MEDULLARY THYROID CANCER and RELATED MEN SYNDROMES

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Grand Rounds
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Thyroid Cancer

• Comprises 95% of all endocrine malignancies and 1.5% of all cancers
• Has the greatest annual percentage increase in incidence of any cancers (4% per year)
• Lifetime risk in US is estimated to be
  – 0.8% for women
  – 0.3% in men
• Median age of diagnosis is 48 years
Categories

• Follicular cell–derived or differentiated thyroid cancer
  – papillary thyroid cancer (PTC)
  – follicular cancer (FC)
  – Hurthle cell cancer (HCC)
  – anaplastic cancer (ATC)
• Non–follicular cell–derived variants
  – medullary thyroid cancer (MTC)
  – Lymphoma
  – metastases
Medullary Thyroid Carcinoma

- Accounts for 5-10% of all thyroid cancers
- Can occur in a sporadic or hereditary forms (part of MEN 2 syndromes)
  - MEN 2A
  - MEN 2B
  - Familial non-MEN medullary thyroid carcinoma (FMTC)
- Originates from the parafollicular cells (C cells) of the thyroid which produce, store, and secrete calcitonin
- These cells comprise 1% of the total thyroid mass and are dispersed throughout the gland
Calcitonin in MTC

- Basal and stimulated serum calcitonin levels correlate with tumor burden and are always elevated in patients with palpable MTC
- Calcitonin excess is not associated with hypocalcemia
- Secretory diarrhea and flushing, most often attributed to elevated calcitonin, are the main paraneoplastic manifestations of advanced MTC
- MTCs may secrete other hormones, including CEA (>50%) and calcitonin gene-related peptide (CGRP)
A solitary mass in a thyroid lobe was removed by total thyroidectomy.
Histologically, MTC can be identified by calcitonin staining and by the presence of amyloid in the tumors.
Clinical Features of Sporadic MTC, MEN 2A, MEN 2B, and FMTC

<table>
<thead>
<tr>
<th>CLINICAL SETTING</th>
<th>FEATURES OF MTC</th>
<th>INHERITANCE PATTERN</th>
<th>ASSOCIATED ABNORMALITIES</th>
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</thead>
<tbody>
<tr>
<td>Sporadic MTC</td>
<td>Unifocal</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>MEN 2A</td>
<td>Multifocal, bilateral</td>
<td>Autosomal dominant</td>
<td>Pheochromocytomas, hyperparathyroidism</td>
</tr>
<tr>
<td>MEN 2B</td>
<td>Multifocal, bilateral</td>
<td>Autosomal dominant</td>
<td>Pheochromocytomas, mucosal neuromas, megacolon, skeletal abnormalities</td>
</tr>
<tr>
<td>FMTC</td>
<td>Multifocal, bilateral</td>
<td>Autosomal dominant</td>
<td>None</td>
</tr>
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</table>
Sporadic vs. Familial MTC

• Sporadic in 70-80% of cases
  – tumors are usually single and have no familial predisposition
  – multicentric or bilateral disease can be present in 30%

• Familial in 20-30%, as part of the MEN2A, MEN2B, or isolated familial syndromes
  – all autosomal-dominant inheritance, result from germline mutations in the \textit{RET} protooncogene
MTC Associated with MEN 2 Syndromes

• Caused by germline mutations in the \textit{RET} gene on chromosome 10
• Gene encodes a transmembrane protein tyrosine kinase
• The mutations are gain-of-function mutations that cause activation of the protein
• More than 30 missense mutations have been described
Familial Medullary Thyroid Cancer

- MTC without any other endocrinopathies in >3 affected family members
- MTC in these patients has a later age of onset and a more indolent clinical course, penetrance is lower
- Many patients with FMTC are cured by thyroidectomy alone, and those with persistent elevation of calcitonin levels do well for many years
- The rate of de novo cases is extremely low
MEN 2A

Medullary thyroid carcinoma
Pheochromocytoma
Hyperparathyroidism
Lichen planus amyloidosis
Hirschsprung disease
MEN2A

