



Secondary Tumors of the Urinary System: An Imaging Conundrum

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Imaging features of metastases to the urinary system may closely mimic primary urinary tract tumors, and differential diagnosis by imaging alone may be problematic or even impossible in some cases. The main purpose of this article was to familiarize radiologists with imaging findings of metastasis to the urinary system on cross-sectional imaging, with an emphasis on abdominal and pelvic computed tomography and magnetic resonance imaging. In addition, we review the clinical importance and implications of metastases to the urinary tract and provide information on diagnostic work-ups.

Keywords: *Urinary system; Metastasis; Kidney; Ureter; Bladder; Urethra; CT; MRI*

INTRODUCTION

The urinary tract may be involved in metastatic spread from other primary cancers. Information on imaging features of secondary urinary tract tumors is very limited and mostly based on anecdotal case reports. A variety of tumors may metastasize to the urinary tract and may present, mostly, with vague and non-specific imaging features. Breast cancer, malignant melanoma, lung cancer, head and neck malignancies, thyroid tumors, colorectal and pancreatic cancers, bone and soft tissue sarcomas, and Merkel cell carcinoma may metastasize to the urinary tract (1-3).

The imaging features of secondary urinary tract tumors have not been very well described in the relevant literature,

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the findings are almost always non-specific, and diagnosis is mostly based on either tissue diagnosis or clinical history. It is not unwise to consider the occurrence of secondary urinary tract tumors in patients with advanced malignancy, but it should also be noted that metastasis to the urinary system may also be the first sign of detectable distant metastasis from an unrelated source (1).

The timely recognition of secondary urinary tract tumors with ultrasonography (US), computed tomography (CT), and magnetic resonance imaging (MRI) is of paramount importance. As the outcome and treatment approaches to primary and secondary urinary tumors may vary significantly, prompt detection and differentiation have the potential to dramatically affect the clinical management. While the main approach to primary tumors is potentially curative surgery, in patients with secondary urinary tumors, surgical intervention can be deferred or may be performed in selected patients.

Renal Metastasis

Metastasis to the kidney is not uncommon, occurring between 7% and 12% of patients with overall cancers at post-mortem examination (4, 5). The actual detection

rate is lower in clinical settings than autopsy data, as the post-mortem studies also include microscopic metastatic involvement, which is generally beyond the resolution of cross-sectional imaging modalities (6). A recent study showed the imaging incidence of metastases to the kidney to be 0.9% (7).

The detection of metastasis in the kidneys is usually a sign of advanced disease and almost always a grave prognosis. The primary site can be almost anywhere in the body, but the most common primary sites are lung, breast, skin (melanoma), and gastrointestinal tract, with lung being the most common (4-6, 8). Although renal metastases from extrarenal malignancies usually present with bilateral involvement, unilateral solitary metastasis may also occur. Hematogenous renal metastases from lung, breast, gastrointestinal tract, and hematologic malignancies and malignant melanoma tend to give rise to bilateral, multiple renal masses, while lung cancer and melanoma may also metastasize via lymphangitic spread, which may result in unilateral perirenal and renal involvement (8, 9).

Despite being extremely rare, it should be noted that in a small percentage of oncologic patients with non-renal malignancy, kidneys may be the only site of metastasis (10). The detection of these patients with solitary metastases is extremely important as these patients may benefit from surgical intervention (11). These solitary metastases are generally clinically silent and discovered during follow-up studies; however, local symptoms like hematuria may also be detected in small percentage of patients (11). These metastatic deposits occur due to hematogenous spread and present as cortical nodules, which likely represent the entrapment of the metastatic cells in glomerular capillary tufts (12). As uroepithelium is not typically involved,

hematuria, even in patients with large masses, is rare (13). The mean duration between the diagnosis of a primary extrarenal tumor and renal metastasis is highly variable, but the mean interval time has been reported to be 2.2 years (8).

The data on the imaging findings of metastases to the kidneys is sparse. The distinction between primary kidney tumors and metastases to the kidneys is of crucial importance as the treatment approaches to these two different clinical entities may be almost completely different.

Although US has been reported as a useful tool for diagnosing renal metastases, it has several limitations (8, 14). Small lesions (1–2 cm) and lesions with similar echotexture to the background renal parenchyma may be hard to discern with US. When detected by US, they appear as homogenous hypoechoic masses without increased through transmission; however, heterogenous or echogenic metastases have also been reported (Fig. 1) (8, 14).

CT is generally the most commonly utilized imaging tool in the imaging follow-up of the abdomen in patients with known malignancy. CT, with its well-known clinical robustness, can also evaluate other sites in the abdomen in addition to the kidneys and may give a better picture of the full extent of tumor load in the abdomen. The CT appearances of renal metastases are mostly non-specific (15). On contrast-enhanced CT, most metastases have been reported to appear as endophytic, ill-defined, small, solid lesions with homogeneous enhancement (Fig. 2) (7). They are typically multifocal and do not distort the kidney contours. They typically enhance less than the background renal parenchyma and mostly appear as either isodense or slightly hypodense (10–40 Hounsfield units [HU]) on unenhanced CT studies (Fig. 3) (16). After contrast agent

