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CASE REPORT

MDCT imaging following nephrectomy for renal cell carcinoma: Protocol optimization and patterns of tumor recurrence

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Abstract

The purpose of this pictorial essay is to review the common and uncommon sites of renal cell carcinoma recurrence throughout the body by examining their appearances on computerized tomography (CT). CT imaging protocols will be discussed. The sites of recurrence have been categorized into 4 groups: chest and mediastinum, abdomen and pelvis, musculoskeletal, and neurological. For each site of recurrence, a representative CT image correlate with discussion is provided. The unique CT appearance of renal cell carcinoma recurrence and how it can be used in lesion detection will be discussed. Renal cell carcinoma recurrences are hypervascular like the primary tumor, which can aid in not only lesion detection but also in some cases, differentiation from other primary tumors. Through CT case review of various sites of recurrence, lesions are shown to be easily seen on arterial phase while sometimes being nearly inconspicuous on venous or delayed phases. Coronal and sagittal reconstructions can also improve diagnostic sensitivity. CT is the most commonly used imaging tool for surveillance of renal cell carcinoma recurrence after nephrectomy. Knowledge of sites of recurrence as well as the utility of arterial phase imaging and multiplanar reconstructions will aid in optimizing detection of disease recurrence.

Key words: Renal cell carcinoma; Recurrence; Computerized tomography; Metastasis; Diagnosis

Core tip: The computerized tomography (CT) imaging appearance of renal cell carcinoma recurrence mimics the appearance of the primary tumor. Just as a majority of renal cell carcinomas are hypervascular, recurrences tend to be hypervascular and are best seen on arterial phase. This paper demonstrates this tendency by giving case examples which review both common and uncommon sites of recurrence. Knowledge of their appearances on CT will help the radiologist in lesion detection and diagnosis, limiting delays in treatment and avoiding unnecessary biopsies.

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INTRODUCTION

According to the National Cancer Institute, over 60000 new cases of kidney cancer are diagnosed annually[1]. Management of such cases will depend on the tumor stage as well as the patient's functional status. Treatment options available include nephrectomy, partial nephrectomy, cryo-

Table 1 Categorization of Disease Recurrence

Anatomic Category	Location
Chest and Mediastinum	Lung
	Lymph Nodes
	Thyroid
Abdomen and Pelvis	Liver
	Nephrectomy Site
	Contralateral Kidney
	Adrenal Gland
	Pancreas
	Spleen
	Stomach
	Intestine
	Ovary
Musculoskeletal	Bone
	Muscle
	Breast
Neurological	Brain
	Spine

Table 2 Most common locations of recurrence and their incidence after nephrectomy

Location	Incidence of Recurrence after Nephrectomy
Lung	38%-71%[3]
Lymph nodes	12%-63% (total within chest, abdomen, and pelvis)[3]
Liver	7%-23%[2]
Nephrectomy site	10%[2,8]
Contralateral kidney	1.2%-10%[3,9]
Adrenal gland	7%-10%[3]
Bone	18%-37%[3]
Brain	2%-15%[3,4]

ablation or radiofrequency ablation, or active surveillance. While nephrectomy has been the traditional management of renal cell carcinomas, nephron sparing procedures are increasingly becoming more common.

After initial treatment, patients will continue to be monitored with imaging in order to detect recurrent or metastatic disease. Following nephrectomy, approximately 20%-40% of patients will develop recurrence. Most will develop recurrence within 2-4 years of nephrectomy[1-3]. One characteristic of renal cell carcinoma is the development of metastases many years after surgical treatment. According to one recent study, 6.4% of patients developed metastases 10 years after their initial surgery[1]. The rate of recurrence and the time to recurrence after nephrectomy is dependent on the stage of the tumor. The lower the stage of the tumor, the lower the rate of recurrence and the longer the time between initial treatment and recurrence[1,4].

The timing of the follow-up as well as the imaging included in the follow-up can vary by institution and specialty organization recommendations. In addition, the computerized tomography (CT) protocols used for surveillance imaging can vary across institutions. As renal cell carcinoma metastases typically follow the vascularity of the primary tumor and most renal cell carcinomas are hypervascular, arterial phase imaging is critical in lesion detection. One recent study reviewed the utility of the dual phase abdominal CT in the detection of renal cell carcinoma metastases. About 75% of the lesions were visualized in the arterial phase and in 9% of patients lesions were only visible in the arterial phase. These lesions were located in the liver, pancreas, and kidney[5]. In this paper, we will demonstrate the increased conspicuity of recurrent and metastatic lesions on arterial phase as compared to venous and delayed phases. We will also show how post processing techniques such as coronal and sagittal multiplanar reconstructions and 3D rendering can also aid in lesion detection. The importance of arterial phase imaging and the post processing techniques will be demonstrated through review of common and uncommon locations of recurrence. All of the images used in this paper were obtained from our institution.

CASE REPORT

At our institution, our CT surveillance protocols for patients with one remaining kidney are similar to the protocols used for the detection, characterization, and staging of renal masses, which was published previously by Sheth *et al*[6]. The protocol includes a multiphase scan after the injection of iodinated contrast (320 mg/mL iso-osmolar contrast with volume according to patient's renal function, between 70-120 cc). With increasing contrast injection rates (now 5 cc/s) and faster scanners, the time delay between onset of contrast administration and imaging of arterial and venous phase has decreased. Arterial (corticomedullary) phase imaging of the abdomen and pelvis is obtained at 25-30 s, previously published at 30-40 s[6]. Venous (nephrographic) phase imaging is obtained of the kidney at 60 s, previously published at 80 s[6]. Delayed phase imaging of the abdomen and pelvis is obtained at approximately 5 min. Axial images are reconstructed in 3 mm thick slices every 3 mm. Sagittal and coronal multiplanar reconstructions are generated at the scanner. Interactive 2D and 3D rendering with volume rendering and maximum intensity projection (MIP) techniques is performed at a separate workstation by an experienced radiologist.

