Protocol for the Examination of Biopsy Specimens From Patients With Carcinoma of the Ureter and Renal Pelvis

Version: 2.2.0.0
Protocol Posting Date: June 2021
The use of this protocol is recommended for clinical care purposes but is not required for accreditation purposes.

This protocol may be used for the following procedures AND tumor types:

Procedure	Description
Biopsy	Includes specimens designated biopsy
Tumor Type	**Description**
Carcinomas	Includes invasive carcinomas of the urinary tract, including urothelial carcinoma and its morphological variants (squamous cell carcinoma, adenocarcinoma, Müllerian carcinoma, neuroendocrine carcinoma, and sarcomatoid carcinoma)

The following should NOT be reported using this protocol:

Procedure
Resection (consider the Ureter and Renal Pelvis Resection protocol)
Cytologic specimens

The following tumor types should NOT be reported using this protocol:

Tumor Type
Lymphoma (consider the Hodgkin or non-Hodgkin Lymphoma protocols)
Sarcoma (consider the Soft Tissue protocol)

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With guidance from the CAP Cancer and CAP Pathology Electronic Reporting Committees.
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Accreditation Requirements
The use of this case summary is recommended for clinical care purposes but is not required for accreditation purposes. The core and conditional data elements are routinely reported. Non-core data elements are indicated with a plus sign (+) to allow for reporting information that may be of clinical value.

Summary of Changes

v 2.2.0.0

- General Reformatting
- Elements that are recommended for clinical care purposes are designated as Core and Conditional (indicated by bolded text), while Non-core elements are now indicated with a plus (+) sign

Reporting Template

Protocol Posting Date: June 2021
Select a single response unless otherwise indicated.

CASE SUMMARY: (URETER, RENAL PELVIS: Biopsy)
Standard(s): AJCC-UICC 8
This case summary is recommended for reporting biopsy specimens, but is not required for accreditation purposes.

SPECIMEN

Specimen (Note A)
___ Renal pelvis
___ Ureter
___ Other (specify): _____
___ Not specified

Specimen Laterality
___ Left
___ Right
___ Not specified

TUMOR

Histologic Type (Note B) (select all that apply)
Urothelial
___ Papillary urothelial carcinoma, noninvasive
___ Papillary urothelial carcinoma, invasive
___ Urothelial carcinoma in situ
___ Urothelial carcinoma, invasive
___ Urothelial carcinoma, nested (including large nested) variant
___ Urothelial carcinoma, microcystic variant
___ Urothelial carcinoma, micropapillary variant
___ Urothelial carcinoma, lymphoepithelioma-like variant
___ Urothelial carcinoma, plasmacytoid / signet ring / diffuse variant
___ Urothelial carcinoma, sarcomatoid variant
___ Urothelial carcinoma, giant cell variant
___ Urothelial carcinoma, poorly differentiated variant
___ Urothelial carcinoma, lipid-rich variant
___ Urothelial carcinoma, clear cell variant
___ Urothelial carcinoma with squamous differentiation
+Percentage of Squamous Differentiation
___ Specify percentage: _____ %
___ Other (specify): _____
___ Cannot be determined
___ Urothelial carcinoma with glandular differentiation
+Percentage of Glandular Differentiation
___ Specify percentage: _____ %
___ Other (specify): _____
___ Cannot be determined

___ Urothelial carcinoma with trophoblastic differentiation
+Percentage of Trophoblastic Differentiation
___ Specify percentage: _____ %
___ Other (specify): _____
___ Cannot be determined
___ Urothelial carcinoma with Müllerian differentiation
+Percentage of Müllerian Differentiation
___ Specify percentage: _____ %
___ Other (specify): _____
___ Cannot be determined
Squamous
___ Squamous cell carcinoma
___ Verrucous carcinoma
___ Squamous cell carcinoma in situ (no invasive carcinoma identified)
Glandular
___ Adenocarcinoma
___ Adenocarcinoma, enteric
___ Adenocarcinoma, mucinous
___ Adenocarcinoma, mixed
___ Adenocarcinoma in situ (no invasive carcinoma identified)
Tumors of Müllerian Type
___ Clear cell carcinoma
___ Endometrioid carcinoma
Neuroendocrine Tumors
___ Small cell neuroendocrine carcinoma
+Percentage of Small Cell Neuroendocrine Component
___ Specify percentage: _____ %
___ Other (specify): _____
___ Cannot be determined
___ Large cell neuroendocrine carcinoma
+Percentage of Large Cell Neuroendocrine Component
___ Specify percentage: _____ %
___ Other (specify): _____
___ Cannot be determined
___ Well-differentiated neuroendocrine carcinoma
+Percentage of Well-differentiated Neuroendocrine Component
___ Specify percentage: _____ %
___ Other (specify): _____
___ Cannot be determined
Other
___ Other histologic type not listed (specify): _____
___ Carcinoma, type cannot be determined: _____
+Histologic Type Comment: _____

Histologic Grade (Note C)
For urothelial carcinoma, other variants, or divergent differentiation
___ Low-grade
___ High-grade
For squamous cell carcinoma or adenocarcinoma
___ G1, well differentiated
___ G2, moderately differentiated

