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Original Research Paper

Oncopathology

RENAL CELL CARCINOMA -AN UPDATED REVIEW

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ABSTRACT Renal cell carcinoma (RCC) is the seventh most prevalent histological kind of cancer in the Western world, and its frequency has been steadily increasing. Renal cell cancer is becoming more common around the world, and the causes are several. Early detection and successful urological operations such as partial or whole nephrectomy can save a person's life. Only around 10% of RCC patients, on the other hand, have typical clinical signs. Over 60% are discovered by chance during a normal ultrasonography scan. The issue of tumor screening and prevention is highly dependent on the source of tumor formation. The genesis, epidemiology, path physiology, risk factors, and therapeutic methods of renal cell cancer are discussed in this review.

KEYWORDS : Renal cell carcinoma, RCC, Aetiology, Path physiology, Histopathology, Treatment

INTRODUCTION:

Hypernephroma, renal adenocarcinoma, and renal or kidney cancer are all terms used to describe renal cell carcinoma (RCC). The primary function of the kidneys is to filter excess water, salt, and waste items from the blood that enters through the renal arteries. Urine is formed from these chemicals. Urine gathers in the renal pelvis in the center of each kidney and then exits through the ureters, which are long, slender tubes. The ureters connect to the bladder, which stores urine until you need to urinate. Tubules are small tubes found in the kidneys. This aid in the filtering of blood, the excretion of waste, and the production of urine. RCC develops when cancer cells in the lining of the stomach proliferate uncontrolled. The kidneys also have other jobs:

- They assist maintain blood pressure by producing the hormone rennin
- They also produce the hormone erythropoietin, which ensures that the body has adequate red blood cells. The bone marrow is tell to create more red blood cells by this hormone. Renal cell carcinomas (RCCs), which originate within Approximately 80% to 85% of all primary renal neoplasms are found in the renal cortex. Transitional cell carcinomas, which arise in the renal pelvis, account for around 8% of all cancers. Oncocytomas, collecting duct tumors, angiomyolipoma's, and renal sarcomas are all uncommon parenchymal epithelial cancers. Nephroblastoma and Wilms tumor are prevalent in children. Medullary renal carcinoma is an uncommon but deadly type of renal cell cancer that develops in people with sickle cell disease. Clear cell, papillary, and chromophobe cancers are some of the less prevalent subtypes.[1][2][3]

Types of kidney cancer:

Renal cell carcinoma:

Renal cell carcinomas account for approximately 9 out of 10 cases of kidney cancer. Although RCC normally develops as a single tumor in the kidney, it is possible to have two or more tumors in one kidney, or even two tumors in both kidneys, at the same time.

RCC is divided into subtypes according on how the cancer cells appear in the lab. Knowing your RCC subtype can help your doctor assess if your cancer is caused by an inherited genetic condition and help you choose the best treatment option.

Clear cell renal cell carcinoma:

Renal cell carcinoma in this kind is the most prevalent. This type of cancer affects about seven out of ten patients with RCC. The cells that make up clear cell RCC seem exceedingly pale or clear in the lab.

Renal cell cancer with non-clear cells:

Renal cell cancer in papillary form: This is the second most prevalent kind, accounting for around one in every ten RCCs. Some, if not all, of these malignancies In the tumor, tiny finger-like projections (called papillae) are generated. These malignancies are known as chromophilic cancers because the cells absorb specific dyes and appear pink when viewed under a microscope.

Renal cell carcinoma of the chromophobe subtype accounts for roughly 5% (5 cases per 100) of all RCCs. These tumors' cells are similarly pale, like clear cells, but they're considerably larger and have other distinguishing characteristics that can be seen when examined closely.

Renal cell carcinoma is a rare kind of cancer that affects the kidneys. These subtypes are extremely rare, accounting for fewer than 1% of all RCCs.:

- Mucinous tubular
- Spindle cell cancer
- Collecting duct RCC
- Multilocular cystic RCC
- Medullary carcinoma
- RCC linked to neuroblastoma

Renal cell carcinoma that hasn't been assigned a classification: Renal cell tumors are sometimes labelled "unclassified" because their appearance does not fall into any of the other categories or because they contain many types of cancer cells.

