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Pathologic Aspects of Gastrinomas in Patients with Zollinger-Ellison Syndrome With and Without Multiple Endocrine Neoplasia Type I

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During the three decades since the recognition of the Zollinger-Ellison syndrome (ZES), major progress has been made in the diagnosis and treatment of this disease. However, the many failed operations in patients with ZES, the existence of primary lymph node gastrinomas, and the surgical approach of patients with ZES and multiple endocrine neoplasia type I (MEN-I) have remained controversial issues. In this review, our experience with the pathology of immunocytochemically identified gastrinomas in 44 patients with ZES is presented and related to the relevant literature. (1) Gastrinomas occur frequently in the duodenum (> 40%) and are commonly small (< 1 cm). They can therefore easily be missed at surgical exploration; lymph node metastases from such occult gastrinomas may be mistaken for primary tumors. (2) Most pancreatic gastrinomas reside in the head of the gland and have a diameter of 1 to 3 cm. (3) Gastrinomas associated with MEN-I are predominantly of duodenal origin and frequently multicentric; sporadic gastrinomas are single and more often pancreatic. Because MEN-I associated pancreatic tumors seldom contain gastrin, ZES in MEN-I patients is almost never cured by resection of the pancreatic tumors. (4) The metastatic potential of most small duodenal gastrinomas seems to be restricted to the regional lymph nodes.

In 1955, surgeons Robert M. Zollinger and Edwin H. Ellison described two patients with jejunal ulcer, marked gastric hypersecretion, recurrent ulceration following conventional surgical therapy, and non-beta-islet cell tumors of the pancreas [1]. In the discussion they referred to four similar cases in the literature [2–5] and postulated that "an ulcerogenic humoral factor of pancreatic islet origin" was responsible for the peptic ulcer disease. Originally they thought that glucagon caused the clinical entity, now known as the Zollinger-Ellison syndrome (ZES), but a few years later gastrin was identified as the hormone accounting for ZES [6]. Gastrinomas, as these tumors were then appropriately called [7], were initially thought to originate only in the pancreas, but in 1961 Oberhelman and collaborators reported ulcerogenic tumors in the duodenum [8]. Subsequent reports describing gastrinomas at other extrapancreatic sites, such as the stomach, jejunum, liver, ovary, kidney, and lymph nodes, further confirmed the notion that gastrinomas may arise from a number of extrapancreatic locations [9–22]. Despite this knowledge, the intraoperative detection of gastrinomas has remained a crucial problem. From surgical series it emerges that 10% to 38% [20, 23–30] cannot be found at laparotomy, and this percentage increases if so-called lymph node gastrinomas in the peripancreatic-periduodenal area are not accepted as primary tumors [31, 32].

Another feature of ZES is its frequent combination with other major endocrine manifestations (hyperparathyroidism, hypoglycemia, prolactinemia) characterizing the autosomal dominant disorder of multiple endocrine neoplasia type I (MEN-I). In the first article on the genetic aspects of MEN-I, which was published by Wermer in 1954, a father and his four daughters were described, who, apart from other endocrine disturbances, had peptic ulcers [33]. The patient reported as "case one" by Zollinger and Ellison in 1955 probably also suffered from MEN-I because she had a positive family history for ulcer disease and possibly hyperinsulinism, as well as multiple pancreatic endocrine tumors [1]. Subsequently many other reports confirmed the common association of ZES with MEN-I, and today the average incidence figure for MEN-I in patients with ZES is 25% [34], although frequencies as low as 9% [20] and as high as 70% [35] have been reported. Conversely, more than 60% of the patients with MEN-I have either ZES or elevated serum gastrin levels [36–40]. The hypergastrinemia in these patients has been ascribed to multiple pancreatic gastrinomas, although the resection of the pancreatic tumors usually fails to eliminate the hypersecretion of gastrin. This failure has led to the conclusion that MEN-I patients should be either totally pancreatectomized or, considering the risk of a total pancreatectomy, be treated medically rather than surgically [41, 42].

We became especially interested in the surgical pathology of gastrinomas after we noticed that immunocytochemical analysis and identification of these tumors was either missing or incomplete in many, if not most, of the major clinicopathologic series reported so far [23–25, 41–44]. In an early study of 201 pancreatic endocrine tumors from 9 MEN-I patients, 8 with ZES, a pancreatic gastrinoma was identified in only 1 patient [40]. This unexpected finding stimulated further investigations.

