Metastatic Renal Cell Carcinoma: Staging and Prognosis of Three Separate Cases.

Abstract

This paper describes the staging, imaging, treatment, and prognosis of renal cell carcinoma. Three case studies are presented on three separate patients with renal cell carcinoma. Each patient shows specific staging, imaging and treatment of renal cell carcinoma, but all demonstrate different metastases to other areas of the body. Each patient was at a higher stage of cancer, but depending on the rate of detection and surgical options, they all had different outcomes.

Introduction

Renal Cell Carcinoma (RCC) is one of the most common causes of cancer death in the United States.\textsuperscript{1} There are several different types of RCC, which are important to understand because they justify the treatment and outcome that the cancer will have on a patient. No matter the subtype of RCC the patient may experience, it must be diagnosed early to minimize chances of metastases to other areas of the body.

Although some patients are diagnosed with RCC in early stages of development, 20-30\% are already in metastatic phases by the time of diagnosis, making the disease harder to treat. Common areas of the body in which the metastases travel to are the lungs, liver, lymph nodes, bones and suprarenal glands.\textsuperscript{1} Identification of the cancer at an early stage is important because depending on what stage the patient is in, outcome, treatment, and survival rate can be determined. Early detection and surgical resection are the two key elements in a longer survival rate of a patient with metastatic RCC. Imaging is essential in early detection and helps to further diagnose RCC.

Symptoms

Some of the more common symptoms of RCC include: hematuria, low back pain, mass in low back or abdomen, anemia, chronic fever, and/or weight loss.\textsuperscript{3-4} Because these symptoms are common for many other cancers as well, other blood work can be done. However, the most helpful test is a microscopic urinalysis identifies squamous cells, indicative of an abnormality.
Many patients don't have any symptoms at the beginning stages of RCC and cancer is diagnosed incidentally due to imaging for unrelated issues.

**Imaging**

Due to the vast technologic advancements in imaging, patients are diagnosed at an earlier stage. This is advantageous because the tumor is still small and can be easily removed.\(^{3-5}\) No matter the modality used, imaging is most effective in measuring the stage of RCC the patient is at. The most common imaging modality used for RCC is computed tomography (CT). However, there are many other imaging studies that may be performed, such as Magnetic Resonance imaging (MRI), Ultrasound, Positron Emission Tomography (PET) scan, Intravenous Pyelogram (IVP), Angiography, chest x-ray and bone scan.\(^3\) If the CT scan shows that the patient’s RCC has spread to other organs, ultrasound is commonly used to see if the kidney mass is solid or filled with fluid. Ultrasound can also be used to help guide the needle during a biopsy of the kidney. PET scans are most commonly used to see if RCC has spread into nearby lymph nodes and to measure the area of metastases. IVP’s are used to analyze kidney function, if a mass has spread throughout the kidney, an IVP could detect it. Angiography is usually combined with a CT to take a look at the arteries and blood vessels, helping further diagnose patients in addition to preparing for surgery. Radiographs and bone scans are done to identify if the metastases has traveled to lung tissue or bone. If these imaging modalities show that the RCC has spread to either, it is indicated that the RCC is at a high stage.\(^3\)

Often times a patient is at a later stage of RCC when it is found, due to incidental findings during imaging for other unrelated symptoms.\(^6\) Some imaging modalities are more helpful than others in detecting what stage a patient is at. CT and MRI are most commonly used in staging tumors of different sizes, whereas ultrasound is used to detect small lesions less than 1cm in diameter or in evaluating tumor thrombus.\(^4-6\) MRI with contrast, specifically gadolinium, enhances arterial or venous tumors.\(^5\) If the RCC has metastasized to more complicated areas of the body, angiography and PET scans are used. Imaging is very helpful in determining the stage of RCC that the patient is in.
Staging

