Challenging Cases in Surgical Pathology and Hematopathology

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EMORY UNIVERSITY SCHOOL OF MEDICINE, DEPARTMENT OF PATHOLOGY
Course Schedule

• 8:00 AM - 9:00 AM: Genitourinary Pathology
• 9:00 AM - 10:00 AM: Gynecological Pathology
• 10:00 AM – 10:30 AM: Break
• 10:30 AM - 12:30 PM: Hematopathology
• 12:30 PM - 1:00 PM: Separate Zoom Continued Discussion and Chat
  • Surgical Pathology
  • Hematopathology
Lara Harik, MD

Disclosures
- Winship Invest Prostate Cancer Research Grant: 2020-2021

Background
- Rotation Director of GU Pathology
- Board Member and Chair of the Education Committee of the Georgia Association of Pathology
Glandular Lesions of the Bladder
Case 1

68 year old male presenting to the urologist for hematuria.

He has hypertension and is otherwise healthy.

He has a family history of breast carcinoma and colon carcinoma.
Adenocarcinoma
Background

Cystitis Cystica Glandularis, Intestinal Metaplasia and Adenomatous change
Primary Adenocarcinoma of Urinary Bladder

BACKGROUND INTESTINAL METAPLASIA AND ADENOMATOUS EPITHELIUM
Glandular Lesions of the Bladder

Benign
- Cystitis Cystica/Glandularis
- Intestinal Metaplasia
- Nephrogenic Adenoma/Metaplasia
- Gender Dependent

Malignant
- Primary
- Secondary
- Metastatic

Benign Ectopic Prostatic Tissue

Mullerianosis
Malignant Glandular Lesions

**Primary**
- Pure Adenocarcinoma
- Urothelial Carcinoma with glandular differentiation

**Secondary**
- Prostatic/Gynecologic
- Colorectal

**Metastatic**
- Breast/Stomach
- Other
Primary Invasive Adenocarcinoma

Rare tumors <5%

Risk Factors: Bladder extrophy, chronic inflammation, irritation and urachal remnants (dome) are risk factors

Can present at high stages: Prognosis depends on stage.

Distinction between primary and secondary tumors could be difficult
Urothelial Carcinoma with Pseudoglandular Spaces
Invasive Adenocarcinoma with Mucinous Features
Urothelial Carcinoma with Glandular Differentiation

Defined as glandular divergent differentiation in the setting of urothelial carcinoma

- Non-invasive (CIS or papillary) and/or invasive urothelial carcinoma
Clear Cell Carcinoma

Very Rare

More common in urethra with female predominance

Thought to be of Mullerian origin

CK, CA125, PAX2 and 8, Napsin, HNF1β: positive
Secondary
Adenocarcinoma

Prostatic
Adenocarcinoma
Secondary Adenocarcinoma:
Colorectal Adenocarcinoma
Helpful Immunohistochemical Panels: Adenocarcinoma with Enteric Differentiation

<table>
<thead>
<tr>
<th></th>
<th>Bladder</th>
<th>Colon</th>
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<tbody>
<tr>
<td>CK7+/CK20-</td>
<td>Around 40%</td>
<td>Less than 1%</td>
</tr>
<tr>
<td>β-catenin</td>
<td>Cytoplasm</td>
<td>Nuclear</td>
</tr>
<tr>
<td>P63/p40/Gata3</td>
<td>+ / -</td>
<td>Usually Negative</td>
</tr>
</tbody>
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Helpful Immunohistochemical Panels:

<table>
<thead>
<tr>
<th>Prostate</th>
<th>Gynecologic</th>
</tr>
</thead>
<tbody>
<tr>
<td>• NKX3.1, PSA, PSAP, Prostein, CK7/CK20</td>
<td>• General: PAX8</td>
</tr>
<tr>
<td>• Clinical / Serum PSA Level</td>
<td>• Endocervical: P16, HPV ISH</td>
</tr>
<tr>
<td></td>
<td>• Endometrial: ER, PR</td>
</tr>
<tr>
<td></td>
<td>• Ovarian Serous: WT1, p53</td>
</tr>
<tr>
<td></td>
<td>• Clinical</td>
</tr>
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</table>

