بسم الله الرحمن الرحيم
THYROID CANCER

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LECTURE OUTLINE

• - Objectives
• - Anatomy
• - Overview
• - Presentation
• - Investigations
• - Types of Thyroid Cancers
Objectives

• 1- Discuss the anatomy of thyroid esp. the lymphatic drainage
• 2- Discuss the etiology of thyroid cancers
• Understand the pathological features of various types of thyroid cancers
• 3- Discuss the presentations of thyroid cancers
• 4- Outline different investigative tools used to diagnose thyroid cancer
• 5- Discuss a plan of management according to the stage
• 6- Various surgical approaches and radioiodine therapies in treating thyroid cancers
PBL

- SWELLING IN THE NECK
- DYSPHAGIA
- DIFFICULTY BREATHING
- HYPO/HYPER-FUNCTION
- NECK PAIN
THYROID ANATOMY

• SHAPE
• POSITION
ANATOMY

The Thyroid gland develops from 2 sources :-

• The Thyroglossal Duct (Base of Tongue at Foramen Cecum)

• Ultimo-branchial Bodies

• Pyramidal Lobe + Isthmus.

• Lateral Lobes
ANATOMY

CONGENITAL ANOMALIES

- Agenesis
- Incomplete Descent
- Thyroglottal Cyst / Fistula
- Extended Descent
- Retrosternal Thyroid
ANATOMY

ARTERIAL SUPPLY

- Superior Thyroid
- Inferior Thyroid
- Thyroidae ima
- Esophageal and Tracheal branches
ANATOMY

VENOUS DRAINAGE

- Superior Thyroid
- Middle Thyroid
- Inferior Thyroid
ANATOMY

LYMPHATIC DRAINAGE

– Deep Cervical
– Pre-Tracheal
– Pre-Laryngeal (Delphian)
ANATOMY

RELATIONS

☐ PARATHYROID GLANDS
  – Superior
  – Inferior
ANATOMY

RELATIONS

- RECURRENT LARYNGEAL NERVE
THYROID CANCERS

- Overview
  - Relatively infrequent (1% of new cancer diagnoses/yr)
  - 3 times higher in women
  - Incidence peaks in the 3rd and 4th decades
  - Favorable prognosis compared with other cancers
  - Treatment requires a multidisciplinary approach
THYROID CANCERS

• **Types:**
  • - Papillary carcinoma (80%).
  • - Follicular carcinoma (10%).
  • - Medullary Thyroid Carcinomas (5-10%).
  • - Anaplastic carcinomas (1-2%).
  • - Primary lymphomas and sarcomas are rare.
PRESENTATION OF THYROID CANCERS

• **Signs and symptoms**
  • General- a painless, palpable, solitary thyroid nodule discovered accidentally.
  • **S+S associated with malignancy in thyroid nodules include:**
    • 1- **Age:** <30 years and > 60 years.
    • 2- **Sex:** Increased rate of malignancy in **males**
    • 3- **Rapid growth** of a nodule. Ominous sign
    • 4- **Painless** (nontender to palpation); sudden onset of pain more strongly associated with benign disease (eg, hemorrhage into a benign cyst, subacute viral thyroiditis)
    • 5- **Hard and fixed.**
Factors suggesting a malignant diagnosis include the following:

1- Age <20 yrs or >70 yrs
2- Male
3- Solid nodules > 3cm
4- dysphagia or dysphonia
5- History of neck irradiation
6- History of thyroid carcinoma
7- Firm, hard, or immobile nodule
8- Presence of cervical lymphadenopathy
Diagnosis

- History taking
- Examination includes a thorough head and neck examination, including cervical lymph nodes.
- Indirect laryngoscopy
- Vocal cord paralysis implies involvement of the recurrent laryngeal nerve.
LABORATORY TESTING

• 1- Serum thyroid-stimulating hormone (TSH) level

• 2- Serum calcitonin levels: (elevated levels are highly suggestive of medullary thyroid carcinoma)
Fine-needle aspiration biopsy FNAB

