

# Protocol for the Examination of Specimens From Patients With Invasive Carcinoma of Renal Tubular Origin

**Wilms tumors and tumors of urothelial origin are not included.**

**Based on AJCC/UICC TNM, 7th edition**

Protocol web posting date: October 2009

## **Procedures**

- Incisional Biopsy (Needle or Wedge)
- Partial Nephrectomy
- Radical Nephrectomy

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## **CAP Kidney Protocol Revision History**

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### **Version Code**

The definition of the version code can be found at [www.cap.org/cancerprotocols](http://www.cap.org/cancerprotocols).

**Version:** Kidney 3.0.0.0

### **Summary of Changes**

No changes have been made since the October 2009 release.

**Surgical Pathology Cancer Case Summary (Checklist)**

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Protocol web posting date: October 2009

**KIDNEY: Biopsy****Note: checklist is optional for biopsy specimens****Select a single response unless otherwise indicated.****\*Procedure**

- \*  Incisional biopsy, needle
- \*  Incisional biopsy, wedge
- \*  Other (specify): \_\_\_\_\_
- \*  Not specified

**\*Specimen Laterality**

- \*  Right
- \*  Left
- \*  Not specified

**\*Histologic Type (Note A)**

- \*  Clear cell renal cell carcinoma
- \*  Multilocular clear cell renal cell carcinoma
- \*  Papillary renal cell carcinoma
- \*  Chromophobe renal cell carcinoma
- \*  Carcinoma of the collecting ducts of Bellini
- \*  Renal medullary carcinoma
- \*  Translocation carcinoma (Xp11 or others)
- \*  Carcinoma associated with neuroblastoma
- \*  Mucinous tubular and spindle cell carcinoma
- \*  Tubulocystic renal cell carcinoma
- \*  Renal cell carcinoma, unclassified
- \*  Other (specify): \_\_\_\_\_

**\*Sarcomatoid Features (Note B)**

- \*  Not identified
- \*  Present
- \* Specify percentage of sarcomatoid element: \_\_\_\_\_%

**\*Histologic Grade (Fuhrman Nuclear Grade) (Note C)**

- \*  Not applicable
- \*  GX: Cannot be assessed
- \*  G1: Nuclei round, uniform, approximately 10 µm; nucleoli inconspicuous or absent
- \*  G2: Nuclei slightly irregular, approximately 15 µm; nucleoli evident
- \*  G3: Nuclei very irregular, approximately 20 µm; nucleoli large and prominent
- \*  G4: Nuclei bizarre and multilobated, 20 µm or greater, nucleoli prominent, chromatin clumped

\* Data elements with asterisks are not required. However, these elements may be clinically important but are not yet validated or regularly used in patient management.

**\*Additional Pathologic Findings**

\* \_\_\_ None identified

\* \_\_\_ Other pathology present (specify): \_\_\_\_\_

**\*Comment(s)**

**Surgical Pathology Cancer Case Summary (Checklist)**

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Protocol web posting date: October 2009

**KIDNEY: Nephrectomy, Partial or Radical****Select a single response unless otherwise indicated.****Procedure (Note D)**

- Partial nephrectomy  
 Radical nephrectomy  
 Other (specify): \_\_\_\_\_  
 Not specified

**Specimen Laterality**

- Right  
 Left  
 Not specified

**\*Tumor Site (select all that apply)**

- \*  Upper pole  
 \*  Middle  
 \*  Lower pole  
 \*  Other (specify): \_\_\_\_\_  
 \*  Not specified

**Tumor Size (largest tumor if multiple)**

- Greatest dimension: \_\_\_\_ cm  
 \*Additional dimensions: \_\_\_\_ x \_\_\_\_ cm  
 Cannot be determined (see "Comment")

**Tumor Focality**

- Unifocal  
 Multifocal

**Macroscopic Extent of Tumor (select all that apply) (Note E)**

- Tumor limited to kidney  
 Tumor extension into perinephric tissues  
 Tumor extension into renal sinus  
 Tumor extension beyond Gerota's fascia  
 Tumor extension into major veins (renal vein or its segmental (muscle containing) branches, inferior vena cava)  
 Tumor extension into pelvicaliceal system  
 Tumor extension into adrenal gland  
      Direct invasion (T4)  
      Noncontiguous (M1)  
 Tumor extension into other organ(s)/structure(s) (specify): \_\_\_\_\_

\* Data elements with asterisks are not required. However, these elements may be clinically important but are not yet validated or regularly used in patient management.