<table>
<thead>
<tr>
<th>Breast</th>
<th>Stomach</th>
</tr>
</thead>
<tbody>
<tr>
<td>• GCDFP15, Mammaglobin, ER, PR</td>
<td>• ? SATB2 (negative in Gastric)</td>
</tr>
<tr>
<td>• Clinical</td>
<td>• Clinical</td>
</tr>
</tbody>
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Glandular Lesions of the Bladder

Benign
- Cystitis Cystica/Glandularis
- Intestinal Metaplasia
- Nephrogenic Adenoma/Metaplasia
- Gender Dependent
- Benign Ectopic Prostatic Tissue
- Mullerianosis

Malignant
- Primary
- Secondary
- Metastatic
Cystitis Cystica/
Cystitis
Glandularis

Benign lesions

Cystitis Cystica: dilatation of Von Brunn nests

Cystitis Glandularis: Columnar lining on top

Up to 60% of autopsy bladders

Reactive process

No evidence of pre-neoplastic potential
Intestinal Metaplasia

Setting of Cystitis Glandularis

Focal or extensive

Presence of goblet cells

No atypia, no increase in mitoses, no infiltration, no necrosis, no complex arborizing architecture

Mucin extravasation can be a pitfall
Is Intestinal Metaplasia a Precursor Lesion

- Data in children show no risk in long term follow-up
- Other data show significant telomere shortening and other chromosomal gains (chrom3, 7, 17, 9p21)
Adenoma and Villous Adenoma
Gender Dependent: Mullerianosis

Endometriosis
Endosalpingiosis
Endocervicosis
Nephrogenic Adenoma/Metaplasia

Benign Lesion

Papillary, Cystic, Glandular

No atypia, necrosis, mitosis, infiltrative pattern

Prior injury/instrumentation

PAX8 positive
Nephrogenic adenoma/metaplasia
Summary of Glandular Lesions

- Wide variety of benign and malignant lesions
- Adenocarcinoma and Urothelial Carcinoma with glandular differentiation have poor prognosis
- Adenocarcinoma of the bladder can have different histologic appearances and the immunoprofile is not specific
- Think about secondary adenocarcinoma and if needed perform stains to exclude the possibility
Updates in Grading of Prostatic Adenocarcinoma
Case 2

75 year old male with an **elevated PSA of 5.97 ng/ml**

He has a history of chronic renal disease and hypertension.

No family history of carcinoma.
How do we Gleason Score this Prostatic Adenocarcinoma?

Gleason Score 3+4 versus 4+3
The 2019 International Society of Urological Pathology (ISUP) Consensus Conference on Grading of Prostatic Carcinoma

Geert J.L.H. van Leenders, MD,* Theokritos H. van der Kwast, MD,† David J. Grignon, MD,‡ Andrew J. Evans, MD,§ Glen Kristiansen, MD,∥ Charlotte F. Kweldam, MD,* Geert Litjens, PhD,¶ Jesse K. McKenney, MD,∥ Jonathan Melamed, MD,++, Nicholas Mostert, MD,++++
Gladell P. Paner, MD,§§ Hemamali Samarasinghe, FRCPA,∥∥∥ Ivo G. Schrooten, MD,¶¶
Jeffry P. Sinko, MD,### Tetsuyori Tsuzuki, MD,*** Murali Varma, MD,†††
Anne Y. Warren, MD, FRCPath,++++ Thomas M. Wheeler, MD,§§§
Sean R. Williamson, MD,|| ISUP Grading Workshop Panel Members,
and Kenneth A. Iczkowski, MD,||||

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The 2019 Genitourinary Pathology Society (GUPS) White Paper on Contemporary Grading of Prostate Cancer