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Table 1. Location of gastrinomas at laparotomy in ZES patients from nine surgical series published between 1981 and 1990.[a]

First author	No. of patients	No. of tumors, by site			
		Pancreas	Duodenum	Peripancreatic lymph node	No tumor detected
Bonfils [23]	92	54	13	—	24
Jensen [24]	42	25	1	—	14
Thompson [25]	27	12	2	—	9
Mignon [26]	125	58	21	13	24[b]
Norton [20]	32	8	1	6	12
Vogel [27]	22	1	4	3	7
Howard [28]	22	7	5	5	5
Kaplan [29]	29	10	11	—	5
Stabile [30]	31	16	3	2	7

[a]Sites outside the pancreas, duodenum, and lymph nodes were not listed.
[b]Patients with "islet cell hyperplasia" only were added to the group of patients in whom no tumor was found.

The results of our studies, which have been performed in close collaboration with a number of pathologists and clinicians from various institutions, have been published recently [32, 45] and are the basis of this review. The questions specifically addressed here are: Why are some gastrinomas difficult to find? Do primary lymph node gastrinomas exist? Why does resection of pancreatic endocrine tumors usually fail to cure hypergastrinemia in MEN-I patients? Are there major differences in the pathology of sporadic gastrinomas versus MEN-I associated gastrinomas?

Location of Gastrinomas: Why Are Some Difficult to Find?

A review of reports from the years 1981–1990, describing the location of gastrinomas in ZES patients, reveals that about 5% to 60% of the gastrinomas that could be detected at laparotomy reside in the pancreas, 3% to 38% in the duodenum, and 0% to 23% in peripancreatic-periduodenal lymph nodes (Table 1) [20, 23–30]. Occasionally, gastrinomas are also identified in other sites, such as the parathyroid [10], stomach [9, 12], jejunum [14, 21], biliary system [46], and kidney [19]. In addition, mucinous cystadenocarcinomas of the ovary [11, 13, 15, 22] and the pancreas [47] with a high content of intraepithelial gastrin cells may cause ZES. The number of these cases, however, is so small that they can be considered exceptions. Consequently, almost all gastrinomas should be found in a rather well defined area comprising the gastrinoma triangle, described by Stabile et al. [48], and the body and tail of the pancreas. In the most recent reports on patients with ZES, however, 17% to 38% of gastrinomas still escape detection at laparotomy (Table 1) [20, 23–30]. In one of the studies, specifically designed to locate and resect gastrinomas in ZES patients, no tumor could be found in 12 of 32 patients (38%) [20].

The most plausible explanation for these operative failures is that gastrinomas may be camouflaged because of their size and their extrapancreatic duodenal location [45, 49]. This point has been illustrated in both early and recent surgical studies as well as in our immunocytochemical analysis of tumor specimens from patients with ZES who underwent a gastrinoma resection [32].

The existence of duodenal tumors with an ulcerogenic potential was first noted by Oberhelman and colleagues [8, 50], and they had emphasized the small size of these lesions. Since then it has been repeatedly shown that duodenal endocrine tumors (gastrinomas and others) may be tiny lesions [45, 51–53]. However, it was not until recently that full attention was drawn to microgastrinomas in the duodenum and their special role in the surgical treatment of patients with ZES [29, 49].

Table 2. Pathologic features of gastrinoma.

Measurement	ZES and MEN-I (no.)	ZES (no.)
Patients		
Total	18	26
Male	11	17
Female	7	9
Location		
Pancreas	1	14
Duodenum	9	10
Only metastasis detected	2	2
No gastrinoma detected	6	0
Number of lesions		
Gastrinoma		
Pancreas	1	1
Duodenum	1–10[a]	1
Other endocrine tumors		
Pancreas	3 to > 100	0
Duodenum	0	0
Size (cm)		
Gastrinoma		
Pancreas	3	1.0 to 6.5
Duodenum	< 0.2 to 2.0	0.5 to 2.0
Other endocrine tumors	< 0.05 to 4.0	—
Metastasis		
Lymph node		
Pancreatic primary	0	7
Duodenal primary	7	4
Liver		
Pancreatic primary	0	3
Duodenal primary	1	2

For details see refs. 32 and 45.
[a]Five of the nine patients with MEN-I had multiple gastrinomas (mean 5).

