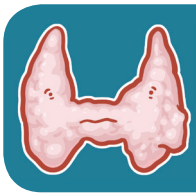

NOTES
NEUROENDOCRINE TUMORS

GENERALLY, WHAT ARE THEY?

PATHOLOGY & CAUSES

- Tumors arising from cells of neuroendocrine origin; most are functional with hormone-secreting capacity
- Can be sporadic; most associated with genetic syndromes

SIGNS & SYMPTOMS

- Mass effect
- Depends on secreted hormone

DIAGNOSIS

DIAGNOSTIC IMAGING

- Location; tumor, lymph node, metastasis (TNM) staging

LAB RESULTS

- Hormone level plasma measurement

OTHER DIAGNOSTICS

- History, physical examination
- Histopathological analysis, tumor grading

TREATMENT

MEDICATIONS

- Chemotherapy; hormonal agonists, antagonists

SURGERY

- Resection

OTHER INTERVENTIONS

- Radiotherapy

CARCINOID SYNDROME

osms.it/carcinoid-syndrome

PATHOLOGY & CAUSES

- Signs, symptoms caused by tumor arising from neuroendocrine cells secreting serotonin
- ⅓ metastasize, ⅓ associated with secondary malignancy, ⅓ multiple tumors
- Most commonly arises from gastrointestinal (GI) tract; followed by lungs, liver, ovaries, thymus
  - Most common small intestine malignancy
  - Appendix most common GI tract site
  - Liver most common site for metastasis; from ileal tumors

SIGNS & SYMPTOMS

- Usually asymptomatic until liver metastasis; symptoms develop occasionally
  - GI tract tumor → hormone secretion → enter into enterohepatic circulation → liver inactivates hormones → no symptoms
  - Liver tumor → hormone secretion → released into circulation + liver dysfunction → symptoms
- Cutaneous flushing
- ↑ intestinal motility, diarrhea
- Collagen fiber thickening, fibrosis
  - Heart valve dysfunction → tricuspid regurgitation, pulmonary stenosis (both right-sided)
- Bronchoconstriction, asthma, wheezing
- Pellagra (niacin/B_3 deficiency)
  - ↑ serotonin synthesis → ↓ tryptophan → ↓ niacin/B_3 synthesis
  - Dermatitis, diarrhea, dementia, death

DIAGNOSIS

DIAGNOSTIC IMAGING

CT scan

- Locate tumors

LAB RESULTS

- Niacin deficiency

Urinalysis

- ↑ 5-hydroxyindoleacetic acid

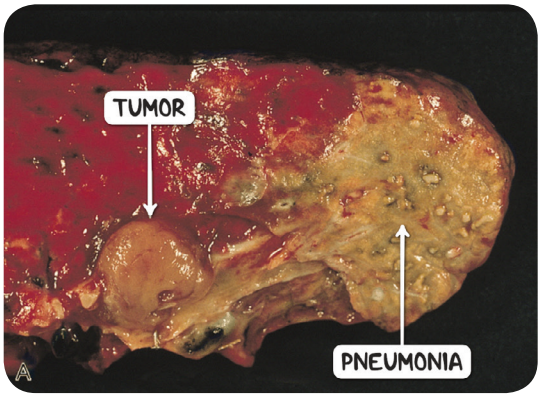

Figure 20.1 The gross pathology a lung carcinoid tumor. The cut surface is firm and yellowish brown. The tumor has obstructed a nearby bronchus, leading to an obstructive pneumonia.

TREATMENT

MEDICATIONS

- Somatostatin analogues
- Niacin supplementation
- Chemotherapy (if malignant)

SURGERY

- Resection

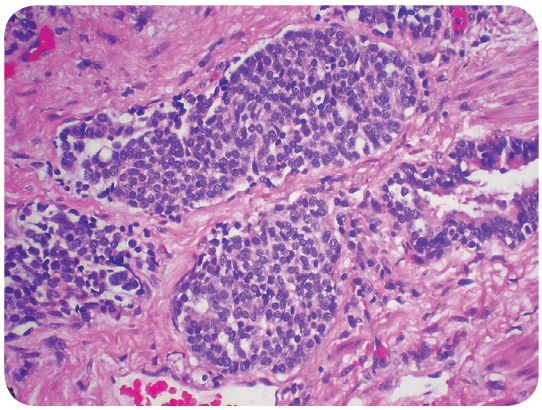

Figure 20.2 The histological appearance of a carcinoid tumorlet. The tumor cells form discrete nests.

