Hashimoto thyroiditis

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- Most common cause of hypothyroidism in western countries.
- It is an autoimmune disease of the thyroid.

Pathogenesis of Hashimoto thyroiditis

I. Hashimoto thyroiditis is caused primarily by a defect in T cells, it is also involves both cellular & humoral responses (induces formation of CD8+ cytotoxic T cells & autoantibodies from sensitized B cells).
These cytotoxic cells are responsible for parenchymal destruction of thyroid.
While those autoantibodies cause hypothyroidism by block the action of TSH that result in further hypothyroidism.

Types of autoantibodies in Hashimoto thyroiditis

1*. Inhibitory anti- TSH receptor antibodies.* That blocks the action of TSH result in hypothyroidism.
2*. Ant thyroglobulin & ant thyroid peroxidase antibodies* are probably formed as a result of tissue destruction & exposure of normally sequestered thyroid antigens to the immune system; these antibodies play a useful role in the diagnosis of Hashimoto thyroiditis but are unlikely to contribute actively to its pathogenesis.

II. There is a significant *genetic component* to disease pathogenesis.
By the followings facts:
1. Increased frequency of disease in first degree relatives of patient.
2. An association has also been found between disease prevalence & the HLA subtypes DR3 & DR5.

Morphology of Hashimoto disease

Gross

- Diffusely & symmetrical enlarged thyroid, the capsule of gland is intact & the gland is well demarcated from adjacent structure.

Microscopically

- Widespread infiltration of thyroid parenchyma by a mononuclear inflammatory infiltrate containing small lymphocytes, plasma cells & well developed germinal centers.
- The thyroid follicles are atrophic & are lined by epithelial cells characterized by presence of abundant eosinophilic, granular cytoplasm, termed **Hurthle** (metaplastic cells) or **Oxyphil** cells.
- The interstitial connective tissue is increased & may be abundant.

But the fibrosis does not extend beyond the capsule of the gland.

Clinical features

- More common in female than male, most prevalent between 45- 65 years of age.
- Presents as painless enlargement of the thyroid gland, usually associated with some degree of hypothyroidism.
- Patient with Hashimoto thyroiditis is at increased risk for the development of B- cells non-Hodgkin's lymphomas within the thyroid gland.

Neoplasms of thyroid gland

❖ Thyroid gland gives rise to variety of neoplasms, ranging from benign adenoma to highly aggressive, anaplastic carcinoma.

❖ Carcinomas of thyroid gland are uncommon, accounting for about 1% of solitary thyroid nodules.

Several clinical criteria provide a clue to the nature of a given solitary thyroid nodule; these criteria are included:-

1. Solitary nodules are more likely to be neoplastic than are multiple nodules.
2. Solid nodules are more likely to be neoplastic than are cystic nodules.
3. Nodules in younger patients are more likely to be neoplastic than are those in older patients.
4. Nodules in males are more likely to be neoplastic than are those in females.
5. Nodules that take up radioactive iodine in imaging studies (cold nodules) are more likely to be neoplastic than hot nodules which are almost always benign.

However fine needle aspiration & histological studies of surgical specimen of thyroid gland give definitive information about the nature of these nodules.

Benign thyroid neoplasms (thyroid adenomas)

- Benign neoplasms derived from follicular epithelium.
- Characteristic features thyroid adenomas are:

1. Solitary, spherical lesion.
2. Compresses the surrounding thyroid tissues.
3. Well capsulated.
4. Microscopically adenoma cells are arranged in uniform follicles that contain colloid, occasionally, the neoplastic cells acquire brightly eosinophilic granular cytoplasm (called oxyphil or Hurthle cell changes).
5. Occasionally, exhibit pleomorphism & atypia.
6. A small proportion of thyroid adenomas are functioning & producing thyroid hormones (***Toxic adenomas)*** & cause clinically thyrotoxicosis.
7. Most of thyroid adenomas are cold nodules on thyroid scan while toxic adenomas are warm or hot, (Up to 10% of cold thyroid nodules are proved to be malignant).

Carcinomas of thyroid

Mostly in adult, although some forms, particularly papillary carcinomas are seen in childhood.

A female predominance in all types of thyroid cancers, most cases of thyroid cancers are derived from follicular epithelium, except for medullary carcinomas which are derived from parafollicular, or C cells.

The major subtypes of thyroid carcinomas are:-

1. Papillary carcinomas (75%-85% of cases).
2. Follicular carcinoma (10%- 20% of cases).
3. Medullary carcinoma (5% of cases).
4. Anaplastic carcinoma (< 5% of cases).