The findings of our studies [32, 45] which also help to clarify this issue, are summarized in Table 2. In 43% of the patients the gastrinomas were found in the duodenum. Most duodenal gastrinomas were small; of the 19 patients, only 2 had a gastrinoma of more than 1 cm in diameter, in 5 patients the tumors were 1 cm in diameter, and the 37 tumors in the remaining 12 patients (5 of them with multicentric lesions) had

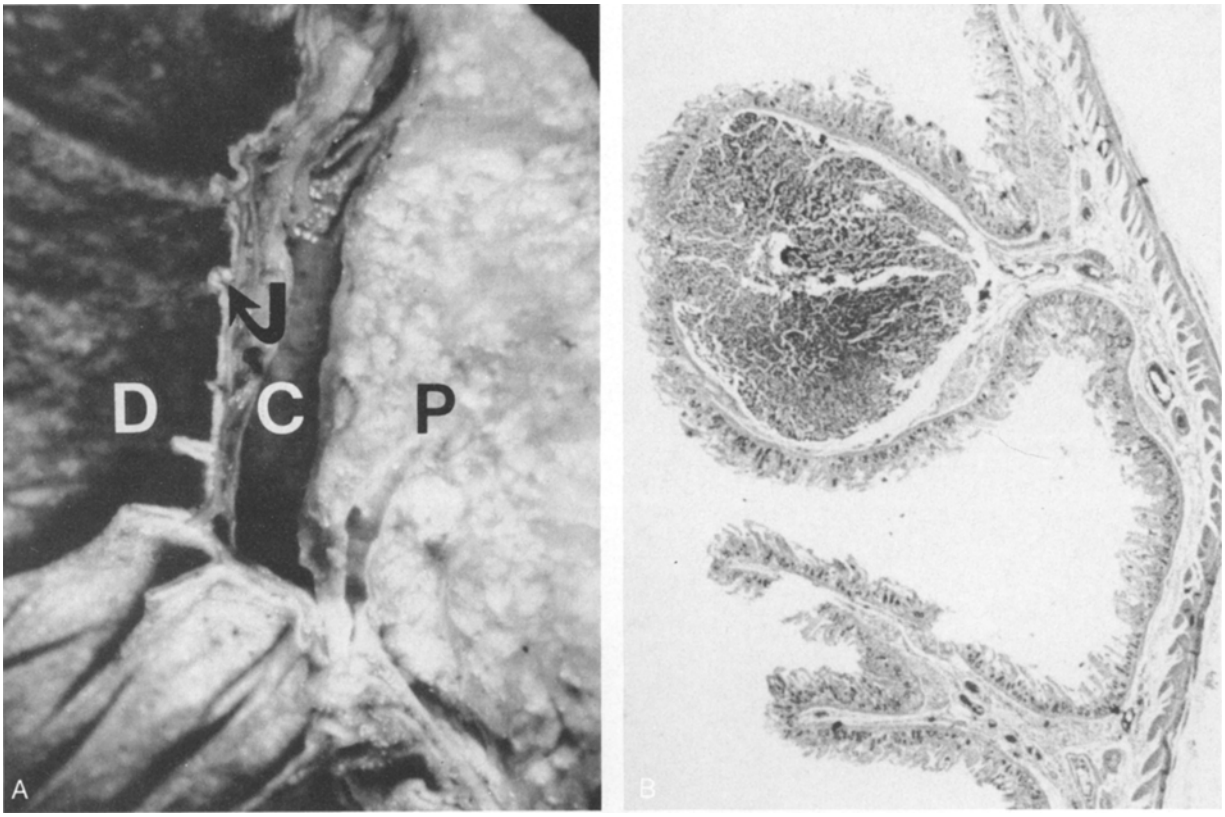

Fig. 1. A. MEN-I. Bisected duodenum (D), common bile duct (C), and head of pancreas (P). The arrow points to a small duodenal gastrinoma. **B.** MEN-I. Duodenal wall; note the comparison between a small submucosal duodenal gastrinoma (at top) and a valve of Kerckring (at bottom). (Reprinted with permission from the publisher.)

a diameter of less than 1 cm, with 28 smaller than 0.6 cm (Fig. 1). Microgastrinomas (i.e., tumors with a diameter smaller than 0.5–0.6 cm) are usually not palpable through the duodenal wall, and their detection often requires duodenotomy and mucosal eversion [49]. Endoscopic transillumination can be helpful for localizing these tumors [54].

The small size of many of the duodenal tumors may also explain a number of "regressions" of gastrinomas described in patients in whom total gastrectomy was performed. This intervention also includes resection of the bulbic region and may thus remove an occult gastrinoma from this portion of the duodenum [55].

