Update on testicular tumours

Dan Berney

ISSP 2016
To cover

1. WHO 2016
2. ISUP testis consultation
3. AJCC TNM 8th ed
4. ICCR testis and RPLND datasets
AVOID MISUNDERSTANDINGS!

I told to cover his eyes with an EYE - PAP.
Nomenclature precursor Germ Cell Tumour (GCT) testis

CIS IGCNU TIN
• CIS
  – Not a carcinoma
• TIN
  – Not intraepithelial
• IGCNU
  – Unclassified/Undifferentiated...
  – The spermatogonial niche
Germ cell neoplasia in situ (GCNIS): evolution of the current nomenclature for testicular pre-invasive germ cell malignancy

Daniel M Berney,1 Leendert H J Looljenga,2 Muhammad Idrees,3 J Wolter Oosterhuis,2 Ewa Rajpert-De Meyts,4 Thomas M Ulbright3 & Niels E Skakkebaek4
GCNIS
GERM CELL NEOPLASIA IN SITU
WHO 2016 Germ cell tumours

- Tumours derived from GCNIS of one type
  - Seminoma
  - Embryonal carcinoma
  - Yolk Sac Tumour, post pubertal type
  - Trophoblastic tumours
  - Teratoma, post pubertal type
  - Teratoma with somatic type malignancy
Seminoma
I am not a choriocarcinoma
Still no place for anaplastic seminoma

- ‘Differentiation’ of seminomas
- Mitotic rate
- Lymphocytic infiltrate
- Cell morphology
Embryonal carcinoma
Trophoblastic tumours

- Choriocarcinoma
- Non-choriocarcinomatous trophoblastic tumours
  - Placental site trophoblastic tumour
  - Epithelioid trophoblastic tumour
  - Cystic trophoblastic tumour
Choriocarcinoma
ETT

- Intermediate trophoblastic cells
- Squamoid monophasic trophoblast cells in cohesive epithelioid nests with abundant eosinophilic cytoplasm
- No biphasic pattern.
- Prominent cell boundaries
- Intracytoplasmic, and extracytoplasmic eosinophilic fibrinoid and globular material
Cystic Trophoblastic Tumor
A Nonaggressive Lesion in Postchemotherapy Resections of Patients With Testicular Germ Cell Tumors

Thomas M. Ulbright, MD, * John D. Henley, MD, * Oscar W. Cummings, MD, * Richard S. Foster, MD, † and Liang Cheng, MD*
# Immunoprofile

<table>
<thead>
<tr>
<th></th>
<th>CTT</th>
<th>ETT</th>
<th>Chorioca.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Inhibin</td>
<td>++</td>
<td>++</td>
<td>+/-</td>
</tr>
<tr>
<td>p63</td>
<td>--</td>
<td>++</td>
<td>-</td>
</tr>
<tr>
<td>hCG</td>
<td>++</td>
<td>++</td>
<td>+++</td>
</tr>
<tr>
<td>HPLC</td>
<td>+/-</td>
<td>++</td>
<td>+++</td>
</tr>
<tr>
<td>Ki-67</td>
<td>&lt;5%</td>
<td>&gt;10%</td>
<td>&gt;10%</td>
</tr>
</tbody>
</table>
Placental site trophoblastic tumour
Teratoma, post pubertal type

- Immaturity
- Atrophy
- GCNIS
Teratoma with somatic type malignancy
Non-seminomatous germ cell tumours of more than one histological type

- Mixed germ cell tumours

Germ cell tumours of unknown type

- Regressed germ cell tumours
Regressed germ cell tumours
Germ cell tumours unrelated to GCNIS

- Spermatocytic tumour
- Teratoma, prepubertal type
  - Dermoid cyst
  - Epidermoid cyst
  - Well-differentiated neuroendocrine tumour (monodermal teratoma)
- Yolk sac tumour, prepubertal-type
- Mixed teratoma and yolk sac tumour, prepubertal-type
Spermatocytic tumour

• Danger of inappropriate chemotherapy
Dermoid Cyst of the Testis
A Study of Five Postpubertal Cases, Including a Pilomatrixoma-Like Variant, With Evidence Supporting Its Separate Classification From Mature Testicular Teratoma

Thomas M. Ulbright, m.d., and John R. Srigley, m.d.

Case series: Adult testicular dermoid tumours – mature teratoma or pre-pubertal teratoma?