**Histologic Type (Note A)**

- Clear cell renal cell carcinoma
- Multilocular clear cell renal cell carcinoma
- Papillary renal cell carcinoma
- Chromophobe renal cell carcinoma
- Carcinoma of the collecting ducts of Bellini
- Renal medullary carcinoma
- Translocation carcinoma (Xp11 or others)
- Carcinoma associated with neuroblastoma
- Mucinous tubular and spindle cell carcinoma
- Tubulocystic renal cell carcinoma
- Renal cell carcinoma, unclassified
- Other (specify): \_\_\_\_\_

**Sarcomatoid Features (Note B)**

- Not identified
- Present
  - Specify percentage of sarcomatoid element: \_\_\_\_%

**\*Tumor Necrosis (any amount)**

- \*  Not identified
- \*  Present

**Histologic Grade (Fuhrman Nuclear Grade) (Note C)**

- Not applicable
- GX: Cannot be assessed
- G1: Nuclei round, uniform, approximately 10  $\mu\text{m}$ ; nucleoli inconspicuous or absent
- G2: Nuclei slightly irregular, approximately 15  $\mu\text{m}$ ; nucleoli evident
- G3: Nuclei very irregular, approximately 20  $\mu\text{m}$ ; nucleoli large and prominent
- G4: Nuclei bizarre and multilobated, 20  $\mu\text{m}$  or greater, nucleoli prominent, chromatin clumped
- Other (specify): \_\_\_\_\_

**Microscopic Tumor Extension (select all that apply)**

- Tumor limited to kidney
- Tumor extension into perinephric tissue (beyond renal capsule)
- Tumor extension into renal sinus
- Tumor extension beyond Gerota's fascia
- Tumor extension into major vein (renal vein or its segmental (muscle containing) branches, inferior vena cava)
- Tumor extension into pelvicalyceal system
- Tumor extension into adrenal gland
  - Direct invasion (T4)
  - Noncontiguous (M1)
- Tumor extension into other organ(s)/structure(s) (specify): \_\_\_\_\_

\* Data elements with asterisks are not required. However, these elements may be clinically important but are not yet validated or regularly used in patient management.

**Margins (select all that apply) (Note F)**

- Cannot be assessed  
 Margins uninvolved by invasive carcinoma  
 Margin(s) involved by invasive carcinoma
  - Renal parenchymal margin (partial nephrectomy only)
  - Renal capsular margin (partial nephrectomy only)
  - Perinephric fat margin (partial nephrectomy only)
  - Gerota's fascial margin
  - Renal vein margin
  - Ureteral margin
  - Other (specify): \_\_\_\_\_

**\*Lymph-Vascular Invasion**

(excluding renal vein and its muscle containing segmental branches and inferior vena cava)

- \*  Not identified  
 \*  Present  
 \*  Indeterminate

**Pathologic Staging (pTNM) (Note G)**

TNM Descriptors (required only if applicable) (select all that apply)

- m (multiple primary tumors)  
 r (recurrent)  
 y (posttreatment)

Primary Tumor (pT)

- pTX: Primary tumor cannot be assessed  
 pT0: No evidence of primary tumor  
 pT1: Tumor 7 cm or less in greatest dimension, limited to the kidney  
 pT1a: Tumor 4 cm or less in greatest dimension, limited to the kidney  
 pT1b: Tumor more than 4 cm but not more than 7 cm in greatest dimension, limited to the kidney  
 pT2: Tumor more than 7 cm in greatest dimension, limited to the kidney  
 pT2a: Tumor more than 7 cm but less than or equal to 10 cm in greatest dimension, limited to the kidney  
 pT2b: Tumor more than 10 cm, limited to the kidney  
 pT3: Tumor extends into major veins or perinephric tissues but not into the ipsilateral adrenal gland and not beyond Gerota's fascia  
 pT3a: Tumor grossly extends into the renal vein or its segmental (muscle containing) branches, or tumor invades perirenal and/or renal sinus fat but not beyond Gerota's fascia  
 pT3b: Tumor grossly extends into the vena cava below the diaphragm  
 pT3c: Tumor grossly extends into vena cava above diaphragm or invades the wall of the vena cava  
 pT4: Tumor invades beyond Gerota's fascia (including contiguous extension into the ipsilateral adrenal gland)

\* Data elements with asterisks are not required. However, these elements may be clinically important but are not yet validated or regularly used in patient management.