Small gastrinomas are difficult for not only the surgeon to detect but also for the pathologist (Fig. 1). Tumors with a diameter of less than 0.5 cm require serial sectioning for identification. If such a small duodenal tumor is present in a gastrectomy specimen, it can easily be missed by routine processing.

Primary Lymph Node Gastrinomas: Do They Exist?

Among the gastrinomas arising outside the pancreas and duodenum, the most common "unusual sites" in which primary gastrinomas have been described are the peripancreatic, periduodenal, and gastrohepatic lymph node regions. There, in the lymph drainage zone of the duodenum and pancreas, isolated, encapsulated gastrin-positive tumors embedded in lymphatic tissue were noted in most of the major series published [16, 18, 20, 23–30, 32, 53, 56–58]. It has been suggested that these lymph node gastrinomas are primary rather than metastatic in origin [16, 18]. The arguments in favor of the primary nature of the lymph node gastrinomas are that no other tumor was found during operation and that, most importantly, removal of the tumor resulted in eugastrinemia and cure.

Careful analysis of the reports describing these patients in detail reveals one group with concomitant or previous gastrectomy [16, 17, 29, 48, 53, 58, 59] and another without such a surgical intervention [16, 60, 61]. In the first group, as has been stressed repeatedly, the gastrectomy specimen could have included a gastrinoma located in the proximal duodenum. Delcore and colleagues [53] specifically mention that in three of their patients occult primary lesions were unwittingly removed as part of a total gastrectomy and were almost missed by the pathologist. This situation also arose in one of our patients, in whom a small gastrinoma was detected only in the resection specimen at microscopy after serially sectioning the duodenum. It is therefore most likely that, in patients who undergo gastrectomy, the lymph node gastrinomas represent metastases of small duodenal gastrinomas rather than primary tumors.

How can we explain the cure of the patients belonging to the second group? Thompson mentioned in the discussion of an

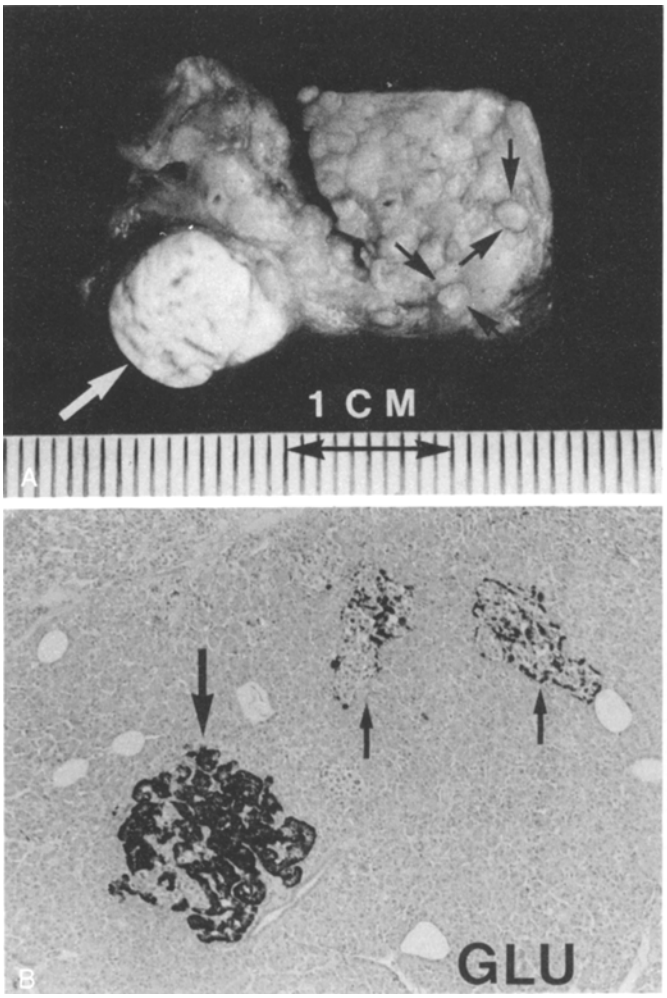

Fig. 2. A. MEN-I. Pancreas specimen: one macroadenoma (white arrow) and two microadenomas (black arrows) are present. B. MEN-I. Pancreas specimen with immunocytochemical staining for glucagon (GLU). One microadenoma is composed predominantly of glucagon cells (large arrow). Two islets are shown (small arrows). (× 125)