- The most important step in the diagnostic evaluation of thyroid nodules.
- Highly accurate
  - mean sensitivity higher than 80%
  - mean specificity higher than 90%.
- Accuracy depends on:
  1 - The cytopathologist's expertise and experience
  2 - The technical skill of the physician performing FNAB
- Highly cost-effective
ASSESSMENT OF THYROID DISEASE

- FNAC
Fine-needle aspiration biopsy FNAB

- Limitations of FNAB include:
  - 1- Hypocellular aspirates
  - 2- Follicular lesions
  - 3- Hürthle cells lesions

(in cystic nodules or poor technique).
Fine-needle aspiration biopsy FNAB

• The recommended thyroid FNAB diagnostic categories in the Bethesda System for Reporting Thyroid Cytopathology and the respective risk of malignancy associated with each include:

  • 1- Benign < 1%
  • 2- Atypia of undetermined significance 5-10%
  • 3- Follicular neoplasm 20-30%
  • 4- Suspicious for malignancy 50-75%
  • 5- Malignancy 100%
  • 6- Nondiagnostic
- Imaging studies:
  1- Neck ultrasonography:
     - Most common modality
     - Limited usefulness for distinguishing between malignant and benign nodules
  2- Thyroid radioiodine imaging: To determine functional status of a nodule (carcinomas are usually cold or hypofunctioning)
  3- Neck computed tomography scanning or magnetic resonance imaging:
     - Play no role in routine management of solitary thyroid nodules.
     - Used to evaluate extension of the lesion, and metastases to the cervical lymph nodes.
     - Avoid iodinated contrast agents.
TYPES OF THYROID CANCERS

• Well-Differentiated Thyroid Carcinoma
  • 1- Papillary carcinoma
    • The most common thyroid malignancy (80%).
    • Papillary carcinoma and follicular carcinoma make up the well-differentiated thyroid carcinomas.
    • Women 3 times more frequently than men.
    • Age at presentation is 34-40 years.
    • Can occur familially, either alone or in association with Gardner syndrome (familial adenomatous polyposis).
TYPES OF THYROID CANCERS

- Radiation exposure, especially during childhood, is associated with the development of papillary thyroid carcinoma. Tumors typically appear after a latency period of about 10-20 years.

- An increased incidence among patients with Hashimoto thyroiditis (chronic lymphocytic thyroiditis).

- A slow-growing tumor that arises from the thyroxine (T4)- and thyroglobulin-producing follicular cells of the thyroid. The cells are TSH sensitive and take up iodine. They produce thyroglobulin in response to TSH stimulation.
TYPES OF THYROID CANCERS

- **Pathology**
  - Whitish invasive neoplasms with ill-defined margins.
  - Unencapsulated.
  - Presence of psammoma bodies, which occur in 50% of papillary carcinomas.
  - Many papillary carcinomas contain areas that show a follicular growth pattern.
  - May be multicentric, with foci present in both the ipsilateral and contralateral lobes.
TYPES OF THYROID CANCERS

- Local invasion
  - Directly through the thyroid capsule to invade surrounding structures.

- Regional and metastatic disease
  - Commonly spreads to the cervical lymph nodes.
  - Clinically in one third of patients at presentation and microscopically in one half.

- Distant spread
  - Typically affects the lungs and bone.
  - Approximately 5-10% of patients develop distant mets.
• **2- Follicular carcinoma**
  - The 2nd most common type (10% of thyroid cancers).
  - Common where dietary intake of iodine is low.
  - 3 times more frequently in women than in men.
  - Age is typically older than with papillary carcinoma (late 4th to 6th decades).
  - Like papillary carcinomas, follicular carcinomas arise from the follicular cells of the thyroid. The neoplastic cells are TSH sensitive as well, taking up iodine and producing thyroglobulin—a feature that is exploited diagnostically and therapeutically.
TYPES OF THYROID CANCERS

- Pathology
  - Encapsulated
  - Fibrosis, hemorrhage, and cystic changes are found in the lesions.
  - Follicular carcinomas are differentiated from benign follicular adenomas by tumor capsule invasion and/or vascular invasion. For this reason, differentiating follicular adenomas from follicular carcinomas is extremely difficult with FNAB cytology and frozen section analysis.
TYPES OF THYROID CANCERS

Local invasion
As it does with papillary carcinoma, with the same presenting features

Cervical metastases
Are uncommon.