Jonathan I. Epstein, MD; Mahul B. Amin, MD; Samson W. Fine, MD; Fernan Algaba, MD, PhD; Manju Aron, MD; Dilik E. Bayraktar, MD; Antonio Lopez Beltran, MD, PhD; Fadi Bismar, MD; John C. Cheville, MD; Maurice Colecchia, MD; Eva Comenetz, PhD; Iliana Weineck da Cunha, MD, PhD; Warick Delgado, MD; Angelo M. DeMarzo, MD, PhD; Ciatovana A. Giannico, MD; Jennifer B. Goodfellow, MD; Charles C. Guo, MD; Donna E. Hansel, MD, PhD; Michelle F. Hirsch, MD, PhD; Jialin Huang, MD, PhD; Peter A. Humphrey, MD, PhD; Rafael F. Jimenez, MD; Francesca Kian, MD; Qingnan Kong, MD; Oleksandr N. Kryvenko, MD; L. Priya Kunju, MD; Pati Lai, MD; Mathew Latoue, MD; Tamara Lohan, MD; Fiona Machner, MD; Cristina Mapi-Galluzzi, MD, PhD; Rohit Mehra, MD; Santosh Menon, MD; Hiroshi Miyamoto, MD, PhD; Rodolfo Montironi, MD; George J. Netto, MD; Jane K. Nguyen, MD, PhD; Adeboye O. Osunkoya, MD; Amil Parwani, MD; Brian D. Robinson, MD; Mark A. Rubbo, MD; Rajal R. Shah, MD; Jeffrey S. So, MD; Hironori Takahashi, MD, PhD; Fabio Tavola, MD, PhD; Maria S. Teitelkova, MD, PhD; Lawrence True, MD; Sara E. Weckler, MD; Ximing J. Yang, MD, PhD; Ming Zhou MD, PhD; Debra L. Zynger, MD; Kelli Trpkov, MD

ISUP: Include IDC in GS
GUPS: Do not include IDC in GS
Is the glass full or empty?
Intraductal Carcinoma of the Prostate

Overall incidence of IDC is lower than 3%

Isolated IDC in needle core biopsies (without concomitant invasive cancer) is between 0.06%--0.3%.

Studies call for aggressive treatment of IDC-P on biopsy, even in the absence of documented infiltrating cancer.

In situ carcinoma or retrograde involvement of invasive carcinoma.

Frequently associated with high-grade/score cancer and poor prognostic parameters at radical prostatectomy.
Intraductal Carcinoma: Diagnostic Criteria

Three major histologic patterns:

Dense solid/cribriform atypical proliferation within ducts/ glands

Loose cribriform/ micropapillary growth with:

Marked nuclear atypia

≥ 6 times normal

Necrosis
Atypical Intraductal Proliferation
Intraductal Carcinoma of the Prostate
What We All Agree On

- Clinically relevant on needle biopsies/TURP
- Should always be mentioned
  - (Bx and Prostatectomies)
- If Intraductal carcinoma is the only lesion: Do not grade it
- Associated with Poor Prognosis when present with GS6/GG1
Intraductal Carcinoma of the Prostate
What is Debated

Should we perform PIN3 to exclude IDC
• When it changes the GS/GG

Lesions which upgrade upgrade to pattern 5 e.g. comedo necrosis?
Reporting Percentage of Gleason Grade 4

Percentage Pattern 4 should be recorded for Gleason score 7 (Grade Group 2 and 3):

3+3 versus 3+4

4+4 versus 4+3
Defining Minor/Tertiary Pattern

Higher grade pattern (4 or 5), which represents <5% of tumor volume.

Needle core Biopsy:
- Minor / Tertiary pattern is incorporated into Gleason score
- Gleason Score (most common+highest)

Radical prostatectomy:
- Gleason Score (most common+second most common ≥5%)
- Minor / Tertiary highest Grade pattern ≤5%
Case 3

51 year old male, previously healthy, with lower urinary tract symptoms, including frequency and urgency up to every 15 minutes. PSA was 5.1

Family history of skin cancer in the mother.
How will you grade this lesion?
Plasmacytoid Urothelial Carcinoma Involving the Prostate
Summary of Prostatic Grading Update

Intraductal carcinoma
- Intraductal carcinoma of the prostate should always be mentioned
- Intraductal carcinoma without invasive carcinoma is not graded.
- Perform PIN3 if the amount of possible IDC changes the GS/GG or invoked a Gleason Pattern 5
- Associated with high GG and stage

Report the percentage of Gleason Pattern 4 in GG2 and GG3

Minor tertiary Pattern are reported only on radical prostatectomy
- High grade pattern ≤ 5%
2020 Virtual Pathology Course

LARA HARIK, MD

ROTATION DIRECTOR,
GENITOURINARY PATHOLOGY

CHAIR, GAP EDUCATION COMMITTEE