T.J. Kendall¹, J.M. Featherstone², G.M. Mead³, M.C. Hayes² & J.M. Theaker¹
Evidence Supporting the Existence of Benign Teratomas of the Postpubertal Testis
A Clinical, Histopathologic, and Molecular Genetic Analysis of 25 Cases

Chen Zhang, MD, PhD,* Daniel M. Berney, FRCPath,‡ Michelle S. Hirsch, MD, PhD,‡
Liang Cheng, MD,* and Thomas M. Ulbright, MD*
Prepubertal type teratoma and variants,
Epidermoid and dermoid cyst

- No GCNIS
- No immature areas
- No evidence of regression
- i12p?
Well differentiated neuroendocrine carcinoma (Monodermal teratoma)

Predominantly benign
Mixed with teratoma
Note mitoses
Yolk sac tumour, prepubertal-type
Mixed teratoma and yolk sac tumour, prepubertal-type

- Very rare
- No GCNIS
- Metastatic disease does occur
- Survival approaches 100%
Sex cord–stromal tumours

• Pure tumours
  – Leydig cell tumour
    • malignant
  – Sertoli cell tumour
    • Malignant
    • Large cell calcifying Sertoli cell tumour
    • Intratubular large cell hyalinizing Sertoli cell tumour
  – Granulosa cell tumour
    • Adult granulosa cell tumour
    • Juvenile granulosa cell tumour
  – Tumours in the fibroma-thecoma group

• Mixed and unclassified sex cord-stromal tumours
  – Mixed sex cord-stromal tumour
  – Unclassified sex cord-stromal tumour
Large cell calcifying Sertoli cell tumour

• Carney complex
  – myxomas
  – lentigines
  – blue naevi
  – Cushing's 2ary to PANH
  – PRKAR1A germ line mutation
Intratubular large cell hyalinizing Sertoli cell tumour
Tumours containing both germ cell and sex cord-stromal elements

- Gonadoblastoma
- 20% phenotypically male
- Most <20 years of age
- Cryptorchidism, hypospadias and gynecomastia
- May present in children under age 2
- Failure of involution of müllerian ducts
A new classification

- GCNIS
- Aligns with the pathogenesis of the disease
- Avoids dangers of mistreatment
When should I request Immunochemistry?
Handling and reporting of orchidectomy specimens with testicular cancer: areas of consensus and variation among 25 experts and 225 European pathologists

<table>
<thead>
<tr>
<th>Use of immunochemistry in the testis</th>
<th>ENUP n (%)</th>
<th>Experts n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Every case</td>
<td>78 (35%)</td>
<td>0 (0%)</td>
</tr>
<tr>
<td>50–100% of cases</td>
<td>75 (33%)</td>
<td>3 (12%)</td>
</tr>
<tr>
<td>10–50% of cases</td>
<td>54 (24%)</td>
<td>9 (36%)</td>
</tr>
<tr>
<td>Fewer than 10% of cases</td>
<td>17 (8%)</td>
<td>13 (52%)</td>
</tr>
<tr>
<td>Never</td>
<td>0 (0%)</td>
<td>0 (0%)</td>
</tr>
</tbody>
</table>

ENUP, European Network of Uro-Pathology.
The End of typing!

• How to stage
• Does it matter?
• What might a clinician need?
ONCOLOGISTS DISAGREE!

“There was some disagreement on your diagnosis.”
<table>
<thead>
<tr>
<th></th>
<th>Risk factors for occult metastatic disease in seminoma CS I</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>No risk factors can reliably be identified for clinical management decisions</td>
</tr>
<tr>
<td>2.</td>
<td>Only tumor size $\geq 3$ cm is accepted as a risk factor</td>
</tr>
<tr>
<td>3.</td>
<td>Only tumor size $\geq 4$ cm is accepted as a risk factor</td>
</tr>
<tr>
<td>4.</td>
<td>Tumor size $\geq 4$ cm and rete testis infiltration are accepted as risk factors</td>
</tr>
<tr>
<td>5.</td>
<td>No statement</td>
</tr>
</tbody>
</table>
Strategy of choice in seminoma CS I should be

1. Surveillance in all patients irrespective of risk factors
   - 30.0%

2. Surveillance and adjuvant carboplatin as equal options irrespective of risk factors
   - 10.0%

3. Surveillance, adjuvant carboplatin and adjuvant radiation as equal options irrespective of risk factors
   - 12.0%

4. Surveillance as standard in low-risk patients, adjuvant carboplatin as the only alternative option high risk patients
   - 26.0%

5. Surveillance as standard low-risk patients, adjuvant carboplatin or radiotherapy as alternative options in high-risk patients
   - 22.0%
<table>
<thead>
<tr>
<th>Table 2. Strategies in clinical stage I seminoma and non-seminoma</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Seminoma</strong></td>
</tr>
<tr>
<td>Risk factors for occult metastases:</td>
</tr>
<tr>
<td>Treatment options:</td>
</tr>
<tr>
<td>Tumor size $\geq 4$ cm</td>
</tr>
<tr>
<td>Invasion of rete testis</td>
</tr>
<tr>
<td>Surveillance (preferred in low risk patients)</td>
</tr>
<tr>
<td>One cycle carboplatin AUC 7</td>
</tr>
<tr>
<td>Adjuvant paraaortic radiation 20 Gy$^{b}$</td>
</tr>
<tr>
<td>Primary RPLND (rarely indicated)$^{c}$</td>
</tr>
</tbody>
</table>