DISCUSSION

In this pictorial essay, we will demonstrate numerous sites of recurrent and metastatic disease. The sites of disease will be organized into the following anatomic categories: chest and mediastinum, abdomen and pelvis, musculoskeletal, and neurological (Table 1). Table 2 lists the incidence of recurrence after nephrectomy for the most common locations of recurrence.

Chest and mediastinum

Lung: The lung is the most common site of recurrence and often the earliest site of recurrence. Chae *et al*[2] reported in their study of post-operative recurrence after

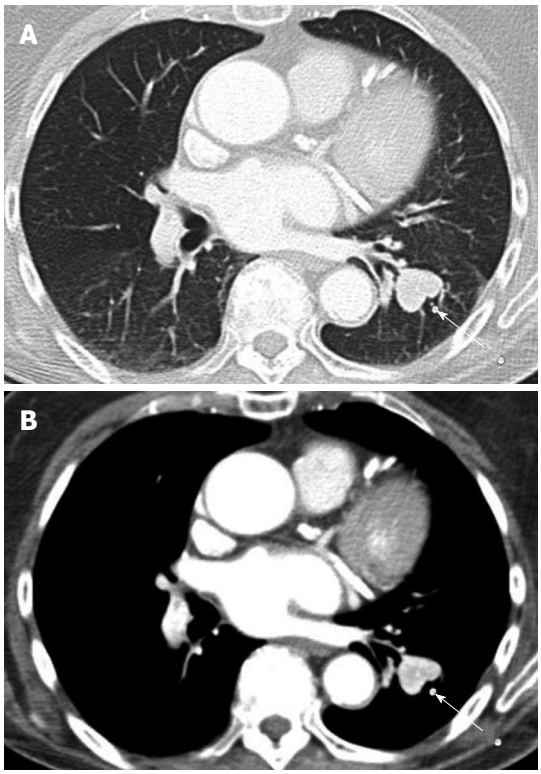

Figure 1 Axial computerized tomography images of the chest in lung and soft tissue windows in an 86-year-old female patient status post nephrectomy who developed pulmonary metastases 10 years later. Note the bright enhancement of the lesion (arrow) on soft tissue windows.

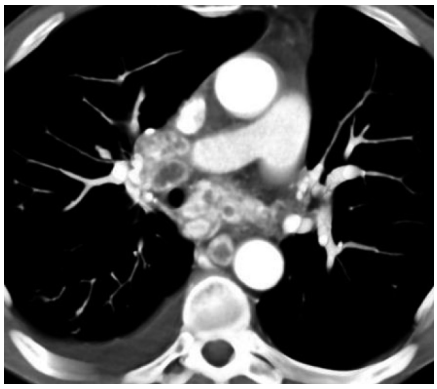

Figure 2 Numerous mediastinal nodes in a 65-year-old male patient status post nephrectomy 6 years earlier. Note the peripheral enhancement and central necrosis.

nephrectomy that the lung was the first site of recurrence in 56% of patients. The appearance of the metastases may be well defined, rounded nodules of varying size or be irregular in shape. They may be singular or multiple. On soft tissue windows, these metastases may enhance as brightly as the pulmonary vasculature (Figure 1). If they are large enough, they may show central necrosis.

Lymph nodes: Lymph node recurrence rates have been reported in up to 63% of cases[2], and can be found in both the chest and abdomen/pelvis. The nodes are usually enlarged, enhance greater than expected for reactive

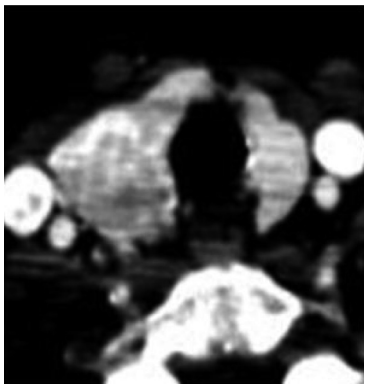

Figure 3 A 67-year-old female status post left partial nephrectomy 2 years prior to this exam. Asymmetric enlargement of the right thyroid gland secondary to a thyroid nodule which was subsequently biopsied as metastatic renal cell carcinoma; Note the nodule enhances as brightly as the remainder of the thyroid.