MULTIPLE ENDOCRINE NEOPLASIA 1 (MEN1)

osms.it/multiple-endocrine-neoplasia-1

PATHOLOGY & CAUSES

- Autosomal dominant disorder
  - *Characterization:* predisposition for endocrine tumor development
- Tumors may be functional/non-functional (NF); benign/malignant; may affect one/more tissues simultaneously

TYPES

Parathyroid

- Most common

Pancreas, duodenum

- Gastrinoma (ZES), insulinoma, glucagonoma, VIPoma

Anterior pituitary adenoma

- Prolactinoma
- *Other:* corticotroph (ACTH) secreting, thyroid-stimulating hormone (TSH) secreting, growth hormone (GH) secreting, NF

Carcinoid

- Thymic, lung, gastric enterochromaffin-like tumor (NF)

Adrenal cortical tumor

- NF

CAUSES

- Mutation of *MEN1* gene located on chromosome 11 (11q13)
  - Encodes protein menin (endocrine organ tumor suppressor)
  - Menin function disruption/inactivation → clonal proliferation → somatic heterozygosity loss of remaining functional allele → endocrine neoplasia formation → primarily affects parathyroid, pituitary, pancreas (3Ps)

RISK FACTORS

- Mutant *MEN1* inheritance

COMPLICATIONS

- *Hyperparathyroidism:* ↓ bone mineral density, nephrolithiasis
- *Pituitary adenoma:* mass effects (e.g. headache, diplopia, visual field defects), Cushing disease, acromegaly
- *Gastrinoma:* peptic ulcer disease, gastrointestinal bleeding
- *Glucagonoma:* necrolytic migratory erythema (NME)
- Metastasis, tumor recurrence

SIGNS & SYMPTOMS

Clinical hormone imbalance, affected organ manifestations

- Hyperparathyroidism
  - Hypercalcemia (e.g. muscle weakness, constipation)
- Pituitary adenoma
  - *Prolactinoma:* menstrual irregularities, galactorrhea, ↓ libido, infertility
  - ↑ *GH:* excessive bone, soft tissue growth; arthralgias
  - ↑ *ACTH:* fat redistribution, plethoric facies, thin skin, striae
  - ↑ *TSH:* hyperthyroidism (e.g. palpitations, tremulousness)
- Pancreatic tumors
  - Glucose dysregulation (insulinomas, glucagonomas); watery diarrhea, hypokalemia, achlorhydria (WDHA) (VIPoma); steatorrhea (somatostatinoma), abdominal pain, gastroesophageal reflux (gastrinoma)
- Carcinoid tumors
  - Dyspnea, wheezing (lung), nausea, vomiting, abdominal pain (gastrointestinal), clinical manifestations of Cushing's syndrome (↑ ACTH from thymic tumor)

Cutaneous manifestations

- Facial angiofibroma, lipoma, collagenoma

DIAGNOSIS

DIAGNOSTIC IMAGING

MRI/CT scan

- Identifies tumor, metastasis, organ structure changes; TNM staging

Upper GI endoscopy

- Identifies gastric, duodenal carcinoid tumors, peptic ulcers; allows biopsy

Endoscopic ultrasound, somatostatin receptor scintigraphy

- Detects pancreatic neuroendocrine neoplasms (PanNETs)

LAB RESULTS

Blood studies

- Parathyroid tumors
  - ↑ basal serum calcium, ↑ serum PTH, hypercalciuria
- Anterior pituitary adenomas
  - ↑ prolactin, ↑ ACTH, ↑ cortisol, ↑ GH
- PanNETs
  - ↑ fasting gastrin, ↑ insulin, ↑ ↓ glucose, ↑ VIP

OTHER DIAGNOSTICS

- History, physical examination
  - Occurrence of ≥ two primary MEN1 tumor types; identification of first-degree relatives with similar findings
- *MEN1* gene-mutation testing

TREATMENT

MEDICATIONS

- Hyperparathyroidism
  - Calcimimetic agents
- Prolactinoma
  - Dopamine agonists
- Gastromas
  - Proton pump inhibitors (PPIs)
- Glucagonomas, insulinomas, somatostatinoma, VIPoma
  - Somatostatin analogue, anti-hyperglycemic agents
- Insulinoma
  - Diazoxide

