Islet 1 (Isl1) expression is a reliable marker for pancreatic endocrine tumors and their metastases.

BACKGROUND: Tracing the origin of a metastasis of a neuroendocrine carcinoma is a challenge. The transcription factors Cdx2 and TTF1 have been found to be helpful in identifying well-differentiated neuroendocrine tumors of gastrointestinal and pulmonary origin, respectively. So far, such a marker is lacking for pancreatic neuroendocrine tumors (PETs) and metastases thereof. Islet1 (Isl1) is a transcription factor expressed in pancreatic islet cells. The aim of this study was (1) to test the specificity and sensitivity of Isl1 as a marker of PETs, and (2) to test the specificity and sensitivity of a panel of markers, including Isl1, Cdx2, and TTF1, for the localization of the primary. DESIGN: One hundred eighty-eight primary gastroenteropancreatic and pulmonary endocrine tumors and 49 metastases thereof were examined. Immunohistochemistry using antibodies directed against Isl1, Cdx2, and TTF1 was performed and the staining results were scored semiquantitatively. RESULTS: Isl1 proved to be a highly specific marker for pancreatic endocrine tumors. In 84 primary PET its specificity was 78.4% (sensitivity 74.3%) and in 18 metastases of PET the specificity reached 100% (sensitivity 77.8%). Strong Cdx2 staining showed a specificity for gastrointestinal origin of 83.9% (sensitivity 82%) in primary tumors and of 100% (sensitivity 40%)
in metastases. Including weakly positive tumors lead to a decreased specificity but an increased sensitivity. TTF1 expression was detected in 2 PET and 1 ileal primary tumor only and was absent in all metastases of gastroenteropancreatic endocrine tumors. CONCLUSIONS: Isl1 is a reliable marker of pancreatic endocrine tumors and metastases thereof. It shows a comparable sensitivity and specificity as Cdx2 as a marker of ileal and appendiceal neuroendocrine tumors and their metastases. TTF1 is very rarely expressed in well-differentiated gastroentero-PETs. Therefore, the panel of Isl1, Cdx2, and TTF1 seems useful for examining metastases of well-differentiated endocrine carcinomas of unknown origin.

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