- MEN2A is the most common hereditary form (66%)
  - presentation in 3\textsuperscript{rd}-4\textsuperscript{th} decade of life
  - 90% of gene carriers will develop MTC (multifocal and bilateral)
  - 60% will develop unilateral or bilateral pheochromocytoma
  - 15-30% will develop hyperparathyroidism
  - The aggressiveness of MTC and the probability of developing pheochromocytoma and parathyroid disease are influenced by the specific \textit{RET} mutation
  - MEN 2A usually has a more favorable long-term outcome than MEN 2B or sporadic MCT
MEN 2B

Medullary thyroid carcinoma

Pheochromocytoma

Musculoskeletal abnormality (*marfanoid habitus, pes cavas, pectus excavatum*)

Mucosal neuromas of the lips, tongue, and conjunctiva

Ganglioneuromatosis of the gastrointestinal tract

Medullated corneal nerve fibers
MEN 2B

- MEN 2B is the rarest and most aggressive of the hereditary MTC syndromes (presents in infancy)
- Once MTC presents clinically, it is rarely curable
- Can be distinguished from MEN2A by the presence of developmental defects and absence of hyperparathyroidism
- Average age of onset of MTC for patients diagnosed with MEN 2B is 10 years
  - all patients develop MTC
  - all patients have ganglioneuromas and mucosal neuromas
  - 50% develop pheochromocytoma
  - >50% of MEN2B cases occur as a result of de novo germline RET mutations
Features of Patients with Hereditary MTC

A Bisected thyroid gland from a patient with MEN 2A showing multicentric, bilateral foci of MTC
B Adrenalectomy specimen from patient with MEN 2B demonstrating pheochromocytoma
C Megacolon in patient with MEN 2B
D Tongue of patient with MEN 2B showing characteristic notching 2ry to plexiform neuromas
Hereditary MTC

- Family members of patients with MEN 2 ideally are screened for the *RET* proto-oncogene
- Workup includes a detailed family history to inquire about the characteristics of MEN 2 in the patient and family members
- If MCT is suspected, serum calcium and urinary catecholamines must be determined to evaluate for hyperparathyroidism and possible pheochromocytoma
Hereditary MTC

- Early diagnosis in hereditary MTC is critical because metastases occur in the early stages of disease.
- Lymph node metastases are rarely present in patients in whom genetic testing establishes the diagnosis of MEN 2A or FMTC in childhood and thyroidectomy is performed before the occurrence of a thyroid mass or elevation of calcitonin level.
Sporadic MTC

- Most cases of sporadic MTC present as a neck mass detected on physical exam
- Lymph node metastases are usually present in these patients by the time of diagnosis
- Diagnosis is made by biopsy (FNA cytology) and measurement of calcitonin levels
- Germline DNA testing for RET gene mutations is recommended for all patients with MTC regardless of family history
  - ~10% of apparent sporadic MTC will have a de novo mutation in the RET protooncogene
MTC Lymphatic Spread

• Spreads within the central neck compartment
• Further lymphatic spread can also occur to the lateral neck compartment
• The outcome of patients with involvement of lower tracheobronchial lymph nodes is equivalent to that of patients with distant metastases
• The incidence of nodal metastases in palpable, established MTC is 80%
Local Invasion of MTC

- May involve adjacent structures by direct invasion or compression
  - trachea
  - recurrent laryngeal nerve
  - jugular veins and carotid arteries

- Possible symptoms
  - stridor and upper airway obstruction
  - hoarseness
  - dysphagia
  - bleeding, arterial stenosis or occlusion
Metastatic MTC

- Distant metastases occur in liver, lung, bone and other soft tissues, including breast
- MTC patients with a palpable mass in the neck have distant metastatic disease in 12-20% of cases
- Occult remote metastases are the likely cause of persistent hypercalcitoninemia after thyroidectomy and extensive lymph node dissection
Spinal metastases from medullary thyroid carcinoma in a patient with MEN 2A
Presentation and Diagnosis
Presentation of MTC