___ G3, poorly differentiated
___ GX, cannot be assessed: _____
Other
___ Other (specify): _____
___ Cannot be assessed: _____
___ Not applicable: _____

Tumor Extent (Note D)
___ Noninvasive papillary carcinoma
___ Carcinoma in situ
___ Invades subepithelial connective tissue
___ Invades muscularis
___ Invades beyond muscularis into peripelvic fat or renal parenchyma (for renal pelvis only)
___ Invades beyond muscularis into periureteric fat (for ureter only)
___ Invades adjacent organs or through the kidney into perinephric fat: _____
___ Cannot be determined: _____

+Lymphovascular Invasion
___ Not identified
___ Present
___ Cannot be determined: _____

+Tumor Configuration (select all that apply)
___ Papillary
___ Solid / nodule
___ Flat
___ Ulcerated
___ Other (specify): _____
___ Cannot be determined: _____

Muscularis Propria (for determining pT category) (Note D)
___ Not identified
___ Present
___ Cannot be determined: _____

+Tumor Comment: _____

ADDITIONAL FINDINGS (Note C)

+Associated Epithelial Lesions (Note C) (select all that apply)
___ None identified
___ Urothelial papilloma
___ Urothelial papilloma, inverted type
___ Papillary urothelial neoplasm, low malignant potential (PUNLMP)
___ Urothelial proliferation of uncertain malignant potential
___ Urothelial dysplasia
___ Other (specify): _____
___ Cannot be determined: _____

+Additional Findings (select all that apply)
___ Inflammation / regenerative changes
___ Therapy-related changes
___ Cautery artifact
___ Cystitis cystica et glandularis
___ Keratinizing squamous metaplasia
___ Intestinal metaplasia
___ Other (specify): _____

COMMENTS

Comment(s): _____

Explanatory Notes

A. History

A relevant history is important for interpretation of all upper urinary tract (renal pelvis and ureter) specimens. A history of renal stones, recent urinary tract procedures, infections, or obstruction can influence the interpretation of random biopsies obtained from patients with hematuria. Any neoplasms previously diagnosed should be specified, including the histologic type, primary site, and histologic grade. Primary tumors may be associated with hereditary nonpolyposis colon cancer (HNPCC) syndrome (Lynch syndrome II). Renal pelvic tumors are more often seen in analgesic abusers, who often have analgesic nephropathy, including papillary necrosis. If prior therapy has been given, it should be described (systemic or intravesical chemotherapy, immunotherapy, radiation, etc). The method of collection and date also should be specified in urine cytology specimens. Cytologic specimens from the ureter or renal pelvis may be over-interpreted if their site of sampling is not stated.

B. Histologic Type

Like the urinary bladder, the vast majority (more than 95%) of carcinomas of the renal pelvis and ureter are urothelial in origin.[1,2,3,4,5,6,7] The most recent 2016 World Health Organization (WHO) classification of tumors of the urothelial tract, including urethra, urinary bladder, ureter, and renal pelvis, is provided in this note. Benign tumors are included in this classification because, within the same patient, a spectrum of differentiation from benign to malignant tumors may be seen, either at the same time or over the clinical course of the disease. The full spectrum of invasive urothelial carcinoma and its variants as found in the urinary bladder may also be found in the upper tract. The distinction between a urothelial carcinoma with divergent squamous, glandular, or Müllerian differentiation, and a pure squamous cell carcinoma, adenocarcinoma or Müllerian is rather arbitrary. Most authorities, including the 2016 WHO classification, require a pure histology of squamous cell carcinoma, adenocarcinoma or Müllerian to designate a tumor as such, all others with recognizable papillary, invasive, or flat carcinoma in situ (CIS) urothelial component being considered as urothelial carcinoma with divergent differentiation. A malignant neoplasm with small cell neuroendocrine carcinoma component arising in the urinary tract is designated as small cell carcinoma.

Lynch syndrome, also known as hereditary nonpolyposis colorectal cancer, predisposes patients to urological cancer, particularly upper tract urothelial carcinoma. Upper tract urothelial carcinoma develops in up to 28% of patients with known Lynch syndrome. Therefore, pathologists should be aware of Lynch syndrome and their important role of identifying Lynch syndrome patients by considering appropriate tissue tests. Recently several guidelines have been published regarding when and what tissue testing is appropriate for screening patients with upper tract urothelial carcinoma.[8,9]

2016 WHO Classification of Tumors of the Urothelial Tract

Urothelial tumors

Infiltrating urothelial carcinoma

- Nested, including large nested
- Microcystic
- Micropapillary
- Lymphoepithelioma-like
- Plasmacytoid/signet ring cell/diffuse
- Sarcomatoid

- Giant cell
- Poorly differentiated

Noninvasive urothelial lesions

- Urothelial carcinoma in situ
- Noninvasive papillary urothelial carcinoma, low grade
- Noninvasive papillary urothelial carcinoma, high grade
- Papillary urothelial neoplasm of low malignant potential
- Urothelial papilloma
- Inverted urothelial papilloma
- Urothelial proliferation of uncertain malignant potential
- Urothelial dysplasia

