Anatomy of the Kidney Revisited: Implications for Diagnosis and Staging of Renal Cell Carcinoma

22

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Abbreviation

RCC Renal cell carcinoma

Introduction

Pathologic stage is the single most important prognostic parameter for renal cell carcinoma (RCC). The tumor, nodes, and metastases (TNM) staging system has two renal-limited categories: a category for local spread outside of the kidney and a category for metastatic disease. The primary mission of the pathologist in evaluation of a tumor nephrectomy is to determine if the tumor is renal limited, or if it has extended locally into veins or into one of the two perinephric fat compartments. Metastatic disease is largely the domain of the clinician (adrenal metastasis excluded). To fulfill this charge, the pathologist must understand the gross and microscopic nuances of the kidney and its environs in order to optimize the dissection strategies, and to permit recognition of invasive behaviors so critical to tissue sampling. Although the basic gross and microscopic anatomy of the kidney is familiar to most pathologists, there are anatomical points that merit specific emphasis with respect to renal neoplasia. This chapter reviews the basic anatomy of the kidney, its neighboring structures within the retroperitoneum, and the numerous potential avenues for distant spread.

Retroperitoneum

The kidneys reside in the retroperitoneum. The retroperitoneum is a large compartment enclosed anteriorly by the peritoneum, posteriorly by the transversalis fascia, and vertebrae superiorly by the 12th rib, and inferiorly by the iliac crest and base of the sacrum [1, 2]. The retroperitoneum is spacious compared to the size of the kidneys, often permitting neoplasms to grow to a large size prior to clinical detection. Thus, symptomatic renal tumors typically are of high stage and have a very poor outcome.

The retroperitoneum is divided into three fascia-invested compartments or spaces: the anterior pararenal space, the perirenal space, and the posterior pararenal space. The anterior pararenal space contains several organs and major vessels, including the pancreas, duodenal loop, ascending and descending colon, and the hepatic, splenic, and proximal superior mesenteric arteries. In large widely invasive tumors, this compartment is occasionally breached leading to composite multiorgan resections. The posterior pararenal space contains fat but no organs.

The perirenal space is home to the kidneys. In addition to the kidneys, it contains the adrenal glands, hilar structures such as the vascular pedicle and its venous tributaries, renal pelvis and ureter, a variable number of hilar lymph nodes and two fat-containing compartments important in renal staging, the peripheral and the central

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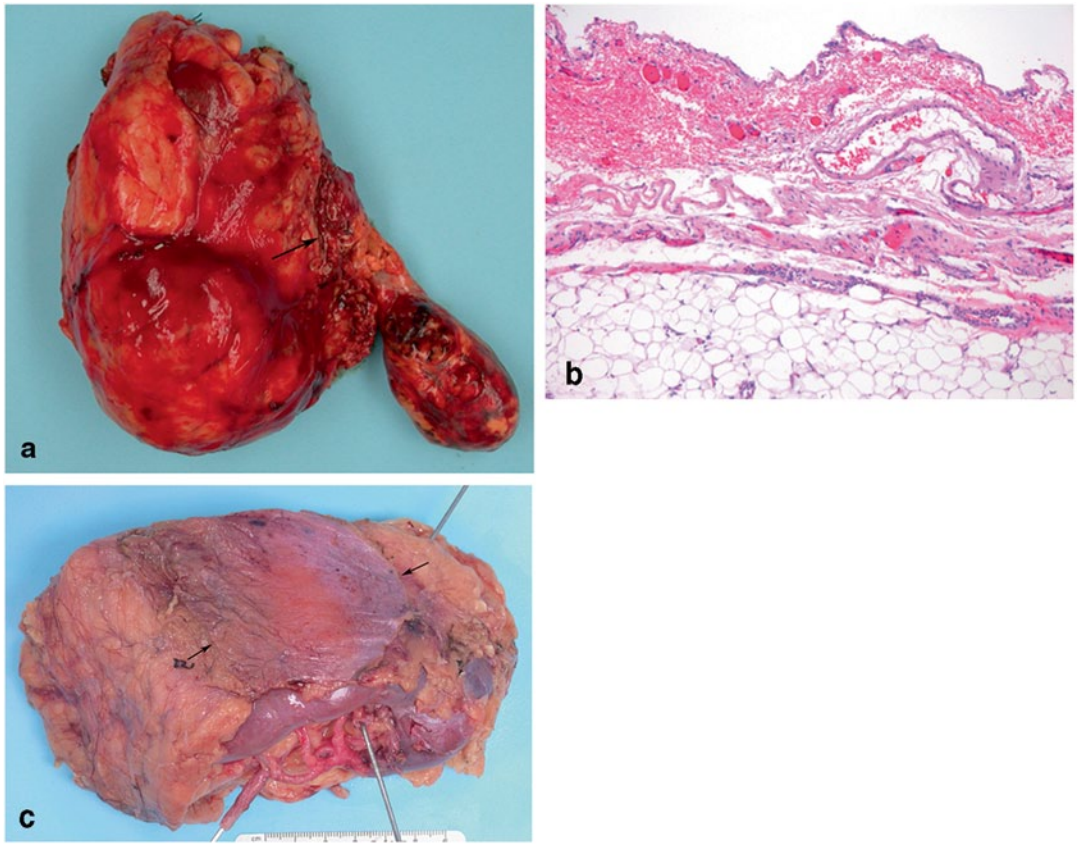

Fig. 22.1 **a** This is a perifascial radical nephrectomy with massive main renal vein involvement by clear cell renal cell carcinoma. Gerota's fascia is intact and visible as a thin delicate connective tissue envelope for the kidney and adrenal. It has been incised medially (*arrow*) exposing more clearly the hilar-perinephric fat. **b** This section shows Gerota's fascia. It is a thin vascularized connective tissue layer that invests the peripheral perinephric fat located below. **c** The anterior pararenal space is thin, overlying the kidneys. Anterior to it is the peritoneum. In this radical nephrectomy, there is a portion of the peritoneum (between *arrows*) covering Gerota's fascia

sinus fat compartments. The anterior and posterior fascial investments of the perirenal spaces are known as Gerota's fascia—a thin connective tissue envelope that provides surgical dissection planes employed during radical perifascial nephrectomy (Fig. 22.1a, b). The posterior layer is a well-defined layer. The anterior layer, however, is more delicate and often adheres to the peritoneum which may be included in radical nephrectomy specimens (Fig. 22.1c). The perirenal space is bounded medially by dense fat and the adventitial connective tissues of the aorta and vena cava that impede communication across the midline of perinephric processes such as urine leaks, hemorrhage, infection, and even neoplastic infiltration.