- Patients with MEN 2A and FMTC have normal appearance
  - diagnosis is made through screening
- >50% of patients with MEN 2B have a de novo mutation and usually present with a thyroid nodule
- In patients with palpable MTC
  - >50% have palpable cervical adenopathy
  - up to 80% have histological lymph node metastases
  - 12-20% present with distant metastasis
- 13% of patients have respiratory complaints
- Occasional index cases of MEN 2 present with clinical pheochromocytoma, Hirschsprung's disease, or hyperparathyroidism before the diagnosis of MTC
Diagnosis of MTC

- Thyroid nodule – FNAB
- Genetic testing for the relevant mutations in the RET gene is widely available and is very accurate and reliable
  - If positive, need to rule out pheochromocytoma before thyroidectomy
- Calcitonin is an invaluable serum marker in screening and follow-up settings - correlates with tumor bulk, lymph node metastases, and systemic metastases
  - basal state & after administration of calcium and pentagastrin
  - more useful than CEA, but high CEA levels are associated with a poorer prognosis
Preoperative Laboratory Testing

“You’ve got to buy a centrifuge machine for these hematocrits, Doctor! I can’t take much more of this spinning chair routine!”
Preoperative Laboratory Testing

• All patients with MTC should be ruled out for MEN2
  – serum calcium level (to screen for hyperparathyroidism)
  – urine or plasma catecholamines (to r/o pheochromocytoma)

• A coexisting pheochromocytoma should be treated prior to the thyroidectomy to avoid malignant hypertension on induction
Preoperative Imaging Studies
Preoperative Imaging Studies

• Used to determine the extent of local neck disease and the presence of systemic metastases
• US of the neck is used to evaluate for abnormal lymph nodes in the central and lateral neck in all patients
• Additional imaging studies are reserved for patients with lymph node metastases or a serum calcitonin level over 400 pg/mL (r/o systemic metastases)
Preoperative Imaging Studies

• CT of the neck, chest, and upper abdomen is useful to evaluate for possible tumor invasion of the upper aerodigestive tract and metastases to the mediastinal lymph nodes, lungs, and liver

• MRI is the most sensitive imaging modality for detection of liver metastases and is complementary with bone scintigraphy for detection of bone metastases
Preoperative Imaging Studies

- Diagnostic laparoscopy has been advocated prior to initial operation in patients with marked hypercalcitoninemia (>1000 pg/mL) to document the presence of liver disease.
- Staging of MTC is based on
  - tumor size
  - extrathyroidal tumor spread
  - local or regional lymph node metastases
  - systemic metastases
### Primary tumor (T)

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>T0</td>
<td>No evidence of primary tumor</td>
</tr>
<tr>
<td>T1</td>
<td>Tumor 2 cm or less in greatest dimension limited to the thyroid <em>(Supplementum to the 6th edition: T1a, tumor 1 cm or less; T1b, tumor more than 1 cm but not more than 2 cm)</em></td>
</tr>
<tr>
<td>T2</td>
<td>Tumor more than 2 cm, but not more than 4 cm, in greatest dimension limited to the thyroid</td>
</tr>
<tr>
<td>T3</td>
<td>Tumor more than 4 cm in greatest dimension limited to the thyroid or any tumor with minimal extra-thyroidal extension (e.g. extension to sternothyroid muscle or perithyroid soft tissues)</td>
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<tr>
<td>T4a</td>
<td>Tumor of any size extending beyond the thyroid capsule to invade subcutaneous soft tissues, larynx, trachea, esophagus, or recurrent laryngeal nerve</td>
</tr>
<tr>
<td>T4b</td>
<td>Tumor invades prevertebral fascia or encases carotid artery or mediastinal vessels.</td>
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</tbody>
</table>
American Joint Committee on Cancer TNM Classification

Regional lymph nodes (N) are the central compartment, lateral cervical, and upper mediastinal lymph nodes