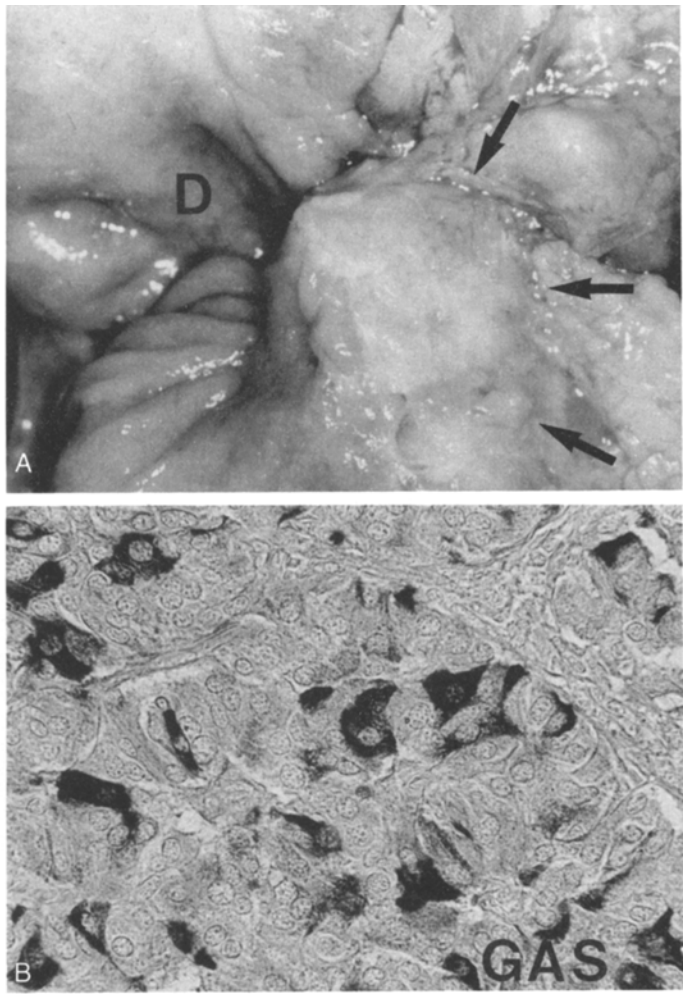

Fig. 3. A. Sporadic gastrinoma: bisected duodenum (D). A macrotumor in the head of the pancreas (arrows) bulges into the duodenum. (Courtesy of Dr. Dralle, Hannover, Germany). B. Sporadic gastrinoma; immunocytochemical staining for gastrin (GAS) in a pancreatic tumor. (× 600)

article by Delcore and colleagues [53] that he observed a patient whose gastrin levels had returned to normal after resection of what was thought to be a "primary liver gastrinoma"; when this patient died, a small pancreatic gastrinoma was found at autopsy, suggesting that the functional activity of small primary gastrinomas may be so insignificant and their growth potential so low they remain undetected during follow-up of the patients.

In our series there are 4 patients in whom the gastrin-containing tumor tissue was restricted to lymph nodes [32, 45]. In the first patient the periduodenal-peripancreatic tumor was removed after a duodenotomy (without eversion nor intraoperative endoscopic transillumination) did not reveal a duodenal primary. The second patient did not undergo duodenotomy, as only a periduodenal mass could be palpated. A third patient underwent a concomitant gastrectomy, and in a fourth patient the tumoral lymph node was found at autopsy. In the two latter patients the duodenum was not cut serially; and as duodenal gastrinomas can be as small as 1 to 2 mm in diameter, we suspect that the primary tumors in the duodenum were missed. The three patients with surgically removed lymph node tumors were cured of ZES, but in the first two patients the resection did not completely normalize the basal serum gastrin levels (which remained in the range of 100–150 pg/ml), and so it is possible that primary tumors are still present in the duodenum. These observations led us to believe that lymph node gastrinomas are metastatic rather than primary in origin, a view shared by others [53, 62, 63].

Why Does Resection of Pancreatic Endocrine Tumors Usually Fail to Cure Hypergastrinemia in MEN-I Patients?

Since the publications of Wermer [33] and Moldawer and associates [64] it is known that patients with MEN-I may have

multiple endocrine tumors scattered throughout the pancreas. This fact has led to the assumption that gastrinomas are multicentric in the pancreas of patients with MEN-I and ZES [65]. However, several large surgical series demonstrated that patients with MEN-I and ZES were not cured by resection of all grossly identifiable pancreatic tumors [20, 25, 26, 41, 42, 66, 67]. Consequently, some groups have considered ZES in patients with MEN-I incurable and excluded them from exploratory laparotomy or attempts at surgical cure [26, 28, 42].