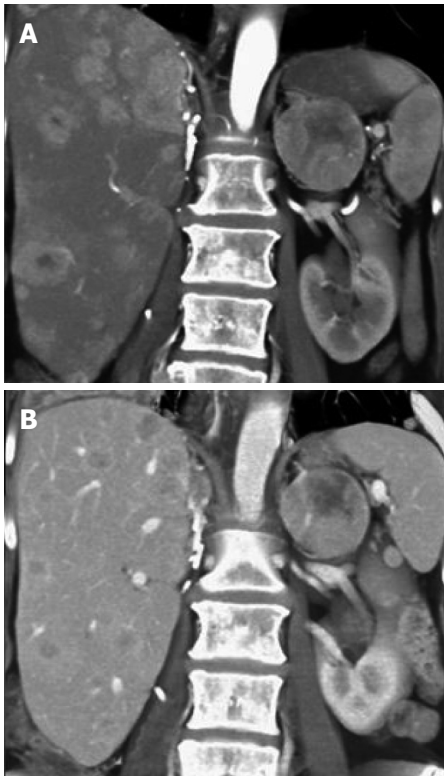

Figure 4 A 67-year-old female with widespread liver metastases after right nephrectomy. Note the increased conspicuity of the liver lesions on arterial phase (A) compared to venous phase (B) coronal volume renderings. A left adrenal metastasis is also seen.

lymph nodes, and often show central necrosis (Figure 2). Thoracic lymph node involvement can include the hilar lymph nodes, subcarinal lymph nodes, and paratracheal lymph nodes. If extensive, the mass effect from the lymph nodes can cause compromise of both the airways and the pulmonary vasculature such that it can be life threatening. Supraclavicular lymph node involvement can also be seen.

Thyroid: More than 150 cases of metastatic renal cell carcinoma to the thyroid (Figure 3) have been reported

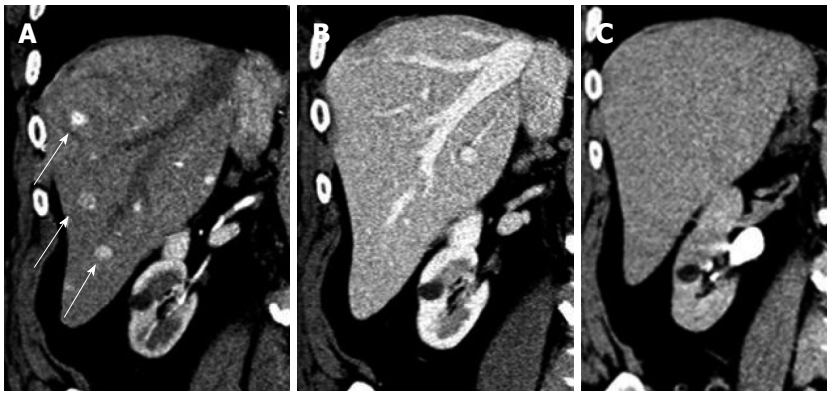

Figure 5 Multiphase exams in another 73-year-old male patient with liver metastases. The liver metastases (arrows) are most obvious on the coronal arterial phase (A), but are subtle or isoattenuating on venous and delayed phases (B, C).

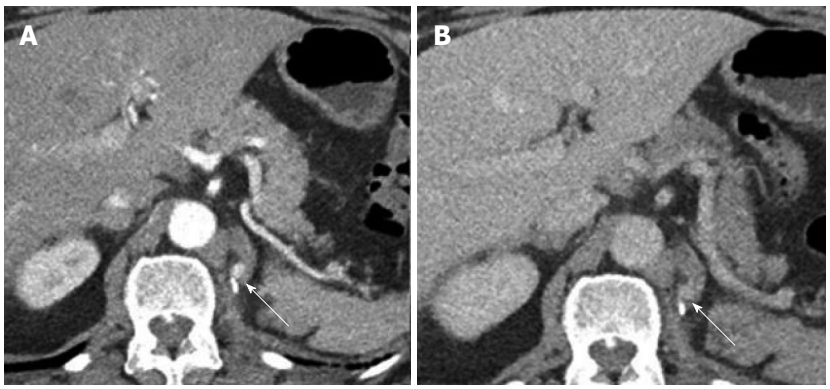

Figure 6 A 65-year-old female patient who underwent nephrectomy more than 10 years prior. Axial VI contrast enhanced computerized tomography (CT) shows 7 mm recurrence in the surgical bed (arrow). The lesion is easily seen on arterial phase (A) and but becomes indistinguishable on the venous phase (B).

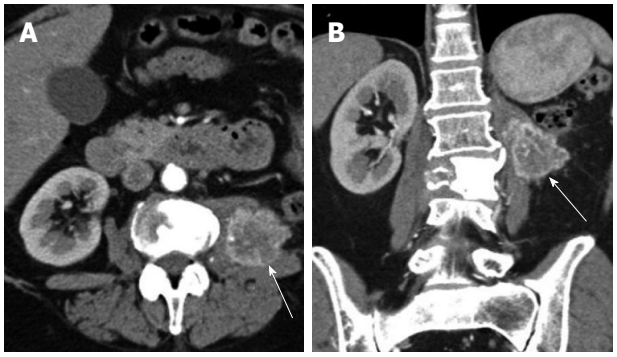

Figure 7 A 60-year-old female status post left nephrectomy with hypervascular recurrence (arrow) on the side of resection, involving the left psoas muscle, seen on axial (A) and coronal images (B).

in the literature[7]. Like other sites of metastases, lesions can occur more than 20 years after nephrectomy. The thyroid's rich blood supply may predispose it to metastatic lesions[7]. Patients may present with cough, as well as breathing and swallowing difficulties due to mass effect from the lesion. It is important to distinguish metastatic lesions from primary thyroid malignancies as they are treated differently. Fine needle aspiration of the nodule can be performed.

Abdomen and pelvis

Liver: The incidence of liver metastasis after nephrectomy has been reported between 7%-23%[3]. Due to their predominately hypervascular nature, the lesions are best seen on arterial phase (Figures 4 and 5), washing out on venous and delayed acquisitions. The lesions may be inconspicuous on non-contrast, venous, or delayed phase images.