SURGERY

- Parathyroid tumor
  - Parathyroidectomy, ethanol ablation

- Pituitary adenoma
  - Gamma knife stereotactic radiosurgery, transsphenoidal surgical resection
- Glucagonoma, somatostatinoma, gastrinoma, insulinoma, VIPoma, carcinoid
  - Tumor resection

OTHER INTERVENTIONS

- Correction of fluid, electrolyte, glucose, nutritional abnormalities
- Radiation therapy (e.g. pituitary adenoma)

MULTIPLE ENDOCRINE NEOPLASIA 2 (MEN2)

osms.it/multiple-endocrine-neoplasia-2

PATHOLOGY & CAUSES

- Autosomal dominant disorder
  - *Characterization:* predisposition for medullary thyroid carcinoma (MTC), pheochromocytoma, primary parathyroid hyperplasia

TYPES

MEN 2A

- Most common type, AKA Sipple syndrome
- Variants
  - Classic MEN2A with MTC, pheochromocytoma, primary hyperparathyroidism (milder than MEN1) (MEN2A with cutaneous lichen amyloidosis (CLA); MEN2A with Hirschsprung disease (HD))
  - Familial medullary thyroid carcinoma (FMTC)

MEN 2B

- Variants
  - MTC
  - Pheochromocytoma
  - *Other features:* mucosal neuromas (eyelid, lip, tongue), intestinal ganglioneuromas, marfanoid habitus, medullated corneal nerve fibers

CAUSES

- Defect in *RET* proto-oncogene located on chromosome 10 (10q11.2)
- Encodes transmembrane tyrosine kinase receptor RET protein (integral to intracellular signalling that regulates cellular differentiation, proliferation)
- Mutation → RET activation → disulfide-linked RET dimerization → intracellular substrate phosphorylation → clinical syndromes

RISK FACTORS

- *RET* mutation presence

COMPLICATIONS

- MTC
  - Hypercalcemia, cardiac arrhythmias, nephrolithiasis
- Parathyroid hyperplasia
  - Hyperparathyroidism, nephrolithiasis, osteoporosis
- Pheochromocytoma
  - Hypertension (therapy-resistant)
- HD
  - Functional bowel obstruction, megacolon, enterocolitis
- Intestinal ganglioneuromas
  - Bowel obstruction
- Metastasis

SIGNS & SYMPTOMS

- MTC/FMTC
  - Palpable neck mass, cervical lymphadenopathy, facial flushing (peptide secretion by tumor), diarrhea (gastrointestinal fluid, electrolyte secretion from excess calcitonin); clinical Cushing's syndrome manifestations (ectopic corticotropin (ACTH) production)
- Parathyroid hyperplasia
  - Fatigue, muscle weakness, altered mental status, bone pain (↓ bone density), flank pain (nephrolithiasis), nausea, vomiting, thirst, frequent urination
- Pheochromocytoma
  - Hypertension, paroxysms of palpitations, tachycardia, excessive sweating, facial flushing, tremors, anxiety (↑ catecholamines)
- HD
  - Vomiting, abdominal distension, constipation
- CLA
  - Scaly, papular, pigmented, lesions in either interscapular region/extensor surface extremities
- Intestinal ganglioneuromas
  - Abdominal pain, gaseous distension
- Dysmorphic facies
  - E.g. upper-eyelid margin thickening, eversion; nodules on tongue, vermilion border of lips

DIAGNOSIS

DIAGNOSTIC IMAGING

CT scan/MRI

- Tumor identification, TNM staging

Thyroid, neck ultrasound

- MTC
  - Calcification presence

LAB RESULTS

- MTC
  - ↑ carcinoembryonic antigen (CEA), ↑ serum calcitonin, pentagastrin/calcium stimulation test (↑ serum calcitonin)
- Parathyroid hyperplasia
  - ↑ basal serum calcium, ↑ serum PTH, hypercalciuria
- Pheochromocytoma
  - ↑ plasma fractionated metanephrines, ↑ 24-hour urine metanephrine

