Allelic deletion of the MEN1 gene in duodenal gastrin and somatostatin cell neoplasms and their precursor lesions.

BACKGROUND: Patients with a multiple endocrine neoplasia type 1 (MEN1)-associated Zollinger-Ellison syndrome (ZES) show multifocal duodenal gastrinomas and precursor lesions. AIMS: To test these lesions for loss of heterozygosity (LOH) of the MEN1 gene locus on chromosome 11q13, and to investigate whether the MEN1-related endocrine cell changes also involved somatostatin cells.

Material and METHODS: Tissue specimens from six patients with MEN1 and ZES were analysed by immunohistochemistry and immunofluorescence. LOH analysis was performed by fluorescence in situ hybridisation (FISH), using probes containing the MEN1 gene locus and the centromere 11 (C11) region. For simultaneous analysis of hormones and allelic deletions, a combined FISH/immunofluorescence protocol was established. RESULTS: 28 of a total of 33 duodenal neuroendocrine tumours (NETs) were gastrin-producing tumours; 13/28 (46.4%) revealed LOH on 11q13 and/or C11. Five of the NETs were somatostatin-expressing tumours, two revealing LOH. Allelic loss was detected in tumours as small as 300 mum (gastrin) and 400 mum (somatostatin) in diameter. The gastrin-producing tumours showed different deletion/retention patterns. Hyperplastic somatostatin cell lesions,
similar to those of the gastrin cells, were present in all patients. The hyperplastic lesions of both cell
types consistently retained both 11q13 alleles. CONCLUSIONS: Allelic deletion of the MEN1 gene
may reflect a pivotal event in the development of multifocal gastrin and somatostatin cell neoplasms in
the duodenum of patients with MEN1. The observation of distinct deletion patterns in small
synchronous tumours supports the concept that each gastrin-producing tumour in an individual MEN1
patient arises from an independent cell clone.

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