Regional Lymph Nodes (pN) pNX: Regional lymph nodes cannot be assessed pN0: No regional lymph node metastasis pN1: Metastasis in regional lymph node(s)

Specify: Number examined: \_\_\_\_\_

Number positive: \_\_\_\_\_

Distant Metastasis (pM) Not applicable pM1: Distant metastasis**Pathologic Findings in Nonneoplastic Kidney (select all that apply) (Note H)** Insufficient tissue (partial nephrectomy specimen with <5 mm of adjacent nonneoplastic kidney) Significant pathologic alterations None identified Glomerular disease (specify type): \_\_\_\_\_ Tubulointerstitial disease (specify type): \_\_\_\_\_ Vascular disease (specify type): \_\_\_\_\_ Other (specify): \_\_\_\_\_**\* Other Tumors and/or Tumor-like Lesions (select all that apply)**\*  Cyst(s) (specify type): \_\_\_\_\_\*  Tubular (papillary) adenoma(s)\*  Other (specify): \_\_\_\_\_**\*Comment(s)**

\* Data elements with asterisks are not required. However, these elements may be clinically important but are not yet validated or regularly used in patient management.

## Explanatory Notes

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### A. Histologic Type

The histopathologic classification published by the World Health Organization (WHO)<sup>1</sup> and the Armed Forces Institute of Pathology<sup>2</sup> is recommended for usage.

Clear cell renal cell carcinoma  
Multilocular clear cell renal cell carcinoma  
Papillary renal cell carcinoma<sup>#</sup>  
Chromophobe renal cell carcinoma  
Carcinoma of the collecting ducts of Bellini  
Renal medullary carcinoma  
Xp11 translocation carcinomas  
Carcinoma associated with neuroblastoma  
Mucinous tubular and spindle cell carcinoma  
Tubulocystic renal cell carcinoma<sup>##</sup>  
Renal cell carcinoma, unclassified

<sup>#</sup> Papillary carcinoma is commonly separated into type 1 and type 2 based mainly on cytomorphological features.<sup>1</sup>

<sup>##</sup> Tubulocystic carcinoma is a distinct low-grade variant of renal cell carcinoma that was not listed in the 2004 WHO classification. Recent papers have elucidated the nature of this tumor.<sup>3-5</sup> This tumor had been previously referred to as a low-grade collecting duct carcinoma.<sup>6</sup> Additionally, there are a variety of other uncommon and emerging carcinomas described in the recent literature.<sup>7</sup>

Occasionally more than one histologic type of carcinoma occurs within the same kidney specimen. Each tumor type should be separately recorded along with its associated prognostic factors.

### B. Sarcomatoid Features

Sarcomatoid carcinoma is not a specific morphogenetic subtype of renal cell carcinoma but is considered as a pattern of dedifferentiation.<sup>1,2</sup> Sarcomatoid change in a renal cell carcinoma is associated with an adverse outcome.<sup>8</sup> Sarcomatoid morphology may be found in renal cell carcinomas of clear cell, papillary, chromophobe, collecting duct, and unclassified subtypes.<sup>9-14</sup> When the background carcinoma subtype is recognized, it should be specified under histologic type (see Note A). Pure sarcomatoid carcinoma or sarcomatoid carcinoma associated with epithelial elements that do not conform to usual renal carcinoma cell types should be considered as unclassified renal cell carcinoma.

There is some indication that the percentage of sarcomatoid component in a renal cell carcinoma has prognostic importance.<sup>13,14</sup>

### C. Histologic Grade

The following grading scheme for renal cell carcinoma developed by Fuhrman et al is recommended and shown below.<sup>15</sup> Beyond clear cell renal cell carcinoma, Fuhrman grading has not been fully established for each histologic subtype of renal parenchymal neoplasia.<sup>16</sup> The protocol does not preclude the use of other grading schemes.<sup>16,17</sup> The

system of grading should be specified in the pathologist's report. Scoring is based on the worst (highest) grade present in the tumor even if it constitutes only a minor component.