Distant metastasis
- High rate of distant metastasis (20%).
- Lung and bone are the most common sites.
TYPES OF THYROID CANCERS

• Treatment of Differentiated Thyroid Cancers
  • - Total thyroidectomy has been the mainstay for treating well-differentiated thyroid carcinoma.
  • - After total thyroidectomy, patients undergo:
    • - Radioiodine scanning to detect regional or distant metastatic disease, followed by -
    • - Radioablation of any residual disease found.
TYPES OF THYROID CANCERS

- **Management of neck**
  - Cervical metastases discovered preoperatively or intraoperatively should be removed by means of en bloc lymphatic dissection of the respective cervical compartment (selective neck dissection) while sparing the nonlymphatic structures.
  - Elective neck dissection (removal of clinically benign neck lymphatic tissue) in a well-differentiated carcinoma is not indicated because postoperative radioiodine treatment effectively treats microscopic lymphatic metastases.
TYPES OF THYROID CANCERS

- Postoperative radioiodine scanning and ablation
  - Because differentiated thyroid tissue and well-differentiated thyroid carcinomas are TSH sensitive and because they take up iodine
  - Radioiodine (\(^{123}\)) can be given in diagnostic doses to detect residual normal or neoplastic tissue in the body
  - Radioiodine (\(^{131}\)) can be given in therapeutic doses to ablate this tissue.
  - \(^{131}\) I or \(^{123}\) I scanning is performed when the patient is in a hypothyroid state
• **Thyroid suppression**

• - After thyroidectomy, patients are given thyroid replacement therapy with T4 (Synthroid) or triiodothyronine (T3, Cytomel).

• - Patients take T4 in daily doses sufficient to suppress TSH production by the pituitary. Low TSH levels in the bloodstream reduce tumoral growth rates and reduce recurrence rates of well-differentiated thyroid carcinomas.
• **Follow-up care**

• Every 6-12 months with serial radioiodine scanning and serum thyroglobulin measurements.

• Thyroglobulin is a useful marker of tumor recurrence because well-differentiated thyroid cancers synthesize thyroglobulin. However, it is useful only after total thyroid ablation.

• Serum antithyroglobulin antibodies are measured in addition to thyroglobulin because their presence invalidates the assay. Thyroglobulin antibody levels should be obtained with each thyroglobulin measurement.

• Rising thyroglobulin level after thyroid ablation suggests recurrence.

• Ultrasonography of the neck can also be used to detect regional recurrences.
**Management of recurrence**

- Recurrences are best treated with **surgical excision** if the disease is clinically evident and surgically accessible.

- **Nonlocalized recurrences detected on the basis of elevated thyroglobulin levels are treated with ¹³¹I**.

- When surgical excision of recurrent disease is not feasible, **external-beam radiation therapy** may be useful.

- **Chemotherapy**, is reserved for tumors that do not respond to other treatments and for palliative care.
Prognostic factors

The long-term disease-free survival with aggressive treatment and management is nearly 90% overall.

Factors associated with prognosis, as listed below.

Age: Cancer-related death is most likely to occur if the patient is >40 years at the time of diagnosis. Recurrences are most common in patients whose disease is diagnosed when they were <20 years or >60 years.

Sex: Men are twice as likely as women to die from thyroid cancer.

Size: Patients with primary tumors >4 cm have increased recurrence and mortality.

Histology:

- Papillary carcinoma 30-year cancer-related death rate of 6%.
- Follicular carcinoma has a 30-year cancer-related death rate of 15%.

