Non-Adenocarcinoma Pancreatic Tumors

Endocrine Tumors

MATTHIAS ROTHMUND • D. BARTSCH

Introduction

Diagnosis, localization and surgical as well as medical treatment of most endocrine pancreatic tumors is nowadays clearly established and not a matter of debate. This is especially true for sporadic benign insulinomas, gastrinomas or more rare tumors like VIPomas or glucagonomas. Controversies still exist in hereditary tumors, mainly in symptomatic gastrinomas and insulinomas, occurring within the syndrome of multiple endocrine neoplasia type I (MEN I). Since the recent description of the mutation in chromosome 11 associated with MEN I [1] the question of how we should deal with asymptomatic patients detected by genetic and/or biochemical screening also became controversial.

Nomenclature

In 1994, a group of noted European pathologists proposed a new classification of neuroendocrine tumors of the lung, pancreas and gut [2]. The classification is made according to the location of the tumors, their histopathological features and growth pattern. It should replace nonspecific terms like “carcinoid tumor” or “endocrine tumor” because it describes more clearly the degree of aggressiveness of these tumors and their expected outcome [3]. It certainly outdates older classifications such as the WHO classification of 1980. In the following chapters we will therefore use the term “neuroendocrine pancreatic” tumors (NPT).

Insulinoma

Sporadic Insulinomas

The insulinoma syndrome is diagnosed by history and a fasting test of up to 72 h duration, measuring glucose, insulin and C-peptide in serum. Before primary operations in sporadic insulinomas only cross-sectional imaging such as ultrasound
is indicated to exclude a malignant metastasizing tumor, the localization of the mostly solitary and benign tumors being made during surgery by meticulous exploration and palpation of the pancreas, including intraoperative ultrasound (IOUS). Both palpation and IOUS have been shown to be more cost-effective than any other imaging procedure performed before surgery [4, 5]. Enucleation of the mostly small (0.5–2 cm) tumors from the head and body and distal resection for tumors in the tail are the preferred surgical procedures and are successful in more than 95% of patients [6].

More sophisticated localization procedures should only be utilized before reoperations. Endoscopic ultrasound and selective intra-arterial calcium injection are most efficient in this situation [7, 8]. Re-operations rather than medical treatment are preferred – the operation being performed in a specialized center [6].

**MEN I Insulinoma**

About 5% of all insulinomas are hereditary and occur as a part of the MEN I syndrome. MEN I insulinomas are rarely malignant and are localized within the pancreas without any preference to a certain region of the gland. They are almost always multiple and pathologists may describe adenomas, microadenomas and hyperplasia of β-cells within the same specimen together with other NPTs (e.g., PPomas). There is also nesidioblastosis in MEN I patients, mainly in children but a few authors have described this even in adults.

Since there is no good medical alternative for the treatment of hypoglycemia and hypoglycemic symptoms caused by MEN I insulinoma, surgery is indicated in these patients as soon as the diagnosis is made. There is some controversy concerning the type of procedure that should be used. Should one only excise tumors demonstrated by preoperative imaging or those which are palpated or demonstrated by IOUS during operation, or is there a standard procedure that can be used in all of these patients? Data published in the last 10 years show that distal pancreatic resection preserving the spleen, combined with enucleation of tumors in the head, can be considered as a standard procedure [9–11]. This makes the routine use of preoperative imaging tests questionable even in MEN I insulinomas.

**Gastrinoma**

Gastrinomas cause symptoms related to the hypersecretion of gastric acid stimulated by hypergastrinemia, mainly peptic ulcer disease and diarrhea, known as Zollinger-Ellison syndrome (ZES). The patient's life is threatened by both the complications of peptic ulcer disease and the progressive growth of the tumors themselves. Most gastrinomas are sporadic, while 20%–30% occur within the MEN I syndrome; 60%–90% of them are malignant, i.e., lymph node metastases and/or liver metastases are found during first exploration; 30% of patients with MEN I gastrinomas will have liver metastases at the time of diagnosis.

The main location of gastrinomas was in the last decade found to be the duodenum, either as solitary (sporadic) or as multiple (MEN I) tumors with diameters