### **Fuhrman Grading System**

Grade X	Cannot be assessed
Grade 1	Nuclei round, uniform, approximately 10 µm in diameter; nucleoli inconspicuous or absent
Grade 2	Nuclei slightly irregular, approximately 15 µm in diameter; nucleoli evident
Grade 3	Nuclei very irregular, approximately 20 µm in diameter; nucleoli large and prominent
Grade 4	Nuclei bizarre and multilobated, 20 µm or greater in diameter, nucleoli prominent, chromatin clumped

### **D. Specimen Type**

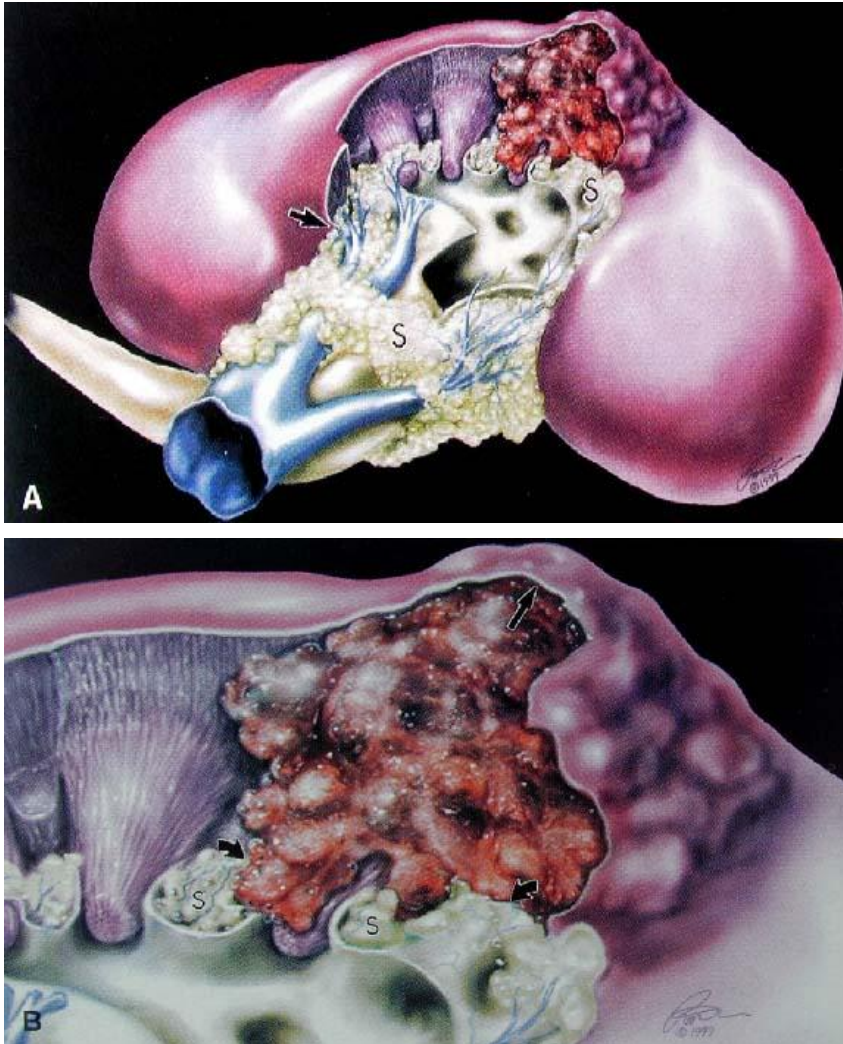
A standard radical nephrectomy specimen consists of the entire kidney including the calyces, pelvis, and a variable length of ureter. The adrenal gland is usually removed en bloc with the kidney. The entire perirenal fatty tissue is removed to the level of Gerota's fascia, a membranous structure that is similar to the consistency of the renal capsule that encases the kidney in perirenal fat. Variable lengths of the major renal vessels at the hilus are submitted.

Regional lymphadenectomy is not generally performed even with a radical nephrectomy. A few lymph nodes may occasionally be seen in the renal hilus around major vessels. Other regional lymph nodes (eg, paracaval, para-aortic, and retroperineal) may be submitted separately.