OTHER DIAGNOSTICS

- Medical history, family history, physical examination
  - *MEN 2A:* ≥ two characteristic neoplasias in individual/close family members
  - *MEN 2B:* mucosal neuromas of lips, tongue; marfanoid habitus; medullated corneal nerve fibers; gut ganglioneuromatosis; MTC
  - FMTC ≥ four MTC cases in families without pheochromocytoma/hyperparathyroidism
- Fine-needle aspiration (FNA) thyroid biopsy
  - *Histological analysis:* MTC with large, pleomorphic, ↑ C cell number
- Rectal biopsy
  - Absent ganglion cells (HD)
- Ophthalmic slit-lamp examination
  - Detects thickened, medullated corneal nerve fibers
- Genetic *RET* mutation testing

TREATMENT

MEDICATIONS

- Tyrosine kinase inhibitors
- Post-surgical hormone replacement
- Hyperparathyroidism
  - Bisphosphonates/calcimimetics (cinacalcet)
- Cutaneous lichen amyloidosis
  - Intralesional steroids, antihistamines, ultraviolet light/laser therapy

SURGERY

- Tumor resection (e.g. thyroidectomy, adrenalectomy, partial/cortex-sparing adrenalectomy)
- Lymphadenectomy

- HD
  - Resect affected colon segment

NEUROBLASTOMA

osms.it/neuroblastoma

PATHOLOGY & CAUSES

- Neural crest cell tumor arising in adrenal gland/spinal cord
- Fetal development → oncogene, tumor suppressor gene mutation → adequate cellular differentiation failure → tumor formation
- Most common infant cancer; most occur in age < five; better prognosis
- Releases chemokines (esp. CXCL12) → stimulates cell growth, migration → metastasis
- Half metastasize to bone

TYPES

- *Three types:* differentiation level

Undifferentiated

- Neural crest cells, AKA small blue round cells; contains nerve fibers, AKA neuropil

Poorly differentiated

- Partially displays characteristics of differentiated, undifferentiated

Differentiated

- Surrounded by myelin, AKA Schwannian stroma; better prognosis

SIGNS & SYMPTOMS

- Related to chemokine release; unspecific
- Fever; weight loss; sweating; fatigue

Mass effect

- Horner syndrome → ptosis, miosis, anhidrosis
- Spinal cord compression syndromes → limb weakness, incontinence
- Abdominal mass

Bone metastasis

- Pain, pathologic fractures
- Skull base fractures → battle, "racoon eyes" sign
- Myelosuppression → anemia, thrombocytopenia, leukopenia → fatigue, easy bruising, frequent infections

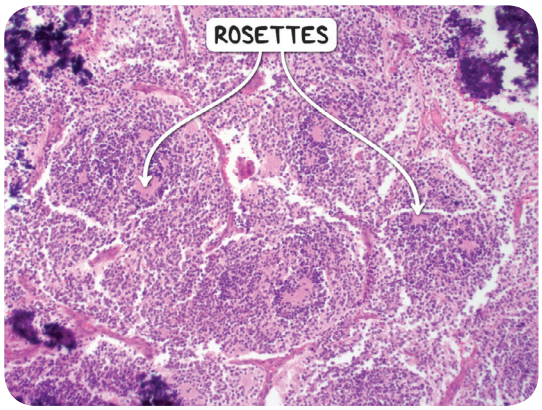

Figure 20.3 The histological appearance of a neuroblastoma demonstrating Homer-Wright rosettes.

DIAGNOSIS

DIAGNOSTIC IMAGING

CT scan

- Renal mass/mass adjacent to spinal nerve roots; confirm diagnosis

LAB RESULTS

- *Catecholamine breakdown products:* VMA, HMA

Complete blood count (CBC)

- Anemia, leukopenia

TREATMENT

MEDICATIONS

- Metastatic
  - Chemotherapy

SURGERY

- Localized
  - Resection
- Metastatic
  - Resection, bone marrow transplant

PANCREATIC NEUROENDOCRINE NEOPLASMS

osms.it/pancreatic-ne-neoplasms

PATHOLOGY & CAUSES

- AKA PanNETs
  - Functional tumors arising from pancreatic neuroendocrine cells
- Unregulated hormone secretion → effect on target organs → hormone-related clinical syndrome

TYPES

Insulinoma

- Rare functional tumor
  - Arises from insulin producing pancreatic beta cells
- Most common functioning PanNET
- Usually benign, indolent, small (< 2cm/0.8in), solitary lesions; rarely malignant
- ↑ insulin secretion → hyperinsulinemia → ↓ hepatic gluconeogenesis → hyperinsulinemic hypoglycemia