<table>
<thead>
<tr>
<th>N</th>
<th>Description</th>
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<tbody>
<tr>
<td>NX</td>
<td>Regional lymph nodes cannot be assessed</td>
</tr>
<tr>
<td>N0</td>
<td>No regional lymph node metastases</td>
</tr>
<tr>
<td>N1</td>
<td>Regional lymph node metastases</td>
</tr>
<tr>
<td>N1a</td>
<td>Metastasis to Level VI (pretracheal, paratracheal, and prelaryngeal/Delphian lymph nodes)</td>
</tr>
<tr>
<td>N1b</td>
<td>Metastasis to unilateral, bilateral, or contralateral cervical or superior mediastinal lymph nodes</td>
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Distant metastases (M)

<table>
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<tr>
<th>M</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>MX</td>
<td>Distant metastasis cannot be assessed</td>
</tr>
<tr>
<td>M0</td>
<td>No distant metastasis</td>
</tr>
<tr>
<td>M1</td>
<td>Distant metastasis</td>
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## Stage Groupings for MTC

<table>
<thead>
<tr>
<th>Stage</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage I</td>
<td>T1N0M0</td>
</tr>
<tr>
<td>Stage II</td>
<td>T2N0M0</td>
</tr>
<tr>
<td>Stage III</td>
<td>T3N0M0, T1N1aM0, T2N1aM0, T3N1aM0</td>
</tr>
<tr>
<td>Stage IVa</td>
<td>T4aN0M0, T4aN1aM0, T1N1bM0, T2N1bM0, T3N1bM0, T4N1bM0</td>
</tr>
<tr>
<td>Stage IVb</td>
<td>T4b, any N, M0</td>
</tr>
<tr>
<td>Stage IVc</td>
<td>Any T, any N, M1</td>
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</table>
MTC Treatment

“We’ve found a mass. The good news is we have weapons of mass destruction.”
MTC Treatment Considerations

• Clinical course of MTC is usually more aggressive than that of differentiated thyroid cancer, with higher recurrence and mortality rates
• MTC cells do not take up radioactive iodine, and radiation therapy and chemotherapy are ineffective
• MTC is multicentric in 90% of patients with the hereditary forms of the disease
• MTC spreads to the lymph nodes in the central neck in 50% of patients with sporadic and hereditary MTC
• Presence of lymph node metastases in the central neck is a risk factor for lateral node involvement
MTC Treatment

• The mainstay of treatment of MTC is surgical
• For sporadic MTC - at least total thyroidectomy with or without central lymph node dissection
  – search for multicentricity
  – allows appropriate staging
• A modified neck dissection is indicated in patients with metastatic lymph nodes in the central or lateral neck (removing lymph nodes from levels II-V)
• Patients with regional lymph node metastases are rarely biochemically cured, even with aggressive bilateral neck dissection
Preventive Surgery

- Best chance of cure in familial MTC is provided by complete surgical resection before malignant transformation or before spread beyond the thyroid gland.
- Preventive thyroidectomy is the goal in patients who are identified by genetic testing to have hereditary MTC but who do not yet display clinical evidence of disease.
- It obviates the need for a central compartment lymph node dissection and its risk of hypoparathyroidism.
Preventive Surgery

- Patients with MEN 2B (highest risk) should have a total thyroidectomy performed as early as possible, before 6 months of age.
- There is an extremely low likelihood of nodal metastases in patients younger than 8 years with MEN 2A or FMTC and in patients with a normal calcitonin level.
- Patients with mutations with MEN 2A should have thyroidectomy before 5 to 6 years of age.
- Management of patients with FMTC is more controversial (indolent disease course)
  - thyroidectomy before 5 to 10 years of age or based on calcitonin levels.
Patient is placed in a supine position with the arms tucked at the sides and a shoulder roll placed lengthwise to extend the neck.
Incision

Transverse collar incision is made two fingerbreadths above the sternal notch along a skin crease.
Raising Flaps

Subcutaneous tissue and the platysma are divided

Skin flaps are raised to the level of

- thyroid cartilage superiorly
- sternal notch inferiorly
- sternocleidomastoid muscles laterally
Thyroid Gland Exposure

Strap muscles are separated in the midline along the median raphe from the prominence of the thyroid cartilage to the sternal notch.
Middle Thyroid Vein

