17607 Gold Plaza
Omaha, NE 68130
(402) 963-4112
(888)WEB-OPIN (932-6746)

Cancer Consultation

JOHN DOE **8/31/2010**

Referral MD: ABC Medical Center MRN #10-12345-1

CancerOpinions MD: Luke Nordquist, M.D., F.A.C.P **68154**

Cancer Type: Kidney Cancer

1. REASON FOR CANCER CONSULTATION FOR JOHN DOE:

"I want to hear from an independent doctor if my primary physician is doing all that can be done to prevent the recurrence of my renal cell carcinoma, again. I have no doubt that my primary physician is the best in his field where I live and is doing all he knows how to do (which may very well be more than most all other doctors). But since I have had a 'rare' recurrence of my cancer in my remaining kidney, I fell it incumbent upon myself to practice this extra bit of due diligence; and seek out a second opinion."

2. SUMMARY OF CANCER HISTORY FOR JOHN DOE:

Mr. Doe is a 53-year-old gentleman with a second primary kidney cancer. His history dates back to December 2005 when he was incidentally found to have a right kidney mass. He had no hematuria (blood in the urine), noticeable abdominal masses, or flank (mid-back) discomfort. His cancer staging workup at that time with a bone scan and CT scan was negative for metastatic disease. He did undergo a confirmatory MRI to further evaluate a lesion seen in his liver on the CT scan. This lesion was felt to be most consistent with a hemangioma (a benign collection of blood vessels). He subsequently underwent a right radical nephrectomy on December 8, 2005. The pathology demonstrated a 5 cm x 4.5 cm x 4.5 cm kidney cancer (Fuhrman grade 3) in the upper pole of the kidney. The subtype of kidney cancer was a mucinous tubular and spindle cell variant. The surgical margins were negative (meaning no microscopic cancer cells obviously left behind at the surgery site). He was monitored expectantly for several years without recurrence. Then a CT scan in September of 2009 demonstrated a slight increase in the size of a low attenuation lesion in the lower pole of the left kidney suspicious for a second kidney cancer. A CT scan on October 7, 2009 confirmed a mass measuring 1.2 cm. Mr. Doe subsequently underwent radiofrequency ablation (RFA) on November 11, 2009 with curative intent. The results were

incomplete. So, he underwent a second RFA procedure on the same mass in December of 2009. Followup CT scan on January 8, 2010 demonstrated no residual tumor enhancement. It did demonstrate a stable mass in the liver consistent with the hemangioma seen on the prior MRI and two stable kidney cysts unrelated to the cancer. The current plan is to continue to follow his remaining kidney with CT scans. The patient is otherwise healthy aside from controlled hypertension and hypercholesteremia. He is asymptomatic aside from some urinary frequency and urgency. He previously smoked one-half pack of cigarettes per day for 20 years which he quit in 2005.

3. THE BASICS ABOUT CANCER

CANCER IN GENERAL

What is a Cancer? Cells in the body normally divide from one cell into 2 cells, and so on. If however, any cell makes a "mistake", called a **mutation,** during the cell division process, the mutated cell starts to replicate or **clone** itself in an uncontrollable manner, this is then a cancer. The type of cancer it turns into is determined by which cell in the body makes the mistake. If it was a breast cell it turns into a breast cancer, if it was a white blood cell it turns into a leukemia, etc. What makes a cancer deadly compared to a benign (non-cancerous) tumor is the fact that cancers have the ability to grow and **invade** like finger-projections through any tissue or structure. This ability to invade tissue allows it to spread to vital organs, making it potentially deadly. When cancers invade blood vessels the cancer gains access to the body's "highway system" and can spread to organs such as the liver, lungs, brain, and bone. When a cancer spreads from its original site to another site in the body it does not change the cancer type. For example, if a breast cancer spread to the liver and bones, it is still breast cancer in the liver and bones. This spreading of a cancer throughout the body is called a **metastasis**.

BASICS OF CANCER TREATMENT

There are **3 main tools** that you and your cancer doctor have to work with when fighting your cancer: **Surgery, Radiation**, & **Chemotherapy**. In general, surgery and radiation are used to treat a localized cancer in one area. Examples would be a cancer confined to the prostate or a cancerous lump in the breast. In these situations, surgery and/or radiation may be the treatment often for possible cure as long as the cancer has not metastasized. Chemotherapy includes many different types of drugs that may be given through a vein, by an injection, or a pill, including newer "targeted" treatments, and hormonal treatments used to treat cancers such as breast or prostate. Chemotherapy gets into the body and goes nearly everywhere the cancer goes. It is mainly used to shrink or control a cancer but in particular cancers the chemotherapy is effective enough to eradicate all of the cancer cells for cure as can be the case with testicular cancer or lymphomas. "Older" chemotherapy

worked primarily by attempting to stop any cell from dividing. It didn't differentiate between normal or cancer cells, but since cancer cells are dividing more than most normal cells, the chemotherapy was able to effect the growth of cancers. Newer treatments called "targeted" therapies attack targets that are found on cancer cells but tend not to be on normal cells so these drugs may be more effective with fewer side effects.

