolocal classification of nephroblastoma (SIOP)

Regression < 66% => subtyping of different tumour components

Regression 66% - 99%
- WT - regressive type (intermediate risk)
- WT – mixed type (intermediate risk)
- WT – epithelial type (intermediate risk)
- WT – stromal type (intermediate risk)
- WT – focal anaplasia (intermediate risk)

Regression 100%
- WT - complete necrotic (low risk)

Diffuse anaplasia

ANAPLASIA ?

No or focal anaplasia

Quantification of regression
SIOP 2001 - Prognosis

Event-Free Survival by histopathological risk

Overall survival by histopathological risk

60 mos EFS - High Risk: 64.1 (95% CI: 58.0 - 70.8)
60 mos EFS - Intermediate Risk: 85.5 (95% CI: 83.6 - 87.4)
60 mos EFS - Low Risk: 94.8 (95% CI: 90.4 - 99.9)

60 mos OS - High Risk: 69.9 (95% CI: 63.4 - 77.1)
60 mos OS - Intermediate Risk: 94.6 (95% CI: 93.2 - 96.0)
60 mos OS - Low Risk: 97.4 (95% CI: 94.4 - 100.0)
Parameters necessary for treatment of pediatric renal tumors (SIOP)

- **Risk group of tumor**
  - Nephroblastomas *(pre-operative treatment)*
    - viable tumor $\rightarrow$ amount of blastema!
  - Anaplasia

- Tumor stage
SIOP 93-01 und 2001

- Patients with unilateral nephroblastomas
- percentage of blastema

Log-Rank \( p = 0.0010704 \)

Log-Rank \( p = 6 \times 10^{-7} \)
Parameters necessary for treatment of pediatric renal tumors (SIOP)

- **Risk group of tumor**
  - **Nephroblastomas** (pre-operative treatment)
  - **Viable tumor**
    - Regression should be assessed on gross specimen
    - Histological types of components will be assessed on H&E slides
Parameters necessary for treatment of pediatric renal tumors (SIOP)

- Regression should be assessed on gross specimen.

If not a complete slice can be prosessed, take representative blocs of viable tumor and make a drawing as bloc guide.
Parameters necessary for treatment of pediatric renal tumors (SIOP)

- Histological types of components will be assessed on H&E slides

Quantification of amount of blastema

(semi-quantitative in slides)
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Parameters necessary for treatment of pediatric renal tumors (SIOP)

- Risk group of tumor

- Tumor stage
  - post-operative chemotherapy
    - stage I → 2 drugs, 4 weeks
    - stage II → 2 drugs, 26 weeks!
    - stage III → 3 drugs and radiotherapy
Parameters necessary for treatment of pediatric renal tumors (SIOP)

- Tumor stage
  - stage II
    - only true viable infiltration of
      - Sinus
      - Hilar area
      - Perirenal fat
      - Viable tumor thrombi
  - don't chase for minimal infiltration
Viable infiltration of perirenal fat
Regressive thrombus -> not stage II
Perilobar nephroblastomatosis in hilar area -> not stage II
Parameters necessary for treatment of pediatric renal tumors (SIOP)

- Tumor stage
  - stage III
    - viable or regressive tumor at resection margin
    - viable or regressive tumor in lymph nodes
  - don't chase for minimal changes
Differential diagnosis
Malignant Rhabdoid Tumor of kidney

• Epidemiology

  Germany: 1 percent of all malignant pediatric renal tumors

  High risk tumor according to the SIOP classification
MRT: Diffuse infiltration of renal parenchyma
INI-Protein
Malignant Rhabdoid Tumor of kidney

Molecular genetics

- Various changes on chromosome 22q
  - hSNF4/INI1 gene (SMARCB1-Gen)
    - Deletions, mutations
Clear cell sarcoma of the kidney

• Epidemiology

  Germany: 1 percent of all malignant pediatric renal tumors

  High risk tumor according to the SIOP classification
Clear cell sarcoma of the kidney

Age at diagnosis

From: AFIP 2004
CCSK: mucoid tumor tissue on cut surface
Clear cell sarcoma of the kidney

- various morphological pattern:
  - 'classical' pattern
  - epitheloid pattern
  - spindel cell pattern
  - sclerosing pattern
  - etc.
CCSK: bland cytology; cave: entrapped renal tubuli
Clear cell sarcoma of the kidney

- Diagnosis can usually be made on H&E stain:
  - typical bland cytology
  - typical vascular pattern
Clear cell sarcoma of the kidney

• Important differential diagnosis

  • Nephroblastoma - blastemal type
    ➢ also high risk tumor!

  • Cellular mesoblastic nephroma
    ➢ low risk tumor!
    ➢ molecular genetics might be necessary
      ➢ t(12;15) translocation
Mesoblastic nephroma

- Most common kidney with the first 6 months of life
- Often already diagnosed in utero
Mesoblastic nephroma

• Epidemiology
  • Age distribution: 90 percent of cases within the first year of life
  • Mean age 2 month
  • Extremely rare in children above 2 years-of-age
  • Sex distribution: almost 1:1 (AFIP 2004)

• Site
  • almost unilateral
Mesoblastic nephroma

Macroscopy

- **'classial' type:**
  - Firm storiforme cut surface

- **'cellular' type:**
  - Cysts and hemorrhages are common
Mesoblastic nephroma

Microscopy

'classical' type:

• Elongated spindle cells in bundles
• Finger-like projection into the renal parenchyma
• Low mitotic activity
Mesoblastic nephroma

Microscopy

*cellular* type:

- Ovoide to round cells
- *pushing border* against the renal parenchyma
- increased mitotic activity
- necrosis and tumor cysts are common
Mesoblastic nephroma

- **Mixed type:**
  - Combination of both growth pattern
Mesoblastic nephroma

Molecular genetics

- t(12;15)(p13;q25) translocation in the cellular type
  - ETV6 gene on chromosome 12
  - NTRK3 gene on chromosome 15

Identical translocation as in infantile fibrosarcoma

No prognostic impact!
Thank you for your attention!