Metastatic Recurrent Small Bowel "Carcinoid": The Role of Blood Neuroendocrine Transcript Analysis in Diagnosis and Management

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Background: A key issue in managing small bowel NETs is detection of disease progression. In most centers, plasma Chromogranin A is used in conjunction with imaging. We report a multi-transcript (n=51 gene) molecular signature for PCR-blood analysis with high sensitivity and specificity (>85%) for GEP-NETs. The PCR score was compared with CgA and imaging in the 5-yr follow-up of a well-differentiated NET GII, T3, N2, M1 small bowel NET.

Methods: Serial blood samples (2008-2013; n=14) were analyzed for CgA (ELISA-DAKO), qPCR performed and transcripts scored. Biomarker measurements were compared to clinical status and imaging (CT/MRI, Octreoscan, PET-CT).

Results: R0 resection (2001) resulted in a PFS of 3 years before ^{11}C-5HTP-PET/CT detection of SI mesenteric lymph node recurrence; re-resection (x2) was undertaken (2005, 2006). CgA and U-5HIAAs were normal. In 2008, ^{11}C-5HTP-PET-CT identified a solitary liver metastasis. Although both CgA and U-5HIAA were normal, the PCR score was elevated. After cryotherapy, PCR scores decreased (30%) but remained abnormal. PCR scores were further elevated (40%) two months prior to ^{11}C-5HTP-PET-CT detection of recurrence in 2009 when five small (<1cm) NELMs and a rib lesion were noted. CgA was transiently elevated (29U/ml). Treatment with Sandostatin LAR 20mg (monthly) was associated with disappearance of metastases. PCR scores were normal in 2010 and PET-CT identified no disease at that time. In 2011, progressively increasing PCR score were noted (2-8); the highest score was concordant with elevated U-5HIAA (CgA normal). ^{86}Ga-DOTATOC-PET/CT identified recurrence in the liver (2013). CgA levels were normal, PCR was elevated (3).

Conclusion: PCR scores were more sensitive than CgA in identifying neuroendocrine lesions. Elevation was evident prior to image-based tumor confirmation. Multi-transcript NET gene panel measurements in blood are more sensitive and specific than CgA in the diagnosis and management of NETs and may have utility as an index of therapeutic efficacy.