

Bladder Pathology

An Introduction

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Outline

- Bladder histology
- Terminology issues
- Natural history of TCC
- Papillary vs. flat lesions
- Divergent differentiation in TCC
- TCC variants: why variants?
- Role of urine cytology

Bladder Histology

- Well developed muscularis mucosae in <5%
- Muscularis mucosae bundles may be relatively organised mimicking detrusor
- Tumour within m mucosae (pT1) may be mistaken for detrusor invasion (pT2)
- Little lamina propria at trigone so detrusor close to surface
- Prominent blood vessels mark the level of muscularis mucosae

Bladder Histology (2)

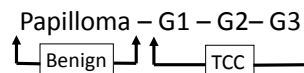
- Detrusor muscle may be interrupted so pT2 may be understaged at TURBT
- Fat often present in lamina propria and Muscularis propria
 - Tumour invading fat in **TURBT** is not pT3

Terminology Issues

- **Superficial TCC**
 - Clinicians: CIS, pTa and pT1
- **Invasive TCC**
 - Pathologists: pT1 at least
 - Clinicians: pT2 at least
- **Muscle invasive TCC**
 - Clinicians: pT2 at least
- **Carcinoma for non-invasive lesions**
 - Basis in natural history of urothelial tumours?

Grading Papillary TCC

WHO 1973



Papilloma

- Rarely recur
- Normal life expectancy
- **Grade 1:** almost normal
- **Grade 3:** like carcinoma in situ

WHO 1973: Problems

- “Carcinoma” for non-invasive tumours
- Large number of tumours end up as G2
- 3 grades of TCC but only 2 Rx options

Natural History of pTa G1 TCC

- Significant recurrence rate (33%), generally as G1 pTa
- Progression rare
- Normal life expectancy
- “carcinoma” because may recur

Re-occurrence rather than recurrence?

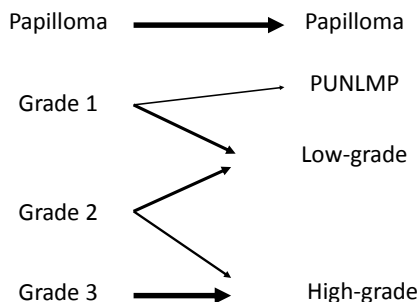
- Related to persistence of causative factor rather than reflecting aggressive tumour behaviour
- “Recurrences” of low-grade TCC often at different site from primary

Grading Papillary TCC

- **WHO 1973**
 - Papilloma – G1 – G2– G3
- **WHO/ISUP 2004**
 - Papilloma
 - Papillary urothelial neoplasm of low malignant potential (PUNLMP)
 - Low-grade urothelial carcinoma
 - High-grade urothelial carcinoma

WHO (1973)

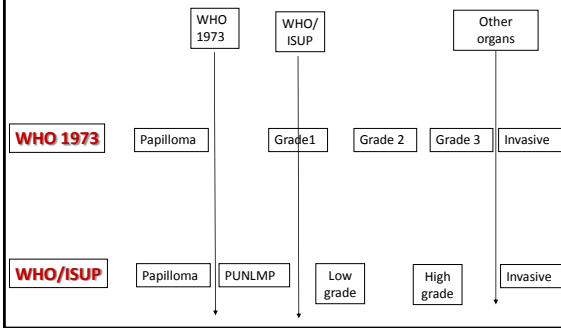
WHO/ISUP (2004)



Natural History of TCC

- **G3 pTa papillary urothelial carcinoma**
 - High recurrence rate (55%), often as invasive (27%).
 - Significant risk of mets/death (25%)
- **pT2 urothelial carcinoma**
 - High risk of mets (50% in 2 years) and death

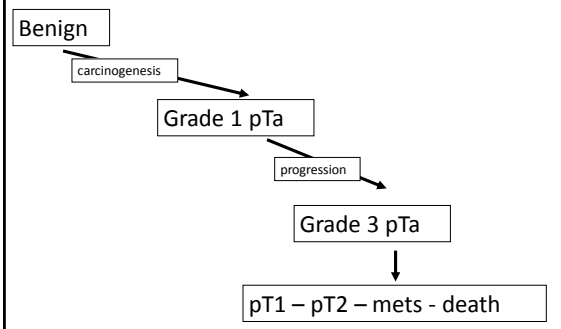
When is it a cancer?



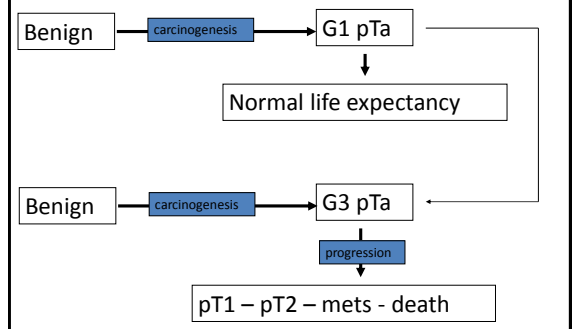
Pathogenesis of Urothelial Neoplasia

- ? 1 disease
- ? 2 distinct diseases

1 Disease Model

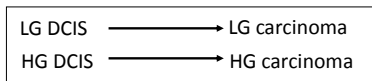


2 disease model



Low-grade and high-grade urothelial neoplasms: Two different diseases?

- Processes that might predispose to adverse outcome have already occurred at time of diagnosis
- Analogous to low-grade and high-grade breast carcinoma



Grade Stage Interaction

- Grade 1 pT1 virtually non-existent
 - Almost always reclassified as pTa or G2
- pT2 disease: grade irrelevant

Relationship of Papillary and Flat lesions

Papillary		Flat
Papilloma	↔	Normal urothelium
PUNLMP	↗	Urothelial hyperplasia
Low-grade TCC	↔	Urothelial dysplasia
High-grade TCC	↔	Urothelial CIS

Divergent differentiation in TCC

- Squamous, glandular and/or small cell differentiation
- Common in high-grade TCC
 - Adverse prognosis
- Small cell carcinoma of bladder often associated with urothelial carcinoma in situ

TCC variants: *Relevance*

- **Histological curiosity**
 - TCC with lipid rich cells
- **Mimics another entity**
 - Plasmacytoid TCC
- **Relevance in mets**
 - TCC with squamous/glandular differentiation
- **Predicts prognosis**
 - Micropapillary TCC
- **Predicts response to therapy**
 - Lymphoepithelioma-like TCC

Role of urine cytology

Advantages

- Non-invasive
- Samples entire surface of bladder and upper tract
- High accuracy in high-grade tumours

Role of urine cytology

Limitations

- Degeneration mimics tumour
- Needs experienced cytopathologist
- Cannot localise tumour
 - May be in bladder, ureter, renal pelvis, urethra
- Low accuracy in low-grade lesions