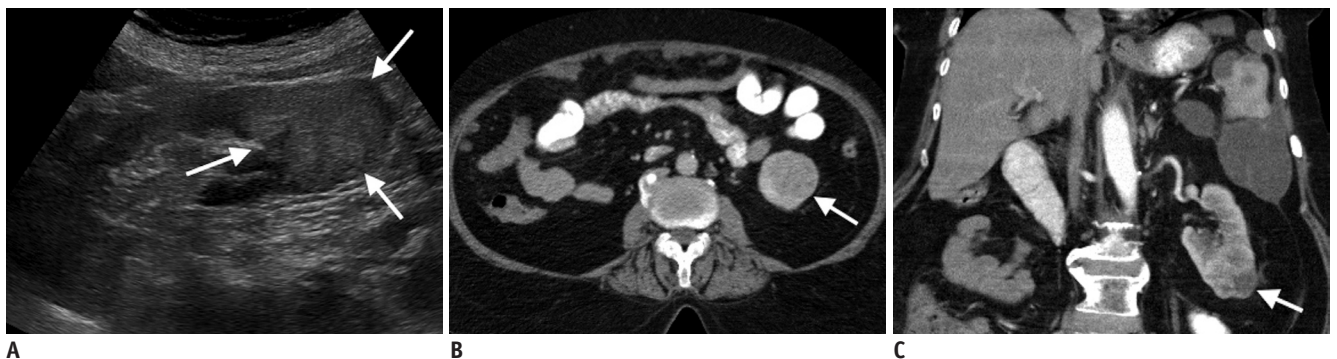


Fig. 1. 75-year-old female patient with known breast cancer with recently detected pulmonary and bone metastases was referred for restaging after chemotherapy.

A. Gray-scale US image demonstrates mildly hyperechoic mass (arrows) in lower pole of left kidney. Lesion is hardly discernible from background renal parenchyma on US image. **B, C.** Axial and coronal contrast-enhanced CT images reveal infiltrative-type hypodense solid mass (arrows) with relatively less enhancement as compared to background renal parenchyma. CT = computed tomography, US = ultrasonography



Fig. 2. 65-year-old female with known lung cancer and brain metastasis.

Post-contrast axial (A) and coronal (B) CT images show hypodense, endophytic solid lesion (arrows) in upper pole of right kidney. Biopsy confirmed metastatic nature of this mass.

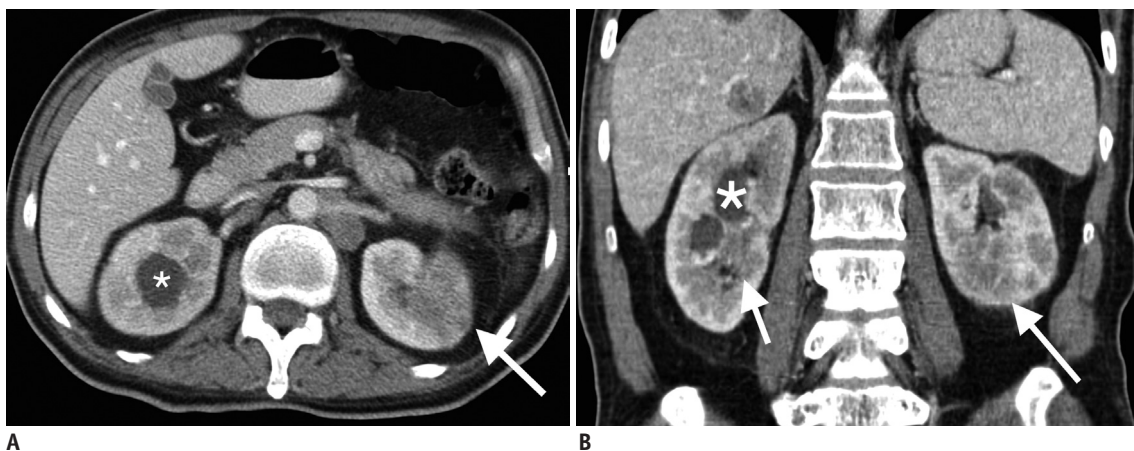


Fig. 3. 53-year-old male patient with known stage 4 lung cancer. Brain and liver metastases were previously detected.

Axial (A) and coronal (B) contrast-enhanced CT images demonstrate hydronephrosis (*) in right kidney due to centrally located hypovascular mass (short arrow). Also note diffusely infiltrative mass (long arrows) in lower pole of left kidney parenchyma. Biopsy confirmed metastatic nature of centrally located right kidney mass.

administration, they tend to mildly enhance (5–15 HU) compared to non-contrast images (15). Multifocality and bilaterality are other helpful clues for diagnosis (17). Metastatic deposits are mostly completely surrounded by renal parenchyma and rarely appear as an exophytic lesion (Fig. 4) (18). Calcification may also be detected within the renal metastases. The underlying reasons for calcification include either secretions from the tumor cells (mucoïd and papillary carcinomas) or cellular differentiation (osteosarcoma and chondrosarcomas) (19). Patel et al. (7) suggested that possibility of renal metastasis in the setting of a renal mass increases when the extrarenal malignancy has a higher stage. In their study, solid nature and endophytic location were significantly higher in renal metastases than primary renal tumors in patients with

extrarenal malignancy (7).