Etiology

1. **Genetic factors**. They are important by the following facts:-
   I. Clustering of thyroid tumors in families.
   II. Familial medullary carcinomas occur in multiple endocrine neoplasia type 2 (disorder associated with gene mutation).
   III. Familial papillary carcinomas have been recently proved to be associated with gene mutation (***RET*** *proto-oncogene)*.
   IV. Other genes abnormalities associated with thyroid carcinomas include (PTEN, APC, p53, PTC).

2. Ionizing Radiation.

- Exposure to ionizing radiation, during the first 2 decades of life, is one of important factors predisposing to the development of thyroid cancer.
- (9%) of people receiving radiotherapy for reactive tonsillar enlargement, tinea capitis during childhood subsequently developed thyroid malignancies.
- The majority of thyroid cancers arising post radiotherapy are papillary carcinomas & most have RET gene abnormalities.

3. Preexisting thyroid diseases.

- Long standing multinodular goiter has been suggested as a predisposing factor in some cases especially in areas with iodine deficiency and this have higher incidence of follicular carcinomas.
- There is **little** evidence that follicular adenomas progress to carcinomas.
- Although most, if not all, thyroid lymphomas are arise from preexisting thyroiditis.

Papillary carcinomas

- Represent about 80% of thyroid cancer.
- Most of cases are presented as nonfunctioning, painless mass within the thyroid or as metastases in the cervical lymph nodes.
- Can occur at any age, even at childhood.

Morphology of papillary carcinomas

Gross

- Either solitary or multifocal lesions.
- May be well demarcated & even encapsulated or infiltrative with ill defined margins.
- May contain areas of fibrosis, calcifications & cysts.

Microscopically

Definitive diagnosis of papillary carcinomas can be made only after microscopic examination, which include:-

1. Nuclear features of neoplastic cells.
   A. Optically clear nuclei due to fine dispersed chromatin, also called ground glass or Orphan Annie nuclei.
   B. Intranuclear inclusions which are due to cytoplasmic invaginations (also are called nuclear pseudo-inclusions).
2. Papillary architecture.

- These papillae can present in some of benign conditions like hyperplastic nodules.
- Papillae of carcinoma differ from those of benign conditions by presences of dense fibrovascular cores.
- Psammoma bodies are often present within the papillae.

3. Lymphatic invasions are often present while blood invasion are uncommon.

Follicular carcinoma

- The second most common thyroid cancer (15%).
- They usually present at older age than the papillary carcinomas.
- The incidence of follicular carcinomas is increased in areas of dietary iodine deficiency (may have relation to the nodular goiter).
- There is no evidence that follicular carcinomas are aroused from preexisting adenomas.
- Clinically follicular carcinomas present most frequently as solitary "cold" thyroid nodules. In rare cases, they may be presented as hyper functional nodules.
- These neoplasms tend to metastasize through the bloodstream to the lung, bone & liver. Regional lymph nodes metastases are uncommon.

Morphology of follicular carcinoma

Gross

Either well demarcated lesions (encapsulated) or infiltrative lesions.

Microscopically

On microscopic level it is difficult to distinguish between follicular adenoma & follicular carcinomas, *so the diagnosis of carcinoma are depending on presence of capsular & / or vascular invasion.*

Medullary Carcinoma of thyroid

- Arise from parafollicular cells (C cells) of thyroid.
- Secretes Calcitonin.
- (80%) of cases are sporadic, while 20% are familial, (mutation in RET gene).
- Most of cases are in adult.

Morphology of medullary carcinoma

Gross

- Either solitary lesion or multicentric. (More with familial cases).
- Large tumors show areas of hemorrhage, necrosis, destruct the capsule.

Microscopically

- Tumor consists of polygonal to spindle cells, arrange in nests, trabecular & even follicles.
- Amyloid deposits are characteristic of these tumors.
- Parafollicular cells hyperplasia in adjacent thyroid tissue (mainly in familial cases).

Clinical features of medullary carcinoma

- Most of cases are presented as mass in the neck.
- Diarrhea due to secretion of VIP substances by the tumor.

Anaplastic carcinoma of thyroid

- Mostly in old patient, aggressive tumors.
- Common in areas of endemic goiter.
- In most of cases deaths occurs in less than one year as a result of aggressive local growth & compress the vital structures in the neck.

Morphology of anaplastic carcinoma

Gross

- Presented as bulky masses that are usually grow beyond the capsule of the gland.

Microscopically
Neoplasms are composed of highly anaplastic cells, exhibiting three distinctive morphologic patterns (Giant cells, Spindle cells & Squamous like cells).

Simple goiter (Multinodular goiter):

- Is the most common thyroid disease.
- **Either endemic or sporadic** (both indicate the presence of goiter due to impaired synthesis of thyroid hormones……. Elevated level of TSH).

Endemic multinodular goiter:

- Occur in areas where iodine supplement by soil, water & food is poor.
- **Called endemic when 10% of population at these areas have goiter.**
- With iodine supplementation, the frequency & severity of endemic goiter is declined significantly.

