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A biomarker and immunomarkers approach for the diagnosis of poorly differentiated neuroendocrine carcinoma

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Background: Pathologic evaluation of tumor tissue is the key for establishing a correct diagnosis and for selecting the appropriate therapy for patients with poorly differentiated neuroendocrine carcinoma (PDNECA). Here, we evaluated the role of histopathology and immunohistochemistry in the diagnosis and subclassification of primary PDNECAs at a single institution with multidisciplinary expertise in neuroendocrine oncology. Methods: Clinico-pathologic data from 80 adult patients, aged: 25-76 yrs (mean 42 yrs years), Patients: 51 M/29 F, with primary PDNECA of the lung 42, colon 33, pancreas 19, gall bladder 3, liver 2 and miscellaneous 17 who had undergone biopsy/resection at our institution were included. Data were collected from pathology archives, consultation files, tumor registries, and social security indexes. All available slides were independently reviewed by 3 pathologists for histological subtyping and immunohistochemical evaluation of each case.

Results: Histopathology was adequate for diagnosing pure small cell (SCCA) and large cell neuroendocrine carcinoma (LC-NECA). Immunohistochemistry was useful in supporting the diagnosis of PDNECA. Overall, chromogranin, synaptophysin, NSE, and CD56 were positive in 44/75 (60%), 72/77 (94%), 24/28 (88%), and 22/25 (88%) cases, respectively. Immunoreactivities for other markers for primary PDNECAs from various organs were as follows: TTF-1, 16/24 (67%) pulmonary and of 0%for nonpulmonary; α-fetoprotein (AFP), 2/2 (100%) in hepatic vs. non-hepatic; anti-cytokeratin (CAM 5.2), 16/19 (85%) pancreatic, 5/6 (83%) pulmonary; CK-7, 15/19 (79%) pancreatic and.83% Pulmonary vs. 28-50% in non-pancreatic/pulmonary/colonic, CDX2 was 100% in small intestine primaries and 100% negative in pancreatic and Gall Bladder NEC, carcinoembryonic antigen (CEA), 5/5 (100%) colonic; CK20, 23/27 (85%) colonic. Ki-67 index ranged from 20-70% (median: 45%). There was a strong correlation between mitotic count and Ki-67 index (*r +0.953*).

Conclusions: Histopathology can be used to subclassify PDNECA cases into small-cell, large-cell, and mixed small and large cell subtypes, as well as other histological subtypes. However, for patients with PDNECA of unknown origin, a panel of immunohistochemical markers (TTF1, CK7, CK20, and CDX2) may be helpful in pointing toward the primary site. Practical utility of AFP to differentiate between primary hepatic and extra-hepatic PDNECA merits further investigation.

Biography

Dr Bukhari completed his doctorate in Surgical Pathology with the theoretical and practical combination of Histopathology, Immunohistochemistry and PCR at the King Edward Medical University in 2007. After his doctorate he attended the special course of Breast Pathology in Harvard School of Public Health in 2009. He has started work with Prof Abbas Iqbal and Eyyad H A Kamel on Chemothearpeutic effect of Sanatinib.e in triple negative patients and HER 2 Positive cases.