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Risk Factors for Sporadic Pancreatic Neuroendocrine Tumors (PNETs): A Single-Center Case Control Study

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Background: Previous analyses have demonstrated that the grade of tumor correlates well with OctreoScan positivity, with lower grade tumors more likely to be positive. We hypothesized that tumor location, grade, Chromogranin A and SST2 immunohistochemical staining will correlate with Octreotide positivity.

Methods: We retrospectively analyzed 37 tumor specimens for tumor grade according to the Wick's grading system of: 1-Well differentiated, 2-moderately differentiated, and 3-poorly differentiated, immunohistochemical staining (IHC) for SST2 receptor, and correlation with OctreoScan imaging. SST2 and Chromogranin A IHC stains were performed and graded 1 +, 2+ or 3+.

Results: There were a total of 40 patients, but only 37 tumor specimens were available for complete analysis by their Wick's grade 1, 2, 3: 13/37, 11/37 and 13/37 respectively. Wick's grade 1: 39% (5/13) were negative and 61% (8/13) positive by OctreoScan imaging. Primary tumor status revealed 77% (10/13) samples were of small bowel and colorectal origin with 54% (7/13) being positive by OctreoScan. The remaining tumor primaries were two pulmonary neuroendocrine and one gastric carcinoid, with all being negative by OctreoScan imaging. Specimens with a Wick's grade 2: 45 % (5/11) were negative and 55% (6/11) positive by OctreoScan imaging. Tumor primaries comprised 36% (4/11) of small bowel and colorectal origin and 18% (2/11) pancreatic neuroendocrine with 50% and 100% respectively being positive by OctreoScan. Those with a Wick's grade 3: 18% (2/11) were negative and 82% (9/11) positive by OctreoScan imaging with 8/11 being of pancreatic neuroendocrine origin. Of the pancreatic neuroendocrine tumors 7/8 were positive by OctreoScan. Of the tumor specimens with 2-3+ staining for STT2, 36% (9/25) had negative OctreoScan and 64% (16/25) were positive. Of those with STT2 IHC 1+ stain, 22% (2/9) and 78% (7/9) were negative and positive respectively by OctreoScan. Of those with a negative SST2 IHC stain 40 % (2/5) and 60% (3/5) were respectively negative and positive by OctreoScan imaging. All tumor specimens had a positive Chromogranin A IHC stain of 1, +, 2+ or 3+. There were 33 specimens 2-3+ by IHC of which 30% (10/33) and 67% (22/33) were respectively negative and positive by OctreoScan with 1 unavailable for analysis. The 3 samples with a Chromogranin A IHC stain of 1+ were all positive by OctreoScan.

Conclusion: In our retrospective analysis a total of 62% (23/37) of the tumor specimens demonstrated OctreoScan positivity, with 90% of pancreatic neuroendocrine tumors being positive. Chromogranin A and SST2 immunohistochemical staining of 2-3+ appeared to correlate with OctreoScan results, but were neither sensitive nor specific. Although published reports have demonstrated a correlation with OctreoScan positivity with lower grade neuroendocrine tumors, our results demonstrate that pancreatic neuroendocrine tumors were most often of a higher grade and consistently OctreoScan positive.