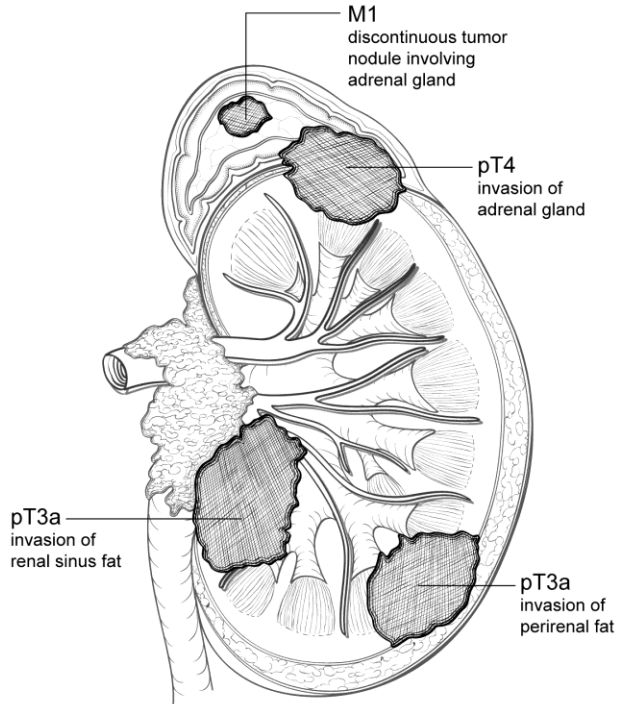
A partial nephrectomy specimen may vary from a simple enucleation of the tumor to part of a kidney containing variable portions of calyceal or renal pelvic collecting system. The perirenal fat immediately overlying the resected portion of the kidney but not to a level of Gerota's fascia is usually included.

### **E. Macroscopic Extent of Tumor**

A careful gross analysis and description of tumor extension in a nephrectomy specimen is important and should guide blocking of tissue samples for histologic assessment. Careful documentation of the tumor extension beyond kidney into perinephric fat and Gerota's fascia provides important staging information. Renal sinus fat involvement in renal cell carcinoma is an under-recognized phenomenon.<sup>18</sup> The renal sinus is an important pathway of spread of renal cell carcinoma (Figure 1, A and B). The renal sinus fat should be carefully assessed and generously sampled in order to detect renal sinus fat involvement. There is evolving literature suggesting that renal sinus fat involvement predicts a more aggressive outcome than peripheral perinephric fat invasion.<sup>19,20</sup> When renal carcinoma involves adrenal gland, it is important to document whether the involvement is contiguous spread of tumor or a separate (noncontiguous) nodule of carcinoma, the latter representing metastatic disease (pM1) (Figure 2).



**Figure 1.** A, Diagram showing the renal sinus fat (S) and its rich venous system that envelops the collecting system. The renal capsule terminates (arrow) just inside the vestibule of the hilum. B, A renal malignancy is constrained by the renal capsule (arrow), yet no fibrous capsule impedes its growth into the vascular tissue of the renal sinus (curved arrows). From Bonsib et al.<sup>18</sup> Reproduced with permission of the American Journal of Surgical Pathology. © 2000 Wolters Kluwer Health.



**Figure 2.** Diagram showing relationship between local tumor extension and pT designation. When a tumor shows direct invasion into the perirenal fat or renal sinus fat it is designated as pT3a. A tumor that directly invades the adrenal gland is designated as pT4 while a tumor that shows discontinuous (noncontiguous) involvement of the adrenal gland is considered metastatic (M1).

### F. Margins

In a partial nephrectomy specimen, the renal parenchymal margin should be inked and histologically assessed. Most partial nephrectomy specimens also contain a portion of perinephric fat overlying the tumor site. The perirenal fat margin should also be assessed. In situations where no perirenal fat is present, the renal capsular margin should be inked and examined histologically.

In radical nephrectomy specimens the ureteric, major vascular (renal vein, renal artery) and soft tissue (Gerota's fascia, renal sinus) margins should be examined and documented in the report.

