Renal Cell Carcinoma Characteristics

Renal Cell Carcinoma (RCC) is a type of kidney cancer. The pathophysiology commonly involves a defect in the VHL gene on chromosome 3. This cancer affects the cells of the proximal convoluted tubule. Risk factors include smoking, nephrolithiasis, and chronic analgesic use. RCC has several notable subtypes including clear cell, papillary, and chromophobic.

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Pathophysiology

Chromosome 3

Chromosome (3) Tree

Alteration of the short arm of chromosome 3 is the most common chromosomal abnormality seen in renal cell carcinoma, especially in the clear cell subtype. Other less common chromosomal aberrations include include trisomy of chromosomes 7 and 17 or loss of the Y chromosome (papillary subtype). Loss of multiple chromosomes (1, 2, 6, 10, 13, 17, and 21) is seen in the chromophobic subtype of renal cell carcinoma.

VHL Gene

Van-hippo Landing-owl

The VHL tumor suppressor gene's inactivation is commonly seen in renal cell carcinoma (25-45% of clear cell carcinoma cases). It can also be associated with tuberous sclerosis (2% of cases of clear cell subtype). VHL gene mutation is found in Von Hippel-Lindau Disease, which is characterized by multiple tumors: renal cell carcinoma, hemangioblastomas, and pheochromocytomas.

Proximal Convoluted Tubule

P-rocks at Opening of Tube

Renal cell carcinoma most commonly arises from proximal convoluted tubule epithelium. However, other kidney segments can also be involved, including distal tubular epithelium (associated with papillary RCC) and intercalated cells of the collecting duct (associated with chromophobic RCC).

Risk Factors

Smoking

Cigarette

Smoking increases the risk of developing renal cell carcinoma. It has a dose-dependent impact. Other toxins like asbestos, heavy metal, and petroleum by-products may increase RCC risk.

Nephrolithiasis

Kidney-throwing Stones

Nephrolithiasis is associated with chronic inflammation and infection, which triggers an alteration in the proliferation of urothelial cells. This can progress to malignancy and explains the increased risk of renal cell carcinoma found in patients with recurrent nephrolithiasis.

Chronic Analgesic Use

Crone A-nail-Jay-Z

Chronic analgesic use, including acetaminophen and non-aspirin NSAIDs, is shown to increase renal cell carcinoma risk. It is expected that the metabolites of these drugs are carcinogenic, but more investigation is needed to understand its biological association. Other renal cell carcinoma risk factors may include hypertension and obesity.

Subtypes

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Clear Cell

Clear Cell

Renal cell carcinoma can be classified based on its cell origin: clear cell, papillary, and chromophobic. Clear cell carcinoma arises from proximal renal tubules and can be found in 85% of cases. Gross findings include a sphere-like mass formed by golden-yellow tissue with focal hemorrhage and necrosis. Microscopic findings include polygonal cells with abundant clear cytoplasm and small nuclei.

Papillary

Paper

Papillary renal cell carcinoma arises from the distal tubular epithelium and is found in 10-15% of all renal cell carcinoma cases. Gross findings include a well-circumscribed and grayish-white mass with frequent hemorrhages and central necrosis. Microscopic findings are divided into two main subtypes. Both subtypes are characterized by papillae with a central fibrovascular core (true papillae) containing foamy histiocytes lined by a single layer of cells. Type 1: basophilic cytoplasm and Type 2: abundant eosinophilic cytoplasm.

Chromophobic

Chrome

Chromophobic renal cell carcinoma arises from intercalated cells of the collecting duct and is found in about 5% of all renal cell carcinoma cases. The tumor can be seen with one or more nodules with a lobulated surface. Microscopic findings are characterized by large, chromophobic polygonal cells which can be hard to differentiate from oncocytoma.

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