Not much has been published about the imaging findings of renal metastases on MRI. These lesions are generally hypointense compared to background renal parenchyma on T1-weighted images (T1WI) while heterogeneously hyperintense on T2-weighted images (T2WI). They mostly hypoenhance after contrast injection. Diffusion-weighted imaging (DWI) may help detection and characterization of kidney lesions (20). Renal metastases present with increased signal intensity on DWIs and decreased signal on apparent diffusion coefficient maps secondary to restricted diffusion of water molecules (Fig. 5) (21).

Renal cell cancer (RCC) is the main differential diagnosis, and differentiation may not be possible, especially in patients with solitary metastases. The most common

subtype of RCC is a clear cell variant that is characterized by its high vascularity, which is an uncommon feature in renal metastases. The relatively hypovascular variants of RCC, such as papillary type, are also well known, and differentiation from metastasis may be difficult or even

impossible in some patients. Hypointensity of papillary type RCC may be helpful for differential diagnosis as the metastatic renal masses are typically hyperintense on T2WIs (9). The infiltration of renal veins and inferior vena cava is also a probable indicator of RCC rather than a metastasis.

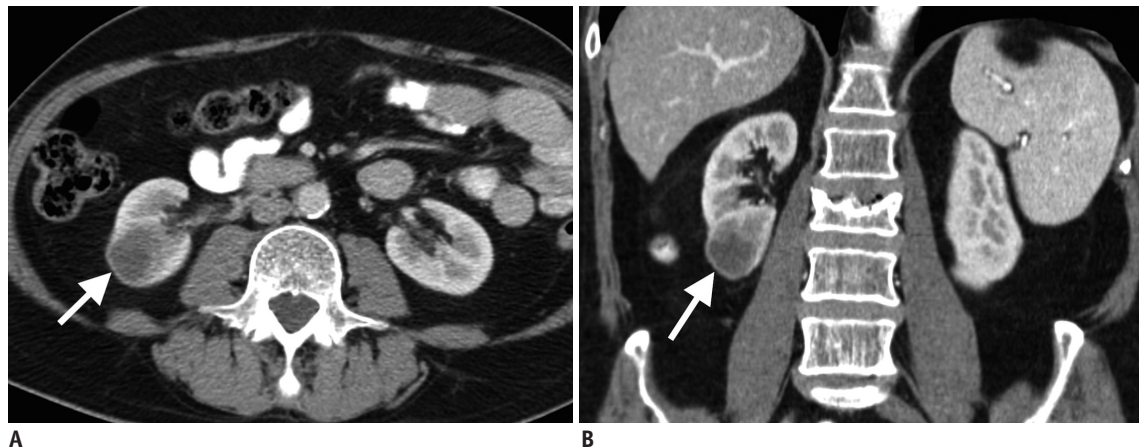


Fig. 4. 66-year-old male patient with known lung cancer and chest wall invasion. No distant metastasis was known at time of this CT scan. Axial (A) and coronal (B) contrast-enhanced CT images reveal low-attenuating, exophytic mass (arrows) that was histopathologically proven to be metastasis from lung carcinoma.

