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FEATURES OF THE IMMUNOHISTOCHEMICAL DIAGNOSTICS OF NEUROENDOCRINE TUMORS

ABSTRACT. Background. The possibility of neuroendocrine tumor (NET) development from almost any organ causes problems in determination of a true primary site after detection of such metastases in lymph nodes or liver. It impels to consider the expression of immunohistochemical organ-specific markers such as cytokeratin (CK) along with the morphological characteristics. **Objective.** Determine the immunophenotype of neuroendocrine tumors of different localizations. **Methods.** Material from 52 patients (30 women and 22 men) aged 31 to 79 years (median 57 years) had been retrospectively analyzed during Jan 2012 – Oct 2014. Material included NET of different localization (9 cases in stomach, 7 in lung, 5 in colon, 3 in small intestine, 3 in larynx, 3 in mammary gland, 2 in pancreas, 1 in cervix and 1 in uterus body) or its metastasis from an unknown primary site (12 in lymph nodes, and 6 in the liver). CK Pan (clone AE1/AE3), Chromogranin A (CHR A) (clone LK2H10), Synaptophysin (SYN) (clone SYP02), CD95 (clone AB3), CK 7 (clone OV-TL 12/30), Vimentin (VIM) (clone V9) were used as a primary monoclonal antibodies. **Results.** 96% of cases have turned out to be CK Pan+, except 2 (3.8%) NET with a localization in lymph nodes. 84.6 % of tumors expressed SYN, except 2 (22.2%) in stomach, 1 (14.3%) in lung, 1 (100%) in uterus body, 3 (25%) in lymph node and 1 (16.7%) in liver metastasis. 82.7% gave a positive staining for CHR A, except for 3 (60%) in colon, 1 (33.3%) in small intestine, 1 (11,1%) in stomach , 3 (25 %) in lymph nodes metastases (both of which are NET with CK Pan-) and 1 (16.7%) of liver metastases. VIM+ were only 4 cases (both of which are NET, 1 (100%) of uterus body and 1 (16.7%) of liver metastasis). Positive cases of CK 7 expression were 6 (66.7%) in stomach NET (all carcinoids), 3 (42.9%) in lung, 1 (20%) in colon, 1 (33.3%) in larynx, 2 (16.7%) in lymph node and 2 (33.3%) in liver metastasis. **Conclusions.** The most common NET phenotype of these localizations is CK Pan+, CHR A+ and/or SYN+, CD95+, VIM-. Expression of CK 7 is intermittent and can not be used to reliably determine the primary site of NET.

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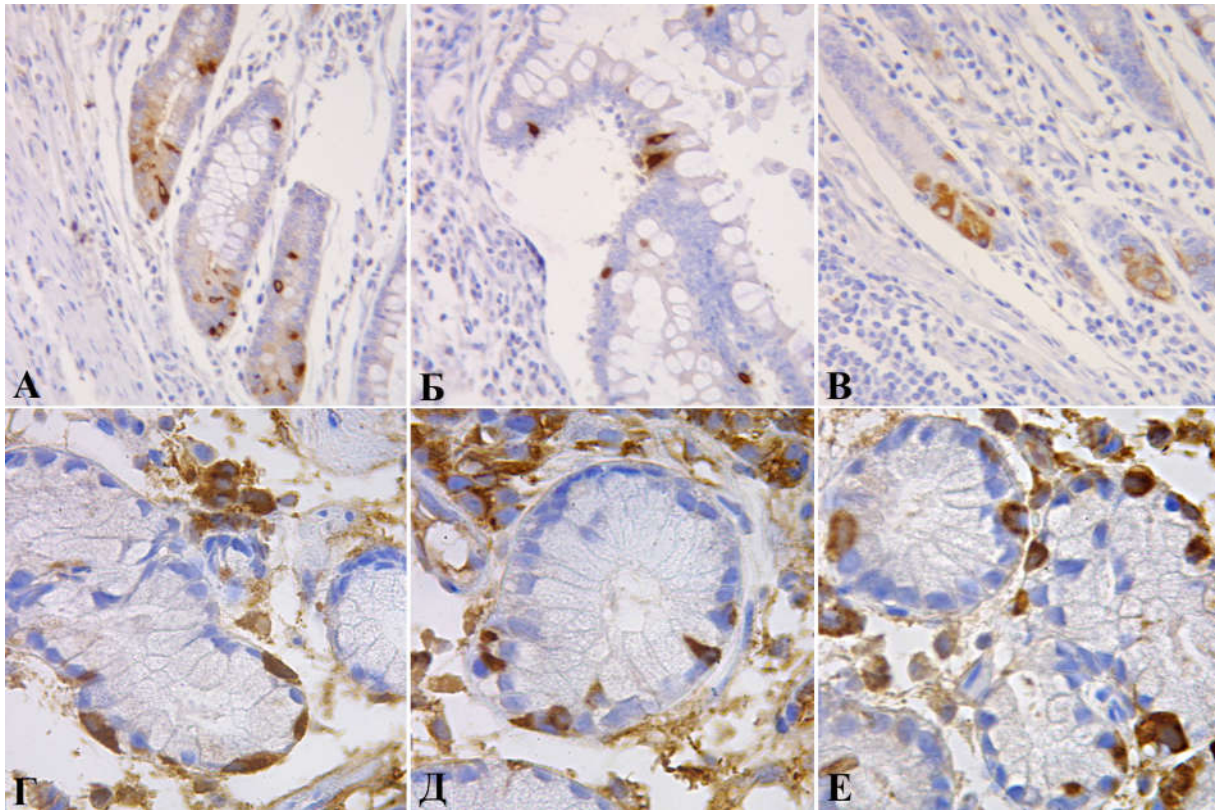


