Chapter 20

ANTİANGİOGENİC AND MOLECULARLY TARGETED THERAPY FOR ADVANCED STAGE CLEAR-CELL RENAL CELL CARCİNOMA

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INTRODUCTİON

Kidney cancer accaunts for approximately 2% of malignancies worlwide 425000 cases diagnosed per year and 137000 deaths(1). Renal cell carcinomas(RCC), originate from renal cortex and %75-80 of these tumors are clear cell carcinomas. There are several distinct subtypes of RCC. Approximately 75 to 85 percent of RCC are clear cell tumors(2-3).other important subtypes include papillary (chromophilic), chromophobe, collecting duct, and medullary carcinomas, as well as oncocytomas. These subtypes including clear cell, have unique genetic abnormalities and gene expressions patterns (4-5). Pathogenesis ofclear cell carcinoma is the best understood.

MOLECULER PATHOGENESİS

Clear cell RCC occurs in sporadic or inherited forms. Von Hippel-Lindau (VHL) disease is the most studied hereditary form of RCC. VHL disease is an autosomal dominant inherited multisystem neoplastic disorder that is characterized by clear cell renal tumors,central nervous system hemangioblastomas, retinal angiomas, tumors of the adrenal gland (pheochromocytoma) and cysts in the pancreas and kidney. VHL occurs in about 1 in 36,000. İn patients with VHL %30 percent develop bilateral, mutifocal renal tumors with clear cell histology. These renal tumors can have metastatic potential when they reach 3 cm (6).

Somatic mutation of the VHLgene is found in up to 92% of tumors from patients with clear cell kidney cancer (7). VHLgene mutation is not found in other subtypes (papillary, chromophobe, collecting duct, medullary, or other types). Becouse of this abnormalityvascular endothelial growth factor (VEGF) is overproduced. InRCC and many other cancers, VEGF plays a significant role. VEGF is tehe most important growth factor that involved in tumor anjiogenesis.

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