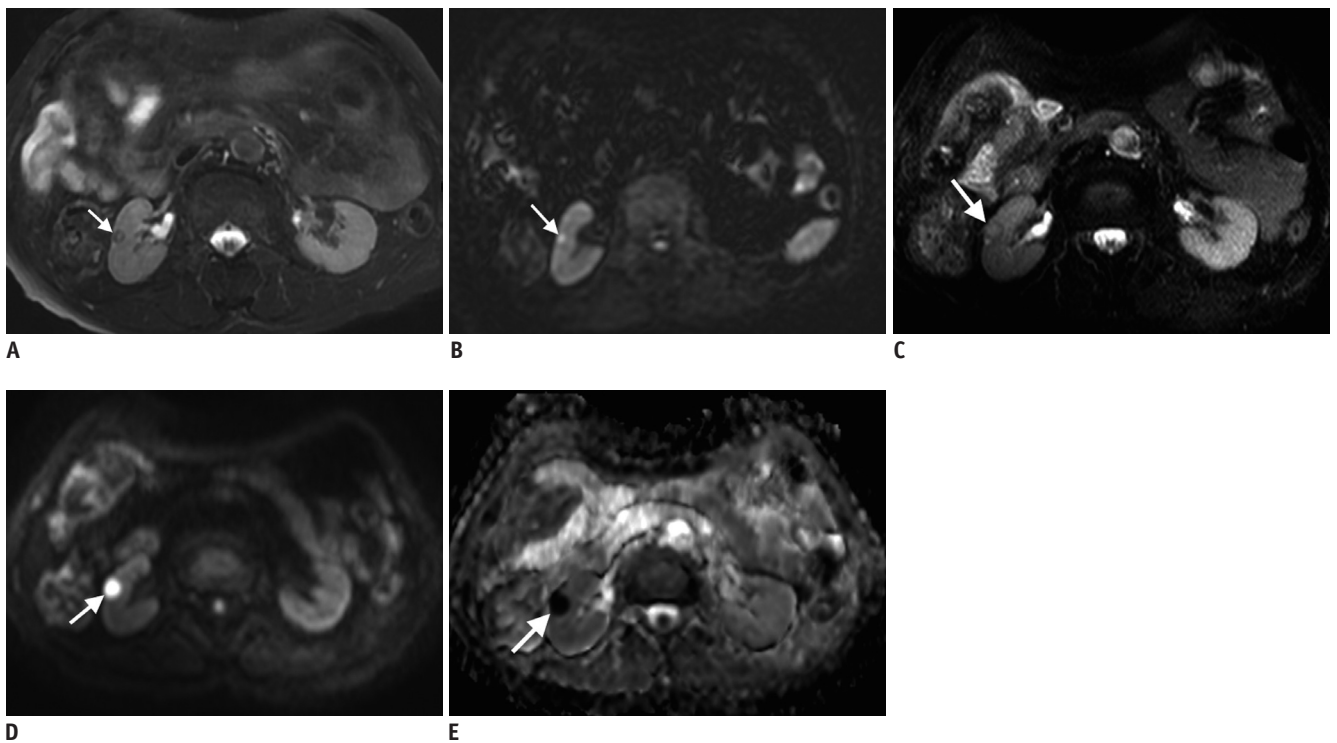


Fig. 5. 74-year-old female patient with known lung cancer and metastatic involvement of left iliac bone. Patient was in clinical remission for two years after last treatment. **A.** Axial fat-saturated T2WI reveals hypointense, focal parenchymal mass (arrow) in subcortical part of right kidney. **B.** Corresponding DWI sequence image shows intense diffuse restriction at location of mass (arrow). Patient refused percutaneous biopsy at that point, and she was placed on close imaging surveillance. **C.** Axial fat-saturated T2WI obtained 3 months after first scan revealed interval enlargement of lesion (arrow). **D.** Corresponding DWI clearly demonstrates focally increased signal suggestive of diffusion restriction (arrow). Percutaneous biopsy confirmed metastatic nature of this lesion. **E.** Apparent diffusion coefficient map confirms true diffusion restriction by demonstrating significant hypointensity at site of lesion (arrow). DWI = diffusion-weighted imaging, T2WI = T2-weighted image

An infiltrative pattern similar to renal metastasis can also be detected in sarcomatoid RCC variants, primary uroepithelial tumors, and primary renal lymphoproliferative disorders (19). A comparison of imaging features of RCC and renal metastases is presented in Table 1.

Metastases to the renal collecting system occur less frequently than renal parenchymal metastases. Imaging differentiation between uroepithelial metastases and primary urothelial tumors may be difficult, as both may appear as diffuse urothelial thickening or as a fungating exophytic mass (Fig. 6) (9).

Metastasis to Perirenal Space

The perirenal space is a well-defined and well-known anatomical compartment that is located in the retroperitoneum. Anatomically, it is limited mainly by anterior and posterior pararenal spaces. It is bounded

anteriorly by the anterior renal fascia (also called Gerota's fascia) and posteriorly by the posterior renal fascia (also called Zuckerkindl's fascia). These fasciae fuse laterally and form the lateroconal fascia. Within this anatomical compartment lie the kidneys, the proximal ureter, perirenal fat, the adrenal glands, bridging connective tissue, and several vessels (22). The left and right perirenal spaces communicate with each other at the midline and with the pelvic retroperitoneal spaces below the iliac fossa (23).

Lung cancer, malignant melanoma, breast carcinoma, and prostate cancer may metastasize to the perirenal space (24, 25). The main underlying reason for the peculiar tendency of lung cancer to metastasize to the perirenal space is the connections between the perirenal and mediastinal lymphatic vessels (25, 26). Infiltrative-type renal metastasis may also invade perirenal space (8).

On cross-sectional imaging, the lesions often appear as several solid lesions around the kidneys (Fig. 7) (24, 27).

Table 1. Imaging Features of Renal Cell Cancer and Metastasis in Kidney

Imaging Features	Renal Cell Cancer (Clear Cell Type)	Metastasis
Involvement	Unilateral	Bilateral
Localization	Cortex	Cortex, medulla or rarely renal pelvis
Size	Large	Small
Growth pattern	Ball-type	Ball- or bean-type
Infiltrative	5%	Common
Calcification	30%	Uncommon
Contour	Smooth or lobulated	Irregular
Multicentricity	Uncommon	Common
Vascularity	Hypervascular	Less vascular
Central necrosis	Common	Uncommon
Venous involvement	Common	Rare

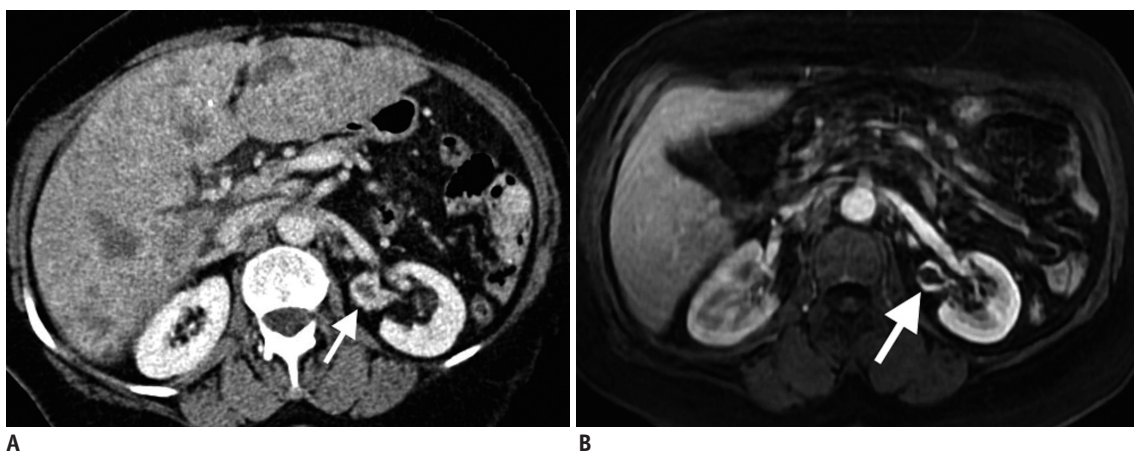


Fig. 6. 64-year-old female with known breast cancer and multiple metastases in liver.