Nephrectomy site: The incidence of local recurrence (Figures 6 and 7) has been reported between 9%-10%[2,8]. The recurrence may also invade the IVC or the adjacent psoas (Figure 7) musculature. Scrutinization of the surgical bed and renal fossa is important in the detection of early recurrence. This may be challenging due to the presence of small bowel or pancreatic tail occupying the surgical bed. Evaluation for hypervascular lesions on arterial phase may help to distinguish tumor from post-surgical changes. Even subcentimeter hypervascular lesions (Figure 6) may be seen on arterial phase.

Contralateral kidney: In a study by Bani-Hani AH *et al*[9] contralateral recurrence (Figure 8) occurred in 1.2% of 2352 patients undergoing surveillance after nephrectomy. The mean time to recurrence was 5.2 years. Positive surgical margins and multifocality of the tumor within the kidney were risk factors for developing contralateral recurrence. Coronal reconstructions may be helpful in lesion detection, especially for those recurrences in the upper and lower poles that may be not as obvious on axial imaging.

Adrenal gland: After nephrectomy, the incidence of adrenal metastasis (Figure 9) has been reported as high as 10%[3]. A study by Weight *et al*[10] regarding the utility of ipsilateral adrenalectomy at the time of nephrectomy

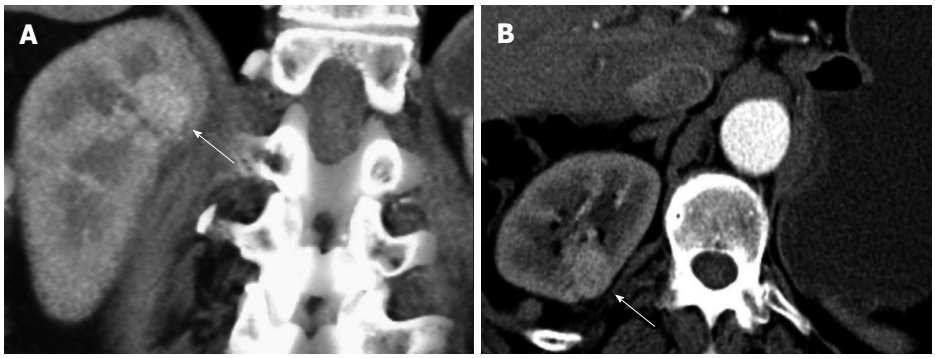

Figure 8 A 72-year-old female status post left nephrectomy who developed a new mass in the contralateral kidney. Note the subtle lesion in the upper pole (arrow), on coronal volume rendering (A) and axial arterial phase CT (B). CT: Computerized tomography.