VIPoma

- Rare functional tumor
  - Arises from pancreatic D-1 cells that produce vasoactive intestinal polypeptide (VIP)
  - AKA Verner–Morrison syndrome/ pancreatic cholera syndrome
- *Malignancy:* 50%
- ↑ VIP secretion
  - Cellular adenylate cyclase, cAMP production by intestinal epithelial cells → secretion of fluid, sodium, chloride into intestinal lumen → high-volume secretory diarrhea

Glucagonoma

- Rare functional tumor
  - Arises from pancreatic glucagon-producing alpha cells
- Usually malignant
- Excessive glucagon
  - ↑ liver's catabolic action → ↑ amino acid oxidation, gluconeogenesis from amino acid substrates → glucagonoma syndrome (amino acid deficiency, ↑ blood glucose, glucose intolerance)
  - Co-secretion of gastrin, VIP, serotonin, calcitonin → diarrhea

Somatostatinoma

- Very rare somatostatin-secreting tumor
  - Arises from pancreatic D-cells
- Commonly located within head of pancreas; may also arise from ampulla, periampullary region of duodenum; rarely in jejunum, liver, colon, rectum
- Usually malignant
  - ↑ somatostatin → digestive organ inhibition → clinical syndrome

RISK FACTORS

Insulinoma

- Multifocal insulinomas associated with MEN 1

VIPoma, glucagonoma

- Associated with MEN 1

Somatostatinoma

- Associated with MEN1, neurofibromatosis type 1 (NF1)

COMPLICATIONS

Insulinoma

- Hypoglycemia, seizures, rarely metastasis

Vipoma

- Dehydration, electrolyte imbalances, metastasis

Glucagonoma

- NME, weight loss (secondary to hyponutrition)
- Diabetes, chronic diarrhea, venous thrombosis (deep vein thrombosis, pulmonary embolism)
- Neuropsychiatric complications (e.g. depression, psychosis, agitation, paranoid delusions)
- Metastasis

Somatostatinoma

- Cholelithiasis, diabetes mellitus, metastasis

SIGNS & SYMPTOMS

Insulinoma

- *Whipple's triad:* hypoglycemia, hypoglycemia signs, intravenous (IV) glucose → symptom resolution
  - *Neuroglycopenic manifestations:* visual disturbances, weakness, confusion
  - *Sympathetic/adrenergic manifestations:* diaphoresis, tremors, palpitations, hunger

VIPoma

- WDHA; stools tea-colored, odorless
- ↑ potassium secretion into large bowel → hypokalemia
- ↓ gastric acid secretion → hypochlorhydria
- ↑ glycogenolysis → hyperglycemia
- ↑ bone resorption → hypocalcemia
- ↑ vasodilation → flushing

Glucagonoma

- Hyperglycemia, weight loss
- NME
  - Erythematous, sometimes painful rash with papules/plaques on face, perineum, extremities; hair loss, nail dystrophy
  - *If mucous membranes affected:* glossitis, angular cheilitis, stomatitis, blepharitis

Somatostatinoma

- Classic syndrome
  - ↓ cholecystokinin → colelithiasis
  - ↓ pancreatic enzyme, ↓ intestinal lipid absorption → steatorrhea
  - ↓ gastrin → hypochlorhydria
  - ↓ insulin → diabetes mellitus
- Abdominal pain
- Weight loss

MNEMONIC: 6 Ds

Glucagonoma symptoms

Dermatitis
Diabetes
Diarrhea
Deep Venous Thrombosis
Decreased Weight
Depression

DIAGNOSIS

DIAGNOSTIC IMAGING

Endoscopic ultrasound

- Insulinoma, VIPoma, glucagonoma, somatostatinoma
  - Detects small tumors, establishes local disease extent, allows for needle biopsy

CT scan/MRI

- Insulinoma, VIPoma, glucagonoma, somatostatinoma
  - Tumor localization, TNM staging

CT scan

- VIPoma
  - Homogeneous, well-circumscribed

lesions; may have cystic regions
- Glucagonoma
  - May appear solid/contain central low-attenuation areas
- Somatostatinoma
  - Isodense; may be cystic

MRI
- VIPoma, glucagonoma, somatostatinoma
  - Low signal intensity on T1-weighted images, high signal intensity on T2-weighted images