A. Axial contrast-enhanced CT reveals nodular wall thickening in left renal pelvis (arrow) with intense contrast enhancement. Also note multiple metastases in liver. **B.** Axial post-contrast T1-weighted image also demonstrates abnormal irregular wall thickening (arrow) with associated brisk contrast enhancement. Urine cytology confirmed uroepithelial metastasis.

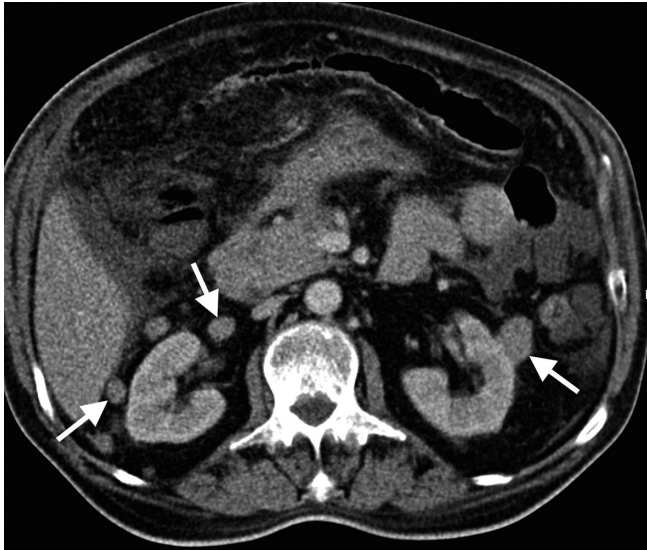


Fig. 7. 65-year-old male with known lung cancer with widespread solid organ and peritoneal involvement in abdomen. Axial contrast-enhanced CT shows bilateral numerous perirenal solid masses (arrows), more prominent on right, consistent with metastases.

The enhancement patterns of these metastatic deposits may differ based on the primary source. Lung and prostate cancers typically hypoenhance during arterial phase; melanoma and breast metastases show brisk arterial enhancement and portal venous phase wash-out (22). Breast cancer metastases may appear infiltrative, which makes them difficult to differentiate from lymphomas from a morphological standpoint. However, brisk enhancement of breast cancer metastases may allow differential diagnosis (22). Based on our experience, primary tumors involving the perirenal areas are rare, except for retroperitoneal mesenchymal tumors. Multifocality of the perirenal lesions may also suggest a secondary process rather than a primary one.

Ureteral Metastasis

Ureters are most commonly affected by tumor extension from adjacent organs, and these involvements should be differentiated from true hematogenous and lymphatic