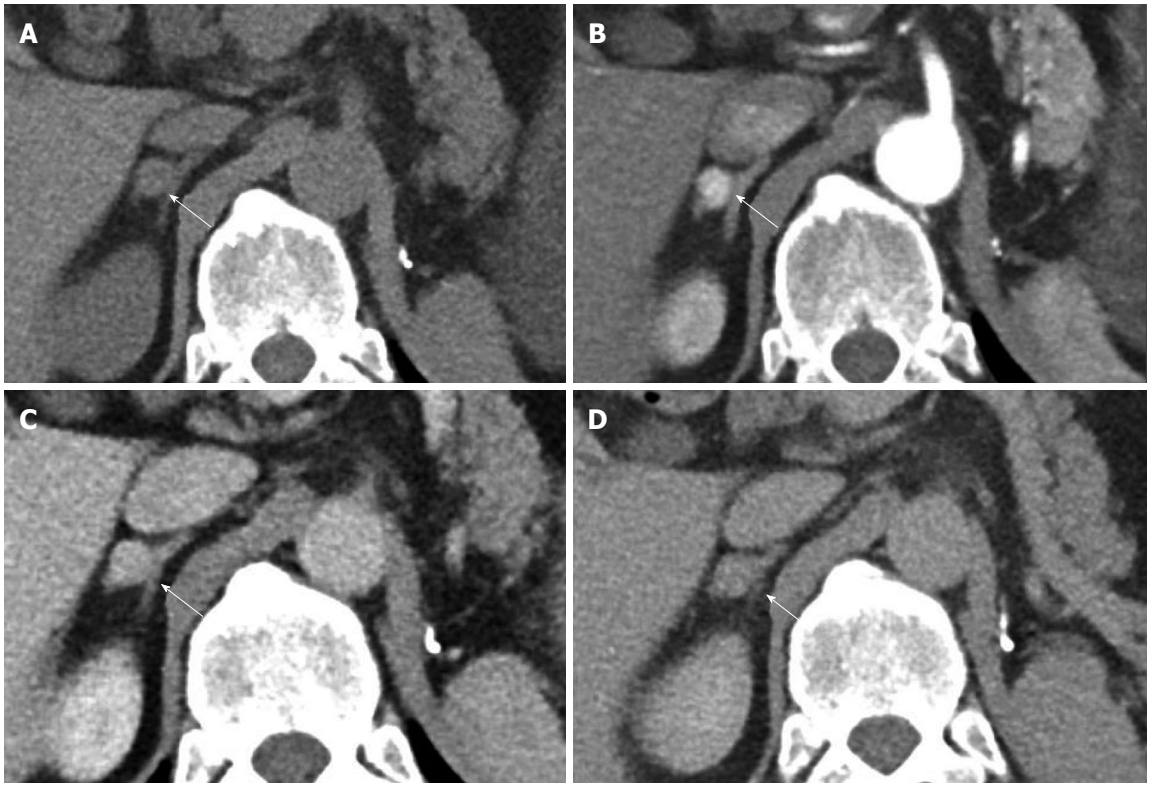

Figure 9 Right adrenal mass in a 54-year-old male patient status post left nephrectomy four years prior to the exam. A: Non-contrast; B: Arterial; C: Venous phase; D: Delayed phase. On non-contrast the lesion measures 33 HU; on arterial phase the lesion measures 180 HU; on venous phase the lesion measures 101 HU; on delayed phase the lesion measures 57 HU (arrow, right adrenal mass). Absolute washout is 65% and the relative washout is 44%. By washout, this lesion is compatible with adenoma. However, the hypervascularity of the lesion (>100 HU) is atypical for adenoma, suggesting metastasis.

reported an incidence of 3.7% for asynchronous adrenal metastasis after surgery. A normal adrenal gland on CT has a 100% negative predictive value for tumor involvement[3]. As with local recurrence, adrenal metastases can be quite small and may only be seen on arterial phase (Figure 10). Owing to their vascularity, they can mimic adrenal adenomas in showing washout. A recent article by Choi evaluated absolute percentage washout (APW) and relative percentage washout (RPW) of known adrenal lesions in patients with RCC and found them to be similar to lipid poor adenomas. Using an APW threshold of 60% and an RPW threshold of 40%, 89% and 95% of known metastases were classified as adenomas[11]. However, the hypervascular nature of the lesion (arterial phase enhancement > 100 HU) is not characteristic of an adenoma. In an investigation comparing the dual phase CT enhancement patterns of adrenal adenoma and pheochromocytoma, arterial phase enhancement > 100 HU was only identified with pheochromocytoma[12], which enhances similar to metastatic hypervascular renal cell carcinoma. As an arterial phase acquisition is a routine part of the renal cell carcinoma CT protocol, review of the arterial phase attenuation should prove sufficient to distinguish a hypervascular renal cell metastasis from

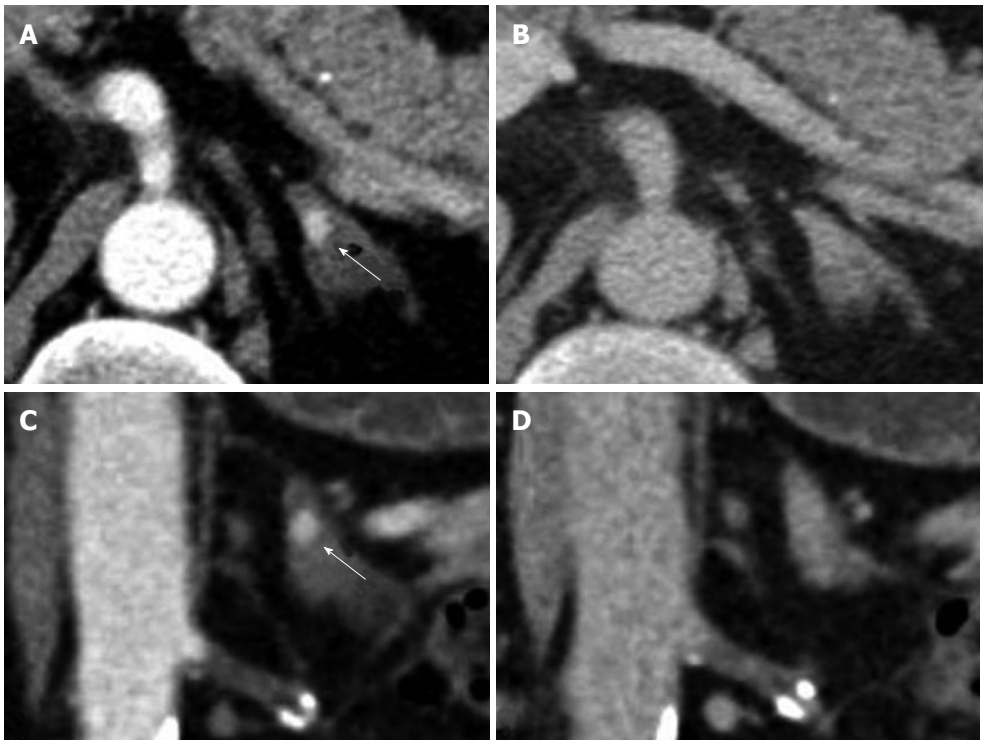

Figure 10 Subcentimeter hypervascular lesion in the left adrenal gland of a 65-year-old male patient who underwent a left nephrectomy 3 years prior. Note despite the small size it is easily seen on axial and coronal arterial phase (A, C) and is virtually undetectable on venous phase (B, D).