Peripheral Perinephric Fat Compartment

The peripheral perinephric fat contains the adrenal gland, and the hilar structures already mentioned. It surrounds the outer aspect of the kidney and is separated from the kidney by the fibrous renal capsule. The quantity of peripheral perinephric fat varies substantially in nephrectomy specimens, especially since adrenal-sparing procedures are often employed. Although it is common practice to weigh nephrectomy specimens, these data provide little useful information. For RCC to qualify as extending into this perinephric compartment, it should be in contact with adipocytes, or in loose connective tissue containing adipocytes.

Renal Parenchyma

The kidney consists of two basic components—the renal cortex and the renal medulla, also known as the renal pyramids because of their distinctive shape [3] (Fig. 22.2). The cortical tissue includes the columns of Bertin, portions of the cortex that dip deeply between the renal pyramids toward the renal sinus fat as mentioned above. The kidney is partially invested by the renal capsule, a dense fibrous tissue layer that covers the peripheral aspects of the kidney and extends a short distance into the renal hilum where it terminates (Figs. 22.2 and 22.3a). The cortical columns of Bertin that extend between the renal pyramids are in direct contact with the renal sinus without an intervening fibrous capsule (Fig. 22.3b). Assuming that the renal capsule provides some resistance to tumor extension outside the kidney into the peripheral perirenal fat, the absence of a capsule between the columns of Bertin and the sinus fat may represent a preferential site for extrarenal extension into the central perinephric sinus fat. This may be especially pertinent for tumors arising in the column of Bertin.

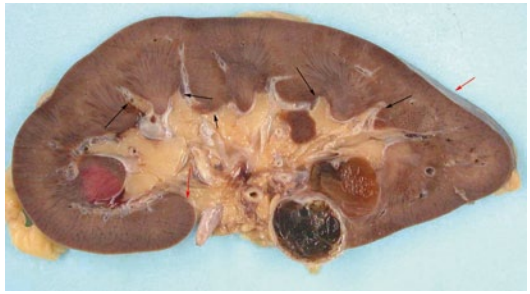

Fig. 22.2 This nephrectomy was bivalved through the lateral mid plane. Most of the perinephric fat was removed. A small portion of the renal capsule is visible to the *upper right* (*red arrow*). The renal capsule curves into the renal sinus a short distance then terminates (*red arrow*). The renal parenchyma consists of the renal cortex and medulla. The cortical columns of Bertin extend between the pyramids and are in direct contact with the renal sinus (*short arrow*). The renal sinus is the central fatty compartment. Wedges of sinus fat extend toward the cortex between the papilla and the columns of Bertin (*long arrows*)

The renal cortex consists of two histological compartments—the cortical labyrinth and the medullary rays. The cortical labyrinth contains glomeruli, proximal and distal convoluted tubules, and the initial portion of the collecting ducts, as well as the renal arteries, veins, and lymphatics. The medullary rays contain parallel tubular segments that course down into the medulla and travel back up to the cortex. It is important to be familiar with the normal histology

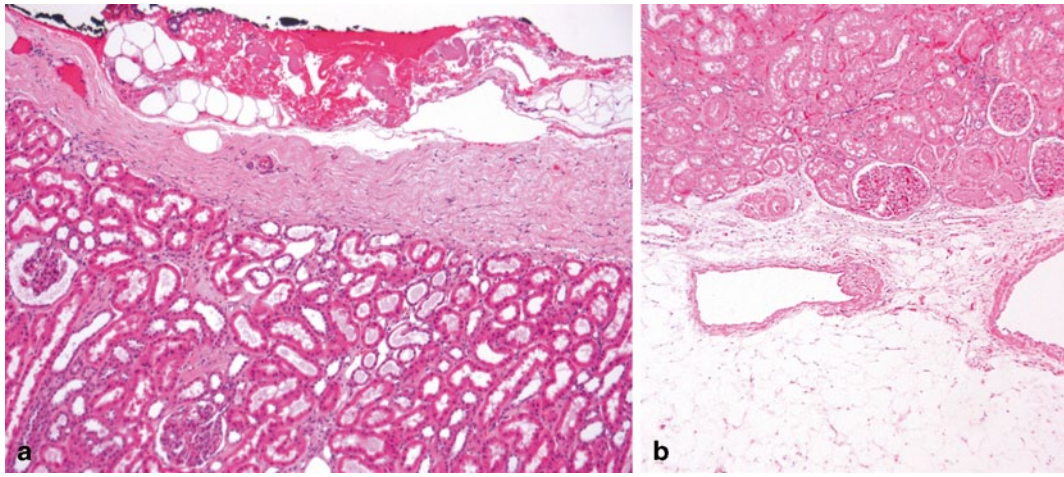

Fig. 22.3 **a** This section shows the dense fibrous renal capsule. It represents a fibrous barrier between the peripheral perinephric fat and the peripheral renal cortex. **b** This image shows the interface between a column of Bertin and the renal sinus fat. Notice the absence of a fibrous capsule. The renal sinus fat with two veins is visible *below*. It is not uncommon for a delicate connective tissue layer to be present between the cortical tissue and the sinus fat as shown here. Involvement of this connective tissue layer is regarded as extension beyond the kidney (pT3a)

of the kidney because the nonneoplastic cortex provides a window into the presence of systemic diseases. Especially important are the common systemic diseases hypertension and diabetes—conditions, that when detected, may have greater prognostic implications than the neoplasm itself. The reader is referred to the recent reviews on this topic that have led to reporting recommendations regarding findings in the nonneoplastic cortex [4, 5].

Central Perinephric Sinus Fat Compartment

The renal sinus is the fatty compartment located within the central confines of the kidney (Fig. 22.2). Involvement of the renal sinus veins was recognized as the primary route of tumor dissemination in nephroblastoma in the early 1980s [6]. A similar role in tumor dissemination for RCC, however, was not shown until 2000 [7]. Inclusion of renal sinus involvement in RCC staging was first codified in the 2002 TNM formulation [8]. Extension into this perinephric compartment is now known to be the most common site of extrarenal extension by RCC. Therefore, understanding the anatomy and histology of this compartment is critical to the accurate staging of RCC [9, 10].