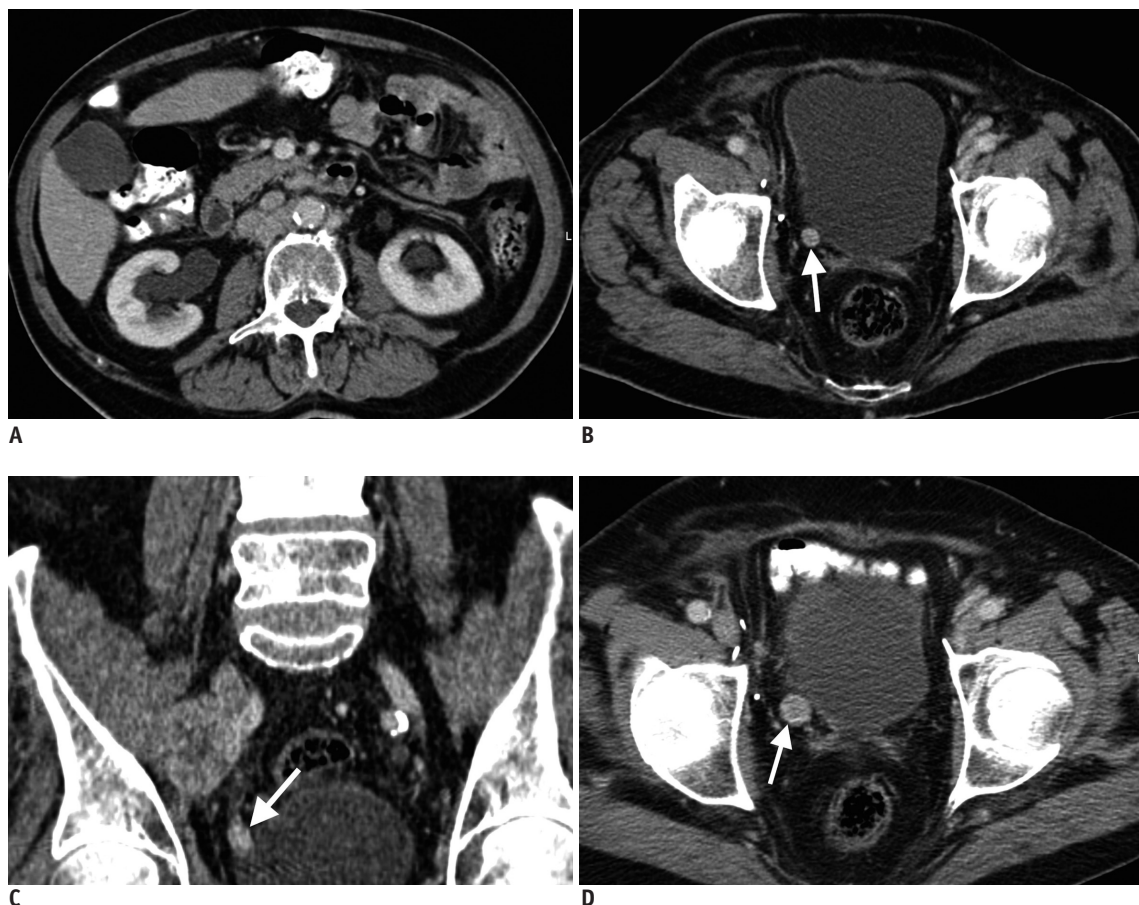


Fig. 8. 55-year-old female patient with known gastric cancer and vertebral metastases presenting with right flank pain. **A.** Axial contrast-enhanced CT demonstrates newly developed pelvicalyceal dilatation in right kidney. Axial (**B**) and coronally reformatted (**C**) CT images demonstrate nodular contrast enhancement in lower third of right ureter (arrows). **D.** Axial contrast-enhanced CT image demonstrated interval enlargement of same lesion (arrow) 4 weeks after index CT and endo-urological biopsy confirmed gastric cancer as primary source.

metastases. Transmural infiltration, or less commonly, diffuse infiltration of the local mucosa with or without muscular layer involvement, may be observed in cases of hematogenous and lymphatic metastases (Fig. 8) (28). This true metastatic involvement of the ureters is an uncommon clinical situation and a very rare cause of ureteral obstruction (29, 30). Since its first description in 1909, only around 400 cases have been reported (29, 31, 32). Autopsy studies have also revealed only rare occurrences of ureteral metastases, and in a series of 10233 consecutive autopsies, the incidence of ureteral metastasis was only 0.37% (33). As the ureters do not have a continuous longitudinal network of lymphatic and blood vessels, they are relatively resistant to metastasis by these two routes (34).

Despite the fact that most of the ureteric metastases are asymptomatic and incidentally diagnosed at autopsy, urinary obstruction may also occur (1, 35, 36). The breast and gastrointestinal systems comprise half of the cases, followed by prostate and uterine cancers comprising 30–40%, with gastric and lung cancers making up the remaining cases (1). Ureters may be involved in partial or full thickness (37, 38). As the periureteral adventitia is rich in blood vessels, this part of the ureter is generally the first layer involved (1).

From an imaging standpoint, the differentiation of ureteral metastasis from primary urothelial tumors might be difficult or even impossible. In our clinical practice, primary uroepithelial tumors of the ureter typically involve a long segment and demonstrate multifocality, whereas secondary tumors usually affect a relatively short segment. Clinical history may also help differential diagnosis as some tumors are more prone to uroepithelial metastasis than others. The

detection of asymmetric wall enhancement, wall thickening, and urinary obstruction are the expected imaging findings. Strictures after stone passage, distal ureteral stenosis due to tuberculosis, amyloidosis, and endometriosis should be considered in the differential diagnosis (Fig. 9). Endoscopic evaluation of the ureters with histopathologic evaluation may be required in most of the cases.

Metastasis to Urinary Bladder

Secondary tumors of the urinary bladder are rare and comprise less than 2% of all bladder cancers (2, 39). The most common primary sources are stomach, breast, and colon cancer and melanoma. Urinary bladder metastases from a primary RCC are rare, with fewer than 40 reported cases in the medical literature, with neck and trigone the most commonly involved sites (2, 40). The metastases may be clinically silent or may present with hematuria. The patients diagnosed with bladder metastasis are generally at an advanced stage, and the prognosis is usually dismal; however, in very rare instances, the bladder may be the only metastatic site (41).

Imaging mostly displays polypoid or non-polypoid diffuse asymmetric wall thickening (Figs. 10, 11). Proper imaging technique is important for both the diagnosis and adequate staging. Differentiation of bladder metastases from primary bladder tumors may be difficult from an imaging standpoint, and pathological diagnosis is almost always indicated.