Other malignancies of the kidneys

Transitional cell carcinomas, Wilms tumors, and renal sarcomas are among the other kinds of kidney cancer. Transitional cell carcinomas begin in the lining of the renal pelvis, not in the kidney itself (where the ureters meet the kidneys). Transitional cells, which resemble the cells that line the ureters and bladder, make up this lining. When examined closely in the lab, cancers that grow from these cells resemble other urothelial carcinomas, such as bladder cancer. These malignancies, including bladder cancer, are frequently connected to cigarette smoking and employment exposure to cancer-causing chemicals.

Blood in the urine and, occasionally, back discomfort are common signs and symptoms of TCC, which are similar to

those of renal cell carcinoma.

Wilms tumor (nephroblastoma) is a type of cancer that almost usually affects youngsters. This form of cancer is extremely uncommon in adults.

Renal sarcomas are an uncommon type of kidney cancer that starts in the kidney's blood vessels or connective tissue. They account for fewer than 1% of all kidney malignancies. Benign (non-cancerous) kidney tumors:

Some kidney tumors aren't cancerous (non-cancer). This means that they do not spread to other parts of the body, but they can still grow and cause issues.

Benign kidney tumors can be removed or destroyed with many of the same procedures that are used to treat kidney cancer, such as surgery or radiofrequency ablation. The size of the tumor and if it is producing any symptoms, the number of tumors, whether the tumors are in both kidneys, and the person's overall health all influence the treatment options.

Angiomyolipoma:
The most frequent benign kidney tumor is angiomyolipoma. Women are more likely to have them. Tuberous sclerosis, a hereditary illness that affects the heart, eyes, brain, lungs, and skin, can cause them to appear sporadically or in persons with the disease.

These tumors are made up of various connective tissues (blood vessels, smooth muscles, and fat). They can normally only be watched if they aren't causing any symptoms. If they begin to cause problems, they may need to be addressed (such as discomfort or bleeding). Oncocytoma: Oncocytomas are uncommon benign kidney tumors that can develop to be extremely large. They're more common in men, and they don't usually spread to other organs, so surgery is usually enough to treat them..

Familial RCC Syndromes
Hereditary RCC is most commonly caused by Von Hippel-Lindau disease. This disease is characterized by multiple, bilateral clear cell RCCs, retinal angiomas, central nervous system hemangioblastomas, pheochromocytomas, renal and pancreatic cysts, inner ear tumors, and epididymis cystadenomas due to abnormalities in the VHL tumor suppressor gene (located at 3p25-26). RCC develops in around 50% of people who have VHL illness. Early age upon diagnosis, bilaterality, and multifocality are all characteristics of these malignancies. RCC is the most common cause of mortality in individuals with VHL disease, owing in part to better care of CNS diseases in VHL disease.

HPRCC (hereditary papillary RCC) is associated with several, bilateral papillary RCCs, as the name suggests. These cancers also present at a young age due to an underlying constitutive activation of the c-Met proto-oncogene (located at 7q31). These tumors, on the other hand, appear to be less aggressive in general than sporadic malignancies.

Hereditary/familial leiomyomatosis and RCC (HLRCC) tumors, on the other hand, are often unilateral, solitary, and aggressive due to a deficiency in the fumarate hydratase (1q42-43) tumor suppressor gene.

Type 2 papillary RCC, which has a more aggressive phenotype, or collecting duct carcinomas are the most common histological types. Extrarenal symptoms include cutaneous and uterine leiomyomas, as well as uterine leiomyosarcomas, which give to the syndrome's name.

