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Case report

Zollinger-Ellison syndrome, duodenal carcinoid (Gastrinoma), and Hyperthyroidism

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Summary. A 43 year old man is presented who suffered from the association of a toxic adenoma of the thyroid gland and a Zollinger-Ellison syndrome (ZES) due to a metastasizing duodenal gastrinoma. There were no other signs of a multiple endocrine neoplasia syndrome, type I (MEN-I). The patient presented here shows that the association of ZES and thyroid disease may also occur in patients with sporadic ZES.

Key words: Zollinger-Ellison syndrome – Duodenal carcinoid – MEN-1 – Hyperthyroidism

Introduction

Involvement of the thyroid gland has been seen in 20–25% of patients with the multiple endocrine neoplasia syndrome, type I, (MEN-I) (Eberle et al. 1981; Greene et al. 1983). The Zollinger-Ellison syndrome (ZES) is the second most frequent manifestation of MEN-I after hyperparathyroidism. We report here on a 43 year old man who – in the interval of only a few months – had to be operated because of a toxic adenoma of the thyroid gland and a malignant gastrin producing carcinoid of the duodenum, accompanied by a ZES, but without the other components of a MEN-I-syndrome.

Case report

A 43 year old man, a chronic alcoholic, was first operated at the age of 35 because of a perforation of the stomach. A further operation was carried out one year later, following massive gastrointestinal bleeding when a partial gastrectomy (Billroth II) was done. Seven years later, at the age of 43 the patient developed symptoms of hyperthyroidism and a hemithyroidectomy was done because of a toxic adenoma.

The same year the patient had to be re-hospitalized twice for further gastrointestinal haemorrhage. At this time a 1,5 cm polyp was located endoscopically beside the papilla of Vater. A biopsy diagnosis of a carcinoid tumour of the duodenum was made. This led to the diagnosis of a ZES with a conspicuous elevation of serum gastrin (960 pg/ml; normally not exceeding 115 pg/ml). A minimal increase of urinary excretion of 5-hydroxy-indoleacetic acid (47,1 μmol/l, normally less than 41,8 μmol/l) was also present. The serum values of ACTH, STH, Glucagon, Insulin, VIP, and Calcitonin were normal.

A duodenotomy with local tumour excision was made. At a further examination of the patient 5 months after the operation serum gastrin had increased to 2991 pg/ml. In spite of this high value, the patient only complained of occasional mid-upper abdominal pain which disappeared after eating. The computer-tomogram of the abdomen showed several nodules in the region of the duodenum interpreted as tumour metastases. The pancreas was normal.

Results

The excised segment of the duodenal wall presented a polypoid, 0,8 cm ulcerated tumour limited to the mucosa and submucosa (Fig. 1). Histologically, this was clearly a carcinoid with a partly trabecular and partly tubular architectural pattern and no obvious polymorphism of cells or nuclei (Fig. 2). Repeated attempts to demonstrate gastrin immunohistochemically within the tumour cells failed. The neuro-endocrine nature of the tumour was, however, proven by its distinct positivity for synaptophysin and chromogranin A. The other polypeptides searched for revealed rare single cells with insulin and somatostatin and negative results for glucagon and PP (pancreatic polypeptide).

Discussion

The syndrome described by Zollinger and Ellison in 1955 is characterized by a marked increase in

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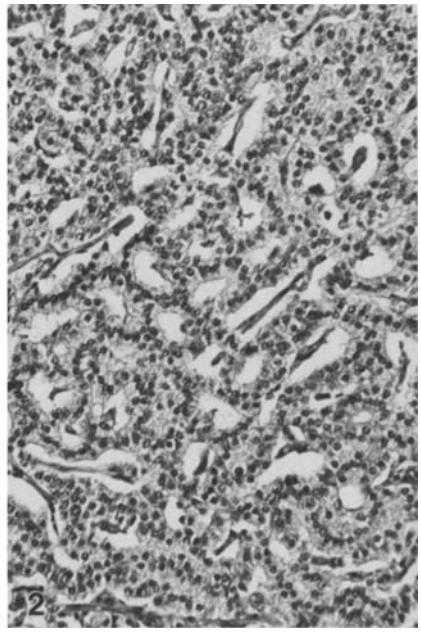

Fig. 1. Transverse cut through the resected duodenal segment showing a small nodule in mucosa and submucosa

Fig. 2. Duodenal carcinoid with typical trabecular and gland-like microscopic pattern (HE, 175×)

gastric acid secretion and recurrent ulceration in the upper gastrointestinal tract and the existence of a gastrin secreting tumour (gastrinoma) most often in the pancreas, but in 13% of the patients in the duodenum (McGuigan 1987). The fact that it was not possible to demonstrate gastrin within the tumour of the patient immunocytochemically may be explained by rapid release of gastrin by the tumour cells, sampling error or a fixation artefact. There is nevertheless little doubt that this tumour has to be regarded as the source of the excessive gastrin in the patient's serum. Duodenal gastrinomas are known to be able to metastasize when they are still small (Stamm et al. 1986).

Gastrinomas can be part of the MEN-I-syndrome, which was first characterized by Wermer in 1954 as a familiar, simultaneous occurrence of hyperplasia or tumours of the anterior pituitary gland, the parathyroids and the islet cells of the pancreas (or, as later added, the endocrine cells of the duodenum). Thyroid disease was repeatedly reported in connection with a MEN-I-syndrome (Brunt et al. 1985; McGuigan 1987; Popa 1980; Greene et al. 1983; Eberle et al. 1981). In our patient there were no signs of either hyperparathyroidism or an adenoma of the anterior pituitary gland.

Our report shows that the association of thyroid disease and ZES may also exist in sporadic ZES without other manifestations of a MEN-I. It represents documentation of an association which may be significant.

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