The advancements in Imaging help identify stages of RCC allowing it to be found early and at a primary stage.\(^3-4\) The staging system that is specifically used with RCC is known as the TNM system. The acronym TNM represents tumor, size, and metastases. The tumor (T) is represented by its size and whether it invades other areas of the body. One of the first areas RCC will spread to is the lymph nodes (N). This portion will describe the extent to which the RCC has traveled into the nodes. The metastases (M) defines the extent of which the cancer has spread to other organs.\(^3-4\) Each letter has sub-categories that are dependent on where the cancer has grown. For example, a sub category of N is N1, which relays that the tumor has spread to neighboring lymph nodes. Certain combinations of the T, N, and M subcategories indicate a particular stage in RCC.\(^3\)

Stages I-IV denotes the size of the tumor found. Stage I represents a tumor 7cm or smaller that is found only in the kidney and has not spread to lymph nodes or distant organs. Stage II designates a tumor larger than 7cm that is found only in the kidney that has not spread to lymph nodes or distant organs. Stage III indicates that the tumor can be any size and has spread into blood stream, neighboring lymph nodes, or tissue surrounding kidneys. Stage IV denotes that the cancer has spread to other organs and can be a range of sizes. These stages, along with the T,N, and M indications, can specifically show what level of cancer the patient has and what their survival rate may be.\(^4\)

Another scale that can determine how aggressive the cancer may be is called the Fuhrman grade. With this grading system RCC is graded on a scale of 1-4, with 1 being a lower grade and 4 being a higher grade of cancer. A biopsy of the cancer is taken and compared to a regular kidney cell. If the biopsy doesn’t have many differences from a regular kidney cell’s nuclei, it is at a low grade of 1. However, if the biopsy has very different features compared to the nuclei of a normal kidney cell, it is at a high grade rated at 4. This scale is most useful for prognosis; the TNM and staging scale is more useful for finding specific information about a patient’s RCC.\(^3-4,7\) Once the stage has been determined, the oncologist will know how to better treat the RCC and can determine options that are available.

Although there are many different scales and grades of staging, it is beneficial to understand what stage the RCC is at. The treatment of the patient is determined by the stage and
size of the patient’s tumor. In order for the patient to have the best chance at survival, the stage must be identified so further treatment can be initiated.

**Treatment**

Depending on the stage of RCC, treatment options may be minimal. However, the most common treatment is surgery. At a lower stage, the patient may only undergo one surgery as well as radiation therapy, but as the RCC advances into higher stages, the patient is likely to have numerous surgeries as well as various therapies. Other treatments for RCC include: ablation, radiation therapy, chemotherapy, targeted therapy, and immunotherapy.²⁻⁶

The most common surgical procedure done for RCC is a radical nephrectomy.⁸ In this procedure, the whole affected kidney, adrenal gland and surrounding tissue is removed. In a less severe case or a situation where the cancer is affecting both kidneys, a partial nephrectomy can be performed, and only the cancerous part of the kidney(s) is removed. RCC is known to metastasize to other areas of the body, commonly to nearby lymph nodes and adrenal glands. “An additional one-third of all patients undergoing nephrectomy for apparent clinically localized disease will go on to develop metastatic disease.” ² (pg.155) Regional lymphadectomy and adrenalectomy are the most common surgical procedures done on patients with metastases to these two areas. When surgery is unsuccessful or cannot be used on a patient, arterial embolization, cryoablation, or radiofrequency can be done to help decreased the spread of cancer. Cryoablation uses cold temperatures to destroy the tumor. Radiofrequency is on the opposite spectrum and uses high energy waves to destroy the tumor with extreme heat. Arterial embolization blocks the area of blood supply to the tumor.²⁻⁶⁻⁸

Other noninvasive treatments can be used, such as radiation therapy, chemotherapy or specific targeted therapies. Radiation therapy is used on people that have poor health conditions and cannot attempt surgery. It can also be paired with other therapies to specifically relieve symptoms caused by RCC. Chemotherapy is used for RCC that has metastasized; however, it is not commonly used until the previously attempted therapies have failed. There are many negative side effects that result from chemotherapy, and, often times, the patient has to pair other medications, such as anti-nausea medications, to help relieve the side effects. Targeted therapies use specific medications to maintain or slow down the growth of RCC. There are many different medications that are used, and they all work to slow the spread of cancer by blocking blood
vessels, cell proteins, growth stimulating molecules, or kinases. These medications are given separate from one another because the result of combining the medication together is still not yet known. There are negative side effects as a result of targeted therapy, but the positive results commonly outweigh the risks.