Urethral Metastasis

Urethral metastases are extremely rare, but occur more

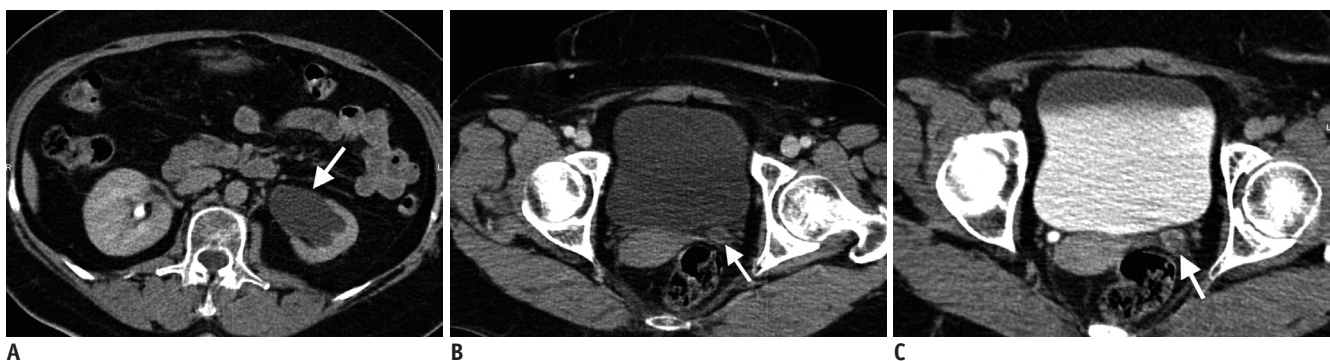


Fig. 9. 64-year-old female with known breast cancer who was in clinical remission for last 5 years. She was referred for annual follow-up CT and was asymptomatic at time of scan.

A. Axial venous phase scan demonstrates moderate-severe hydroureteronephrosis (arrow), with significant loss of renal parenchyma, on left kidney. **B.** Axial venous phase scan demonstrates faint enhancement of lower left ureter (arrow). This was transition point of left dilated ureter. **C.** Enhancement becomes more pronounced on urographic phase image (arrow). Endo-urologic biopsy confirmed non-neoplastic cells but amyloid deposit.

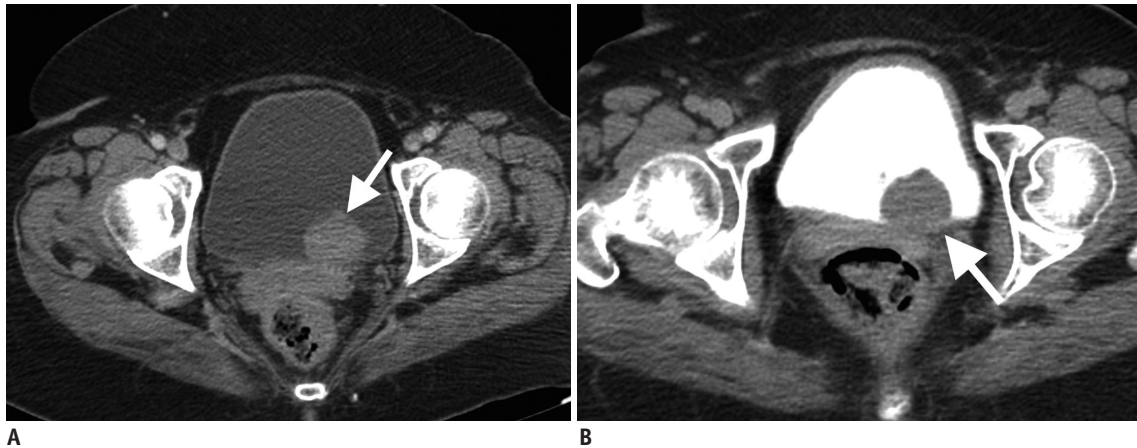


Fig. 10. 61-year-old female with known RCC and retroperitoneal lymph node metastases presenting with hematuria.
A. Axial contrast-enhanced CT image demonstrates polypoid lesion located close to left ureteral orifice (arrow). There was no evidence of hydronephrosis in left kidney on upper level images (not shown). **B.** Axial urographic phase image clearly shows filling defect (arrow) created by same polypoid lesion. Cystoscopic biopsy confirmed metastatic RCC. RCC = renal cell cancer

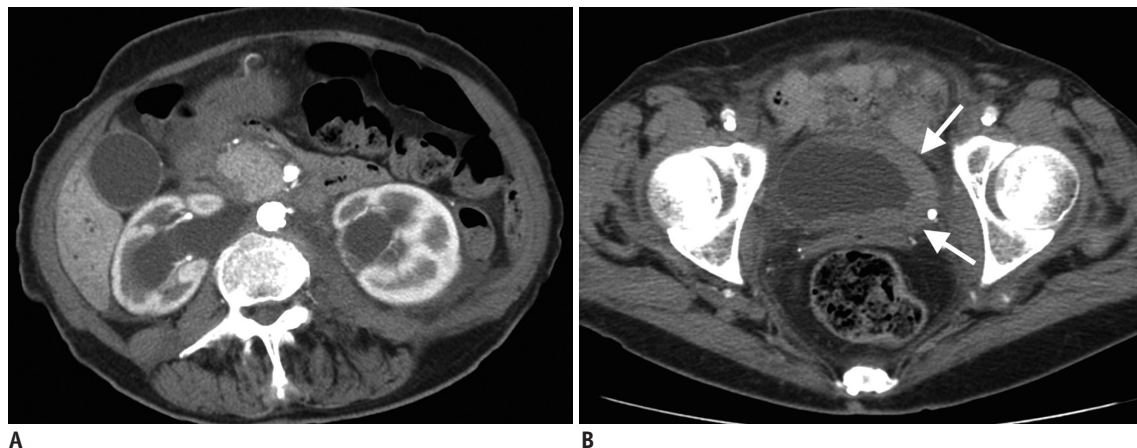


Fig. 11. Bladder metastasis in 74-year-old female with known breast cancer, which was last treated 10 years ago; she was in clinical and imaging remission since then. She recently presented with polyuria and gross hematuria.
A. Bilateral dilatation of renal collecting system is seen on axial contrast-enhanced CT image. **B.** Axial contrast-enhanced CT image demonstrates asymmetric thickening (arrows) in left lateral wall of bladder. Chest CT was also negative. Cystoscopic biopsy confirmed metastatic breast cancer.

