

Abstract

Background: A gastrinoma is a gastrin-secreting tumor. More than 80% of gastrinomas arise from a triangle defined as the union of the cystic and common bile duct superiorly, the neck and body of the pancreas medially, and the second and third portions of the duodenum inferiorly. Rarely, primary tumors as well occur in a variety of ectopic sites, including the body of the stomach, jejunum, peripancreatic lymph nodes, omentum, splenic hilum, liver, gallbladder, ovary, and the common bile duct. Over 50% of gastrinomas are malignant and can metastasize to regional lymph nodes and the liver.

Aim of the Work: The aim of the work is to evaluate the recent modalities in diagnosis and management of gastrinoma in pancreaticoduodenal triangle and how to avoid missing cases of gastrinoma.

Methodology: The management of gastrinoma has developed due to advances in medical therapies, diagnostic and imaging investigations and improvements in surgical technique. Gastrin has been identified as the humoral agent responsible for Zollinger-Ellison syndrome.

Conclusion: Zollinger-Ellison syndrome is characterized by severe peptic ulcerations, hypersecretion of gastric acid, and non-beta islet cell tumors of the pancreas. Further studies with longer follow-up are necessary to conclusively describe the natural history of this condition, identify factors predictive of recurrence and survival, and make categorical recommendations regarding treatment and to avoid missing cases of gastrinoma.

Keywords: Recent modalities, surgical management, pancreaticoduodenal triangle

Contents

Subjects	Page
List of abbreviations.....	II
List of Figures.....	III
List of Tables	VII
• Introduction	1
• Aim of the Work	7
• Chapter (1): Surgical Anatomy and Histology of Pancreaticoduodenal Triangle	8
• Chapter (2): Pathophysiology of Gastrin Releasing Tumors	46
• Chapter (3): Clinical Manifestations of Gastrin Releasing Tumors	55
• Chapter (4): Investigations	60
• Chapter (5): Management of Gastrin Releasing Tumors	84
• Summary and Conclusion	115
• References	119
• Arabic Summary	

List of Abbreviations

Abbrev.	Meaning
ACh	: Acetylcholine
AJCC	: American Joint Committee on Cancer
BAO	: Basal acid output
Ca	: Calcium
CBD	: Common bile duct
CT	: Computed tomography
DJ	: Duodenojejunal
EGD	: Esophagogastroduodenoscopy
EGF	: Epidermal growth factor
ENETS	: European Neuroendocrine Tumor Society
EUS	: Endoscopic ultrasound
FAP	: Familial adenomatous polyposis
FDG	: Fluorodeoxyglucose
Fig.	: Figure
FSG	: Fasting Serum Gastrin
GCT	: Gastro-colic trunk
GDA	: Gastroduodenal artery
GEPNETs	: Gastroenteropancreatic neuroendocrine tumors
GERD	: Gastroesophageal reflux disease
GI	: Gastrointestinal
GI NETs	: Gastrointestinal neuroendocrine tumors
GRP	: Gastrin releasing peptide
H2Rs	: Histamine H2 receptor
HA	: Hepatic artery

List of Abbreviations

HDL	: Hepatoduodenal ligament
HE	: Staining Hematoxylin and eosin staining
HGF	: Hepatocyte growth factor
HV	: Hepatic vein
HV-IRG	: Heptic vein- Immune Reactive Gastrin
IDS	: Intra operative Duodenoscopy
IGF1	: Insulin-like growth factor-1
IMV	: Inferior mesenteric vein
IOS	: Intraoperative secretin test
IOUS	: Intraoperative US
IPDV_s	: Inferior pancreaticoduodenal veins
IRG	: Immune Reactive Gastrin
IV	: Intra venous
IVC	: Inferior vena cava
LGV	: Left gastric vein
LS	: Laparoscopic surgery
M cells	: Microfold cells
MALT	: Mucosa-associated lymphoid tissue
MEN	: Multiple Endocrine Neoplasia
MEN I	: Multiple Endocrine Neoplasia type 1
MRI	: Magnetic resonance
NET_s	: Neuroendocrine tumors
NIH	: National Institutes of Health
NSAID	: Non-steroidal anti-inflammatory drug
PD	: Pancreatoduodenectomy
PET	: Positron emission tomography
PNET_s	: Pancreatic neuroendocrine tumors
PP	: Pancreatic polypeptide

List of Abbreviations

PPI	: Proton pump inhibitor
PPPD	: Pylorus-preserving pancreaticoduodenectomy
PPTD	: Pancreaspreserving total duodenectomy
PRRT	: Peptide receptor radionuclide therapy
Pts	: Patients
PUD	: Peptic ulcer disease
PV	: Portal vein
RGEV	: Right gastro-epiploic vein
RGV	: Right gastric vein
SASI	: Selective angiography with secretin injection
SMA	: Superior mesenteric artery
SMV	: Superior mesenteric vein
SPA	: Splenic artery
SPDVs	: Superior pancreaticoduodenal veins
SPECT	: Single photon emission computed tomography
SRS	: Somatostatin receptor scintigraphy
SST	: Secretin Stimulation Testing
SV	: Splenic vein
TNM	: Tumor, node, metastasis
UGI	: Upper gastrointestinal
UICC	: Union for International Cancer Control
ULN	: Upper limit of normal
US	: Ultrasound
ZES	: Zollinger-Ellison syndrome