The middle thyroid vein is divided, and the lobe of thyroid is mobilized anteromedially.
Superior Thyroid Vessels

The superior pole vessels are identified by exerting downward traction on the upper pole of the thyroid gland and individually ligated close to the thyroid gland to avoid injury to the external branch of the superior laryngeal nerve.
Antero-medial Mobilization

Areolar tissue between the common carotid artery and the thyroid lobe is dissected using a combination of blunt and sharp techniques, facilitating the anterior and medial rotation of the thyroid lobe.
Thyroidectomy

- Inferior thyroid artery is delineated
- Recurrent laryngeal nerve is identified, traced through its entire course and preserved
- Routine exposure of the recurrent laryngeal nerve has been shown to reduce the rate of nerve injury
- Intraoperative nerve monitoring is not necessary and should not be used in lieu of routine exposure of the recurrent laryngeal nerve
Division of Inferior Thyroid Vessels

Inferior pole of the thyroid gland is mobilized by ligating the tertiary branches of the arteries and veins close to the thyroid gland to preserve the blood supply to the inferior parathyroid gland.
Clearing the Trachea

Remaining thyroid lobe and ligament of Berry are separated from the recurrent laryngeal nerve, preserving the blood supply to the superior parathyroid gland.
Excision of the Lobe

Remaining thyroid lobe and ligament of Berry are separated from the recurrent laryngeal nerve, preserving the blood supply to the superior parathyroid gland.
Thyroidectomy

- Contralateral lobe of the thyroid gland is removed in an identical fashion.
- Sternohyoid muscles are re-approximated in the midline, leaving the inferior aspect open (3-4cm) to allow blood to decompress into the subcutaneous space if bleeding develops.
- A drain is not used.
Parathyroidectomy

- Leave the parathyroid glands in situ if possible
- If devascularised – autotransplantation
  - Send a small piece for frozen-section (for confirmation)
  - the gland is sliced and autotransplanted into the sternocleidomastoid muscle in patients with sporadic MTC, MTC of MEN2B, and FMTC
  - In patients with MEN2A and a \( RET \) mutation, parathyroid gland should be autotransplanted into the brachioradialis muscle of the nondominant forearm (associated with a high risk of hyperparathyroidism)
Parathyroidectomy

• Patients are maintained on calcium and vitamin D supplementation for 4-8 weeks postop
• Parathyroidectomy with autotransplantation is done in all patients with gross parathyroid enlargement or biochemical evidence of parathyroid disease at the time of operation for MTC
Surgery for Palpable Disease

- Risk for more extensive nodal metastatic disease is increased
- Total thyroidectomy, parathyroidectomy with autotransplantation, central neck dissection, and ipsilateral level II to V node dissection (maybe bilateral)
- Persistent disease, evidenced by elevation of calcitonin levels, is present in more than 50% of patients after surgery for palpable MTC
- A successful operation with a good prognosis is predicted for patients with smaller masses and in whom calcitonin levels are undetectable after surgery
Persistent or Recurrent Disease

• Patients who present with palpable MTC often have elevated calcitonin levels following primary surgery, indicating residual or recurrent MTC

• Currently, there is no defined role for chemotherapy or radiation therapy in these patients

• Reoperation for patients with recurrent disease can be done with curative or palliative intent

• Evidence of distant metastases is a contraindication to surgery unless some palliative benefit can be identified
  – prevent invasion or compression of the airway
  – debulk large tumors that cause profuse, intractable diarrhea secondary to hormone secretion
Postoperative Care

- Postoperatively, patients are started on a replacement dose of thyroid hormone.
- No need to treat with TSH-suppressive doses of thyroid hormone or radioiodine, because the C cells are not responsive to TSH and don’t concentrate radioiodine.
- Subsequent follow-up consists of periodic physical examination and measurement of serum calcitonin and CEA levels to detect recurrent disease.
Follow-up