When we reviewed the pathology of the tumors reported in the series mentioned above, we found that the resected tumors were not routinely identified as gastrinomas by immunocytochemistry. Immunocytochemical findings are also missing or incomplete in other major reports on gastrinomas [23, 24, 28]. However, considering the capability of the pancreatic MEN-I tumors of producing different hormones (e.g., insulin, glucagon, somatostatin, pancreatic polypeptide, vasoactive intestinal polypeptide, growth hormone-releasing factor, and neurotensin) and the unpredictability of their hormone production without appropriate analysis at the tissue level, immunocytochemical examination of the tumors in correlation with their location, size, and functional parameters is essential for correct diagnosis. If this kind of investigation is not performed, certain questions will remained unsolved. Which tumor is producing gastrin? Is there a correlation between size and functional activity? Are there multiple gastrinomas? Do they show any preferential location?

In our recent investigations [32, 45] (Table 2) of 15 pancreatic specimens from 18 MEN-I patients with ZES, multiple endocrine tumors (range 3 to > 100) were detected in each pancreas. Most were microadenomas (< 0.5 cm), but a few macrotumors with diameters up to 4.0 cm were also present in each specimen (Fig. 2A). When the tumors were screened with a battery of antisera to hormones, it was found that the microadenomas stained predominantly for pancreatic polypeptide, glucagon (Fig. 2B), or insulin, whereas the few macrotumors (> 0.5 cm) contained either pancreatic polypeptide, glucagon, somatostatin, insulin, vasoactive intestinal polypeptide (VIP) or a combination of hormones. The presence of macrotumors producing insulin or VIP was combined with symptoms of hypoglycemia and watery diarrhea, respectively. These symptoms, which accompanied ZES in 4 patients, disappeared after removal of the respective pancreatic tumors. Only 1 of our 18 MEN-I patients with ZES had a grossly visible pancreatic gastrinoma (Table 2). He was relieved of his symptoms after tumor resection. None of the other patients (except one who had scattered gastrin-positive cells in a microadenoma) showed pancreatic gastrinomas, but in 9 patients one or more duodenal endocrine tumors were identified by either the surgeon or the pathologist. All these duodenal tumors stained predominantly for gastrin; and in those patients whose tumors were surgically removed, serum gastrin returned to normal or near-normal levels [45]. These observations suggest that gastrinomas associated with MEN-I occur more frequently in the duodenum than has previously been assumed. Perhaps the duodenum is the preferential site of gastrinomas in patients with MEN-I, because in the 8 patients in whom no gastrinoma was found in the available tissue specimens, or only a "lymph node gastrinoma" was detected, a duodenal gastrinoma could not be excluded. The duodenum should therefore be the first site examined for gastrinomas in patients with MEN-I.

Are There Major Differences in the Pathology of Sporadic Gastrinomas Versus MEN-I-Associated Gastrinomas?

To study whether gastrinomas of patients with sporadic ZES differ in their pathology from those occurring in the setting of MEN-I, we compared these tumors with regard to site, size, number, and malignancy rate [32].

The most striking feature of the gastrinomas observed in our 26 patients with the sporadic form of ZES was solitary occurrence, in either the pancreas or the duodenum. More than 50% of the gastrinomas resided in the pancreas and had a diameter of more than 2 cm (Fig. 3); half of them occurred in the head of the gland and the other half in the body and tail. These findings confirm the observations of others [68, 69]. The duodenal gastrinomas comprised 38%, a slightly higher percentage than noted in most other series [7, 70–72]. All were observed in the proximal part of the duodenum, which seems to be their preferential site [73], although some have also been described in more distal portions of the duodenum [49, 73]. In 2 patients, the only gastrinoma tissue detected occurred in periduodenal lymph nodes; and, as has been discussed, these lesions were considered metastases from occult duodenal primary tumors. Taken together, our findings confirm that most sporadic gastrinomas are located in the gastrinoma triangle [48], but approximately one-fourth of the tumors may also occur outside this triangle (i.e., in the body and tail of the pancreas).

