COMPREHENSIVE ANALYSIS FOR MUTATIONS IN A PATIENT WITH RENAL CELL CARCINOMA AND ADPKD

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Case Study: Renal cell carcinoma (RCC) is known to be more prevalent in autosomal dominant polycystic kidney disease (ADPKD) patients compared to the general population. The genes such as VHL, PBRM1, SETD2, KDM5C, PTEN, BAP1, MTOR, and TP53 are represented as significantly mutated in RCC. Whole exome and transcriptome sequencing was performed for paired RCC, normal kidney tissue, and peripheral blood (paired triple set) from a patient diagnosed with ADPKD and RCC. An 68-yr-old male with ADPKD came to the hospital for managing a left renal incidental mass found in the computed tomography (CT) scan. A 2.4x2.7x2.7cm early-enhanced-washout nodule was seen at the left kidney interpolar area, and was suspected to be RCC. The patient underwent left partial heminephrectomy and was indeed diagnosed with RCC. DNA from his blood, tissue from the tumor, and ADPKD tissue were extracted. The stop-gained mutation in PKD2 (p.Arg742Ter), which is well known as a pathogenic variant at ADPKD, was identified in the paired triple set. For the tumor, the somatic missense VHL mutation (p.Ser65Leu) was found, which known as pathogenic at Von Hippel-Lindau syndrome. As for the somatic copy number alterations, loss of chromosome 3p, which is the most commonly involved pattern (frequency: 91%), was detected. In the RNA expression, angiogenesis seems to have been upregulated in the VEGF signaling pathway. In the event of a twofold change in the expression of HIF1A in the tumor compared to the normal proliferation, the expression should be activated by the MAPK signaling pathway, including NRAS and MAPK1 expression. In summary, we identified PKD2 germline stop-gained mutation and characterized VHL somatic missense mutation with 1 copy deletion at chromosome 3p in DNA level as well as up-regulation of MAPK and VEGF signaling pathway in RNA level on RCC from an ADPKD patient.

Figure 1. A 2.4 x 2.7 x 2.7cm sized, early enhanced-washout nodule was seen at left kidney interpolar area, suspected renal cell carcinoma
Figure 2. The renal cell carcinoma with negative margin was identified in the frozen section biopsy performed during the operation.