The renal sinus begins at the renal hilum and fills the space between the pelvicalyceal system and the renal parenchyma. The renal sinus has a complex three-dimensional structure [1, 2, 11]. There are pyramidal extensions of the sinus containing fat and interlobar vessels between the renal pyramids that separate the minor calyces from the columns of Bertin (Fig. 22.2). These slender cords of sinus approach within 1–1.5 cm of the renal capsule. Therefore, it is no surprise that sinus tissue is commonly present in partial nephrectomy specimens. This should be looked for grossly at the partial nephrectomy resection margin and when the specimen is sectioned (Fig. 22.4a, b) because sinus fat and sinus veins will occasionally be involved. Most renal pyramids and minor calyces angle toward the central portion of the renal sinus from the anterior and posterior planes of the kidney. Therefore, in a bivalved specimen and in kidney sections, the sinus tissue can be encountered completely surrounded by renal parenchyma (Fig. 22.5a, b).

The renal cortex of the columns of Bertin is in direct contact with the renal sinus without an intervening capsule in contrast to the peripheral renal cortex as previously mentioned (Figs. 22.2 and 22.3b). The renal tubules of the cortical column of Bertin tissue may contact adipocytes directly, or may be separated by loose connective tissue fibers. Involvement of either constitutes the renal sinus involvement. The renal pyramids,

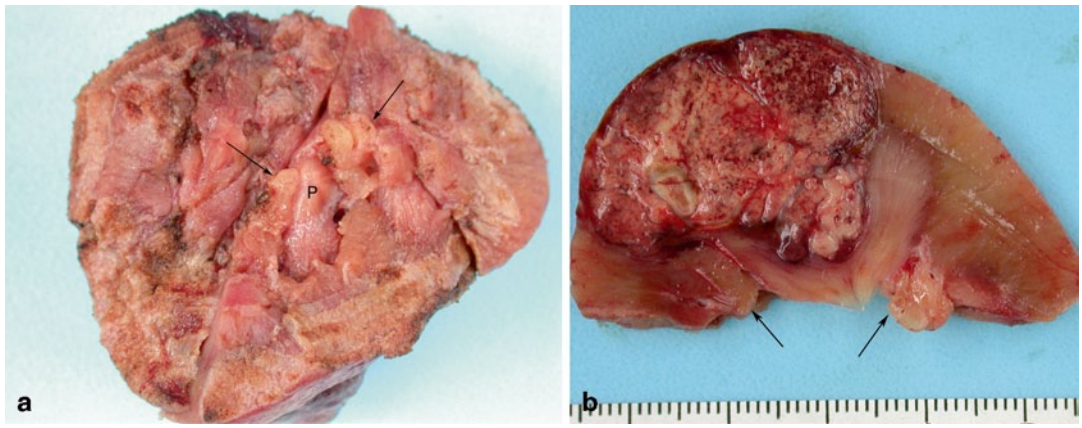

Fig. 22.4 **a** This image shows the surgical resection margin of a partial nephrectomy. Several renal papillae (*P*) can be seen. In addition, two wedges of renal sinus fat are also visible (*arrows*). **b** This cut surface of the above specimen shows a papillary RCC. Notice the two wedges (*arrows*) of sinus fat flanking the renal pyramid

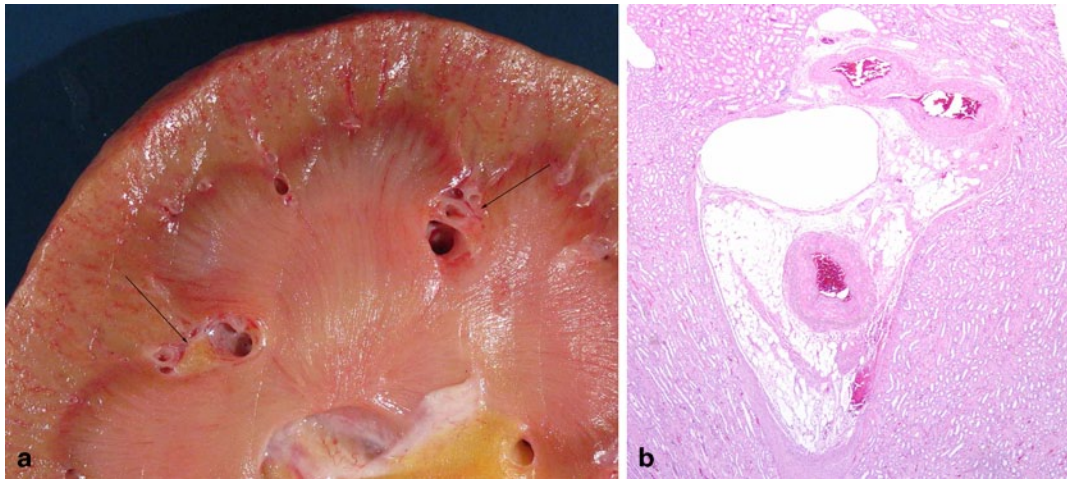

Fig. 22.5 **a** This bivalved kidney shows a compound renal pyramid in the center with two islands of renal sinus (*arrows*) seen in cross section that are completely surrounded by renal parenchyma. **b** In this section of the kidney, there is an island of renal sinus surrounded by the cortex to the top and renal pyramids on both sides. There is a thin-walled interlobar vein adjacent to the cortex that would be easily accessible to a RCC if developing in this area

by contrast, are nested within minor calyces and are not in direct contact with the renal sinus. When RCC involves the collecting system, it usually indicates sinus involvement because it would be uncommon, but not impossible, for a slender cord of tumor to breach only the papillary tip without also invading the renal sinus. The renal sinus' defining attribute is its lush vascularity discussed in detail below.