- Yearly screenings for MTC recurrences and other manifestations of the syndrome must be conducted.
- In patients with a calcitonin level less than 150 pg/mL, an US of the neck is sufficient for further evaluation.
- If serum calcitonin levels remain persistently high, further imaging is necessary to locate other potential sites of metastases.
- Recommended imaging studies include CT of the chest, MRI of the liver, and bone scintigraphy.
- Unfortunately, documentation of recurrent MCT by biochemical means is often associated with unresectable recurrence in distant metastatic locations.
Follow-up

- For MEN 2 syndromes, routine yearly plasma or 24-hour urine screens must be performed to rule out a pheochromocytoma
  - If catecholamines or metanephrines become elevated, MRI or CT are repeated to localize the tumor
- MEN 2A patients must have lifelong screening for evidence of hyperparathyroidism
  - Graft-dependant hyperparathyroidism may occur in patients with parathyroid autografts -> debulking
Prognosis

- Prognosis is related to disease stage
- 10 year survival is ~75%, but decreases to 45% in patients with lymph node involvement
- Before the use of screening techniques, average life expectancy was 50 years for patients with MEN 2A and 30 years for patients with MEN 2B
- MTC in the MEN 2 syndromes is usually indolent and slow-growing, but it is lethal in many patients with distant metastases
- Patients with MEN 2A and FMTC have a better long-term outcome than patients with MEN 2B or sporadic tumors
External Beam Radiation Therapy

- Is an option for grossly positive or microscopically positive margins following surgery and for high-volume disease involving the central and lateral compartments of the neck.
- Not endorsed by the ATA as a substitute for surgery or as a general adjuvant therapy for patients with elevated calcitonin postoperatively.
Pheochromocytoma

• Occurs in 40-60% of MEN 2A and MEN 2B patients
• Arise in adrenal medullary cells that synthesize, store, and secrete catecholamines
• In MEN 2, pheochromocytomas are often multifocal, with bilateral tumors
• As opposed to the sporadic form of the disease, malignant and extra-adrenal pheochromocytomas are very rare within MEN 2 populations
• Pheochromocytomas rarely precede the development of C-cell abnormalities in MEN 2 syndrome
Pheochromocytoma

• Classic signs and symptoms
  – hypertension, headache, heart palpitations, anxiety, and tremulousness

• Complications of unrecognized disease
  – malignant hypertension, stroke, myocardial infarction, cardiac arrhythmias, and sudden death during unrelated surgical procedures, biopsies, or childbirth

• Pheochromocytomas may be clinically silent in up to 60% of MEN 2 cases, where they are detected by biochemical testing
Diagnosis of Pheochromocytoma

- Biochemical screening is done by measurement of plasma or 24-hour urine catecholamines and metanephrines.
- If the test is positive or borderline, imaging is needed to determine whether a pheochromocytoma is present.
- Most MEN 2A and MEN 2B patients have some degree of adrenal medullary hyperplasia.
- Adrenal CT or MRI can detect tumors 1 cm or larger.
- MRI may distinguish a pheochromocytoma from an adrenal adenoma, which occurs in up to 9% of normal patients.
A, CT scan of the neck in a patient with MEN 2A and untreated medullary thyroid carcinoma (arrow) with adenopathy

B, Abdominal computed tomography scan of the same patient showing cystic left pheochromocytoma (arrow)
Treatment of Pheochromocytoma

• Partial or complete adrenalectomy is recommended in patients with MEN 2A and MEN 2B who are found to have a pheochromocytoma

• It is important to medically stabilize the patient before surgery to avoid any perioperative events due to excessive catechol secretion

• Preoperative $\alpha$-blockade is achieved by administration of phenoxybenzamine (40-200 mg/day) for 5 days to 2 weeks before surgery

• The dose is titrated to the lowest blood pressure tolerated and a $\beta$-blocker is added to the treatment regimen if tachycardia or cardiac arrhythmia present
Treatment of Pheochromocytoma

• During operation, it may be necessary to control paroxysmal hypertension with short-acting antihypertensives (sodium nitroprusside or phentolamine)

• Patients with MEN 2A and MEN 2B are ideally suited to laparoscopic adrenalectomy because the pheochromocytomas arising in these syndromes are rarely malignant and almost never extra-adrenal

