Pancreatic Neuroendocrine Tumors in VHL Disease

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Pancreatic lesions in patients with VHL disease can manifest as simple pancreatic cysts, serous cystadenomas and pancreatic neuroendocrine tumors (pNET). More than 60% of the VHL patients have at least one type of pancreatic lesion. In most cases VHL-associated pNET are nonfunctional and do not demonstrate hormonal hypersecretion. Chromogranin A can be useful especially in follow-up, but its specificity is low. At the age of 40 at least 50% of the patients has a pancreatic manifestation in the majority pancreatic cysts. The natural history of VHL-associated pNETs varies between nonlinear tumor growth, stability and sometimes decrease of the lesion, without identifying factors responsible for tumor behavior. We have shown that endoscopic ultrasound (EUS) is superior to CT/MRI + Somatostatin receptor scintigraphy for detecting pancreatic solid lesions in VHL disease. Although the EUS performs well in early detection of pNETs, its role in VHL standard surveillance is unclear. The optimal surveillance for pancreatic NET has not been established yet. But it has already shown that the presence of a exon 3 germline mutation increases the risk on malignant potential. The treatment of pNET has to be balanced with the presence and progression of the multiplicity of the other non-pancreatic VHL-associated tumors. Surgery should be considered for pNETs larger than 2-3cm or with a doubling time of <500 days. Local lymph node or distant metastases have been reported in 13% of patients with a pNET. In general, guidelines for sporadic pNET are also used for VHL-associated metastatic pNET. Surgical resection should be considered if more than 90% of tumor burden can be resected and risk of peri-operative mortality is low. First-line medical treatment for progressive metastatic low-grade pNET is a somatostatin analog. Currently no preference exists for second-line treatment and the choice between PRRT with Lu177-DOTATATE, everolimus, sunitinib or chemotherapy is mainly based on tumor and patient characteristics.