Fig. 1. Neuroendocrine cells in gastrointestinal tract (internal control), intensive cytoplasmic reaction with Synaptophysin marker, immunohistochemical method, counterstain with Mayer's hematoxylin. A. Numerous ones among epithelial cells of glands ($\times 200$). Б. In mucosa, with elongated processes reaching the gut lumen ($\times 200$). В. Polymorphous ones with secretory granules ($\times 200$). Г, Д, Е – Tumor cells of neuroendocrine origin around the glands with positive internal control. ($\times 1000$).

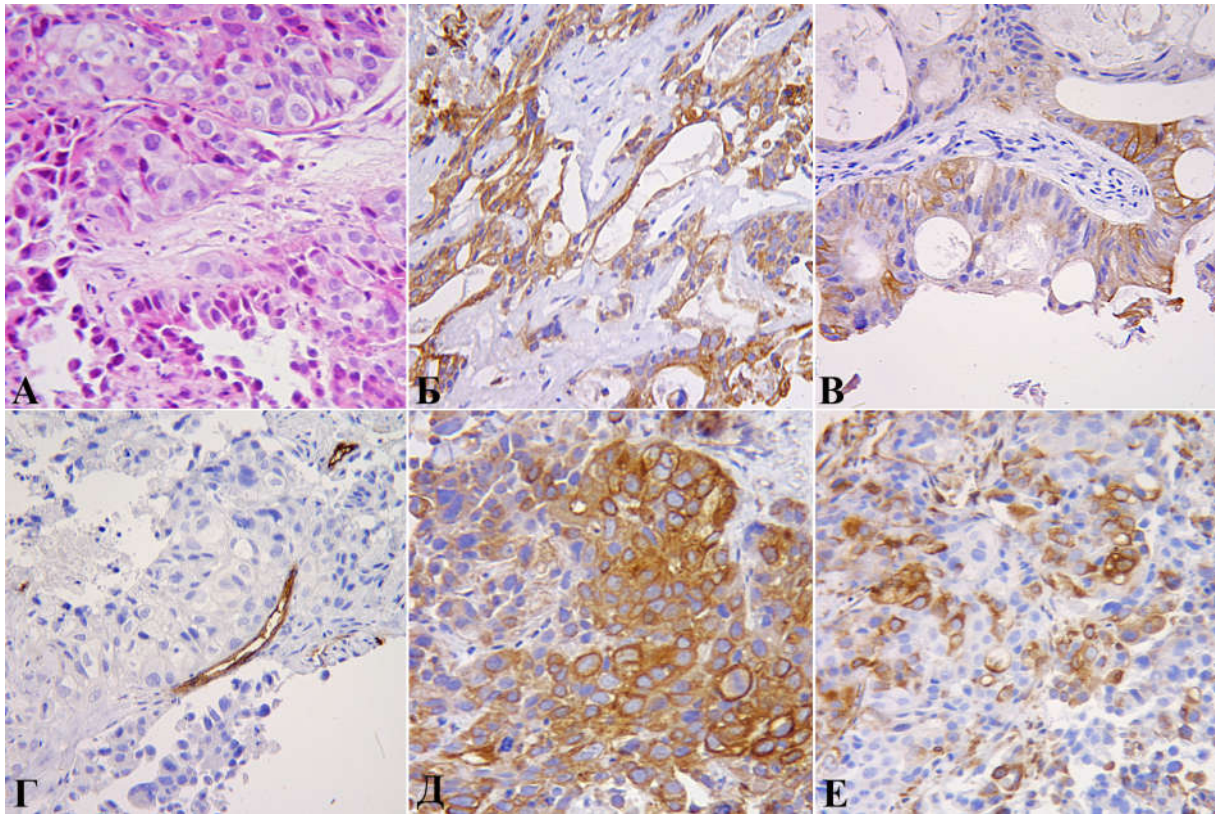


Fig. 2. A. Neuroendocrine carcinoma of gastrointestinal tract, Hematoxylin&Eosin staining, $\times 400$. Б. Cytoplasmic reaction of tumor cells with Cytokeratin Pan, immunohistochemical method, counterstain with Mayer's hematoxylin, $\times 400$. B'. Cytoplasmic reaction of a part of cells with Cytokeratin 7 marker, immunohistochemical method, counterstain with Mayer's hematoxylin, $\times 400$. Г. Negative reaction of tumor cells with Vimentin disproving their mesenchymal origin, immunohistochemical method, counterstain with Mayer's