Birt-Hogg-Dube is linked to numerous chromophobe RCCs, hybrid oncocytictumors (having characteristics of both chromophobe RCC and oncocytoma), and oncocytoma due to a deficiency in the tumor suppressor folliculin (17p11). Patients with Birt-Hogg-Dube are less likely to develop clear cell RCC or papillary RCC. Facial fibrofolliculomas, lung cysts, and the development of spontaneous pneumothorax are examples of non-renal symptoms.

Tuberous sclerosis can cause clear cell RCC if abnormalities in TSC1 (located at 9q34) or TSC2 (16p13) are present. Multiple benign renal angiomyolipomas, renal cystic disease,cutaneous angiofibromas, and pulmonary lymphangiomyomatosis are the most common causes.

Succinate dehydrogenase RCC can result from abnormalities in the SDHB (1p36.1-35) or SDHD (11q23) subunits of the succinate dyhydrogenase complex, which can cause chromophobe RCC, clear cell RCC, and type 2 papillary RCC. Paragangliomas, both benign and malignant, and papillary thyroid cancer are examples of extrarenal presentations. These tumors are aggressive in general, and thorough surgical resection is recommended.

Finally, Cowden syndrome can result in papillary or other RCCs, as well as benign and malignant breast tumors and epithelial thyroid malignancies, due to abnormalities in PTEN (10q23).

Etiology:
The specific cause of RCC is unknown to medical specialists. The modifications tell the cells to multiply and expand quickly. The aberrant cells clump together to produce a tumor that can spread beyond the kidney.

Risk factors for the disease:
- Family history of RCC
- Older age.
- Having acquired cystic kidney disease (especially in dialysis patients)
- Hypertension
- Obesity
- Smoking cigarettes
- Hepatitis C
- Exposure to certain dyes, asbestos, cadmium (a metal), herbicides, and trichloroethylene (solvents).
- Polycystic kidney disease
- (an inherited disorder that causes cysts to form in the kidneys)
- African American race,
- Sickle cell disease
- Renal stones.[4][5]
- Certain inherited syndromes like von Hippel-Lindau disease, Birt-Hogg-Dube syndrome, tuberous sclerosis complex, hereditary papillary renal cell carcinoma or familial renal cancer.
- Chronic abuse of certain prescribed medications such as nonsteroidal anti-inflammatory drugs used to treat arthritis, and medications for fever and pain relief such as acetaminophen,
- aspirin, ibuprofen.

Prevention:
Taking steps to improve your health may help reduce your risk of kidney cancer. To reduce your risk, try to:
- Give up smoking. Quit smoking if you're a smoker. Support groups, medications, and nicotine replacement products are just a few of the choices for quitting smoking. Inform your doctor of your want to quit, and the two of you will discuss your choices.
- Keep a healthy weight. Maintain a healthy body weight. Reduce the quantity of calories you consume each day if you're overweight or obese, and aim to be physically active most days of the week. Inquire with your doctor about other healthy weight-loss options.

- Maintain a healthy blood pressure level. At your next appointment, request that your doctor check your blood pressure. If your blood pressure is high, you can talk to your doctor about ways to lower it. Exercise, weight loss, and dietary adjustments are all examples of lifestyle improvements that can help. Some people may require assistance.

Epidemiology:

In adults, RCC is the most frequent kind of kidney cancer. The incidence of RCC varies around the world, with the highest rates being found in the Czech Republic and North America. Every year, roughly 63,000 new cases and nearly 14,000 deaths occur in the United States. RCC incidence rates in the United States have been increasing since the mid-2000s. Since the 1980s, the majority of the increases have been in early-stage malignancies.[6]

Pathophysiology:

RCC develops in the proximal renal tubular epithelium, which is a type of kidney tissue. Nonhereditary and hereditary types are both sporadic. Both variants have structural changes on the short arm of chromosome 3. (3p).

- Families with a high risk of getting kidney cancer were examined, resulting in gene cloning. Oncogenes (VHL, TSC) and tumor suppressors (VHL, TSC) were the genes whose mutations resulted in RCC development (MET).

