Different patterns of chromogranin A and Leu-7 (CD57) expression in gastrointestinal carcinoids: immunohistochemical and confocal laser scanning microscopy study*

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Thirty-seven carcinoids of the gastrointestinal tract were studied with immunohistochemical staining for chromogranin A (CgA) and Leu-7 (CD57). The aim of this study was to distinguish and describe the differences in patterns of distribution of immunostaining of these two non-specific neuroendocrine markers in neuroendocrine tumors of different degree of differentiation (typical, vs. atypical carcinoids) at different gastrointestinal sites. Selected 5 tumors from this group were studied in detail using confocal laser scanning microscopy (CLSM) and double immunofluorescence staining to disclose the patterns of distribution of CgA and CD57 positive granules within the individual tumor cells. Prominent differences in the patterns of immunohistochemical staining for both studied markers related to the degree of differentiation of the tumors were observed in studied neoplasms. Regular (diffuse) strongly positive immunoreaction for CgA predominated in typical carcinoids, whereas atypical tumors were characterized by irregular patchy staining. Both typical and atypical tumors displayed predominantly irregular patchy staining for CD57. The results of CLSM study indicate that different modes of CgA and CD57 expression and/or co-expression can occur in neuroendocrine tumors. Neoplastic cells that contained either CgA positive neuroendocrine granules (NEG), or Leu-7 positive NEG, were frequently observed in different areas of the tumor samples, especially in atypical carcinoids. Varying number of cells revealed co-localisation of both CgA and Leu-7 within the NEG. Similar co-localisation of CgA and CD57 was found in non-neoplastic Kultschitski cells of the mucosa of small intestine. In conclusion, our results suggest that the differences in CgA and CD57 expression in human neuroendocrine tumors are related to the degree of differentiation of the neoplasms and probably reflect the degree of maturation (functional state) of neuroendocrine granules within the neoplastic cells.

Key words: Gastrointestinal carcinoid, chromogranin A, Leu-7 (CD57), immunohistochemistry, confocal laser scanning microscopy.

Neuroendocrine tumors of gastrointestinal (GI) tract represent a group of relatively rare malignant epithelial neoplasms characterized by less aggressive biological behavior compared to GI carcinomas, distinctive histological appearance and by expression of markers suggesting neuroendocrine differentiation of neoplastic cells [8, 23]. The histogenetic background of these tumors has not been clarified yet, however, the origin of these tumors from enterochromaffine epithelial cells, which belong to amine precursor uptake and decarboxilation system (APUD) or diffuse neuroendocrine system (DNES) is widely accepted [1, 15]. Several markers of neuroendocrine differentiation are recently conventionally used in histological diagnosis and characterization of neuroendocrine tumors [6, 13, 16, 22]. Among them, chromogranin-A (CgA) and Leu-7 (CD-57), proteins, located in the core of neuroendocrine granules (NEG), have a special significance [9, 17, 20, 25]. Never-

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