WHY DO CANCERS RECUR?

It takes approximately 1 billion cancer cells to make a 1cm tumor (Approximately 1/3 inch in size). A cancer needs to be about this size to reliably show up on cancer detection scans such as a CT scan, bone scan, MRI, PET scan, etc. So when a cancer appears to be confined to its original site of origin and it is surgically removed, a majority of the time the surgeon will get it all and you would be cured, but if any cells are left behind undetected, these cancer cells may eventually grow and show up as a recurrence.

4. THE BASICS ABOUT KIDNEY CANCER

The kidneys are vital organs which serve to filter the body's blood and remove impurities, excess minerals, salts, and water. The impurities and excess are eliminated from the body in the form of urine. The kidneys also produce hormones that affect blood pressure and red blood cell production.

The kidneys are located in the back of the abdomen in a cavity called the retroperitoneum, so pain related to the kidneys tend to cause back pain and not abdominal pain. The body can function normally with just one kidney. Through a process called dialysis, the body can survive with no functioning kidneys.

In 2010, there will be an estimated 58,000 cases of kidney and renal pelvic caner in the US. Cancers that are found in the kidney start in the kidney and rarely, if ever, spread from somewhere else in the body to the kidney. A cancer which starts in the kidney can simply be referred to as a kidney cancer. The most common type of kidney cancer (90%) is called renal cell carcinoma (RCC). Not all kidney cancers are the same. Different subtypes of RCC behave quite differently, both with regard to how aggressive they are in the patient and how they respond to treatment:

1. Clear cell or Conventional cell kidney cancer is the most common subtype (75%) and has a varying aggressiveness depending on its grade (Fuhrman grade 1-4). Grade 1 is the least aggressive and grade 4 the most aggressive. Clear cell RCC is the cell type associated with the von Hippel Lindau (VHL) gene mutation in hereditary kidney cancer.
2. Papillary (types 1 and 2) is the second most common sub-type (15%). It often affects both kidneys and is more common in African Americans.
3. Chromophobe (5%) commonly behaves less aggressively and does not tend to spread outside the kidney until late in the disease.

4. Oncocytoma (5%) is a slow growing sub-type that behaves as a benign tumor and rarely, if ever, spreads, so it does not tend to be life-threatening.
5. Collecting Duct (Bellini Duct)(<1%) is a rare sub-type which acts more like a bladder cancer and frequently spreads outside the kidney early in the disease. Medullary renal cell cancer is a collecting duct variant which occurs in patients with sickle cell trait.
6. Mucinous Tubular and Spindle Cell Carcinoma (MTSCC) a rare, recently identified, slower growing sub-type which rarely spreads
7. Sarcomatoid is a more aggressive variant of kidney cancer that is found in up to 15% of other kidney cancer subtypes (chromophobe and clear cell) and frequently spreads outside the kidney.

Other less common types of cancer associated with the kidney include: lymphomas, carcinoids, and transitional cell carcinomas (TCC). Transitional cell carcinomas occur in the area of the kidney (renal pelvis) responsible for collecting the urine before it moves into the bladder. Transitional cell carcinomas act and are treated similar to bladder cancers.

The most common risk factor for causing kidney cancer is smoking, which causes nearly 30% of kidney cancers. Other factors associated with an increased risk of developing kidney cancer include the male sex, obesity, black race, high fat diet, high blood pressure, long term dialysis, and genetic disorders such as Von Hippel-Lindau Syndrome and Tuberous Sclerosis.

There is no screening test currently available or recommended for early detection of kidney cancer. Many kidney cancers are detected incidentally on CT scans or ultrasounds which are being done for other purposes. Common symptoms of a patient with kidney cancer include: blood in the urine, back pain, abdominal mass, high blood pressure, fatigue, anemia, and weight loss.

When a kidney cancer does spread from the kidney, the sites of the body it tends to spread to include: lymph nodes, adrenal glands, liver, lungs, bone, and the brain. CT scans and bone scans are commonly done after a diagnosis of kidney cancer to determine if the cancer has spread or is confined to the kidney. A biopsy of a suspicious mass in the kidney is often unnecessary and it is not uncommon for the surgeon to proceed to surgery without a prior biopsy to remove a tumor for both treatment and diagnosis. If there is clear evidence of widespread metastasis at the time of the discovery of the kidney mass, a biopsy may be taken from an area of metastasis, instead of from the kidney.