Histopathology:

Subtypes of renal cell cancer include:

- The most common type of cell, with a cytoplasm rich in glycogen and lipids. This subtype is most likely linked to a 3p deletion.
- Bilateral chromophilic masses are common and can be linked to trisomy 7/17.
- Large polygonal cells are found in chromophobic lesions, while 3p deletion is uncommon.
- Eosinophilic cells predominate in oncocytoma lesions, but chromosomal abnormalities are infrequent. These lesions have the lowest chance of spreading.
- Collecting duct cancer is an extremely aggressive cancer that affects young people and commonly manifests as advanced disease.

Clinical features:

- A lump in the abdomen, lower back
- Blood in the urine
- Unexplained weight loss
- Loss of appetite
- Fatigue
- Vision problems
- Persistent pain in the lower back
- Excessive hair growth (in women)
- Fever
- Night sweats
- Anaemia
- High levels of calcium in your blood
- High blood pressure

DIAGNOSIS:

If your doctor suspects you have RCC, he or she will inquire about your personal and family medical histories. After that, they'll do a physical examination. Swelling or lumps in the abdomen, or swollen veins in the scrotal sac in men, can all be signs of RCC (varicocele).

If RCC is suspected, your doctor will order a number of tests to get an accurate diagnosis. These may include:

- Complete blood count — a blood test conducted by drawing blood from your arm and sending it to a lab for evaluation
- CT scan —an imaging test that allows your doctor to take a closer look at your kidneys to detect any abnormal growth
- Abdominal and kidney ultrasounds — a test that uses sound waves to create a picture of your organs, allowing your doctor to look for tumors and problems within the abdomen
- Urine examination — tests used to detect blood in the urine and to analyze cells in the urine looking for evidence of cancer
- Biopsy —the removal of a small piece of kidney tissue, done by inserting a needle into the tumor and drawing out a tissue sample, If you are diagnosed with RCC, additional tests will be performed to determine if and where the cancer has spread. This is referred to as staging.

Stages of Kidney Cancer

When your doctor discovers a kidney lesion that could be cancer, the following step is to establish the tumour's extent (stage). Additional CT scans or other imaging tests that your doctor deems necessary may be included in your kidney cancer staging testing.

The stages of kidney cancer are denoted by Roman numerals ranging from I to IV, with the lowest stages denoting kidney cancer. The cancer has spread to the lymph nodes or other parts of the body by the time it reaches stage IV.

Approximately one-third of individuals with RCC have cancer that has spread at the time of diagnosis.

From there, they'll do some tests that could include:

- Urine tests
- Blood tests
- Biopsy
- Tests to see how well your liver is working
- Ultrasound which uses sound waves to make a picture of the organs inside your body
- CT scan a test that uses a powerful X-ray to make detailed pictures inside your body
- Nephrectomy, when doctors remove part of one of your kidneys, or sometimes the whole kidney, to check it for renal cell carcinoma.

Treatment / management:

- Treatment is determined by the tumor's stage. For stage I renal cell carcinoma localized to the kidney and measuring less than 7 cm, nephrectomy or partial nephrectomy is the treatment of choice and is usually curative. Patients with bilateral tumors and tiny cortical tumors may benefit from radiofrequency ablation or cryotherapy. Imagery monitoring is an option in elderly patients with a short life expectancy who are not good surgical candidates, as many renal cell cancers are slow growing.
- Laparoscopic radical nephrectomy is the therapy of choice for stage II renal cell carcinoma.
- The standard of therapy for stage III renal cell carcinoma is open radical nephrectomy. When an abdominal CT scan reveals signs of adrenal or lymph node invasion, an adrenalectomy or extensive lymph node dissection is advised.
- Renal cell cancer at stage IV is incurable. Palliative care is provided. Tumor embolization, external-beam radiation therapy, and nephrectomy are among the treatments available, but they are not intended to cure the patient; rather, they are intended to prolong survival and provide palliation. Immunotherapy and chemotherapy can help patients live longer. Bisphosphonates and Xgeva are two drugs that may be used to lower the risk of problems from bone metastases.[7][8]

Surgery:

this might entail a variety of treatments. The damaged kidney is removed (nephrectomy). A complete (radical) nephrectomy

entails the removal of the entire kidney, as well as a border of healthy tissue and, in certain cases, additional adjacent tissues such as lymph nodes, the adrenal gland, or other structures.A nephrectomy can be done through a single incision in the abdomen or side (open nephrectomy) or a series of tiny incisions in the belly (laparoscopic nephrectomy) (laparoscopic or robotic-assisted laparoscopic nephrectomy).