Renal Parenchymal Vasculature

The renal parenchymal vasculature has two components [1–3, 11–14]. There is a minor system of small vessels, the stellate arteries and veins, which supply and drain, respectively, the superficial cortex through the renal capsule (Fig. 22.6a). These arteries and veins are themselves supplied by, and drain into, the major hilar vessels. An in-

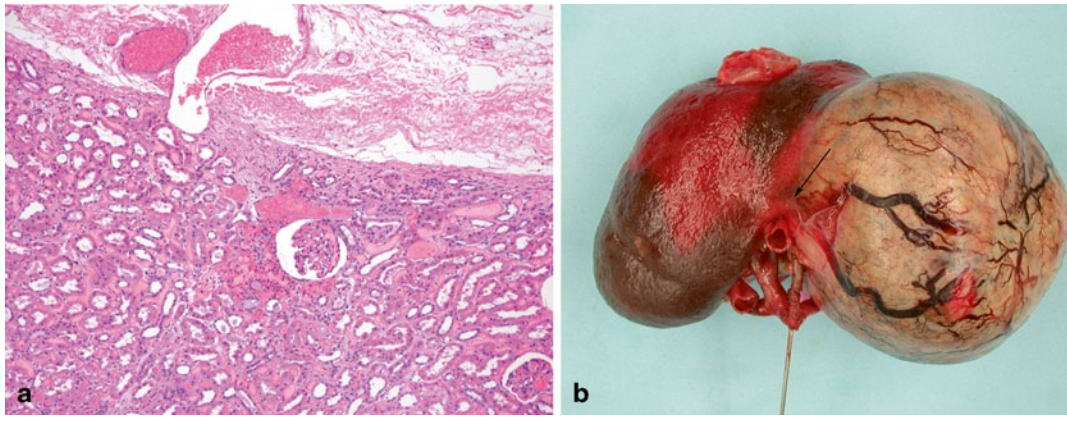

Fig. 22.6 **a** A small dilated stellate vein can be seen in this image traversing the fibrous renal capsule. **b** The perinephric fat and renal capsule have been removed from this nephrectomy specimen exposing the intact tumor capsule. Notice the engorged veins that drape across the tumor capsule. They disappear (*arrow*) as they approach the hilum to drain into hilar veins

travenous tumor in the peripheral perinephric fat represents a tumor that has gained access to the stellate system or may be there by retrograde extension from the hilar connection of the stellate veins (see below). It may be that the venous engorgement occasionally observed in tumor capsules represents this system of veins (Fig. 22.6b).

The major renal parenchymal vasculature resides in the central cortical labyrinth. The arteries and veins travel in parallel as they ascend from, and descend to, the renal sinus, respectively. The renal parenchymal veins are distinctive compared to veins in most other organs because they lack a smooth muscle media (Fig. 22.7a, b). They are essentially very large capillaries. The absence of a smooth muscle media assumes importance with respect to the recognition of retrograde cortical venous invasion and the possibility of multifocal tumors, issues addressed in Chap. 24.

The interlobular veins of the cortex progressively enlarge as they approach the corticomedullary junction to form the arcuate veins. The arcuate veins drain into the interlobar veins that travel between the pyramid and enter the renal sinus. There are elaborate anastomoses between these large veins that encircle the renal pyramids and minor calyces. The interlobar veins converge within the renal sinus forming segmental veins that course anterior to the renal pelvis. Once veins enter the sinus, they acquire a smooth muscle media as discussed below. There are no arteries or veins in the renal medulla, only arterioles, venules, and capillaries.

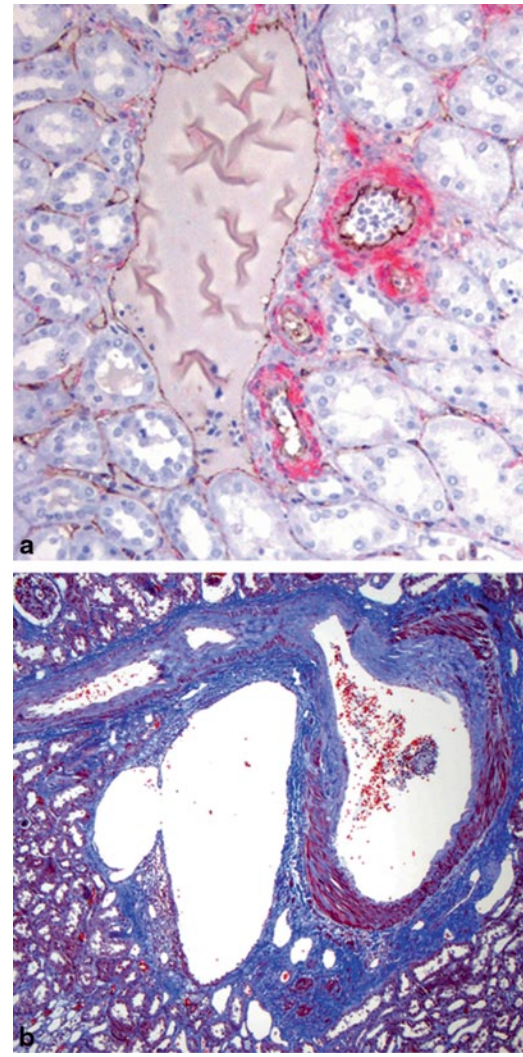

Fig. 22.7 **a** This image shows a cortical interlobular vein to the *left* with small interlobular arteries and arterioles to the *right*. The arteries and veins are always adjacent. Notice that the vein lacks a smooth muscle media and resembles the peritubular capillaries in the surrounding cortex. *Red:* actin smooth muscle; *brown:* CD 31 immunoperoxidase stains. **b** This is the corticomedullary junction. The cortex is to the *top*. Abundant smooth muscle can be seen in the media of the artery to the *right*. However, the arcuate vein to the *left* is devoid of medial smooth muscle. Masson's trichrome stain

Arterial Supply to the Kidney

The kidney's blood supply is disproportionately high compared to that of other organs. Although the kidneys represent only 1% of the body mass, they receive 25% of the cardiac output, five times the blood flow through the coronary arteries [15]. Since only 1% of the glomerular filtrate is normally excreted as urine, there is a comparably impressive venous return that exits the renal sinus through the renal veins. Thus, tumors arising within the kidney are heavily perfused with a voluminous venous return that potentiates venous metastases.