hematoxylin, $\times 400$. Д. Intensive cytoplasmic reaction of the majority of cells with Synaptophysin, immunohistochemical method, counterstain with Mayer's hematoxylin, $\times 400$. E Intensive cytoplasmic reaction of a part of cells with Chromogranin A, immunohistochemical method, counterstain with Mayer's hematoxylin, $\times 400$.

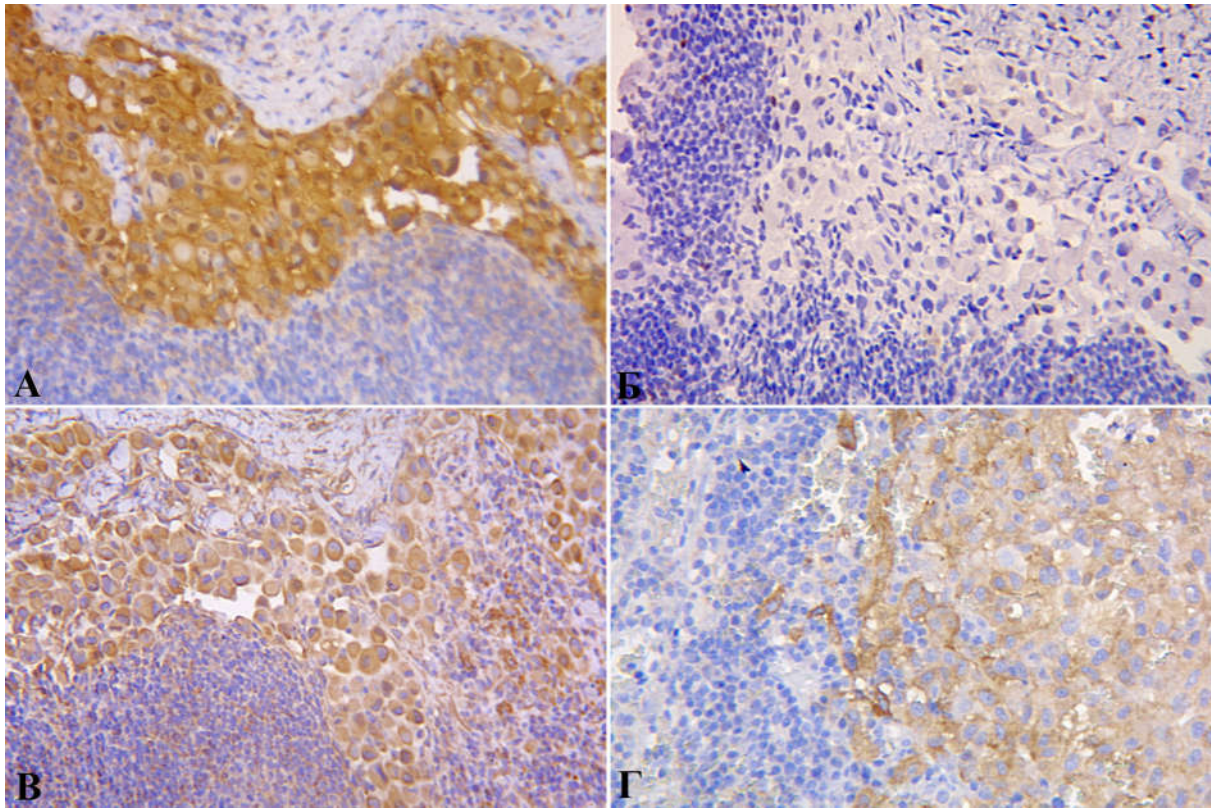


Fig. 3. A. Neuroendocrine carcinoma axillary lymph node metastasis without primary tumor, intensive cytoplasmic reaction of tumor cells with Synaptophysin, immunohistochemical method, counterstain with Mayer's hematoxylin, $\times 400$. Б. Negative reaction of tumor cells with Vimentin, immunohistochemical method, counterstain with Mayer's hematoxylin, $\times 400$. B. Moderate cytoplasmic reaction with Chromogranin A, immunohistochemical method, counterstain with Mayer's hematoxylin, $\times 400$. Г. Mixed membrane-cytoplasmic reaction of a part of cells with Cytokeratin 7 marker, immunohistochemical method, counterstain with Mayer's hematoxylin, $\times 400$.

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