• Contraindications to the laparoscopic approach include large tumors (>8-10 cm), malignant pheochromocytomas, and existing contraindications to laparoscopy
Parathyroid Disease in MEN 2A

• Hyperparathyroidism occurs in 10-35% of patients
• It is rarely the initial presenting problem
• It is characterized by multiglandular hyperplasia (<1/5 patients has a single parathyroid adenoma)
• Parathyroid hyperplasia, in the absence of hyperparathyroidism, is common in MEN 2A
• Parathyroid hyperplasia is not found in patients with sporadic MTC or in patients with MTC in MEN 2B syndrome
Diagnosis of Parathyroid Disease

• All known MEN 2A carriers need to be screened annually for the presence of hyperparathyroidism by serum calcium measurements
• PTH levels are measured if the serum calcium is high or borderline
Treatment of Parathyroid Disease

- The need for isolated parathyroidectomy in MEN 2A patients is rare
- Routine total parathyroidectomy with autotransplantation at the time of thyroidectomy is usually performed regardless of gross appearance of the parathyroid glands
- Should hyperparathyroidism occur at a later time in these patients with forearm grafts, surgical removal of all or a portion of the graft can be done
Question

With regard to medullary thyroid carcinoma, which of the following statements is/are correct?

A. It is derived from a dedifferentiated variant of the same cell that produces papillary and follicular carcinomas
B. It’s pattern of metastatic spread is almost exclusively to distant sites
C. The serum calcitonin level is useful for diagnosis and management
D. The prognosis is approximately the same as that of papillary carcinoma
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A. It is derived from a dedifferentiated variant of the same cell that produces papillary and follicular carcinomas

B. It’s pattern of metastatic spread is almost exclusively to distant sites

C. The serum calcitonin level is useful for diagnosis and management

D. The prognosis is approximately the same as that of papillary carcinoma
Question

Are the following characteristics of medullary thyroid carcinoma associated with its sporadic form, its hereditary form, or both?

A. Contains parafollicular cells that secrete calcitonin
B. Multifocal and bilateral
C. Associated with MEN-IIA and MEN-IIB
D. Worse prognosis
E. Treatment consists of total thyroidectomy with central node dissection
Are the following characteristics of medullary thyroid carcinoma associated with its sporadic form, its hereditary form, or both?

A. Contains parafollicular cells that secrete calcitonin - Both
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D. Worse prognosis
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Are the following characteristics of medullary thyroid carcinoma associated with its sporadic form, its hereditary form, or both?

A. Contains parafollicular cells that secrete calcitonin - **Both**
B. Multifocal and bilateral – **Hereditary MTC**
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D. Worse prognosis
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C. Associated with MEN-IIA and MEN-IIB – Hereditary MTC
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Answers

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B. Multifocal and bilateral – **Hereditary MTC**
C. Associated with MEN-IIA and MEN-IIB – **Hereditary MTC**
D. Worse prognosis – **Hereditary MTC**
E. Treatment consists of total thyroidectomy with central node dissection - **Both**
With regard to the management of a patient with MTC, which of the following statements is/are correct?

A. The patient should be screened for hyperparathyroidism and pheochromocytoma
B. Total thyroidectomy is the procedure of choice
C. If cervical lymph node metastasis are present and no distant metastasis are evident, neck dissection results in little benefit with regard to long-term survival
D. If pheochromocytoma is found, adrenal surgery should precede the thyroid surgery
E. If hyperparathyroidism is found, it may be surgically managed at the time of thyroidectomy by removing the two largest parathyroid glands
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E. If hyperparathyroidism is found, it may be surgically managed at the time of thyroidectomy by removing the two largest parathyroid glands
Question

With regard to genetic analysis in patients with thyroid cancer, which of the following is/are true about the ret proto-oncogene?

A. Is associated with anaplastic thyroid cancer
B. Is located on chromosome 10
C. Is associated with familial MTC
D. Is associated with MEN-IIA and MEN-IIB
E. Is associated with follicular cancer of the thyroid
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