$^{a}$Validity of risk factors have been challenged in recent analyses.
PROGNOSTIC FACTORS IN SEMINOMAS ARE DIFFERENT FROM NON-SEMINOMAS
SEMONOMAS

• SIZE
• RETE TESTIS INVASION
• CLINICAL STAGE
• ? Pathological stage?
• ?VI
NON SEMINOMAS

- % Embryonal carcinoma
- Vascular invasion
- ? Pathological stage
PATHOLOGIC STAGING (UICC 7th edition)**(Note 16)**

- m - multiple primary tumours
- r - recurrent
- y - posttreatment

**Primary tumour (pT)**

- pTX: Primary tumour cannot be assessed
- pT0: No evidence of primary tumour
- pTis: Germ cell neoplasia in situ
- pT1: Tumour limited to testis and **epididymis** without vascular/lymphatic invasion; tumour may invade tunica albuginea but not tunica vaginalis
- pT2: Tumour limited to testis and epididymis with vascular/lymphatic invasion, or tumour extending through tunica albuginia with involvement of tunica vaginalis
- pT3: Tumour invades spermatid cord with or without vascular/lymphatic invasion
- pT4: Tumour invades scrotum with or without vascular/lymphatic invasion
<table>
<thead>
<tr>
<th>pT Category</th>
<th>pT Criteria</th>
</tr>
</thead>
<tbody>
<tr>
<td>pTX</td>
<td>Primary tumor cannot be assessed</td>
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<tr>
<td>pT0</td>
<td>No evidence of primary tumor</td>
</tr>
<tr>
<td>pTis</td>
<td>Germ cell neoplasia <em>in situ</em></td>
</tr>
<tr>
<td>pT1</td>
<td>Tumor limited to testis (including rete testis invasion) without lymphovascular invasion</td>
</tr>
<tr>
<td>pT1a</td>
<td>Tumor smaller than 3 cm in size</td>
</tr>
<tr>
<td>pT1b</td>
<td>Tumor g 3 cm or larger in size</td>
</tr>
<tr>
<td>pT2</td>
<td>Tumor limited to testis (including rete testis invasion) with lymphovascular invasion OR Tumor invading hilar soft tissue or epididymis</td>
</tr>
<tr>
<td>pT3</td>
<td>Tumor invades spermatic cord with or without lymphovascular invasion</td>
</tr>
</tbody>
</table>
\( pT2 = \) invasion of epididymis

\( pT2 = \) invasion of hilar soft tissue
MICRO:
DO NOT BOTHER!

• Count mitoses
• Give a ‘grade’
• Quantitate inflammation
Neoplasia of the Testis - Orchidectomy
Histopathology Reporting Guide

<table>
<thead>
<tr>
<th>Family/Last name</th>
<th>Date of birth</th>
</tr>
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<tbody>
<tr>
<td>Given name(s)</td>
<td></td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Patient identifiers</th>
<th>Date of request</th>
<th>Accession/Laboratory number</th>
</tr>
</thead>
</table>

Elements in **black text** are REQUIRED. Elements in **grey text** are RECOMMENDED.
MAXIMUM TUMOUR DIMENSION (select all that apply) (Note 5)

- Cannot be assessed
- Maximum dimensions (largest tumour)
  - mm \( \times \) mm \( \times \) mm
- Greatest dimensions of additional tumour nodules
  - mm \( \times \) mm \( \times \) mm
  - mm \( \times \) mm \( \times \) mm
  - mm \( \times \) mm \( \times \) mm

TUMOUR FOCALITY (Note 4)

- Cannot be assessed
- Indeterminate
- Unifocal
- Multifocal

\[ \downarrow \]

Number of tumour nodules
HISTOLOGICAL TUMOUR TYPE (select all that apply) (Note 8)

- Germ cell tumour *(specify type and percentage)*
  - [ ]
  - [ ]
  - [ ]
  - [ ]

- Other *(specify)*
  - [ ]
  - [ ]
MICROSCOPIC EXTENT OF INVASION (Note 9)

Rete testis of stromal/interstitial type
- Not submitted
- Not involved
- Involved

Epididymis
- Not submitted
- Not involved
- Involved

Hilar fat
- Not submitted
- Not involved
- Involved

Tunica albuginea (white fibrous capsule around testicular parenchyma)
- Not submitted
- Not involved
- Involved
• Accurate typing is by far the most important factor in a testicular tumour. WHO 2016 is an advance.
• Seminomas and non-seminomas have different prognostically important histological features.
• Tumour size, vascular invasion, interstitial rete testis invasion and % EC should always be reported.
• TNM stage has been improved…but may be used less by oncologists than other criteria.
• Due to their rarity, these tumours are challenging even for experts. Don’t hold back from getting advice.