Case 4

- A 7 year old boy presented with a renal tumour
- Primary nephrectomy done (non-SIOP patient)
Case 4

- Dg: Anaplastic sarcoma of the kidney
ANAPLASTIC SARCOMA OF THE KIDNEY

- 20 cases in NWTS, SIOP & UKCCSG files (~14,000 cases) (Am J Surg Pathol 2007)
- Identified in a group of anaplastic WT/sarcomas
- Another 6 cases reported since
- Age: 10 m – 41 yrs
  - Median 10 yrs, mean 12 yrs
  - 10 cases under 5 yrs
  - 17 cases under 15 yrs
- F : M = 1.5 : 1          R : L = 3 : 1
- No bilateral cases
Microscopy

- usually a number of cysts present
- spindle cells arranged in a fasicular pattern
- primitive mesenchymal cells with a myxoid stroma
- cellular anaplasia with atypical mitoses
- benign or malignant cartilage
- small foci of osteoid with osteoclast-like giant cells
- no classical blastema
Spindled cells fascicles
CCSK – like pattern
CCSK-like pattern
Blastema-like areas
Blastema-like with anaplasia
Immunohistochemistry

- Vimentin - 5/5 cases
- Desmin - 4/6 (focally)
- MyoD1 - 0/5
- Myf4 - 1/4 - focal weak nuclear positivity
- PGP9.5 - 4/5 focal
- p53 – 3/6

- CAM5.2 - uniformly negative
- NB84a - negative in 4/4 cases
- CD34 - negative in 5/6 cases
- CD99 - negative in 5/5 cases
- WT1 – negative in 6/6
ASK

Differential diagnosis

• Anaplastic Wilms’ tumour
• Malignant mesenchymoma
• Mesenchymal chondrosarcoma
• Undifferentiated sarcoma (of liver)
ASK

Diagnosed as
- unusual WT
- anaplastic WT
- CCSK, RTK
- sarcomas
- malignant mesenchymoma

- 5 cases – stage unknown
- Stage 1 – 7 cases
- Stage 2 – 5 cases
- Stage 3 – 4 cases
- Stage IV – 2 cases
Follow up (16 pts)

- Different treatments given
- 7 patients lost to follow-up
- 6 developed metastases (lung, liver, bone)
- 1 local recurrence
- 4 died
- 12 patients NED on follow-up
  - 5 stage I
7/8 ASK showed at least one DICER1 mutation

**DICER1** syndrome - an autosomal dominant hereditary tumour predisposition syndrome

cause by pathogenic variants in the **DICER1** gene

**DICER1** gene located on chromosome 14q32.13

Cystic nephroma – anaplastic sarcoma of the kidney (1 case)

? Surveillance for cystic nephroma patients
• DICER1 is mutated pleiotropic tumour predisposition syndrome
  • (OMIM 601200)

Mesenchymal cell tumours/lesions

Choong et al, 2012

TRENDS in Molecular Medicine

- PNB: Malignant, ages <24 months (n<10)
- PPP: Malignant, Cystic PBP, ages 0-3 years (n>100)
- Cystic/solid & solid PBP, ages 2-6 years (n>200)
- CN: Benign, ages 0-4 years (n=45)
- MNG/DTC: Benign/malignant, ages 5-40 years (n>50)
- OSCST (S.LCT): Malignant, ages 2-25 years (n>50)
- CBFMS: Malignant, ages 10-20 years (n<10)

• 1st Mutation
  • inactivates

• 2nd Mutation affects miRNA generation

Dicer lesion
Surveillance in predisposed individuals

- The International DICER1 Symposium (2016) - recommendations for testing and surveillance guidelines for individuals with DICER1 pathogenic variants

- Limited evidence re efficacy and risk-benefits
- Different strategies in different countries
- Advantage: early detection (lower stage)