Multiple Endocrine Neoplasia Type 1 (MEN1): Loss of One MEN1 Allele in Tumors and Monohormonal Endocrine Cell Clusters But Not in Islet Hyperplasia of the Pancreas.

Abstract:

Context: The occurrence of multiple small pancreatic endocrine tumors in patients suffering from multiple endocrine neoplasia type 1 (MEN1) represents a unique possibility to study early neoplasms and their potential precursor lesions. To date, it is unknown whether small islet-like endocrine cell clusters found in MEN1 patients are neoplastic or rather hyperplastic. It is also unclear whether microadenomas develop from islets.

Design: We hypothesized that monohormonal endocrine cell clusters observed in MEN1 patients are small neoplasms with loss of heterozygosity of the MEN1 locus. Using a technique combining fluorescence in situ hybridization of the MEN1 locus and the centromeric region of chromosome 11q with hormone immunostaining, we examined resection specimens from four MEN1 patients. We focused our investigations on the following: 1) typical microadenomas; 2) monohormonal endocrine cell clusters; 3) endocrine and exocrine structures entrapped in microadenomas; and 4) morphologically normal islets. Results: Loss of one MEN1 allele was found in all 27 microadenomas and 19 of 20 (95%) monohormonal endocrine cell clusters. By contrast, it was absent in islets and ductal or acinar structures. Our results indicate that monohormonal endocrine cell clusters
represent a minute form of microadenomas. Conclusion: The frequent presence of single nonneoplastic insulin cells in microadenomas and the occurrence of microadenomas in islets suggest an islet origin of microadenomas. Islet hyperplasia does not seem to be an obligatory stage in pancreatic MEN1-associated tumor development.