ACADEMIA ONE
PEER REVIEWED JOURNALS
Open Herald: Periodical of Methodical Research
Volume 1, Issue 8, December, 2023
ISSN (E): 2810-6385
Website: https://academiaone.org/index.php/6

Etiology, Treatment and Prevention of Kidney Cancer

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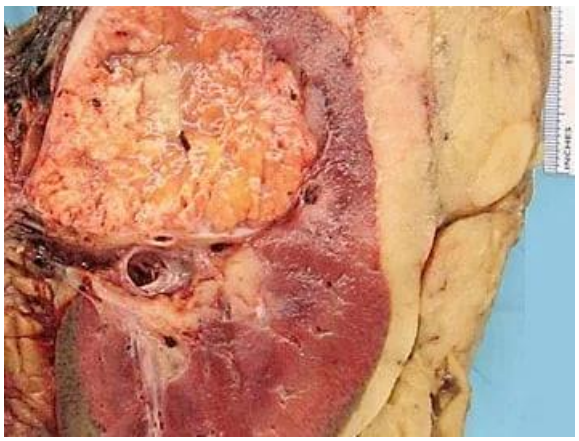
Annotation: Renal cell carcinoma, a disease arising from malignant epithelial cells in the kidneys. Renal cell carcinoma is responsible for about 90 percent of kidney cancers in adults.
Key words: carcinoma, renal, kidney, blood, bone.

Carcinoma, a cancerous growth of surface (epithelial) tissues of the skin, digestive tract, blood vessels, and various organs. Carcinoma cells tend to invade surrounding healthy tissues and give rise to secondary growths (metastases) distant from the original tumour. In addition to the skin and digestive tract, carcinomas may develop in the reproductive tract, mucous membranes, lungs, and other internal organs and glands, including the liver, pancreas, thyroid, ovaries, and prostate. Cancers of the nervous system, blood, bone, and muscle are not carcinomas.

Adenocarcinomas are tumours in which the cancerous cells are arranged in the form of glands. Stomach cancers are usually adenocarcinomas, beginning in the glandular cells of the stomach lining. The most common type of pancreatic cancer is also an adenocarcinoma. Prostate cancer in men and breast cancer in women are most commonly adenocarcinomas, as are many lung cancers.



Picture 1, renal cell carcinoma

Causes and symptoms

Renal cell carcinoma appears to be caused by both genetic and environmental factors. Mutations in chromosome 3 have received special attention as an underlying cause. Men are twice as likely as women to develop this cancer, and the majority of cases are diagnosed in people between 50 and 70 years old. Smoking is believed to double the risk of developing renal cell carcinoma; exposure to asbestos and cadmium are also suspected risk factors. Two rare disorders, tuberous sclerosis and von Hippel-Lindau syndrome, are often associated with renal cell cancers. Other risk factors include a family history of kidney cancer, long-term kidney dialysis, and obesity.

As with many cancers, the symptoms of renal cell carcinoma are often associated with other disorders. Symptoms include blood in the urine, unexplained pain in the side or lower back, a lump in the abdomen, anemia, fatigue, fever, loss of appetite, and unexplained weight loss. Because kidney cancer may affect the ability of the kidneys to regulate fluid levels in the body, high blood pressure or

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swelling of the feet or ankles may also occur. In many cases, symptoms do not appear until the disease has progressed to an advanced stage. Diagnosis

If cancer is suspected, a thorough examination is conducted to confirm its presence. Diagnosis is routinely made by means of multiple imaging techniques, including standard X-rays, computed tomography (CT) scans, magnetic resonance imaging (MRI), and ultrasound. A dye may be injected into a vein and allowed to travel to the kidney in order to improve X-ray contrast. Although no laboratory test exists for diagnosing renal cell carcinoma, urinalysis may reveal blood in the urine, and a blood test may reveal anemia, elevated liver enzymes, or elevated calcium levels. Results of these tests may indicate the possibility of kidney cancer and thus allow early diagnosis and treatment. Once renal cell cancer has been diagnosed, its stage is then determined to indicate how far the cancer has progressed. Stage I tumours are less than 7 cm (about 2.75 inches) and are confined to the kidney, whereas stage II tumours are larger than 7 cm. Stage III tumours have spread to the tissues surrounding the kidney, the adjacent adrenal gland, the major blood vessels of the kidney, or nearby lymph nodes. Stage IV cancers have spread (metastasized) to other areas of the body such as the liver, lungs, colon, pancreas, or bone. Approximately one-third of renal cell carcinomas have already metastasized by the time of diagnosis.