Squamous cell neoplasms

Squamous cell carcinoma

Verrucous carcinoma

Squamous cell papilloma

Glandular neoplasms

Adenocarcinoma, NOS

- Enteric
- Mucinous
- Mixed

Villous adenoma

Tumors of Müllerian type

Clear cell carcinoma

Endometrioid carcinoma

Neuroendocrine tumors

Small cell neuroendocrine carcinoma

Large cell neuroendocrine carcinoma

Well-differentiated neuroendocrine tumor

Paraganglioma

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1. Delahunt B, Amin MB, Hofstader F, Hartmann A, Tyczynski JE. Tumours of the renal pelvis and ureter. In: Eble JN, Sauter G, Epstein JI, Sesterhenn IA, eds. *World Health Organization Classification of Tumours: Pathology and Genetics of Tumours of the Urinary System and Male Genital Organs*. Lyon, France: IARC Press; 2004:150-153.
2. Murphy WM, Grignon DJ, Perlman EJ. Tumors of the ureters and renal pelves. In: *Tumors of the Kidney, Bladder, and Related Urinary Structures*. *AFIP Atlas of Tumor Pathology*. Series 4. Washington, DC: American Registry of Pathology; 2004:375-379.
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8. Mork M, Hubosky SG, Rouprêt M, et al. Lynch syndrome: a primer for urologists and panel recommendations. *J Urol*. 2015;194(1):21-29.
9. Rouprêt M, Babjuk M, Compérat E, et al. European Association of Urology Guidelines on Upper Urinary Tract Urothelial Cell Carcinoma: 2015 update. *Eur Urol*. 2015;68(5):868-879.

C. Histologic Grade

The grading system is identical to that for urinary bladder neoplasms. Flat intraepithelial lesions and papillary and invasive lesions are graded separately. There has been significant controversy in the classification of these lesions.[1] Due to variable classification systems and the need for a universally acceptable system, the World Health Organization/International Society of Urological Pathology (WHO/ISUP) consensus classification was proposed.[2] This system is utilized in the WHO 2004 classification,[3] the 2004 Armed Forces Institute of Pathology (AFIP) fascicle,[4] and 2016 WHO classification,[5] and has been validated by many studies to be prognostically significant. Other systems (that were being used previously) may still be used according to institutional preference. Urothelial carcinomas of the renal pelvis tend to more often be high grade[6,7] compared to urinary bladder carcinomas.

Flat and papillary urothelial hyperplasia has been renamed as “urothelial proliferation of uncertain malignant potential” in 2016 WHO classification.

Squamous carcinomas and adenocarcinomas may be graded as well differentiated, moderately differentiated, and poorly differentiated.

References
1. Amin MB, Murphy WM, Reuter VE, et al. Controversies in the pathology of transitional cell carcinoma of the urinary bladder. In: Rosen PP, Fechner RE, eds. *Reviews of Pathology*. Vol. 1. Chicago, IL: ASCP Press; 1996:1-39.
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classification of urothelial (transitional cell) neoplasms of the urinary bladder. *Am J Surg Pathol.* 1998;22:1435-1448.
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D. Extent of Invasion

Depth of invasion and pathologic stage are the most important prognostic indicators for patients with neoplasms of the upper urinary tract.[1,2] A critical role of the surgical pathologist is to diagnose the depth and extent of invasion into the subepithelial connective tissue/lamina propria (pT1), muscularis propria (pT2), or beyond (pT3 or pT4). The patterns of invasion are similar to the urinary bladder, except that for renal pelvis carcinoma, the type of tumor involvement of the kidney, when present, impacts stage. Also, it is important to note that the lamina propria is absent beneath the urothelium lining the renal papillae in the pelvis and is thin along the minor calyces.[3] As in the urinary bladder, in papillary tumors, invasion occurs most often at the base of the tumor and very infrequently in the stalk. Tumor infiltrating the lamina propria is pT1, and, like the urinary bladder, there is no accepted approach for assessing depth of lamina propria invasion. However, pathologists are encouraged to provide some assessment as to the extent of lamina propria invasion (ie, focal versus extensive, or depth in millimeters, or by level – above, at, or below muscularis mucosae). Designation of a tumor as merely muscle-invasive is inappropriate, but the type of muscle invasion, ie, muscularis mucosae (pT1 tumors) versus muscularis propria (pT2 tumors) invasion, needs to be clearly stated. Descriptive terminology, such as “urothelial carcinoma with muscle invasion, indeterminate for type of muscle invasion,” may be used when it is not possible to be certain whether the type of muscle invaded by the tumor is hypertrophic muscularis mucosae or muscularis propria. For renal pelvic tumors, in-situ extension of carcinoma into renal collecting ducts and renal tubules does not affect stage, while carcinoma invading into the renal parenchyma is pT3. Renal pelvic carcinoma that invades through the kidney into perinephric fat is pT4. Patients with upper tract urothelial carcinoma often present at higher stage compared to patients with urinary bladder carcinoma.[4,5]

References

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