Germ cell tumours

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Old histogenetic Concept of Germ cell tumours

- Pluripotent (primordial) germ cell
  - Gonadoblastoma
    - Seminoma/Germinoma/Dysgerminoma
  - Embryonal carcinoma
  - Extra-embryonal structures
    - Immature teratoma
    - Mature teratoma
    - Yolk sac tumor
    - Chorio carcinoma
  - Mixed malignant Germ cell tumour
<table>
<thead>
<tr>
<th>Typ</th>
<th>Lokalisation</th>
<th>Phänotyp</th>
<th>Alter</th>
<th>Ursprungselle</th>
<th>Genomisches Imprinting</th>
<th>Genotyp</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Hoden/Ovar</td>
<td>(unerleses) Teratom/Dottersacktumor</td>
<td>Neugeborene/ Kinder</td>
<td>frühe PGC/Gonozyten</td>
<td>biparental/ partiell verloren</td>
<td>diploid (Teratom) Zugewinne: 1q, 12(p13), 20q Verluste: 1p, 4, 6q</td>
</tr>
<tr>
<td>2</td>
<td>Hoden</td>
<td>Seminom/ nicht-seminomatös</td>
<td>&gt; 15 Jahre (Median 35 u. 25 J.)</td>
<td>PGC/Gonozyten</td>
<td>verloren</td>
<td>aneuploid (+/- triploid) Zugewinne: X, 7, 8, 12p, 21 Verluste: Y, 1p, 11, 13, 18</td>
</tr>
<tr>
<td>Ovar</td>
<td>Dysergerinom nicht-dysergerinomatös</td>
<td>&gt; 4 Jahre</td>
<td>PGC/Gonozyten</td>
<td>verloren</td>
<td>diploid/tetraploid</td>
<td></td>
</tr>
<tr>
<td>Dysergetische Gonaden</td>
<td>Dysergerinom nicht-dysergerinomatös</td>
<td>konnatal</td>
<td>PGC/Gonozyten</td>
<td>verloren</td>
<td>diploid/tetraploid</td>
<td></td>
</tr>
<tr>
<td>vorderes Mediastinum</td>
<td>Seminom/ nicht-seminomatös</td>
<td>Adoleszenten</td>
<td>PGC/Gonozyten</td>
<td>verloren</td>
<td>diploid/tri-tetraploid</td>
<td></td>
</tr>
<tr>
<td>Gehirn (Mittelwass) (Glandula pinealis/ Hypothalamus)</td>
<td>Germinom/ nicht-sominomatös</td>
<td>Kinder (Median 13 J.)</td>
<td>PGC/Gonozyten</td>
<td>verloren</td>
<td>diploid/tri-tetraploid</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>Hoden</td>
<td>spermatozyt. Seminom</td>
<td>&gt; 50 Jahre</td>
<td>Spermatogonien/ Spermatozyten</td>
<td>teilweise komplett paternal</td>
<td>aneuploid Zugewinn: 9</td>
</tr>
<tr>
<td>4</td>
<td>Ovar</td>
<td>Dermoidzyste</td>
<td>Kinder/ Erwachsene</td>
<td>Oogonien/ Oozyten</td>
<td>teilweise komplett maternal</td>
<td>(nahe) diploid, diploid/ tetraploid, peridiploid</td>
</tr>
<tr>
<td>5</td>
<td>Plazenta/ Uterus</td>
<td>hydatiforme Mole</td>
<td>Reproduktionsphase</td>
<td>leere Eizelle Spermatozoen</td>
<td>komplett paternal</td>
<td>diploid (XX und XY)</td>
</tr>
</tbody>
</table>

PGC: primordiale Keimzelle (primordial germ cell)
Type 1 Germ cell tumors

• **Age:** Infants, children

• **Histology:**
  - Teratoma (mature/immature) and Yolk sac tumor

• **Sites:**
  - Saccroccocygeal, testis, ovary, mediastinum, neck, brain (rarely)

• **Genetics:**
  - Teratoma (diploid), Yolk sac tumor (aneuploid)
  - Gains on chromosomes 1q, 12(p13), 20q
  - Losses on chromosomes 1p, 4, 6q
Teratoma