**Prognosis**

The outcome of RCC is highly dependent on follow-up appointments. In combination with treatment options, especially surgery, prognosis can be positive. During the follow up visit, the patient can be evaluated through imaging, blood work, and physical examinations to determine whether or not the cancer has spread or is under control. The outcome of the patient is also determined by the stage of RCC that the patient is in. Although many people live much longer than five years, a scale has been made to show the survival rate according to the five years following treatment. A patient with stage I RCC has a survival rate of 81%, stage II has a survival rate of 74%, stage III’s survival rate is 53%, and stage IV’s survival rate is 8%. Without treatment patients have a very low survival rate of less than 10%. The prognosis is much higher on patients that have detected a tumor early on with no metastases compared with a patient that has metastatic RCC. Surgical removal increases the chance of survival rate; however, there are areas of the body that RCC can metastasize to, such as bone, which decrease the five year survival rate to 7%. There are many factors that can affect the outcome of the patient; however, with treatment and close follow ups, the prognosis is good and can result in longer survival rates.

**Case Report 1**

Milovic et al presented a 35 year old patient who was diagnosed with RCC stage III after a (CT) scan of the abdomen. The CT revealed a left kidney tumor and nodules which had metastasized into the lungs. The patient had a left radical nephrectomy, as well as chemotherapy. Fifteen months later, the patient had a right partial radical nephrectomy and a left lung metastasectomy after a post-operative CT scan that indicated a 30mm nodule in the left lung, as well as a 3 cm mass in the right kidney (see **Figure 1**). During the left lung metastasectomy, three lesions, 60mm, 45mm, and 25mm in size, were found and removed.
Due to these findings, the previous CT scan was referred to, and the same right kidney tumor that was earlier mistaken as a cyst, due to its size, was apparent. (see Figure 2). The patient had an abdominal ultrasound, as well as a CT, a couple months later after the patient became ill and had symptoms of nausea and vomiting. The CT revealed a large mass in the abdominal wall, which called for another resection. At another post-operative appointment (the patient complained of right testes pain), an ultrasound presented a 21mm mass in the testes, resulting in an orchiectomy (see Figure 3). One month later, a head CT displayed that the RCC had metastasized to the parieto-temporal bone, as well as the brain, causing the patient to start three cycles of chemotherapy. This patient’s RCC metastasized so quickly that the resections of cancerous areas, in addition to the therapies, weren’t effective enough, and the patient died two years after his first surgery.

Case Report 2

Wang et al\textsuperscript{2} presented a 63 year old patient that had 8 operations due to multiple recurrences of metastatic RCC after the first nephrectomy. In 2001, the patient had a CT scan that showed a right adrenal mass and many masses of the left kidney, resulting in a left partial nephrectomy and a right adrenalectomy. The left partial nephrectomy was repeated two more times, once in 2004 and again in 2007, because of metastatic RCC recurrence. After a histopathological evaluation, the patient was diagnosed with Fuhrman grade ¾ RCC. The patient had a radical nephrectomy of the left kidney in 2007, and again in 2010. When evaluating for a possible kidney transplant, an ultrasound was done which showed a nodule in the pancreas. A CT scan was also performed, showing numerous small nodules throughout the pancreas (see Figure 4). After several surgeries in 2011 on the pancreas, including a distal pancreatic resection, the patient didn’t show signs of tumors in 2012 during the follow up appointment.