A patient will be assigned a “stage” for their cancer depending on the extent and location of the kidney cancer present in the body. There are specific criteria for each stage but a general outline for each stage is shown below:

Stage 1: Cancer limited to the kidney only and is smaller than 7cm (~3 inches). The estimated 5 year survival rate for Stage 1 kidney cancer is 96%

Stage 2: Cancer limited to the kidney only and is larger than 7cm (~3 inches). The estimated 5 year survival rate for Stage 2 kidney cancer is 82%

Stage 3: Cancer has spread to lymph nodes near the kidney or grown into major blood vessels. The estimated 5 year survival rate for Stage 3 kidney cancer is 64%

Stage 4: Cancer has spread to other parts of the body outside of the kidney such as bones, liver, or lungs. The estimated 5 year survival rate for Stage 4 kidney cancer is 23%

Recurrent: cancer that comes back after treatment

Cancers limited to the kidney are most frequently treated with curative intent by surgical removal of the cancer by removing the entire kidney (nephrectomy) or a portion of the kidney involved with a tumor (partial nephrectomy), when possible. Other treatment options for a small kidney cancers limited to the kidney include radiofrequency ablation (RFA) which destroys the cancer by electricity/heat or cryoablation which destroys the cancer by freezing. These last two options can be done as an outpatient.

There is currently no evidence for giving any added treatment (adjuvant treatment) once all of the known cancer has been removed although that is commonly done in other cancers such as breast and colon cancer. There are current research studies looking to see if a short course of a treatment after surgery has a higher cure rate than is seen with surgery alone but today the answer is not known and the current recommendation is to follow patients with no additional treatment unless the cancer recurs.

Occasionally if a kidney recurs or spreads to a limited area, surgery to remove that isolated metastasis will prove beneficial. It is also thought to be beneficial to remove the primary kidney cancer by surgery even if the cancer has already spread to sites outside of the kidney. This is called cytoreductive nephrectomy.

Until the last few years there were limited drug treatment options for a kidney cancer which had recurred or spread beyond the kidney (Stage 4). Historically, the two most commonly used treatments had been IL-2 and interferon. Both were designed to boost the body's natural defenses to fight the cancer, but both were associated with significant side effects and actually helped only a small portion of patients.

More recently a number of "targeted" drug treatments have been developed and FDA approved for treating kidney cancer which has recurred or spread outside of the kidney. Several of these treatments are pills. Current target drug treatments for kidney cancer include: Sutent®, Nexavar®, Torisel®, Avastin®, Afinitor®, and Votrient®. These drugs work by various methods but attempt to target only the cancer cells and not normal cells. This makes "targeted" therapies more effective at killing the cancer cells with fewer side effects.

Several additional experimental targeted treatments (ie. Axitinib) are still being studied and not yet available for general use.

Radiation's role in kidney cancer is typically reserved for treating a single site, such as in the bone or brain, where the kidney cancer has spread and is causing significant side effects. Radiation is rarely used to treat kidney cancers that are confined to the kidney.

If a patient has had all of the kidney cancer removed and they are potentially cured, the patient will need to be followed on a regular basis with a physical exam, blood work and images such as cat scan or ultrasound. They will also need to be monitored for declining kidney function. It is recommended that the patient have a check up every six months for 2 years and then yearly for 5 years. Occasionally more frequent follow up visits are recommended if the patient is at high risk of having a recurrence of their kidney cancer. If a kidney cancer does recur after surgery, most of the time it recurs within 3 years of the surgery and the most common site of the kidney cancer recurrence are the lungs.

This background information was intended to provide you with a simplistic overview of your type of cancer. For more detailed educational material about your type of cancer, we suggest the *American Society of Clinical Oncology website:* *http://www.cancer.net/patient/Cancer+Types*

5. CANCER TREATMENT OPTIONS FOR JOHN DOE:

The pathology from Mr. Doe's initial surgery in 2005 was consistent with a recently described subtype called mucinous tubular and spindle cell variant. This subtype tends to grow more slowly than conventional kidney cancer and rarely metastasizes; however, there have been reported cases of this subtype metastasizing so this warrants occasional imaging to evaluate for metastatic disease. The second mass that Mr. Doe was found to have, although not biopsied, was also consistent with a kidney cancer by CT scan. The second kidney cancer was most likely a new primary kidney cancer and not spread or related to the previous kidney cancer. Fortunately, the second kidney cancer was found when it was small allowing for a potentially curative kidney-sparing procedure with RFA. Other potentially curative options at that time would have included partial nephrectomy, cryoablation, or possibly CyberKnife, which is still being investigated. Mr. Doe has a very high likelihood of being cured from these two episodes of kidney cancer.

