Congenital Paediatric Tumours
Case 1

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History

- 2/12 female, born at 37/40
- Left sided weakness; not using left hand and leg much
- Sibling aged 6 - fit and well.
- O/E:
  - Mild left sided weakness
  - Holding left hand flexed
Radiology (Head)

- MRI head showed a large heterogeneous part solid/part cystic mass centred predominately within the right frontal lobe
Radiology (Kidney)

• Abdominal CT showed a large heterogeneous non-enhancing mass arising from the mid/upper pole of the left kidney
Intracranial biopsy (Slide 1)

- Sheets of large atypical cells
- Vesicular nuclei
- Prominent nucleoli
- Abundant cytoplasm with many some showing pale inclusion bodies (aggregates of intermediate filaments)
- Necrosis

- Immunohistochemistry
  - INI-1 lost
  - Vimentin positive; perinuclear accentuation
  - Patchy keratin, desmin and EMA staining
  - Negative: synaptophysin, myogenin, CD99, WT1, C45, CD7, ALK
INI1 loss
Nephrectomy Specimen (Slide 2)

- Largely viable tumour
- Similar to morphology to the CNS lesion
- INI1 lost
- Extension beyond tumour capsule into renal parenchyma
- Present in hilar fat and at inked hilar margin
- Renal sinus involvement with ureter and vascular invasion
- Stage III (SIOP and UMBRELLA)
Diagnosis

• Clinically considered to be two separate tumours
  – Atypical teratoid/rhabdoid tumour (WHO Grade IV)
  – Malignant rhabdoid tumour of the kidney

• Multiple primary rhabdoid tumours are highly suspicious for Rhabdoid Tumour Predisposition Syndrome

• Screening of the SMARCB1 gene showed c564del heterozygote, confirming Rhabdoid Tumour Predisposition syndrome
Treatment

- Too young for radiotherapy.
- 2 cycles of chemotherapy on the EU rhabdoid protocol
- Intensive chemotherapy protocol; each cycle comprised of
  - Doxorubicin
  - 14 days later by Ifosfamide, Carboplatin and Etoposide
  - A further 14 days later, Vincristine, Cyclophosphamide and Actinomycin D
  - Cycle repeats.
  - GCSF support to maintain bone marrow function.
- Consolidation with high dose chemotherapy with Carboplatin and Thiotepa and peripheral blood stem cell rescue.
Outcome

• Unfortunately developed renal failure due to Ifosfamide; not able to have full chemotherapy regimen.
• Subsequent intracranial recurrence and died 10 months after initial diagnosis.
Rhabdoid tumours 1

- Rare; 1-2% of Childhood tumours
- Majority (60%) are <1 yr, rare > 5 yrs.
- Can occur anywhere, but most common in the brain and kidneys
- Highly aggressive, generally lethal; med. survival is less than 1 year
  - Often present with metastatic disease; lung, liver, LN
  - Invasive pattern
  - Poor response to chemotherapy and radiotherapy
- Younger age associated with poorer prognosis
Rhabdoid tumours 2

- Cell origin currently unknown
- Diagnosis of exclusion
  - Other tumour may have rhabdoid features but retain INI1
- Associated with loss of the SMARCB1 gene (22q,11.2)
  - Some have mutations in the SMARCA4 gene; these retain SMARCB1 expression
- INI1 loss can be seen in other aggressive tumours
Rhabdoid Tumour Predisposition Syndrome

• Consider RTPS as a diagnosis
  – multiple primary tumours
  – and/or in families with a history of rhabdoid tumour.
• Germline inactivation of 1 allele of a gene
  – SMARCB1 gene -> RTPS1
  – SMARCA4 gene -> RTPS2.
• Children -> generally develop rhabdoid tumours at a younger age
• Adults -> have a tendency to develop multiple schwannomas.
• Whether the germline mutation has an impact on survival remains unclear.
• Genetic counselling is recommended for families of patients with ATRT/MRTK due increased risk of RT in carriers of the germline mutation
Which of these statements about rhabdoid tumour is false?

• They are associated with INI1 loss (SMARBC1 gene).
• They are highly aggressive.
• Good response to chemotherapy and radiotherapy
• Associated with early metastases to lung, liver and lymph nodes.
• Synchronous rhabdoid tumors are highly suspicious for rhabdoid predisposition syndrome (>1 primary rhabdoid tumor).
References

• Rhabdoid Tumor Predisposition Syndrome Sredni ST, Tadanori T. Pediatric and Developmental Pathology 18, 49–58, 2015

• Germline Nonsense Mutation and Somatic Inactivation of SMARCA4/BRG1 in a Family with Rhabdoid Tumor Predisposition Syndrome R Schneppenheim et al Volume 86, Issue 2, 12 February 2010, Pages 279-284

• https://www.pathologyoutlines.com/topic/softtissuerhabdoidtumor.html

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