List of Figures

<u>No.</u>	<u>Figure</u>	<u>Page</u>
<u>1</u>	Gastrinoma triangle.	8
<u>2</u>	Diagrammatic sagittal section showing the position of the duodenum in relation to the aorta and the superior mesenteric artery.	11
<u>3</u>	Four configurations of the suspensory ligament of Treitz.	12
<u>4</u>	The arterial supply of the duodenum.	13
<u>5</u>	The venous drainage of the duodenum and pancreas: anterior.	17
<u>6</u>	The venous drainage of the duodenum and pancreas, and formation of the hepatic portal vein: posterior.	17
<u>7</u>	Low-power micrograph showing several circular folds in the wall of the ileum.	23
<u>8</u>	Anterior relationships of the pancreas.	25
<u>9</u>	Posterior relationships of the pancreas. Anterior.	26
<u>10</u>	The five parts of the pancreas. The line between the body and the tail is arbitrary.	26
<u>11</u>	A, Regions and anterior surfaces and borders of the pancreas. B, Anterior relations of the pancreas.	28
<u>12</u>	Anatomic relationships of the pancreas with surrounding organs and structures.	30
<u>13</u>	Cross sectional CT scan of pancreas at the level of the uncinate process.	32

<u>No.</u>	<u>Figure</u>	<u>Page</u>
<u>14</u>	Variations of the pancreatic ducts.	33
<u>15</u>	Diagram of the relations of the pancreatic and common bile ducts.	36
<u>16</u>	The arterial blood supply of the pancreas.	38
<u>17</u>	Lymph nodes draining the pancreas.	41
<u>18</u>	Pancreatic tissue. Exocrine acinar cells.	43
<u>19</u>	Gastrin on oxyntic parietal cells.	50
<u>20</u>	(a) Algorithm for diagnosis of gastrinoma. (b) Algorithm for differential diagnosis of gastrinoma in patients with gastric outlet obstruction and hypergastrinemia. (c) Algorithm for differential diagnosis of gastrinoma in patients with chronic renal failure and hypergastrinemia.	61
<u>21</u>	Algorithm for the diagnosis of Zollinger–Ellison syndrome .	65
<u>22</u>	Somatostatin receptor scintigraphy (SRS; a) and computed tomography (CT; b) in a patient with ZES.	73
<u>23</u>	(a) Computed tomography showing peripancreatic lymph node. (b) MRI demonstrating metastatic liver disease in a patient with Zollinger-Ellison syndrome from a large pancreatic gastrinoma.	74
<u>24</u>	Octreotide scan demonstrating positive uptake in a patient with metastatic Zollinger- Ellison syndrome.	74
<u>25</u>	Calcifications on CT are predictive of intermediate-grade, lymph node , and liver metastasis.	75

<u>No.</u>	<u>Figure</u>	<u>Page</u>
<u>26</u>	Imaging modalities for gastrinoma.	76
<u>27</u>	Duodenal gastrinoma visualized by 68Ga-DOTATOC-PET/CT. Arrow indicates a duodenal gastrinoma.	77
<u>28</u>	(A) Schematic diagram of SASI test (B) Results of super SASI test.	78
<u>29</u>	(A) An example of the intraoperative duodenoscopy in a patient with MEN-1 and ZES. (B) In the duodenal specimen after the PPTD. (C) Microscopic photo showing multiple submucosal tumors confirmed to be microgastrinomas by immune-histochemical staining with an antigastrin antibody.	93
<u>30</u>	A flow chart showing the localization and treatment of sporadic gastrinoma. CT and/or SRS are performed initially for the detection of distant metastases.	94
<u>31</u>	A flow chart showing the localization and treatment of tumors in patients with ZES and multiple endocrine neoplasm type 1.	95
<u>32</u>	(a) En bloc surgical specimen by PPTD. (b), which were confirmed to be gastrinomas by antigastrin antibody staining (c). The patient has been disease free for 2 years postoperatively.	97
<u>33a</u>	PPTD. The entire duodenum is resected, while preserving the whole pancreas. A functional major papilla is preserved by only stripping off the mucosa.	97

<u>No.</u>	<u>Figure</u>	<u>Page</u>
<u>33b</u>	b. PPTD. The entire duodenum is resected, while preserving the whole pancreas.	98
<u>34</u>	Step two: Extended Kocher maneuver	100
<u>35</u>	Step three: Lymphadenectomy of gastrinoma triangle	101
<u>36</u>	Step four: Opening the duodenum to identify and remove duodenal gastrinomas	104
<u>37</u>	Intraoperative duodenoscopy reveals a tiny submucosal tumor in the proximal second part of the duodenum (yellow arrows), which was pathologically diagnosed to be a gastrinoma.	106

List of Tables

<u>No.</u>	<u>Table</u>	<u>Page</u>
<u>1</u>	Clinical features of patients with ZES and PUD.	57
<u>2</u>	Clinical manifestations suggestive of ZES.	58
<u>3</u>	The American Joint Committee on Cancer Staging for Neuroendocrine tumor of the small intestine.	82
<u>4</u>	A comparison of the American Joint Committee on Cancer and the European Neuroendocrine Tumor Society TNM staging systems on pancreatic neuroendocrine tumors.	83



Introduction





Aim of the Work





CHAPTER (1)

Surgical Anatomy and Histology of Pancreaticoduodenal Triangle





CHAPTER (2)

Pathophysiology of Gastrin Releasing Tumors





CHAPTER (3)

Clinical Manifestations of Gastrin Releasing Tumors