The average five-year survival rate for all stages of renal cell carcinoma combined is more than 60 percent. The five-year survival rate is very low once the cancer has spread to distant organs. Survival is considerably higher when the cancer is detected early; many of these patients often go on to live long, healthy lives.

Diagnostic imaging, the use of electromagnetic radiation and certain other technologies to produce images of internal structures of the body for the purpose of accurate diagnosis. Diagnostic imaging is roughly equivalent to radiology, the branch of medicine that uses radiation to diagnose and treat diseases. However, other technologies—including ultrasound, which employs sound waves to visualize tissues, and endoscopy and similar methods in which a flexible optical instrument is equipped with a camera for imaging—may also be used.

X-ray imaging

X-rays, used since 1895, were the first type of radiation to provide images of the interior of the body. X-rays pass through bodily tissues and also have the property of darkening photographic film when they strike it. As they penetrate tissues, the X-rays are absorbed differentially, with denser objects such as bones absorbing more of the rays and thus preventing them from reaching the film. Soft tissues, on the other hand, absorb fewer rays; the result is that in an X-ray photograph of the interior of the body, bones show up as lighter areas and soft tissues show up as darker ones on the exposed film.

A limiting factor in X-rays when used alone is the inability to distinguish between adjacent, differentiated soft tissues of roughly the same density (i.e., it is not possible to produce contrasting tones between such objects on the exposed film). To obtain this contrast, a contrast medium—a liquid or gaseous substance that is comparatively opaque to X-rays (radiopaque) or comparatively transparent to them—is injected into the body. Contrast-medium fluids can be injected into naturally occurring body cavities, injected into the bloodstream and lymphatic vessels, swallowed or introduced by enema for study of the digestive tract, or injected around organs to show their external contour. Different contrast media thus allow the X-ray imaging of particular types of soft internal structures, such as the arteries and veins in angiography, the passage of blood through the heart in angiocardiography, the gallbladder and biliary channels in cholecystography,

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the spinal cord in myelography, and the urinary tract in urography. Virtually any part of the body can be examined for physiological disturbances of the normal structures by X-ray analysis. X-ray motion-picture films can record the body processes as the contrast media enter and leave parts of the body.

Other imaging techniques have been developed using X-rays. In tomography, X-ray images of deep internal structures can be obtained by focusing the rays on a specific plane within the body. A more complex variation of this technique is computed tomography, known as a CT scan.

Nuclear medicine

The scanning of radioactive isotopes that have been injected into the tissues is a medical specialty called nuclear medicine. Both isotope scanning and X-ray photography are used in brain scanning. An imaging technique related to isotope scanning is positron emission tomography. Another type of diagnostic imaging is nuclear magnetic resonance, which creates images of thin slices of the body using very-high-frequency radio waves. Ultrasound is a technique in which high-frequency sound waves are used for detecting abnormalities in internal organs. The varieties of radiation that are used in diagnostic imaging continues to expand, along with the techniques for using them.

Endoscopy and related procedures

Procedures such as endoscopy, laparoscopy, and colposcopy make use of generally flexible optical instruments that can be inserted through openings, either natural or surgical in origin, in the body. Many scope instruments are fitted with small video cameras that enable the physician or surgeon to view the tissues being examined on a large monitor. A number of scopes also are designed to enable tissue biopsy, in which a small sample of tissue is collected for histological study, to be performed in conjunction with visual analysis.

Treatment

Unlike many other cancers, renal cell carcinoma generally does not respond well to chemotherapy or radiation. Therefore, surgery is usually necessary. A nephrectomy, or removal of kidney tissue, is the most common procedure. Partial nephrectomy removes only a portion of the kidney, while the more common radical nephrectomy removes an entire kidney plus the adrenal gland. Often local lymph nodes are also removed.

Although chemotherapy and radiation treatments are generally not effective in curing renal cell carcinoma, they may be used in conjunction with surgery or in cases where, because of generally poor health, surgery is not indicated. In addition, targeted therapies, such as temsirolimus and everolimus, may be used to treat advanced renal cell carcinoma, and biological therapies involving the immune system may be used to combat the disease in its various stages.