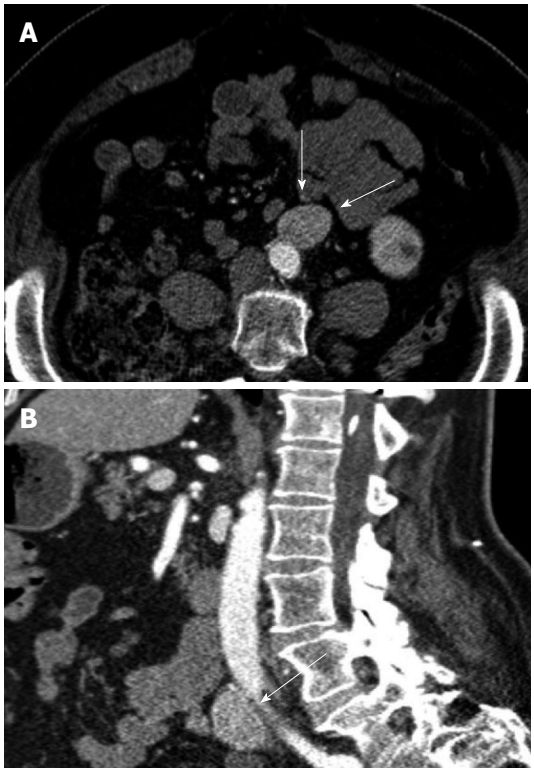

Figure 11 A 55-year-old female status post right nephrectomy. Axial (A) and sagittal (B) images of left para-aortic lymphadenopathy in patient who underwent right nephrectomy six years earlier. The patient also had left supraclavicular lymphadenopathy (not shown).

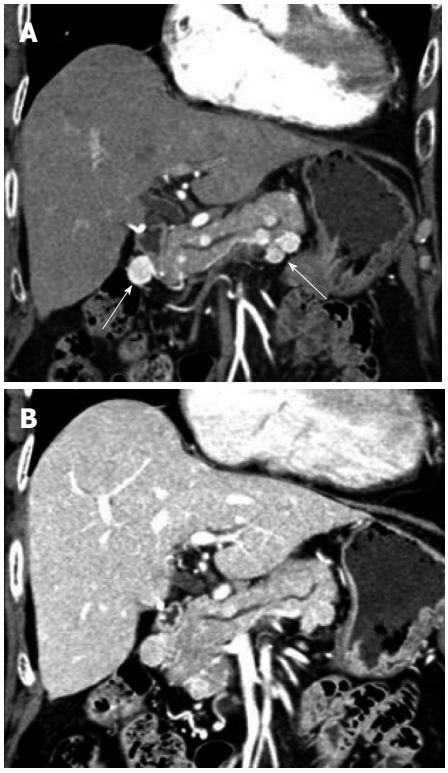

Figure 12 A 66-year-old female status post left radical nephrectomy 12 years earlier. Multiple rounded hypervascular masses within the pancreas on arterial phase (A) which are nearly isodense to the pancreas on venous phase (B), coronal volume renderings.

an adrenal adenoma.

Lymph nodes: In the abdomen and pelvis, lymph node

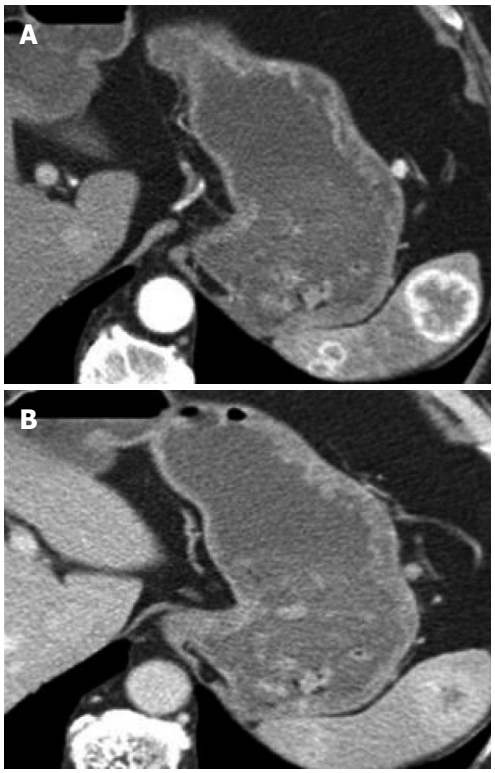

Figure 13 A 64-year-old male status post right nephrectomy that developed splenic metastases 7 years later. Note the increased conspicuity of the lesions on arterial phase (A). On venous phase, the lesions are nearly isodense to the spleen (B).

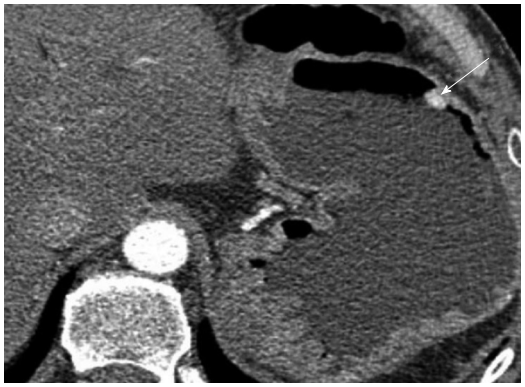

Figure 14 A 65-year-old male status post left radical nephrectomy in who developed a gastric metastasis (arrow) 5 years later. The patient subsequently underwent partial gastrectomy.

recurrence is most often in the retroperitoneum (Figure 11), up to 33% of recurrences[3]. Many will be enlarged and show conspicuous enhancement. It is difficult by CT to determine metastatic involvement to normal sized nodes; however, the incidence of microscopic lymph node invasion has been reported as low as 5%[3]. Mesenteric lymph nodes can also be involved.