Local invasion: indicates aggressiveness and worsens the prognosis.

Distant metastasis: Distant metastasis at initial examination is associated with a 68.1-fold increase in the death rate.
3- Hürthle Cell Carcinomas

- Rare (2-3% of all thyroid malignancies).
- The overall 5-year survival rate is 50-60%.
- Occur more commonly in women
- Fifth decade of life.
- The clinical presentation is similar to that of other thyroid malignancies.
- About 75-100% of the tumor is composed of Hürthle cells, which are also known as oxyphilic, oncocytic, Askanazy, or large cells.
- Hürthle cells can be found in a variety of benign thyroid conditions, such as Hashimoto thyroiditis, Graves disease, and multinodular goiter.
- Benign neoplasms, called Hürthle cell adenomas, that contain more than 75% Hürthle cells can also occur.
3- Hürthle Cell Carcinomas

- Considered a variant of follicular carcinoma
- Like follicular carcinoma, is differentiated from Hürthle cell adenoma by the presence of capsular invasion, vascular invasion, or both. Hürthle cell tumors identified on FNAB findings cannot be categorized as malignant or benign.
- behave aggressively.
- high risk for recurrent and metastatic disease.
- most often do not take up radioactive iodine, thereby removing the diagnostic and therapeutic benefits that papillary and follicular carcinomas have.
- Surgery is the mainstay of treatment.
- Because tumors do not take up iodine and are not TSH sensitive, thyroid suppression and radioiodine therapy have little value.
- External-beam radiation therapy can used to treat metastatic disease.
4- Medullary Thyroid Carcinoma

- 5% of all thyroid malignancies.
- Slight female preponderance.
- Arise from the parafollicular C cells of the thyroid gland (neural-crest derivatives which produce calcitonin).
- About 75% occur sporadically, and 25% occur familially. Familial cases are commonly multifocal.
- New germline mutations can also occur without a positive family history, but with the risk for passing on the syndrome.
• **4- Medullary Thyroid Carcinoma**
• The FMTC syndromes consist of MEN 2A, MEN 2B, and FMTC. They are inherited in an autosomal dominant fashion. Children inheriting an FMTC syndrome have a **100%** risk of developing MTC.
• **1- MEN 2A (Sipple syndrome)**
  - **MTC**: almost always develops by the second decade.
  - **Pheochromocytoma** (in 50% of patients)
  - **Hyperparathyroidism** (in 10-20% of patients).
• **4- Medullary Thyroid Carcinoma**
• **2- MEN 2B**
  - **MTC**
  - has the most aggressive biologic features
  - Usually develops by the age of 10 years
  - High propensity for rapid growth and metastasis.
• - **Pheochromocytoma** (in 50% of patients)
  - **Marfanoid habitus**
  - **Ganglioneuromatosis**.
• **3- FMTC**
• - **MTC** alone and usually develops during adulthood.
MULTIPLE ENDOCRINE NEOPLASIA

- M.E.N. I
- M.E.N. II A
- M.E.N. II B
• 4- Medullary Thyroid Carcinoma

• Genetic testing for MTC:

• Genetic testing is now the mainstay in the diagnosis of the FMTC syndromes (MEN and FMTC)

