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Primary Gastro-entero-pancreatic Poorly Differentiated Neuroendocrine Carcinoma: Clinico-pathologic and Survival Analysis in 68 Cases

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Background: Primary gastro-entero-pancreatic poorly differentiated neuroendocrine carcinomas (GEP-PDNECAs) are highly aggressive neoplasms with a very poor prognosis. This study was conducted to evaluate the immuno-morphological spectrum of GEP-PDNECA, and survival in patients treated with systemic platinum and etoposide.

Methods: Clinico-pathologic and survival data were analyzed on 68 adult patients with GEP-PDNECA who had undergone biopsy / resection at MCC or outside institution. Data sources: Pathology archives, consultation files, tumor registry and social security index. All available slides were reviewed independently by two pathologists and tumors were histologically sub-typed.

Results: Patients: 41 M/27 F. Age: 25-76 yrs (mean 42 yrs). Sites: Colo-rectum 39, pancreas 19, small intestine 4, stomach 3, colon/small-intestine/pancreas 3. Sixty-three of 68 (93%) patients presented with lymph node/distant metastases. 37/68 (54%) tumors were classified as small cell carcinoma (SCCA), 16/68 (24%) large cell carcinoma (LCCA), 5 (7%) mixed small and large cell (MSLCCA) and 10 (15%) poorly differentiated carcinoma with neuroendocrine features (PDCA-NEF). Tumors were positive for chromogranin in 38/65 (55%), synaptophysin in 62/67 (92%), and CD56 in 17/21 (81%) cases. Fifty-eight of 68 (85%) patients were treated with platinum and etoposide. Overall survival at 1, 3 and 5 years was 85%, 40% and 24% respectively. Patient survival was independent of age (r= 0.1022), sex (r= -0.909) and histologic subtype (r=0.1028) (p= 0.128) but was related to distant metastases (r=0.306; p=0.0383).

Conclusions: Diagnosis of GEP-PDNECA can be based on histo-morphologic features and expression of neuroendocrine markers. Because of variable immunoreactivities of basic markers of neuroendocrine differentiation, a multi-marker neuroendocrine diagnostic panel will be prudent to avoid under-diagnosis of GEP-PDNECA, especially in the metastatic setting. Although survival of GEP-PDNECA patients following platinum and etoposide therapy in our series was relatively favorable, it will be critical to identify novel therapeutic targets/biomarkers to improve patient survival in these clinically aggressive neuroendocrine cancers.