One of the first observations in a nephrectomy for RCC is examination of the vascular hilum, and in particular, assessment of the hilar vessels. Although there are countless variations in the organization of the renal arteries (and veins as discussed below), there are a few generaliza-

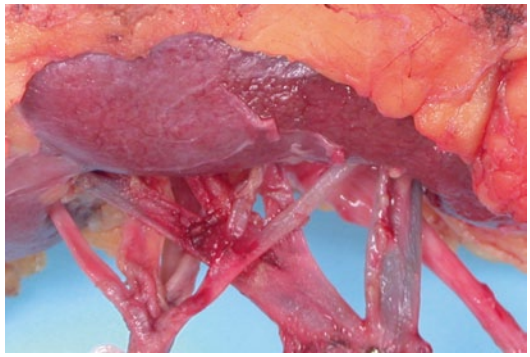

Fig. 22.8 This image shows the vascular hilum of a left kidney. Notice that the arteries and vein are located anterior to the renal pelvis. The artery on the *left* has five segmental branches. The main renal vein on the *right* is formed by the confluence of four tributaries. Notice that the segmental renal arteries and veins interdigitate

tions that apply to most nephrectomy specimens [3, 11–14]. The most common arterial arrangement is for the main renal artery to give rise to an anterior and posterior division. Four segmental arteries arise from the anterior division to supply the upper and lower poles and the anterior kidney. The posterior division continues as the posterior segmental artery. The segmental arteries sequentially branch into the interlobar arteries that enter the renal parenchyma giving rise to six to eight arcuate arteries, from which the interlobular arteries are derived that ascend to the renal capsule. These arteries are all end arteries. There is a vascular junction between the anterior and posterior blood supply 1–2 cm posterior to the lateral convex border of the kidney. This is known as "Brödel's bloodless line of incision," a useful landmark for surgical entry to the kidney [11].

Although the arteries play no role in tumor dissemination or staging, documentation of significant atherosclerotic disease is important because of its role in nephrosclerosis. The major grossing issue related to renal arteries is their frequent tendency to intertwine with the major tributaries of the main renal vein at the renal hilum (Fig. 22.8). This complicates the dissection of the renal veins and may explain the all too frequent occurrence of stapling of arteries and veins together, especially with laparoscopic resections.

Renal Sinus Veins

Once the interlobar veins enter the renal sinus fat, they lose their association with the renal arteries and acquire a smooth muscle media [10]. The smooth muscle of the sinus veins is remarkably variable in quantity and organization. The sinus veins may have a thick layer of smooth muscle that abruptly transitions into a thin layer or no muscle, or the muscle may have only a loose association with the actual vascular lumen (Fig. 22.9a, b). This is noteworthy because the TNM staging definition of sinus vein involvement employs the term "muscular containing vein" [8].

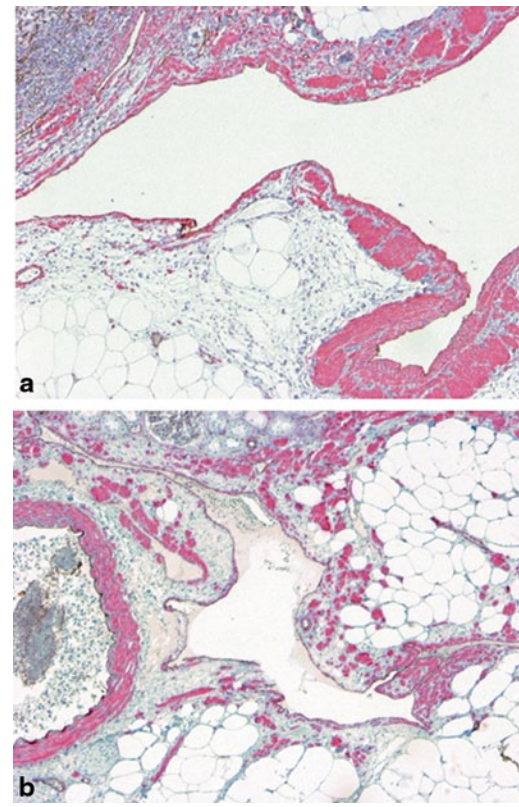

Fig. 22.9 **a** This large sinus vein has just exited the renal parenchyma. Notice the abrupt transition from scant to nonexistent smooth muscle on the *left,* to a very thick smooth muscle media on the *right*. Does only the portion to the *right* qualify as a "muscle containing vein"? What if the tumor was present only in the portion to the *left*? **b** This large sinus vein has a large quantity of smooth muscle in the vicinity on the *right* and to the *bottom,* but no muscle to the *left*. Is this a "muscle-containing vein"? Fully expanded it would be at least 1 cm in size, possibly even larger

Since large caliber sinus veins may have little or no muscle, or the muscle may become attenuated or destroyed when involved by a tumor, this qualification is counterproductive. Furthermore, it has been clearly demonstrated that at least in clear cell RCC, venous involvement begins with entry into large veins that drain the tumor [10]. Therefore, the author contends that any sinus vein involved regardless of size, or quantity of smooth muscle, should be regarded as significant and assigned a pT3a stage designation.

The multiple proximal tributaries of the main renal vein within the renal sinus are large veins that may normally range up to 1–2 cm in diameter. They can become much larger when involved by a tumor. Gross appreciation of the impressive sinus venous system, however, requires sectioning the kidney though its "venous plane." The venous plane is offset from the mid plane of the kidney. There are no large sinus veins posterior to the renal pelvis. The veins that drain the posterior kidney cross over the minor calyces anterior to the renal pelvis, to join the anterior veins before exiting through the renal hilum to form the main renal vein. The venous plane will be missed with sectioning through the lateral mid plane or sectioning through the collecting system. Compare the kidney in Fig. 22.2 sectioned along the lateral mid plane in which the sinus veins are inconspicuous and cut in cross section, with the kidney in Fig. 22.10, which was sectioned through the venous system along probes placed within the major renal veins.

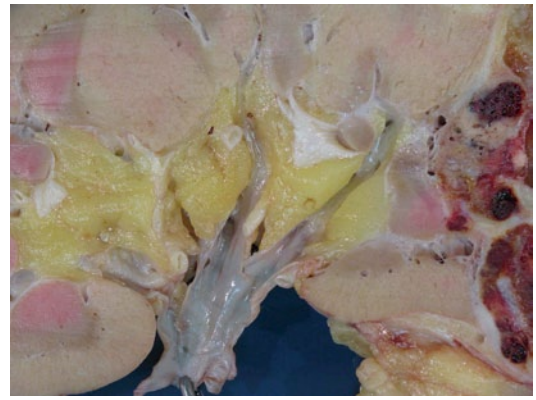

Fig. 22.10 This nephrectomy specimen was venous perfusion fixed allowing visualization of the sinus venous system. The specimen was opened through the venous plane by placing probes within the primary tributaries of the main renal vein and cutting along that plane. The pelvis would be deep to this plane