Case Report 3

The third case was a patient that was admitted to the Emergency Room (ER) of a local hospital with chest and abdominal pain after a four- wheeling accident. The patient had been sent to the ER from an immediate care facility after x-rays were taken and many rib fractures were apparent. Once the patient arrived at the hospital, a CT was done of the chest, abdomen, and
pelvis. The CT results displayed an unexpected case of RCC that had metastasized into the left renal vein into the inferior vena cava near the border of the heart (see Figure 5). There were small soft tissue nodules near the left renal vein, as well as thickening of the left adrenal gland. The patient was again admitted to the ER about a month later, due to chest pain. A CT chest angiogram was performed that revealed pulmonary thrombosis and fluid around the heart. The RCC could have caused the resulting blood clots. The patient followed up with urology and oncology for further treatment. This case exemplifies that not every patient has immediate symptoms of RCC. It also shows that incidental findings from imaging, due to trauma or other issues, are very common. Although the patient’s RCC had already metastasized into nearby areas, with proper surgery and continual imaging, his prognosis was more optimistic than if he had come in later due to symptoms of RCC.

Discussion

In these 3 separate case studies, patient 1 had RCC stage IV due to the metastases, as well as the size of tumors that were found. The prognosis was poor, and there were a limited amount of treatments that could be done. However, in case 2, although the patient had metastases, surgical removal of the areas the cancer had spread to was viable. Follow-up visits, along with consistent imaging, helped maintain and control the cancer. In case 3, the patient’s cancer was already in a higher stage due to the amount of metastases that were already present. Considering that the patient had follow up visits at another facility, the prognosis and treatment are unknown.

Although each patient may have specific needs due to the stage of RCC, the initial testing and imaging that each patient may receive is similar. All 3 patients underwent common imaging such as CT and MRI, and, most likely, had initial blood testing to show a complete blood count. After the results of the imaging are determined, the patient may then need specific surgeries or treatment. In the cases presented, patient 2 continued consistent follow up care and was able to successfully have surgical resections until there were no metastases present. The RCC in patient 1, on the other hand, had metastasized to bone and caused a shortened survival.
Conclusion

RCC, like any other cancer, is very unpredictable. There are many factors that must be identified in order to diagnose the type and stage of RCC, which, in turn, will assist in successfully treating the cancer. Although there are different treatment options available, this cancer is dependent on the patient’s health, the stage of RCC, and continual follow up imaging. As shown in the above cases, prognosis and survival rate is reliant on how the patient’s body responds to surgery and treatment. Early detection will offer the longest survival rate; however, with a disciplined follow up regimen, continuous imaging, and surgical resection of tumors, the patient has a more promising chance of survival.
References


Figures and captions:

**Figure 1.** A CT image of a 3cm RCC found in right kidney, overlooked earlier as a small cyst. Image courtesy of Milovic N, Lazic M, Aleksic P, et al. Rare locations of metastatic renal cell carcinoma: A presentation of three cases. Milit Med Pharmaceut J 2013; 70(9):881-886. doi: 10.2298/VSP120515014M
Figure 2. The initial CT image before any surgery had been performed. A large left kidney tumor is shown as well as a cystic formation in the right kidney that was mistaken as a cyst, later to be diagnosed as RCC of the right kidney. Image courtesy of Milovic N, Lasic M, Aleksic P, et al. Rare locations of metastatic renal cell carcinoma: A presentation of three cases. Milit Med Pharmaceut J 2013; 70(9):881-886. doi: 10.2298/ VSP120515014M
Figure 3. Ultrasound of a 21mm mass in the right testes. The echoheterogeneous mass is a result of RCC metastases into the right testes. Image courtesy of Milovic N, Lazic M, Aleksic P, et al. Rare locations of metastatic renal cell carcinoma: A presentation of three cases. Milit Med Pharmaceut J 2013; 70(9):881-886. doi: 10.2298/ VSP120515014M
**Image A:** Coronal view of left renal mass  **Image B:** Transverse view of left renal mass

**Figure 5:** A CT with contrast, showing two separate views of a left kidney mass that extends into the left renal vein and inferior vena cava. Image courtesy of a local hospital.