frequently than primary tumors of the urethra. Metastasis to the urethra most commonly results from prostate, bladder, lung, and colorectal cancers (42, 43). Urethral and penile metastases may result from hematogenous involvement, instrumental spread, retrograde lymphatic spread, and direct extension. Retrograde lymphatic spread was reported to be responsible especially for metastasis from colon cancers (42). Superficial US performed with a linear probe can detect metastasis in the urethra. Abundant secondary tumoral involvement of urethra presents as solid nodular or cylindrical mass with heterogeneous contrast-enhancement (Fig. 12). Superior soft-tissue resolution makes MRI a preferred imaging modality in assessment of secondary tumors of the urethra in terms of location, size, and local

extension. Differentiation between primary urethral cancers and secondary urethral extension of adjacent malignancies such as rectal, vaginal, and cervical tumors can be accomplished with MRI.

The Role of Percutaneous Biopsy in Diagnosis

The urinary system is frequently the site of percutaneous biopsies, and the kidneys are the most frequently biopsied organs. Adequate pre-procedural imaging and patient work-up is of utmost importance (44). The probability of a renal mass being a metastasis in patients with extrarenal malignancy is almost equal to the likelihood of its being a primary renal tumor (7). Since imaging features of

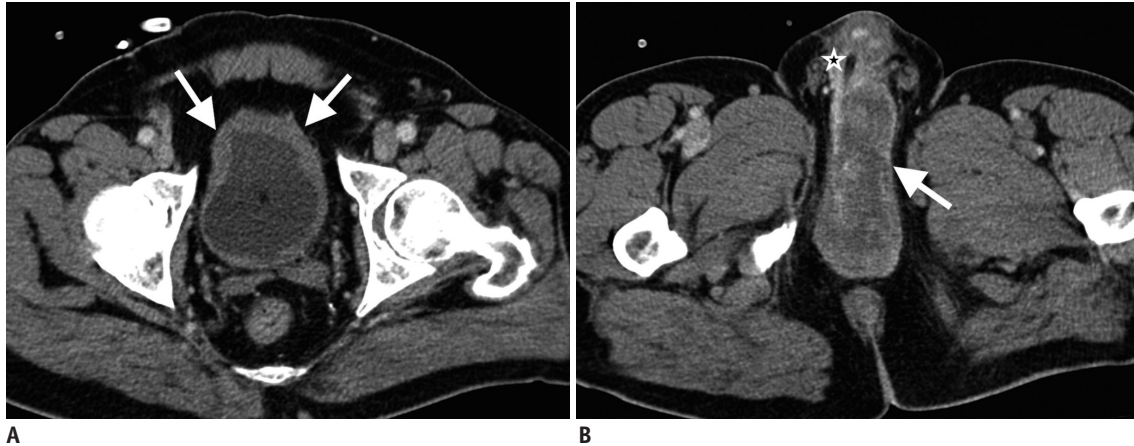


Fig. 12. Urethral metastasis in 57-year-old male with known neuroendocrine tumor of bladder and no known metastasis elsewhere.
A. Axial urographic phase CT image shows asymmetric wall thickening (arrows) in anterior bladder wall. Cystoscopic biopsy revealed neuroendocrine tumor of bladder. **B.** Axial post-contrast CT image of same patient, who presented with difficult urination. CT image demonstrates extensive tumor infiltration (arrow) in penile shaft and ureter (also note urinary drainage catheter-*). Endo-urologic biopsy confirmed metastatic neuroendocrine tumor.

urinary system metastases cannot exclude the possibility of a primary tumor of the urinary system, histopathologic examination of renal masses in patients with an extra-urinary malignancy is necessary in the management of and the decisions regarding the treatment options of these patients (3, 7, 10, 40). The percutaneous biopsy of solid renal and perirenal lesions are generally straightforward, but cystic lesions may deserve further attention, as the biopsy yields may be lower in these lesions (45). Targeting the solid parts of patients' cystic lesions may be more helpful in the diagnosis of semisolid renal and perirenal lesions (44).

Bladder lesions may also be diagnosed with percutaneous biopsy. This approach may be even more important in patients who have difficulties with retrograde endourological procedures due to urethral stenosis (46).

CONCLUSION

Metastasis to the urinary system in patients with non-urinary system primary tumors is a relatively rare clinical phenomenon. Early diagnosis and evaluation of these subjects is important to obtain a satisfactory patient outcome. Given the ever-increasing role of cross-sectional imaging in the oncologic patient population, it would not be irrational to predict that this diagnosis will be more commonly made in the near future.

Ethical Approval

All procedures performed in studies involving human participants were in accordance with the ethical standards

of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent was obtained from all individual participants included in the study.

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