Main Renal Veins and Their Systemic Venous Connections

The right renal vein is shorter than the left renal vein by 2–4 cm because the vena cava lies to the right of the aorta (Fig. 22.11a). Although there are important differences between the left and

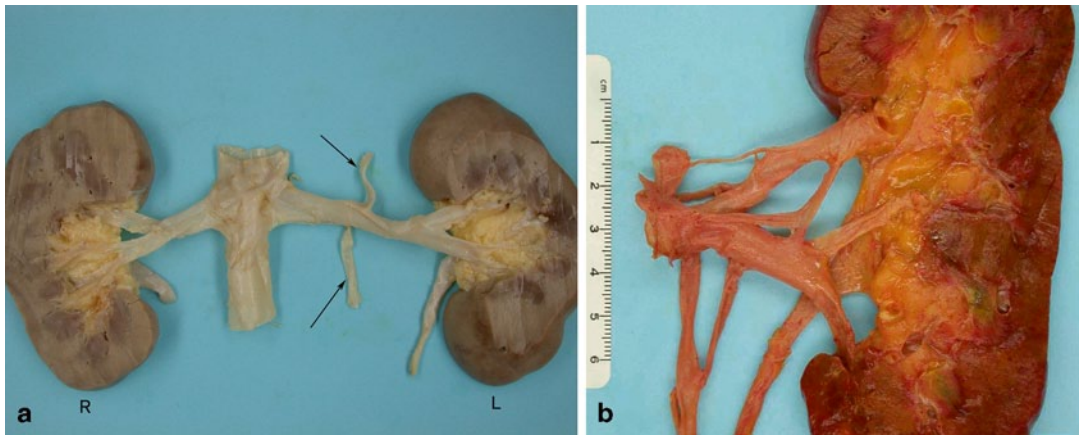

Fig. 22.11 **a** This autopsy specimen shows the short right renal vein and the much longer left renal vein. The main renal veins on both sides begin outside of the renal hilum as two large primary tributaries merge. The left renal vein (*right side*) is fed by the left adrenal vein to the *top* and the left gonadal vein to the *bottom* (*arrows*). **b** This autopsy left kidney shows complicated interconnection of the hilar veins. The main renal vein begins several centimeters outside of the renal hilum. There are interconnections between the primary tributaries of the main renal vein and a thin connection to the large left adrenal vein pointing upwards. The gonadal veins are to the *bottom*

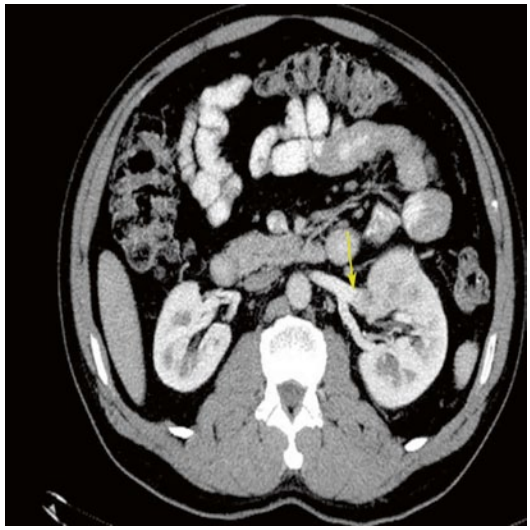

Fig. 22.12 This computed tomography (CT) scan shows a RCC in the left kidney. The tumor extends into a large primary tributary of the left main renal vein (*arrow*). The author reported this as a positive left main renal vein, unaware that it was only a tributary and another branch vein was present draining the opposite pole

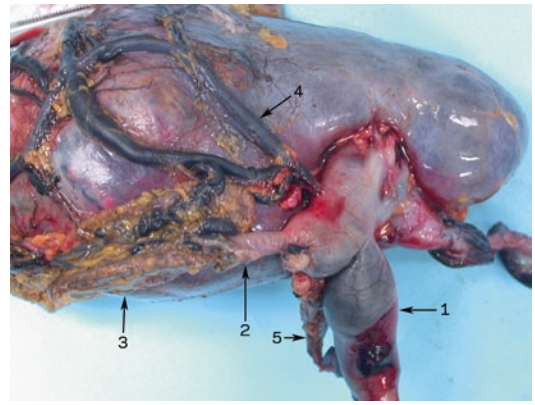

Fig. 22.13 This is a left radical nephrectomy showing venous engorgement due to the main renal vein involvement (*1*). Notice the adrenal vein (*2*) and adrenal gland (*3*), capsular veins (*4*) posterior lumbar vein (*5*), ureteral veins to the *right*. It is easy to envision once the tumor occludes the main renal vein for the tumor to preferentially extend into the other veins and metastasize to the adrenal gland, vertebral venous plexus via the lumbar vein or down the ureter to the pelvis. In addition, when a tumor is found in the capsular vein in the perinephric fat, it is conceivable that it arrived via retrograde flow from the main renal vein

right main renal veins, a feature that they have in common is the frequent occurrence of anomalies. This seems to make every nephrectomy specimen a unique developmental experiment and a dissection challenge for the pathologist.

It is common for more than one major vein to be present at the vascular resection margin of a nephrectomy specimen because the convergence of the primary tributaries of the right and left segmental veins to form the main renal vein often occurs outside of the renal hilum (Figs. 22.8 and22.11a, b). This is more common on the left side where there may be two to three large renal vein tributaries to examine for venous involvement [13–15]. Unfortunately, when there are large main renal vein tributaries located outside of the renal hilum, this can result in disagreement between the pathologist and the radiologist about the status of the main renal vein (Fig. 22.12). The radiologist will report the main renal vein involvement when the tumor is within the final point of convergence of all venous tributaries forming a single vein which may be several centimeters beyond the renal hilum. However, the pathologist will often report a main renal vein involvement when a large caliber renal vein at the renal hilum is occluded by a tumor, often unaware that on imaging studies this vein was only a large tributary of the main renal vein. A similar conundrum is created when multiple "main" renal veins attach directly to the vena cava. This is also common. Approximately 24–30 % of right renal veins will have two to three separate vena cava attachments, while 10 % of left renal veins will have two separate vena cava attachments [13–15].