Mr. Doe's biggest concern will be the development of another new primary kidney cancer in the remaining kidney. If not detected early enough, when the tumor is small, treatment could require more extensive therapy, which could render the kidney non-functioning, leading to the need for lifelong dialysis. Currently, there are no treatments that we could give to prevent the development of a new kidney cancer. There are ongoing clinic trials in the U.S. investigating whether a short course of targeted treatments (Sutent or Nexavar) could increase the chance of cure over surgery alone, but the final answer is still unknown. To be eligible for this trial you must have complete resection of the tumor and be enrolled in the trial within a few months after your surgery. There is no role for radiation to the kidney. If

curing Mr. Doe at any cost was the only goal, removal of his remaining kidney would likely accomplish cure, but this radical approach would also leave him requiring lifelong dialysis. I would not recommend such a radical approach.

Mr. Doe will need lifelong follow-up with physical exams, labs, urinalysis, and imaging to detect any additional new tumors when they are still very small, again to spare as much of the remaining functioning kidney as possible. Standard follow-up is done with "contrast" CT scans. The dilemma is that the IV contrast can be damaging to the remaining kidney function. It will be necessary to make sure his kidneys are functioning optimally prior to each scan. Unfortunately, non-contrast CT scans are not as sensitive at detecting small cancers. Other ways of monitoring should also be considered such as MRI, ultrasound, and urinalysis. As part of his imaging either a CT scan or X-ray of his chest should be included to evaluate for pulmonary metastasis.

The following link will take you to a list of current research studies which may be available to you within the United States.

http://www.cancer.gov/search/psrv.aspx?cid=163674&protocolsearchid=8123536

Please note that the URL will expire after 75 days from 8/31/2010. For your convenience, I have also sent this link in an email to you.

6. CURRENT RECOMMENDATIONS FOR JOHN DOE:

It is my opinion that Mr. Doe should be followed every 6 months for the next 2 years with physical exam, urinalysis, Chest x-ray, and an abdominal/pelvic CT scan with contrast, if possible. After the 2 years, he should continue with yearly follow-ups and scans. According to Mr. Doe's medical records, his most recent creatinine level (blood test which estimates the kidney function) was 1.2mg/dL with a GFR (also a test estimating kidney function) of 60. Both of these values are within normal limits. At this point as long as these values remain stable I feel that it would be allowable to continue with contrast CT scans at follow-up visits. I would recommend that Mr. Doe remain well hydrated prior to each contrast CT scan to optimally protect his kidneys. If Mr. Doe's kidney function declines, again one could consider MRI or ultrasound as alternate ways of imaging. Ultrasound, much like a non-contrast CT scan, is less sensitive for detecting small kidney cancers. There is no clear answer to how long Mr. Doe should be followed with scans, but I would suggest a minimum of 10 years. If his kidney function remains normal, I see no reason to even stop at that point. If another kidney cancer occurs in the remaining kidney, all of the above options; cryoablation, RFA, partial nephrectomy, or possible CyberKnife could be considered, however, I would

seriously consider a biopsy to confirm a cancer prior to proceeding with additional treatment procedures which could further harm the kidney function.

If metastatic disease develops in a limited area, one could consider surgical resection, radiation, or RFA of the isolated cancer. This can still be potentially curative. If multiple sites of metastatic disease develop, then targeted drugs (Sutent, Nexavar, Afinitor, Torisel, Votrient, or Avastin) or a clinical trial should be implemented. I attached a list of several clinical trials currently ongoing in the U.S. that could possibly have results that may have a bearing on Mr. Doe's situation or future treatment options. At this time there are currently no clinical trials in the U.S. that Mr. Doe would appear to qualify for or given the time from his initial diagnosis, the subtype of his kidney cancer, the RFA, the second cancer, and the fact that Mr. Doe currently has no known active disease evident.

Thank you for allowing me the opportunity to participate in your cancer care.

Luke Nordquist, MD, FACP

CancerOpinions make every effort to produce a consult that provides you with a better understanding of your type of cancer and all the treatment options available to you. Yet we realize that cancers and treatments can be complicated and difficult to understand. If after reviewing your consult you still have questions regarding its content, talk with your referring physician, or have your referring physician contact us at 1-888-WEB-OPIN (932-6746).