Pancreas: Metastatic lesions to the pancreas (Figure 12) are rare, but renal cell carcinoma's predisposition for unusual sites of metastases also includes the pancreas. In

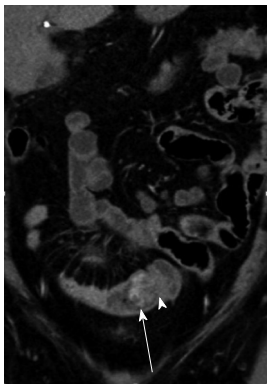

Figure 15 A 60-year-old female status post left nephrectomy presenting with a small bowel metastasis. Note a subtle intraluminal enhancing mass (arrow) serving as lead point for short segment intussusception (arrowhead). The lesion is best appreciated on coronal MPR images in arterial phase.

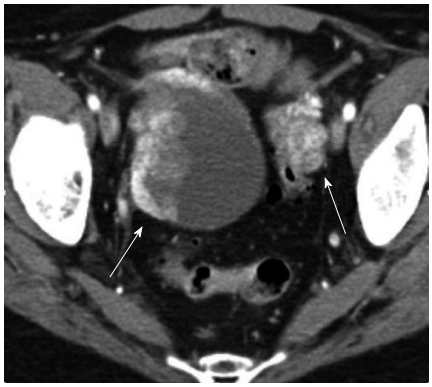

Figure 16 A 60-year-old female status post left radical nephrectomy with liver and bony metastases and with bilateral ovarian metastases. Axial computerized tomography (CT) image in arterial phase shows a large cystic and solid mass seen in right ovary and solid hypervascular mass in left ovary. The solid components of the cystic mass are hypervascular on arterial phase.

an autopsy study of patients with renal cell carcinoma, less than 2% had metastasis to the pancreas. Nonetheless, renal cell carcinoma is the most common tumor to metastasize to pancreas[13]. Late recurrences more than 10 years after initial surgery have been reported[14]. Due to the hypervascular nature of the metastases, these lesions could be confused with pancreatic neuroendocrine tumors which are also typically vascular. Multiplicity of the pancreatic lesions, evidence of additional sites of recurrent or metastatic disease elsewhere in the body, and even biopsy may be useful in distinguishing the two entities. If there is limited involvement within the pancreas, patients may go on to surgical resection, such as undergoing a Whipple procedure for lesions in the pancreatic head.

Spleen: While other cancers are more commonly known to metastasize to the spleen such as lung, melanoma, and breast cancer, renal cell carcinoma rarely spreads to the spleen (Figure 13). A review of the literature of splenic metastases from renal cell carcinoma by Moir *et al*[15] produced 8 such cases. Despite this low number, autopsy

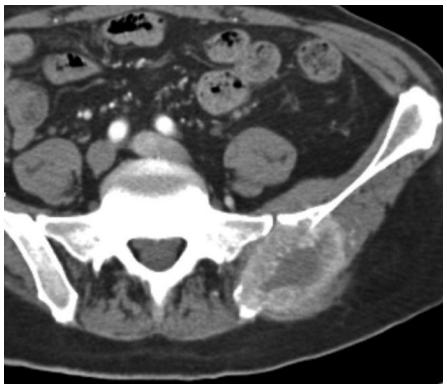

Figure 17 A 63-year-old male status post right nephrectomy subsequently developed bone metastasis in the left iliac wing. Axial arterial phase image shows a lytic lesion with a soft tissue component that shows prominent enhancement peripherally with central necrosis.

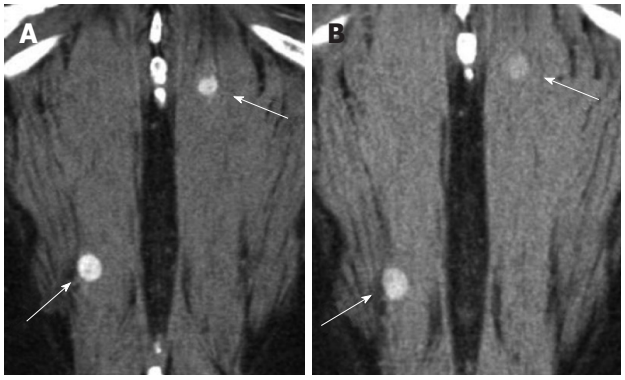

Figure 18 A 66-year-old male status post left nephrectomy, developed metastases within the paraspinal muscles 3 years later. These small lesions (arrows) are often best visualized on the coronal arterial acquisition (A) and inconspicuous on venous (B) and delayed phase.

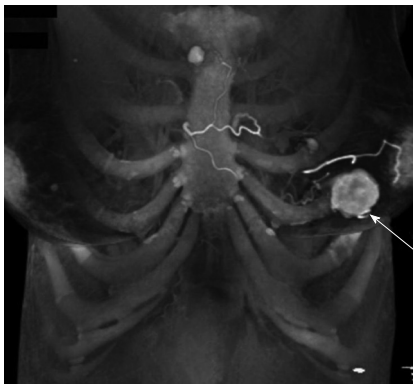

Figure 19 A 67-year-old female with widespread metastatic renal cell carcinoma. A hypervascular metastasis (arrow) in the left breast, seen on this 3D volume rendered image in coronal arterial phase.

studies of patients with renal cell carcinoma have reported an incidence of splenic metastases of 4.6%[15].