GLP-1 scintigraphy
- Insulinoma
  - Identifies insulinoma via radiolabeled GLP-1 receptor imaging

Somatostatin receptor scintigraphy
- VIPoma, glucagonoma, somatostatinoma
  - Detects metastases via radiolabeled form of somatostatin analog octreotide (Indium-111 [111-In]) pentetreotide

Functional PET imaging with 68-Ga DOTATATE
- Glucagonoma, somatostatinoma
  - Detects small tumors

LAB RESULTS

Insulinoma
- Overnight fasting plasma levels/72 hour fast test (inpatient)
  - ↓↓ glucose, ↑ insulin, ↑ proinsulin, ↑ C-peptide

VIPoma
- *Hormonal assay:* ↑ plasma VIP
- ↓ stool osmotic gap (<50mOsm/kg)

Glucagonoma
- *Hormonal assay:* ↑ plasma glucagon
- ↑ glucose

Somatostatinoma
- *Hormonal assay:* ↑ somatostatin
- ↑ glucose

OTHER DIAGNOSTICS
- Histopathological analysis, grading
  - Determines degree of pleomorphism, hyperchromasia, mitotic activity

TREATMENT

MEDICATIONS

Insulinoma
- *Diazoxide:* inhibits insulin release, enhances glycogenolysis

VIPoma
- Somatostatin analogue

Glucagonoma, somatostatinoma
- Somatostatin analogue
- Anti-hyperglycemic agents

SURGERY

Insulinoma, VIPoma, glucagonoma, somatostatinoma
- Resection
- Ultrasound-guided fine needle ethanol ablation (insulinoma only)

OTHER INTERVENTIONS

Insulinoma
- Oral carbohydrate administration; IV glucose

VIPoma
- *Manage complications:* fluid, electrolyte replacement
- Treat metastatic disease (e.g. chemotherapy, radiation)

Glucagonoma, somatostatinoma
- Correct nutritional deficiencies
- Treat metastatic disease (e.g. chemotherapy, radiation)

PHEOCHROMOCYTOMA

osms.it/pheochromocytoma

PATHOLOGY & CAUSES

- *Pheo* = dark; *chromo* = colored; *cyto* = cell; *oma* = tumor
- Arises from chromaffin cells in adrenal medulla; secretes catecholamines
- *Rule of 10s:* 10% bilateral; 10% in children; 10% metastasize; 10% calcify; 10% extra-adrenal
- Most common adult adrenal medulla tumor
- Most common in older biologically-male individuals; may be part of inherited syndrome (25%)
  - MEN 2A, MEN 2B → *RET* proto-oncogene mutation
  - Von-Hippel-Lindau (VHL) → *VHL* gene mutation
  - Neurofibromatosis type 1 (NF1) → *NF1* mutation → impaired neurofibromin function

SIGNS & SYMPTOMS

- Catecholamine excess-related → ↑ epinephrine, norepinephrine, dopamine
- Sweating, anxiety, palpitations, tachycardia, transient, episodic hypertension, headaches
- May be associated with polycythemia

MNEMONIC: Ps

Pheochromocytoma symptoms

Perspiration
Palpitation
Pallor
↑ Blood **P**ressure (BP)
Pain (headache)

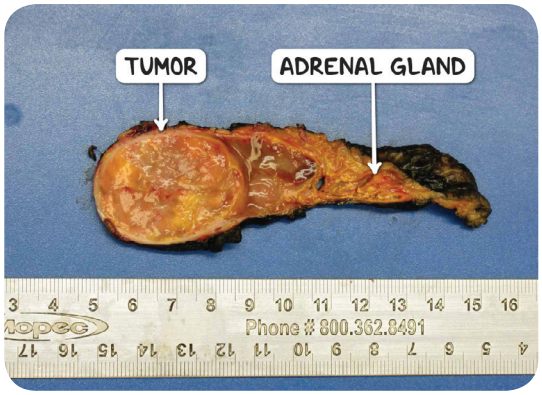

Figure 20.4 The gross pathological appearance of an adrenal pheochromocytoma. The tumor has been bissected revealing a hemorrhagic and necrotic cut surface.