The renal veins frequently receive one or more extrarenal venous tributaries, such as the adrenal, ureteric, gonadal, lumbar, and segmental veins (Fig. 22.13). The left adrenal vein drains into the main renal vein or one of its large tributaries while the right adrenal vein drains directly into the vena cava (Figs. 22.11a, b and 22.14). The gonadal vein and lumbar vein frequently join the main renal veins after they exit the renal sinus (Fig. 22.14). This occurs in 58 % of cases on the left side, but only 3 % of cases on the right side. When these veins do not drain into the main renal vein, they drain directly into the vena cava and are close to the origin of the main renal vein and represent potential avenues for intravenous

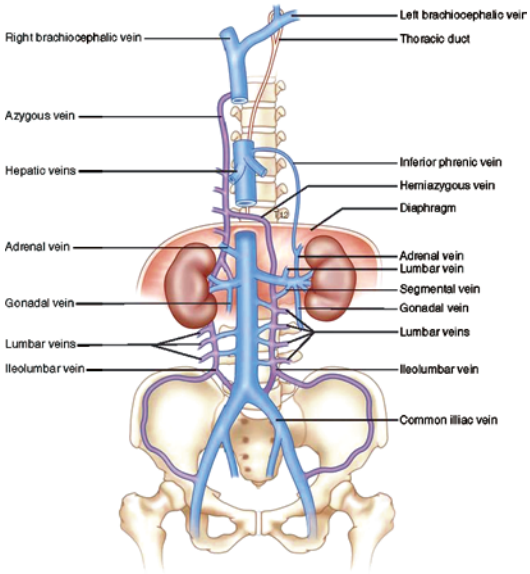

Fig. 22.14 This diagram shows the diverse venous interconnections between the renal veins and the hemiazygous and azygous systems which communicate with the iliac veins and the lumbar veins at each intervertebral space providing avenues for metastatic spread to pelvic and vertebral venous systems

dissemination of a tumor to pelvic or more widespread locations when the main renal vein is involved.

The multiple venous connections of the main renal veins are significant because they communicate with the hemiazygous veins on the left side and azygous veins on the right side which are in turn connected with the common iliac veins (Fig. 22.14). The lumbar veins at every intervertebral disc connect to the vertebral venous system. The vertebral venous system consists of a venous labyrinth within each disc and several longitudinal sinuses that extend along the entire spinal column. Inferiorly, this system communicates with the sacral, pelvic and prostatic veins. Superiorly, it communicates with the intracranial venous system which is composed of the cortical veins, the dural sinuses, the cavernous sinuses, and the ophthalmic veins. The subsequent venous drainage of the intracranial systems ultimately flows into the jugular veins to the superior vena cava.

In 1940, Batson employing intravenous injection with X-rays studies demonstrated that the vertebral venous system was a low pressure, valveless system that permits bidirectional blood flow [16, 17]. With changes in intracranial pressure, blood flows into the vertebral venous system. With the valsalva maneuver, or straining, coughing, sneezing, etc., blood flows from intrathoracic, abdominal, and retroperitoneal veins into the vertebral venous plexus and the intracranial venous system. Thus, cancers of the kidney can spread to the pelvic bones and organs, the vertebral skeleton, and demonstrate the seemingly paradoxical behavior of bypassing the heart and lungs to metastasize to the skull, brain, and head and neck sites [16, 18–20]. Batson commented about the vertebral venous system: "We have a vast intercommunicating system of veins…constantly and physiologically the site of frequent reversals of flow. During these reversals a pathway up and down the spine exists which does not involve the heart or lungs. It provides a ready vehicle for the explanation of 'aberrant' metastatic patterns and removes the stumbling block of the absence of lung involvement." Some of these complex venous interconnections are demonstrated in a left nephrectomy (Fig. 22.13) and in a venous diagram provided (Fig. 22.14).

Renal Lymphatics

Hematogenous dissemination is the principle invasive pathway for RCCs. However, it is important to be familiar with the lymphatic drainage of the kidney and the diverse nodal stations that lymphatic metastases may involve because lymph node dissections have demonstrated that from 7 to 17% of patients have hilar or locoregional lymph node metastases [19, 20]. This occurs more commonly with certain RCC types, particularly papillary and chromophobe RCCs [19].

There are two lymphatic systems in the kidney [21, 22]. Similar to the stellate arteries and veins, there is a minor capsular lymphatic system

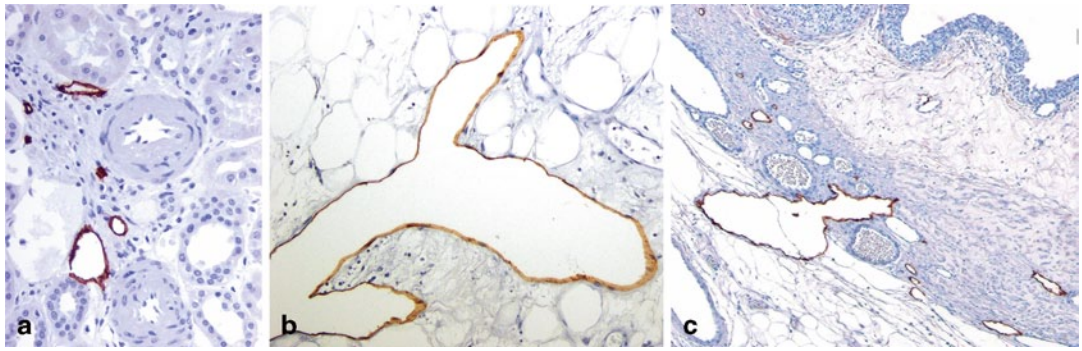

Fig. 22.15 **a** This image is from the superficial cortical labyrinth. It shows multiple small cortical lymphatic endothelia stained with podoplanin. The lymphatics are associated with the arterial-venous system. The vein on the *left* is larger than the several stained lymphatics. **b** This is a lymphatic within the sinus fat. It consists of an endothelial cell lining without a smooth muscle media. **c** The pelvis mucosa is invested with numerous lymphatics. These allow the intralymphatic tumor to spread along a pelviureteral pathway

that drains the superficial cortex and courses toward the renal hilum to join the major lymphatic system that exists through the renal sinus. The major lymphatic system travels with the arterial-venous structures. In the mid to upper cortex, one or more small lymphatics of the caliber of peritubular capillaries are located within the connective tissue investment of interlobular arteries (Fig. 22.15a). Lymphatics lack smooth muscle so they are indistinguishable from capillaries and veins unless stained with a marker specific for lymphatic endothelium.