• Children of parents known to have MEN or FMTC are tested for RET mutations to guide therapy and future genetic counseling.
• **Biochemical testing for MTC**
  • Because MTC cells produce calcitonin, elevated serum calcitonin levels are diagnostic of MTC.
  • Routine measurement of serum calcitonin has low yield in investigating all solitary thyroid nodules because of the uncommon nature of MTCs.
  • Plasma calcitonin levels are commonly increased before clinical evidence of MTC appears.
  • Although this finding was once the mainstay in diagnosing familial forms of MTC, results of genetic testing have largely supplanted it.
  • This level is most commonly used now as a tumor marker to identify residual and metastatic disease after thyroidectomy to treat MTC.
**Pathology**
- Fairly well circumscribed but unencapsulated.
- Most tumors arise in the middle and upper third of the thyroid lobes, commensurate with the location of the parafollicular C cells in the thyroid gland.
- Sporadic tumors are unilateral, and inherited forms usually involve both thyroid lobes.
- In the stroma, characteristic deposits of amyloid are commonly observed, giving a green birefringence on Congo red staining (this is a feature unique to MTC).
- The finding of C-cell hyperplasia with MTC should raise the suspicion for familial disease.
• **Treatment**
  • - Both sporadic MTCs and FMTCs are treated with total thyroidectomy and lymphatic dissection.
  • - Metastasis to the cervical lymph nodes is common in patients with MTC, particularly those with familial forms with multicentricity and bilaterality of the primary tumor. - Lymph node metastases can occur in more than 50% of patients.
  • *Prophylactic thyroidectomy* in patients with MEN 2A and MEN 2B
  • - Most patients who inherit these syndromes develop MTC in the first decade of life.
• **Follow-up care**
  - Annual measurement of serum calcitonin.
  - Carcinoembryonic antigen is another tumor marker associated with the recurrence of MTC, and it may also be used for surveillance.
  - Neck, abdominal, and pelvic CT or MRI may be used to detect disease if metastasis or recurrence is suspected.
  - Radionuclide studies and selective venous catheterization with sampling of calcitonin levels can be performed to localize recurrences.
  - **Radiation therapy** is used in an adjuvant setting and to treat patients with surgically inoperable recurrences and metastases.
  - Because MTC does not concentrate iodine, radioiodine therapy has no role in follow-up care or treatment.
  - MTC is relatively insensitive to chemotherapy,
• **Prognosis**
  
  - Worse than that of patients with well-differentiated carcinoma, with MEN 2B having the worst prognosis.
  
  - The **10-year survival rate is 65%**.
  
  - Young age, small primary tumor, low stage of disease, and completeness of initial resection improve survival.
5- Anaplastic Thyroid Carcinoma

- Very rare (1.6% of all thyroid cancers)
- Most aggressive of all thyroid malignancies.
- One of the worst survival rates of all malignancies in general.
- Progression of disease is rapid, and most patients die from local airway obstruction or complications of pulmonary metastases within 1 year.
- Female-to-male ratio of about 2-3 : 1.
- Present later than other thyroid malignancies (mostly in the 6th or 7th decade)
- As many as 50% of patients present with associated symptoms due to local invasion.
• **Physical examination:**
• - Firm thyroid mass or masses.
• - About 30% of patients have vocal cord paralysis.
• - Cervical metastases are palpable on examination in 40% of patients.
• - At least one half of patients already have distant metastases at the time of diagnosis. The most common sites of involvement are the lungs, bones, and brain.
• **Pathology**
• - Areas of focal necrosis and hemorrhage.
• - The tumor often extends through the capsule of the thyroid gland itself.
• - Anaplastic thyroid carcinoma is believed to arise from a preexisting, well-differentiated thyroid carcinoma, therefore areas of well-differentiated thyroid carcinoma are often found within it.
• **Treatment**
  - Neck dissection is added to manage palpable cervical metastases.
  - Complete excision is often impossible, therefore total or subtotal thyroidectomy is performed as the extent of the disease permits. Tracheal and laryngeal resection is usually not performed to remove disease because of the poor prognosis in these circumstances.
  - Tracheotomy is needed in cases with airway compromise due to tracheal invasion.
  - External-beam irradiation added postoperatively or used as primary treatment in unresectable cases is effective in improving local control.
  - Chemotherapy is added for palliation.
  - Chemotherapy and radiation therapy are typically administered in combination.
• **Prognosis**
• - poorly responsive to multimodality therapy.
• - median survival is 8.1 months.
• - Young age, unilateral tumors, small tumors (< 5 cm), no local invasion of the surrounding tissue, and a lack of cervical metastases are relatively favorable prognostic indicators.
• - Long-term survival should prompt a reconsideration of the diagnosis of anaplastic thyroid carcinoma; the original tumor is usually found to be a variant of MTC or thyroid lymphoma.
6- Primary Thyroid Lymphoma