Stomach: Patients with metastases to the stomach (Figure 14) usually have other sites of metastases within the

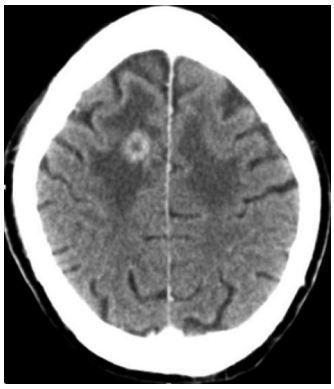

Figure 20 A 81-year-old male status post left radical nephrectomy with bilateral frontal lobe metastases. Enhancing lesion in the right frontal lobe with surrounding vasogenic edema. Vasogenic edema is also seen in the left frontal lobe secondary to another metastatic lesion located more inferiorly.

body. Patients may present with gastrointestinal bleeding, epigastric pain, or dyspepsia. Pollheimer *et al*[16] reported a 0.2% incidence rate of metastases over a 22 year period. The study found that a gastric mass in a patient with a history of renal cell carcinoma is twice as likely to be a primary gastric tumor rather than a metastasis[16]. If this is the patient's only site of disease, the patient may be treated with partial gastrectomy.

Intestine: Bianchi reported that large intestine metastases contributed 1.3% to the total number of metastases in renal cell carcinoma patients, and small intestine metastases (Figure 15) contributed 1.1%[17]. Patients may present with abdominal pain, gastrointestinal bleeding, or intussusception. Most are treated surgically followed by chemotherapy.

Ovary: Ovarian metastases are thought to occur through hematogenous spread *via* the renal vein to the ovarian veins, with a higher predilection for left sided renal tumors due to the retrograde flow *via* the gonadal vein. Autopsy studies have reported ovarian metastases (Figure 16) in 0.5% of patients with renal cell cancer. Only 21 cases have been reported in the literature[7].

Musculoskeletal

Bone: The second most common site of recurrence is in the skeletal system. Patients are not screened for bone metastases unless they are symptomatic or have metabolic abnormalities suggestive of bone metastases, therefore such metastases may be found incidentally on surveillance CTs of the chest, abdomen, and pelvis. In the study by Chae *et al*[2], the bone was the initial site of recurrence in 29% of patients[2]. The incidence of bone metastases has been reported as high as 45% in T3 patients[4]. The lesions are typically lytic and can have an associated soft tissue component that enhances similar to the primary tumor (Figure 17).

Muscle: In a review of the literature, only a total of 35 case reports of muscle involvement (Figure 18) have

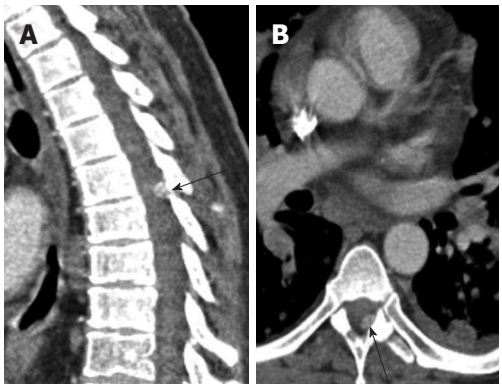

Figure 21 A 56-year-old male with diffuse metastatic disease and an enhancing dural based nodule. A. Lesion in the thoracic spine (arrow) seen on sagittal image. B. Corresponding axial CT with lesion (arrow). Subsequent magnetic resonance imaging showed a dural based metastasis.

been published. One of the cases reported involved multiple muscle metastases in a patient who had undergone radical nephrectomy 19 years prior[7]. Intramuscular metastases may be small and only well visualized during the arterial phase. Coronal and sagittal reconstructions may be helpful as they may emphasize the distortion of the muscle plane by the tumor.

Breast: Metastases to the breast from extramammary malignancies are rare. The incidence of metastases in autopsy studies range from 5%-6%, and of those cases, 3% are attributable to a renal tumor. The most common malignancies to metastasize to the breast include melanoma, lymphoma, and lung cancer[18]. A review of the literature by Ganapathi *et al*[19] in 2008 reported 15 case reports of renal cell carcinoma metastases to the breast (Figure 19). The hypervascularity of the metastasis helps to distinguish it from a primary breast carcinoma and may help to avoid unnecessary biopsy.

Neurological

Brain: Brain metastases (Figure 20) usually occur in later stages of disease and their incidence has been reported between 2%-15%[3,4]. Patients are not typically screened from brain metastases. Typically patients are symptomatic, leading to their diagnosis. If a solitary lesion is present, this may be treated surgically.

Spine: Most often the metastases to the spine are extramedullary (Figure 21) rather than intramedullary. Nevertheless, the presence of an intradural metastasis is a poor prognostic indicator and a sign of advanced disease. A review of the literature by Jost *et al*[20] in 2009 reported 32 cases in the literature of intradural metastases from renal cell carcinoma. Use of sagittal reconstructions to visualize the spinal canal longitudinally may help in lesion conspicuity.

Conclusion

In this pictorial essay we have demonstrated common and uncommon sites of metastatic recurrence in patients status post nephrectomy for renal cell carcinoma. A recent study by Jain *et al*[5] demonstrated the importance of arterial phase imaging in lesion detection within the liver, pancreas, and kidney. This case series confirms the utility of arterial phase imaging in detecting lesions elsewhere in the body by taking advantage of the metastases' hypervascularity. Lesion hypervascularity may also help to distinguish a metastatic lesion from a second primary as in the cases of adrenal or breast metastases and thereby avoid unnecessary diagnostic procedures or therapies. Coronal and sagittal reconstructions are also helpful in lesion detection, specifically in evaluating for contralateral recurrences and spinal metastases, respectively.

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