The small lymphatics enlarge and become more numerous as they descend along the interlobular vessels to the corticomedullary junction. As the corticomedullary junction is approached, the lymphatics stray from the arterial adventitia although they remain associated with the arterial-venous structures. The cortical lymphatics are invariably smaller than the adjacent veins. The lymphatics continue to travel with the arcuate and interlobar vessels until they enter the renal sinus. There are no lymphatics among the glomeruli and renal cortical tubules, or in the renal medulla, unless inflammation-associated neolymphangiogenesis occurs [23]. It is not known if such new lymphatics are actually functional and connected to the native lymphatics.

The largest caliber lymphatics occur within the renal sinus where they appear to lose a vascular association and are scattered throughout the sinus fat (Fig. 22.15b). Sinus lymphatics may have an interrupted smooth muscle media, but most often the lymphatics consist solely of a thin endothelial cell layer as the lymphatics within the renal parenchyma. There are numerous lymphatics within the renal pelvic muscularis allowing pelviureteral lymphatic spread of RCC (Fig. 22.15c).

Most Lymph exit through the renal hilum and flows to the hilar lymph nodes and/or the locoregional lymph nodes. That said, most radical nephrectomy specimens will not contain any hilar lymph nodes. In a recent study in which all of the hilar fat was examined histologically, only 20 % of cases had lymph node tissue identified [24]. The primary locoregional drainage for the right kidney are the precaval, postcaval, and interaortocaval lymph nodes, while the primary locoregional drainage for the left kidney are the paraaortic, postcaval, and postaortic lymph nodes [22, 25].

Lymphatic involvement in RCC is very unpredictable. Only a third of patients with positive locoregional nodes will have positive hilar lymph nodes because the renal lymph may follow a number of alternate routes and not only bypass hilar lymph nodes, but may even bypass locoregional lymph nodes and flow to more distal nodal stations, such as the pelvic and thoracic lymph nodes [25, 26]. As shown in the drawing from the classic lymphatic injection studies of Parker in

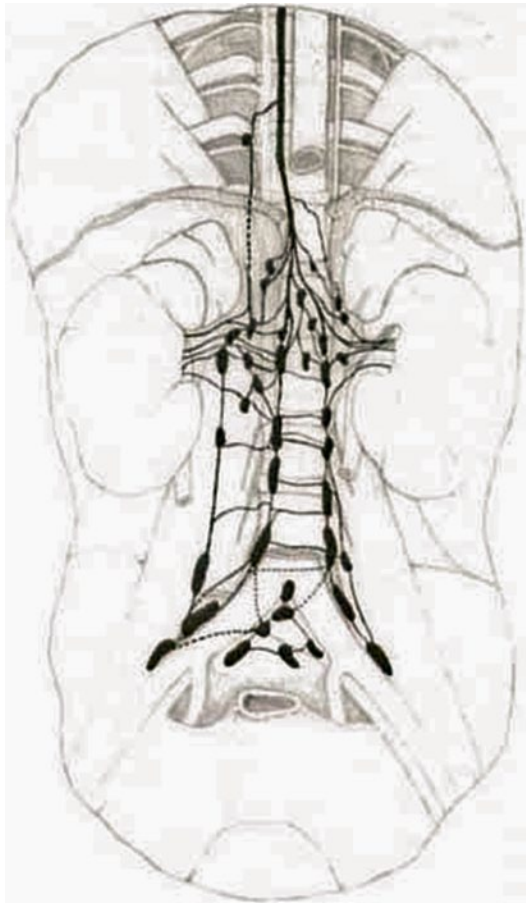

Fig. 22.16 This diagram by Parker shows the elaborate lymphatic intercommunications between the locoregional nodal stations and the pelvic and thoracic nodal stations. Notice the most superior lymphatic pathway to the thoracic duct that allows the lymph to flow from the kidneys directly into the brachiocephalic vein potentially bypassing all nodal stations. (Used with permission from Parker [22])

1935, there are three parallel tracks that an intralymphatic tumor can follow up and down the aorta and the vena cava [22] (Fig. 22.16). Renal lymphatics may connect directly to the thoracic duct without passing through any intervening lymph node stations (Fig. 22.16). This occurs more often on the right side than the left side (38 versus 15 %). This allows intralymphatic RCC to flow into the left brachiocephalic vein and metastasize to the lungs without nodal involvement. The unpredictability of lymphatic spread may explain the lack of survival advantage afforded by lymph node dissections resulting in a decreasing incidence of routine regional lymph node dissection in RCC treatment [26]. It has also hampered implementation of sentinel lymph node biopsy in operative staging of RCC which is technically feasible [27].

Conclusion

The kidneys and their environs are complex and important to understand not only for specimen handling and pathologic staging purposes, but also for understanding the phenomenal potential of RCC to spread to seemingly anomalous sites. The kidneys have four coverings—the renal capsule, the perinephric fat, Gerota's fascia, and the anterior and posterior pararenal spaces. They are cushioned internally and externally by perirenal fat compartments. These many layers would seem to impart numerous barriers to distant spread. However, the kidney's uniquely voluminous arterial blood supply, with its equally impressive venous return, allows RCC to circumvent these barriers because the majority of RCCs gain access to the venous outflow prior to any another type of extrarenal extension. This becomes an even greater liability since the renal veins not only drain directly into the largest caliber vein of the body, the vena cava, but also freely interconnect with the azygous and hemiazygous systems and the large volume, low pressure, and the valveless bidirectional cerebrospinal venous system. Collectively, these interconnected venous highways allow metastases to travel to the liver and lungs, descend into the pelvis, or bypass the abdominal and thoracic organs with seemingly paradoxical metastases to the brain, head, and neck.

The renal lymphatics, although representing a minor metastatic pathway, not only flow into the hilar and locoregional nodes but may directly connect to the pelvic and thoracic nodal stations allowing the lymphatic tumor spread to bypass the more proximal nodal stations. This compromises the ability of the urologist to surgically control locoregional lymphatic spread. Direct lymphatic connections to the thoracic duct bypassing nodal stations allows the intralymphatic

tumor to spread via hematogenous routes to the lung, even in the absence of intravenous invasion by the primary tumor.

The countless number of venous and lymphatic pathways available to RCC explains why no bone, organ, or body site is immune to RCC metastases. Furthermore, these anatomic complexities underscore the fact that when we generate a pathologic stage, it represents the least stage of the process, but not necessarily the true stage of the process. The tumor may have already escaped the confines of the specimen and its environs by the time of our examination.

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