Unlike sporadic gastrinomas, all MEN-I-associated gastrinomas were found in the gastrinoma triangle; more specifically, most originated in the duodenum. In addition, the MEN-I-associated duodenal gastrinomas were frequently multicentric, whereas the sporadic gastrinomas were solitary lesions. All other features (i.e., histologic pattern, distribution, and size) were common to both types. Approximately 85% had a diameter of less than 1 cm; the smallest lesions (< 0.5 cm) were encountered in the MEN-I group. This finding again emphasizes the small size of most duodenal gastrinomas, a feature that, as already discussed above, is likely responsible for the many failures to detect gastrinomas at surgical exploration.

The malignancy rate of the MEN-I-associated gastrinomas was 50%. However, if not only the 10 patients in whom we identified gastrinomas are considered but the 2 patients with "lymph node gastrinomas" are added, the malignancy rate increases to 58% (7 of 12 patients). This figure is similar to that found in our series of sporadic duodenal and pancreatic gastrinomas and compares well with the respective data extracted from the literature [8, 25, 29, 34, 39, 44, 65, 72]. We therefore cannot confirm previous reports that ascribe a higher malignancy rate to sporadic gastrinomas [34, 65]. The lone difference regarding malignancy seems to be that only patients with the sporadic form of ZES had massive liver metastasis; 3 patients had a primary pancreatic gastrinoma and 2 a duodenal gastrinoma. Malignant gastrinomas may thus be of two categories: one with a good prognosis because of a limited metastatic potential and tumor spread restricted to regional lymph nodes, and another with an unfavorable prognosis because of a high metastatic capacity. A similar observation was made by others who identified two prognostic groups: those with and those without hepatic metastases at initial examination [74]. In our series most of the duodenal gastrinomas and all MEN-I-associated gastrinomas belong to the first group. The good prognosis

of duodenal gastrinomas, sporadic as well as MEN-I-associated, was also noted by Friesen's group [53, 73]. It is still unclear whether MEN-I in itself represents favorable factor in the survival of gastrinoma patients, because Stabile and Passaro [74], as well as Friesen's group, described a considerable number of MEN-I patients with ZES whose deaths were related to liver metastasis. So far no histologic or other criteria (DNA content, AgNOR number) that would help to predict prognosis have been established.

Whereas the pancreas of patients with ZES and MEN-I is usually studded with microadenomas [40, 75], and their duodenum may contain multiple tumors, patients with the sporadic form of ZES normally have no other tumors than gastrinomas in their pancreas or duodenum. Islet hyperplasia and nesidioblastosis have been described in the latter patients [14, 76–79], but a quantitative study performed on the pancreas of 8 patients with gastrinoma and 9 control patients could not confirm these findings [80]. We are also not able to find an objective difference between the extratumoral pancreas of patients with the sporadic type of gastrinoma and control pancreata.

The stomach in patients with sustained tumor hypergastrinemia induces parietal cell hyperplasia as well as enterochromaffin-like (ECL) cell hyperplasia. However, multiple ECL cell tumors in the fundus of the stomach—well known long-term sequelae of patients suffering from pernicious anemia with chronic type A gastritis—appear to be uncommon in patients with sporadic ZES [81]. They have, however, been reported in patients with ZES and MEN-I and were also observed in 1 patient of our series. In these instances they most likely represent another neoplastic manifestation of the MEN-I syndrome rather than being the result of a trophic potential of gastrin [81, 82].

Conclusion

Our studies on the surgical pathology of gastrinomas were based on immunocytochemical screening of all lesions removed from patients with ZES. The findings that emerged may have the following clinical implications for the diagnosis and treatment of gastrinomas.

In patients with the sporadic type of gastrinoma, localization procedures should be focused primarily on finding the tumor in the pancreas, where 50% to 60% of the tumors, with a size ranging between 1 and 6 cm, may be expected. If this approach remains negative, the duodenum, particularly its proximal part, is the next site to be carefully investigated. As about 80% of the duodenal gastrinomas are smaller than 0.6 cm, some may be found only after endoscopic transillumination and duodenotomy [49, 55]. When a nodule is found in the pancreas or duodenum during surgical exploration and it shows an endocrine growth pattern by intraoperative frozen section, this tumor is most likely the gastrinoma, because sporadic gastrinomas appear to be solitary lesions. It is recommended regional lymph nodes be removed to eliminate possible micrometastases.

In patients with ZES as a component of MEN-I, the duodenum should be the first site examined for gastrinomas; characteristically, these tumors are multiple and small (< 0.6 cm). In the pancreas there may be also one or more macrotumors (> 0.5 cm), but these lesions are only exceptionally the source of hypergastrinemia. Removal of the non-gastrin-secreting pancreatic tumors is debatable if the patient does not, in addition to ZES, suffer from hypoglycemia or the Verner-Morrison syndrome. The fact that one of the pancreatic macrotumors may become malignant, however, argues in favor of resection [67].