The tumor in the kidney is removed (partial nephrectomy). The surgeon eliminates the tumour plus a narrow margin of good tissue surrounding it rather than the entire kidney in kidney-sparing surgery, also known as nephron-sparing surgery. It can be performed openly, laparoscopically, or with the help of robotics.

Small kidney malignancies are commonly treated with kidney-sparing surgery, which may be an option if you only have one kidney. To preserve kidney function and limit the risk of later consequences, such as renal disease and the need for dialysis, kidney-sparing surgery is generally recommended over a total nephrectomy when possible.

Your doctor's recommendation for surgery will be based on the type of cancer you have and its stage, as well as your overall health. Dialysis or a kidney transplant are required if both kidneys are removed.

Radiation therapy:

To kill cancer cells, radiation therapy uses high-powered energy beams from sources such as X-rays and protons.

- Chemotherapy is a treatment that uses chemicals to kill cancer cells. Depending on the medication, it can be given orally or intravenously. This permits the medications to reach cancer cells that have spread to other parts of the body through the bloodstream.
- Biologic therapy, also known as immunotherapy, works in conjunction with your immune system to combat cancer. Enzymes or chemicals produced by the body are employed to protect the body from cancer. Immunotherapy works by interfering with the immune system's natural processes.
- Targeted therapy is a type of cancer treatment that is relatively new. Drugs are employed to kill cancer cells while causing no harm to healthy cells. Some medications act by blocking blood flow to the tumor, effectively "starving" it and shrinking it. Targeted medication treatments can kill cancer cells by inhibiting these aberrations.

Clinical trials:

These are research studies that allow you to explore the most cutting-edge treatments for kidney cancer. Clinical trials are used to evaluate the safety and efficacy of prospective medicines. Other clinical studies are attempting to discover novel methods for preventing or detecting disease. If you want to participate in a clinical trial, talk to your doctor about the benefits and risks.

Options may include:

- Frozen cancer cells treatment (cryoablation). Using ultrasound or other imaging guidance, a unique hollow needle is introduced through your skin and into the kidney tumor during cryoablation.
- A treatment that uses heat to kill cancer cells a specific probe is placed through your skin and into the kidney tumor during radiofrequency ablation, and the location of the probe is guided by ultrasound or other imaging. An electrical current is passed through the needle and into the cancer cells, heating or burning them.

Prognosis:

The prognosis is determined by the stage of the cancer and the histology of the cell type.

- Stage 1 has a 5-year survival rate of 90%.
- The 5-year survival rate for Stage 2 is 50%.
- Stage 3 gas has a 5-year survival rate of 30%.
- Stage 4 has a 5-year survival rate of 5%

The best 5-year survival rate for papillary RCC is 90%. Clear cell cancer has the second-best 5-year survival rate, at 70%.

CONCLUSION:

Renal cell carcinoma has been on the rise in recent years. Its identification, staging, therapy evaluation, and follow-up all rely heavily on imaging.

Environmental risks are a serious concern in terms of prevention and the need to screen populations at risk. Genetic predisposition/hereditary disorders, obesity, smoking, various nephrotoxic industrial chemicals, drugs, and natural/manmade radioactivity are all factors, and environmental risks are a serious concern in terms of prevention and the need to screen populations at risk.

The exciting new class of immunomodulatory drugs that are currently in clinical trials and could form the basis of a new therapeutic approach for advanced RCC patients.

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