- 2-5% of all thyroid malignancies.
- Most are non-Hodgkin B-cell tumors.
- The incidence peaks in the 6th decade of life.
- Female-to-male ratio of 4:1.
- Highly associated with chronic lymphocytic thyroiditis (Hashimoto thyroiditis).
- The risk of primary thyroid lymphoma increases 70-fold in patients with chronic lymphocytic thyroiditis compared with the general population.
• **6- Primary Thyroid Lymphoma**

• - The most common clinical presentation is an enlarging thyroid mass.

• - Patients may have clinical or serologic evidence of hypothyroidism.

• - Local extension into the aerodigestive tract or surrounding tissues

• - Regional and distant lymphadenopathy is common.

• - FNAB is considered less reliable with this lesion than with other thyroid malignancies. May be difficult to differentiate from chronic lymphocytic thyroiditis.

• - Surgical biopsy of the lesion is preferred
• **Staging of thyroid lymphomas**

  - Important for therapeutic and prognostic purposes.
  - Involves CT scanning of the brain, neck, chest, abdomen, and pelvis, as well as bone marrow biopsy.
  - Most 1ry thyroid lymphomas are localized to the thyroid and are therefore classified as stage IE (localized to an extranodal site).
  - Involved regional lymph nodes increase the stage to IIE.
• **Treatment and prognosis**
  - **Stage IE lymphomas**
    - Treated with total thyroidectomy followed by postoperative radiation therapy.
    - Surgical excision should not be performed if local infiltration into surrounding tissues is evident.
    - 5-year survival rate of up to 85%.
  - **Stage IIE lymphomas**
    - Treated with combined chemotherapy and radiation therapy.
    - 5-year survival rate to about 35%.
  - Lymphomas at stages higher than this worsen the prognosis.
• **7- Sarcoma of the Thyroid Gland**

  - Uncommon.
  - Aggressive tumors that most likely arise from stromal or vascular tissue in the gland.
  - Should be differentiated from anaplastic thyroid carcinomas, which can appear sarcomatous.
  - The treatment for thyroid sarcomas is total thyroidectomy.
  - Radiation therapy may be used in an adjunctive setting. - Most sarcomas are unresponsive to chemotherapy.
  - Recurrence is common.
  - Overall prognosis is poor.
Extent of Thyroidectomy

- Lobectomy (+ isthmectomy)
- Subtotal thyroidectomy
- Total thyroidectomy
- Extended thyroidectomy.
THYROID SURGERY

• Care must be taken during thyroid surgery in order to:

• 1- Avoid injuring the recurrent laryngeal nerve.

• 2- Avoid injuring or devascularizing the parathyroid glands. If a parathyroid gland is inadvertently removed, reimplant it in the sternocleidomastoid muscle or on the volar surface of the forearm after slicing it into small pieces and marking it with a surgical clip.

• 3- During superior dissection, remember the nearby location of the external branch of the superior laryngeal nerve, which innervates the cricothyroid muscle.

• 4- Ensure meticulous hemostasis.
THYROID SURGERY

- **Preoperative considerations**
- Vocal fold mobility should always be determined before thyroid surgery.
- If lobectomy for biopsy is planned, discuss the potential need for completion thyroidectomy with the patient.
• **Postoperative care**
  
  - If a surgical drain is placed, maintain it until its output has diminished sufficiently.
  
  - Hypocalcemia may occur in patients who have undergone total thyroidectomy.
  
  - Assess for hypocalcemia by inquiring about perioral paraesthesia. In a patient with hypocalcemia, tapping on preauricular region overlying the trunk of the facial nerve may cause ipsilateral contraction of the face (Chovstek sign).
  
  - Measure ionized calcium postoperatively. Hypocalcemia may require calcium and vitamin D supplementation.