It is at present not clear whether the duodenum should be opened in patients with MEN-I who have no symptoms of ZES but who are subjected to laparotomy for other endocrine tumors. One of our patients, who had a surgical intervention for insulinoma, became hypergastrinemic 2 years later, just before she died of a cerebral vascular accident. At autopsy two duodenal gastrinomas were found (2 and 4 mm in diameter). The occurrence of a second symptomatic endocrine pancreatic or duodenal tumor in patients who have ZES and MEN-I is low but not exceptional. Five of 18 patients in our series had two symptomatic endocrine tumors, either synchronic or metachronic. In a study of Chiang and colleagues [83] only 1 patient of 45 developed a second symptomatic tumor. Interestingly, it occurred in a patient with the sporadic type of gastrinoma. MEN-I patients should certainly always be screened extensively before laparotomy to determine the presence of various functioning endocrine tumors.

In the near future it may be possible to perform intraoperative immunocytochemistry for peptide hormones by microwave technique, a method that has already been described for insulin [84]. Because it is a rapid procedure, it could help to determine the hormonal function of the various endocrine tumors of MEN-I patients during surgical exploration.

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Résumé

Depuis sa découverte, d'importants progrès ont été réalisés dans le diagnostic et le traitement du syndrome de Zollinger et Ellison (SZE). La raison du taux élevé d'échecs chirurgicaux, l'existence de gastrinomes lymphatiques ganglionnaires primitifs et la meilleure approche thérapeutique du patient ayant un SZE associé à un syndrome de néoplasie endocrine multiple de type I (MEN-I) restent des sujets débattus. Dans cette revue, nous décrivons notre expérience avec 44 cas de SZE en rapport avec un gastrinome identifié par l'immunocytochimie. Les gastrinomes sont souvent (> 40%) localisés au duodénum et fréquemment de petite taille (< 1 cm), rendant leur découverte peropératoire problématique. Les métastases ganglionnaires de ces tumeurs sont souvent prises pour la tumeur primitive. La plupart des tumeurs pancréatiques se trouvent dans la tête pancréatique et ont une taille comprise entre 1 et 3 cm. Les gastrinomes associés aux MEN-I sont essentiellement d'origine duodénale et fréquemment multicentriques. Les gastrinomes sporadiques sont uniques et le plus souvent pancréatiques. Parce que les tumeurs pancréatiques MEN-I ne sécrètent que rarement de la gastrine, les SZE/MEN-I ne sont habituellement pas guéris par la résection de la tumeur pancréatique. Le potentiel métastatique de la plupart des petits gastrinomes d'origine duodénale semble limité aux ganglions lymphatiques régionaux.

Resumen

Notable progreso se ha logrado en las tres décadas transcurridas desde el reconocimiento del síndrome Zollinger-Ellison (SZE). Sin embargo, las numerosas operaciones fallidas en pacientes con SZE, la existencia de gastrinomas primarios en ganglios linfáticos y el aproche a los pacientes con SZE y síndrome de neoplasia endocrina múltiple Tipo 1 (SNEM-1), siguen siendo temas de controversia. En la presente revisión se informa nuestra experiencia con la patología de gastrinomas inmunocito-químicamente identificados en 44 pacientes con SZE y se la relaciona con la literatura. (1) Los gastrinomas ocurren frecuentemente en el duodeno (> 40%) y generalmente son pequeños (< 1 cm), por lo cual fácilmente pueden pasar desapercibidos en la exploración quirúrgica; las metástasis ganglionares de tales gastrinomas ocultos pueden ser confundidos con tumores primarios. (2) La mayoría de los gastrinomas pancreáticos residen en la cabeza de la glándula y tienen un diámetro entre 1 y 3 cm. (3) Los gastrinomas asociados con el SNEM-1 son preponderantemente de origen duodenal y con frecuencia multicéntricos; los gastrinomas esporádicos son únicos y muy frecuentemente pancreáticos. Puesto que los gastrinomas asociados con SNEM muy rara vez contienen gastrina, el SZE en pacientes con SNEM-1 casi nunca puede ser curado mediante la resección de los tumores pancreáticos. (4) El potencial metastásico de la mayoría de los pequeños gastrinomas duodenales parece estar limitado a los ganglios linfáticos regionales.

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