Chemotherapy, the treatment of diseases by chemical compounds. Chemotherapeutic drugs were originally those employed against infectious microbes, but the term has been broadened to include anticancer and other drugs.

Until the end of the 19th century, most drugs were derived either from minerals or from plants. The researches of Louis Pasteur in France and Robert Koch in Germany laid the foundations of bacteriology. It was Paul Ehrlich, however, who made the greatest contribution to the science (chemotherapy) he named. The problem facing medical scientists was to produce a disinfectant that would destroy parasites within a living animal without serious damage to the host.

William H. Perkin, in England, made the first aniline dye (1856) as a result of abortive attempts to synthesize quinine, the sole antimalarial drug available at that time. About 30 years later, Ehrlich found that a synthetic dye, methylene blue, has antimalarial properties. He had been led to this by a study of the specific staining of organs of an animal or of a parasite following the injection of a

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synthetic dye. From these studies there emerged (1901–04) Ehrlich's well-known "side-chain" theory, in which he sought for the first time to correlate the chemical structure of a synthetic drug with its biological effects. In 1903 Ehrlich invented a dye, trypan red, which was the first drug to show activity against trypanosomal infections in mice. Ehrlich's greatest triumph, however, was the discovery (1910) of the organic arsenical drug Salvarsan, which proved to be effective in the treatment of syphilis. The discovery of other chemotherapeutic agents followed, including mepacrine, proguanil, and chloroquine. The discovery of Prontosil in the early 1930s proved that antibacterial agents could be developed. Prontosil was the forerunner of the sulfonamide drugs, which came to be widely used for the treatment of bacterial infections in humans and domestic animals.

The discovery of penicillin by Sir Alexander Fleming in 1928, and its practical development by Sir Howard Florey and Ernst Chain, marked another important advance in bacterial chemotherapy. Penicillin, which did not become widely used until World War II, was the first of the so-called antibiotics, and it was followed by other important antibiotics such as streptomycin, the tetracyclines, and the macrolides.

Antibiotics, whether they are produced by living organisms (usually fungi or bacteria) or artificially synthesized, have transformed the modern management of diseases caused by bacteria and most other microorganisms. Paradoxically, the more widely they are used, the greater the likelihood that drug-resistant bacteria will emerge. Bacteria may develop resistance to drugs in several ways: mutation changes in genetic composition; transduction, whereby resistance is transferred from a resistant to a nonresistant strain; transformation, in which a bacterial cell takes from its environment the genes from a resistant form to acquire resistance; and conjugation, in which the organism acquires resistance by cell-to-cell contact.

Drug modes of action vary. For example, some may act on the bacterial wall, others affect cell membranes, some modify the molecular mechanism for duplication, some change the nucleic acid metabolism, and others change the intermediary metabolism of two interacting organisms.

Cancer chemotherapy is an increasingly important aspect of drug treatment. Alkylating agents (that work by impairing cell division) and antimetabolites (that interfere with enzymes and thus block vital cell processes) are used cytotoxically to attack malignant cells. Steroid hormones are used in the treatment of breast and prostate cancers, and corticosteroids are used to treat leukemia and lymphatic cancers. The periwinkle plant derivatives vincristine and vinblastine have been used effectively in treating Hodgkin's disease and leukemia.

The alkylating agents and antimetabolites have serious drawbacks. As they cannot distinguish between healthy and malignant cells, these drugs also interfere with actively multiplying noncancerous cells. They also reduce the body's resistance to infection. Work is being done on tumour-specific agents that attack only cancer cells.

Another area where chemotherapy has had a major, albeit controversial, impact is mental illness. Severe depression, anxiety, and schizophrenia are now treated with various drugs.

Concomitant with the successes of drug therapy has come increasing concern about attendant dangers. Stringent controls are operated by such regulatory agencies as the Food and Drug Administration in the United States and the Committee on Safety of Medicines in the United Kingdom. These bodies ensure the safety of pharmaceuticals before they are placed on the market and monitor any side effects thereafter. Public demands for "watchdog" agencies were triggered in large part by the 1962 Thalidomide tragedy, when thousands of severely deformed children were born to users of that insufficiently tested drug.

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