### G. TNM and Stage Groupings

The TNM staging system of the American Joint Committee on Cancer (AJCC) and the International Union Against Cancer (UICC) for renal cell carcinoma is recommended.<sup>21,22</sup>

By AJCC/UICC convention, the designation "T" refers to a primary tumor that has not been previously treated. The symbol "p" refers to the pathologic classification of the TNM, as opposed to the clinical classification, and is based on gross and microscopic examination. pT entails a resection of the primary tumor or biopsy adequate to evaluate the highest pT category, pN entails removal of nodes adequate to validate lymph node metastasis, and pM implies microscopic examination of distant lesions. Clinical classification (cTNM) is usually carried out by the referring physician before treatment during initial evaluation of the patient or when pathologic classification is not possible.

Pathologic staging is usually performed after surgical resection of the primary tumor. Pathologic staging depends on pathologic documentation of the anatomic extent of disease, whether or not the primary tumor has been completely removed. If a biopsied tumor is not resected for any reason (eg, when technically unfeasible) and if the highest T and N categories or the M1 category of the tumor can be confirmed microscopically, the criteria for pathologic classification and staging have been satisfied without total removal of the primary cancer.

### Stage Groupings

Stage I	T1	N0	M0 <sup>#</sup>
Stage II	T2	N0	M0
Stage III	T1 or T2	N1	M0
	T3	N0 or N1	M0
Stage IV	T4	Any N	M0
	Any T	Any N	M1

<sup>#</sup> M0 is defined as no distant metastasis.

### TNM Descriptors

For identification of special cases of TNM or pTNM classifications, the “m” suffix and “y,” “r,” and “a” prefixes are used. Although they do not affect the stage grouping, they indicate cases needing separate analysis.

The “m” suffix indicates the presence of multiple primary tumors in a single site and is recorded in parentheses: pT(m)NM.

The “y” prefix indicates those cases in which classification is performed during or following initial multimodality therapy (ie, neoadjuvant chemotherapy, radiation therapy, or both chemotherapy and radiation therapy). The cTNM or pTNM category is identified by a “y” prefix. The ycTNM or ypTNM categorizes the extent of tumor actually present at the time of that examination. The “y” categorization is not an estimate of tumor prior to multimodality therapy (ie, before initiation of neoadjuvant therapy).

The “r” prefix indicates a recurrent tumor when staged after a documented disease-free interval, and is identified by the “r” prefix: rTNM.

The “a” prefix designates the stage determined at autopsy: aTNM.

### Additional Descriptors

#### Residual Tumor (R)

Tumor remaining in a patient after therapy with curative intent (eg, surgical resection for cure) is categorized by a system known as R classification, shown below.

RX	Presence of residual tumor cannot be assessed
R0	No residual tumor
R1	Microscopic residual tumor
R2	Macroscopic residual tumor

For the surgeon, the R classification may be useful to indicate the known or assumed status of the completeness of a surgical excision. For the pathologist, the R classification

is relevant to the status of the margins of a surgical resection specimen. That is, tumor involving the resection margin on pathologic examination may be assumed to correspond to residual tumor in the patient and may be classified as macroscopic or microscopic according to the findings at the specimen margin(s).

### Lymph-Vascular Invasion

By AJCC/UICC convention, vessel invasion (lymphatic or venous) does not affect the T category indicating local extent of tumor unless specifically included in the definition of a T category. In all other cases, lymphatic and venous invasion by tumor are coded separately.

### H. Pathologic Findings in Nonneoplastic Kidney

It is important to recognize that medical kidney diseases may be present in nonneoplastic renal tissue in nephrectomy and nephroureterectomy specimens.<sup>23,24</sup> Arterionephrosclerosis (or hypertensive nephropathy) and diabetic nephropathy are seen in approximately 30% and 20% of cases, respectively. Other medical renal diseases that have been identified include thrombotic microangiopathy, focal segmental glomerulosclerosis, and IgA nephropathy. The findings of greater than 20% global glomerulosclerosis or advanced diffuse diabetic glomerulosclerosis are predictive of significant decline in renal function 6 months after radical nephrectomy.<sup>24</sup> Evaluation for medical renal disease should be performed in each case; PAS and/or Jones methenamine silver stains should be applied if necessary. Consultation with a nephropathologist should be pursued as needed.

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