- Most common type of germ cell tumor (51.3% of germ cell tumors in the Kiel Pediatric Tumor Registry)

- Usually all three types of germ cell layers

- Degree of 'maturity' depends on amount of immature elements:
  - Grading by Gonzalez-Crussi (1982)
    - Grade 0 (mature) - Grade 3 (immature)
  - Norris (1976); Thurlbeck (1960)
Teratoma

- Degree of 'maturity' depends on amount of immature elements:
  - Grading by Gonzalez-Crussi (1982)
    - Grade 0 (mature)
    - Grade 1 (<10 percent)
    - Grade 2 (10 – 50 percent)
    - Grade 3 (> 50 percent)
  - Norris (1976); Thurlbeck (1960)
Immature teratoma of the mediastinum
Yolk sac tumours

- Second most common type of germ cell tumours (18.3% of cases in the KTR)

- Large morphological variability:
  - Pseudo papillary
  - Polyvesicular ('vitelline')
  - Mikrocystic
  - Endometrioid
  - Hepatoid
  - Parietal
  - Mesenchyma-like
Endometrioid variant of YST
Hepatoid variant of YST: AFP staining
Yolk sac tumours

- Immunohistochemistry:
  - Cytokeratin-positive
  - AFP-positive
  - Glypikan 2-positive
  - SALL4-positive
In about 28% of pediatric teratomas the microfoci of YST are initially not seen (Heifetz, 1998)

- Recurrences with YST components are often found in cases with incomplete resection

- Nevertheless:
  - Recurrences with YST components can also occur in initially 'mature' teratomas
Yolk sac tumour 'microfoci' in teratoma

- Identification of YST microfoci very important

- If the serum AFP level is elevated in children above 6-9 months of age, a YST component should be suspected
Type 2 Germ cell tumors

- **Age:**
  - Testis: above 14 years
  - Ovary: probably above 4 years
  - Medastinum: Adolescents
  - Brain: Children

- **Histology:**
  - Seminoma/Dysgerminoma/Germinoma
  - Non-seminomatous:
    - Teratoma, embryonal carcinoma, Yolk sac tumor, choriocarcinoma
    - \( \rightarrow \) all are malignant

- **Genetics:**
  - mostly aneuploid
  - Gains on chromosomes X, 7, 8, 12p, 21
  - Losses on chromosomes Y, 1p, 11, 13, 18
Seminoma/Dysgerminoma/Germinoma

- As pure tumours more infrequent as other germ cell tumours (9.7% of cases in the KTR)
- mostly in the ovary or CNS
Seminoma/Dysgerminoma/Germinoma
IGCNU in about 90 percent
Embryonal Carcinoma and choriocarcinoma

- As pure tumors rare in children (2.1% bzw. 0.6% of cases in the KTR)

- Embryonal Carcinoma components can occur in mediastinal and testikular mixed germ cell tumours in adolescents

- Beta-HCG-positive giant cells cells can cause mild elevation of serum beta-HCG
Malignant transformation in germ cell tumours

- Very rare in children
- Some cases with neuroblastoma, Wilms tumor, plexus carcinoma, etc. have been reported
- In adults a PNET-like malignant transformation can occur
GCT with malignant (somatic) transformation: PNET-like
Type 4 Germ cell tumors

- **Age:**
  - Ovary: Children/Adults
  - ?? Testis: young boys

- **Histology:**
  - Mature Teratome (‘Dermoid cyst’)

- **Genetics:**
  - euploid/near euploid
Genetics of Germ cell tumours

- Adult malignant GCT:
  - Gain on chromosome 12, Isochromosome 12
  - (not in ovarian mature teratomas (‘Dermoid cysts’))

- YST children:
  - Gain on chromosome 1q and 20q
  - Loss on chromosome 1p and 6q (LOH)
  - Maybe also seen in immature teratoma

- Pure mature teratoma children:
  - No molecular changes yet found
• Germ cell tumors in children are different from adult germ cell tumors
  - in morphology
  - in biology
  - in molecular genetics
Thank you for your attention!