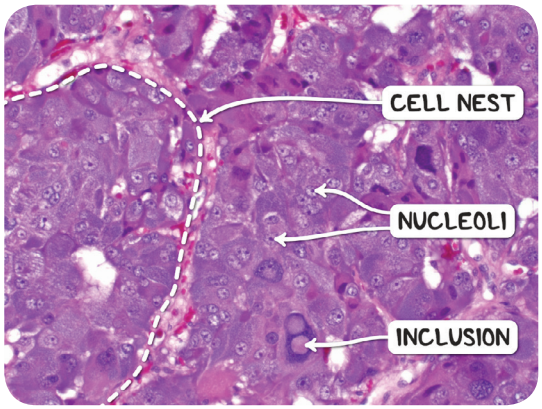

Figure 20.5 The histological appearance of an adrenal pheochromocytoma. The tumor cells are arranged in nests and display prominent nucleoli and occasional nuclear inclusions.

DIAGNOSIS

DIAGNOSTIC IMAGING

CT scan/MRI

- Suprarenal mass; confirm diagnosis

LAB RESULTS

Screening

- Urinary, serum catecholamine breakdown products → homovanilic acid (HMA), vanilmandellic acid (VMA)

CBC

- Polycythemia

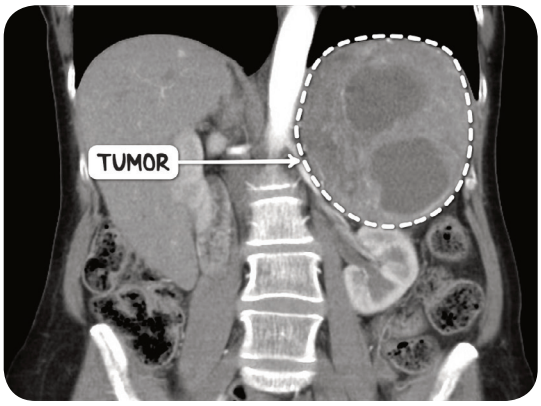

Figure 20.6 An abdominal CT scan in the coronal plane demonstrating a large adrenal pheochromocytoma on the left hand side.

TREATMENT

SURGERY

- Removal (requires pre-operatory preparation)
  - Block alpha effects with phenoxybenzamine → give beta blocker

ZOLLINGER–ELLISON SYNDROME (ZES)

osms.it/zollinger-ellison_syndrome

PATHOLOGY & CAUSES

- AKA gastrinoma syndrome
- Functional gastrin-secreting tumor
  - Most commonly arises from "gastrinoma triangle" (head of pancreas, curve of duodenum, cystic, common bile duct)
- Usually malignant
- ↑ gastrin secretion
  - ↑ gastric acid output from parietal cells, enterochromaffin-like (ECL) → malabsorption, mucosal lining erosion (stomach, duodenum)
  - Inhibition of sodium, water absorption by small intestines → loose stools
- May co-occur with other PanNET syndromes

RISK FACTORS

- 20–30% of cases associated with MEN1
- More common in biologically-male individuals

COMPLICATIONS

- Diarrhea, steatorrhea, peptic (potential for bleeding, perforation), esophageal strictures, pancreatitis (with duct obstruction)
- Most gastrinomas malignant

SIGNS & SYMPTOMS

- Abdominal pain; gastroesophageal reflux; nausea, vomiting; dysphagia; weight loss; loose stools; gastrointestinal (GI) bleeding

DIAGNOSIS

DIAGNOSTIC IMAGING

Upper endoscopy

- Enlarged gastric rugal folds, esophagitis, ulcer presence

Endoscopic ultrasound

- Gastrinomas appear as hypoechoic, homogeneous masses

Somatostatin receptor scintigraphy

- Somatostatin analog (111 indium-DTPA-D-Phe1 octreotide) administered, somatostatin analog binds to somatostatin Type II receptors on gastrinomas
- Visualize gastrinoma(s), metastatic lesions

LAB RESULTS

- *Basal (fasting) gastrin levels:* ↑ serum gastrin

Secretin stimulation test

- Secretin administered IV
- If ZES tumor present
  - ↑ serum gastrin > basal levels
- If other cause of hypergastrinemia
  - Gastrin inhibition

OTHER DIAGNOSTICS

- MEN1 screening

TREATMENT

MEDICATIONS

- Chemotherapy
  - Metastatic disease

SURGERY

- Resection

OTHER INTERVENTIONS

- Proton pump inhibitors
  - ↓ gastric acid
- Somatostatin analog
  - ↓ gastrin levels; may slow tumor growth