Sporadic multinodular goiter

- Less common than endemic goiter.
- In female more than male.
- Common in puberty or young adult (increased demands).
- Could be due to ingestion of substances interfering with synthesis of thyroid hormones (e.g. cauliflower).
- Or could be due to hereditary enzymatic defect (decreased synthesis of thyroid hormones).

Pathogenesis of multinodular goiter

- There is hypertrophy & hyperplasia of thyroid follicular cells by elevated level of TSH.
- At early stage….. Diffuse enlargement of thyroid gland which is called (diffuse nontoxic goiter), in this stage the follicles are lined by crowded columnar cells.
- (Sometimes result in formation of Papillae).
- If dietary iodine is increased……. Colloid goiter (dilated follicles lined by flat cells).
- Colloid grossly appears brown, glassy & transparent.
- With time, repeated attacks of stimulation & involution will result in formation of irregular enlargement or called nodular or multinodular goiter.

Gross

- Asymmetrical enlargement of thyroid, may reach massive size.
- On cut section nodular surface with variable amount of colloid.
- Areas of fibrosis, hemorrhage, calcification & cystic change.

Microscopically
Colloid rich follicles lined by flat epithelium, with many areas of hypertrophy & hyperplasia.

Clinical features
Mass in the neck, compress on airways, dysphagia, compress the veins of neck.

Complications

1. Toxic multinodular with hyperthyroidism (cardiac symptoms without ophthalmopathy & dermatopathy of Graves 'disease).
2. Long stand multinodular goiter may result in anaplastic carcinoma.
3. Sometimes result in hypothyroidism.

Pathology of parathyroid glands

Most common pathologic processes are (**Hyperparathyroidism & hypoparathyroidism**).

Hyperparathyroidism

- Either (primary, secondary & tertiary hyperparathyroidism).
- In secondary & tertiary cases are due to chronic renal failure, while in primary cases are due to diseases of parathyroid glands.

Primary hyperparathyroidism

- Common, important cause of hypercalcemia.

Causes of primary hyperparathyroidism are:-

1. Adenomas of parathyroid glands (common cause 80%- 90% of cases).
2. Bilateral adrenal hyperplasia (10% to 20% of cases).
3. Carcinoma of parathyroid glands (less than 1% of cases).

- Usually in adult female, either sporadic or familial.

Clinical features

In fact, *primary hyperparathyroidism* is the most common cause of ***clinically silent hypercalcemia,*** while ***apparent hypercalcemia*** is almost always associated with *underlying non parathyroid malignancy*.

Clinical features of primary hyperparathyroidism are due to increase level of PTH in the blood which results in followings:-

1. GIT disturbances (peptic ulcer, constipation, pancreatitis & gallstones).
2. CNS disturbances (depression, seizures).
3. NEUROMUSCULAR disturbances (hypotonia & weakness).
4. Renal problems (due to renal stones & obstructive uropathy).
5. Bones pain (due to osteoporosis or osteitis fibrosa cystica).
6. Polyuria & polydipsia.

Morphology of parathyroid adenoma

1. Parathyroid adenomas are almost invariably confined to single glands & the remaining glands are normal in size.
2. Most of adenomas are weighted between 0.5 & 5 gm.
3. Microscopically adenomas are composed of uniform, polygonal cells (chief cells) with small centrally located nuclei.
4. In most of cases, at least a few nests of larger cells containing eosinophilic granular cytoplasm (oxyphil cells).
5. Mitotic activity is rare in these adenomas, but it is not uncommonly to find pleomorphic cells within these adenomas.
6. Unlike the normal parathyroid parenchyma, adipose tissue in adenoma is inconspicuous.

Morphology of parathyroid hyperplasia

1. Parathyroid hyperplasia is multiglandular process.
2. It is chief cells hyperplasia, which involve the glands either diffusely or multinodular pattern.

Morphology of parathyroid carcinoma

1. Usually firm, hard infiltrative mass, that adheres to surroundings.
2. Usually larger than adenoma (> 5g).
3. Two important criteria for carcinomas (invasion of adjacent tissue & metastasis).

Hypoparathyroidism

- *Less common than hyperparathyroidism.*

Causes

1. Surgical ablation: removal of glands during thyroidectomy.
2. Congenital absence: if associates with thymic aplasia & cardiac anomalies are called (Di George syndrome).
3. Autoimmune hypoparathyroidism: due to defect in cellular & humeral immunity (autoantibodies & defect in T- cells function).

Clinical features

Mostly due to Hypocalcaemia & include ***tingling of muscles, spasm of muscle, facial grimacing & carpopedal spasm.***

- Also ***cardiac arrhythmias, convulsion, cataract, calcification of basal ganglia & dental abnormalities.***

THANKS