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Lec : NEOPLASMS OF THE THYROID, PATHOLOGY OF PARATHYROID GLAND

Note: I brought a lot of information from the book to make this lecture easier to understand

let’s go ;)}
Neoplasmas of the thyroid

thyroid nodules >> mainly we have 2 types of thyroid nodules

-- neoplastic nodules (benign = adenoma; malignant = carcinoma)
-- non neoplastic nodules (less common)

-- Several clinical criteria provide a clue to the nature of a given thyroid nodule:

** Solarity young nodules : are more likely to be neoplastic than are multiple nodule

(gland with just single nodule >> neoplastic)
(gland with multiple nodules = non neoplastic)

so in solarity young nodules the most common to be neoplastic single nodule

** Nodules in younger patients are more likely to be neoplastic than are those in older patients. (older patient with non neoplastic very common)

** Nodules in males are more likely to be neoplastic than are those in female

** If a patient have a history of radiation "for example" due to treatment of lymphoma, he will be at high risk to develop malignancy like papillary thyroid carcinoma.

** If we give a patient radioactive iodine >> increase uptake of that radioactive molecule in the thyroid gland thats what we call it hot nodules ,, in contrast to cold nodule which can not uptake that radioactive iodine

hot nodules more benign than cold nodules (malignancy 10% in cold)

Adenomas

as we know from histology, thyroid gland composed mainly from follicle (epithelial cells) so we call it follicular adenoma

follicular (cuz follicle in thyroid)

adenoma (cuz epithelial cell)

*foliclular adenoma : mass in thyroid, just one mass, cuz as we said more than one mass it become non neoplastic

* single mass : 2 types

- non functional,, most common,, without symptoms just compression

- functional or toxic adenomas : symptoms here

** they are differ from each other by genetics causing
-Nonfunctional----- RAS, PAX8/PPARG fusion gene
-toxic adenomas---- TSHR, α-subunit of Gs (GNAS ----autonomy---- thyrotoxicosis)

*may be we have follicular carcinoma too

how to differentiate between adenoma and carcinoma??

according to capsule , so we find well-defined, intact capsule without invasion in adenoma ,,but in carcinoma and due to high invasion we do not able to find a capsule

so in adenoma no invasion to capsule and adjacent thyroid tissue vice versa for carcinoma

Multinodular goiter: its another type of tumor in thyroid , but here we talk about multiple nodules not single one ,,in addition to another feature( no capsule here)

so as we see capsule its a marker for adenoma

**Uniform follicles >>whats that means??

in normal thyroid we can observe that the follicle its not a same , there will be a differences, but in adenoma all the follicle will be the same

look at that grossly appearance it's easy to see that clear ,well defined capsule so absolutely its follicular adenoma

**Hürthle cell adenoma:

very like follicular adenoma but the difference due to abundant amount of eosinophilic cytoplasm lead to cell eosinophilic appearance

**endocrine atypia

can not differentiate between follicular adenoma and carcinoma!

at the beginning of lecture we have talked about hot and cold nodules So

**cold nodules---10% of cold nodules eventually prove to be malignant,,nonfunctional and most common type of follicular adenoma

**hot nodules ...malignancy is rare---- toxic adenoma (toxic adenoma the same to functional adenoma"we said that earlier)

-so cold nodules >> nonfunctional adenoma

-hot nodules>> functional or toxic adenoma
to diagnose follicular adenoma we need
- ultrasonography: type of radiation and most common in thyroid cysts and lesion
- fine needle aspiration biopsy (FNA);

Take a sample from the tumor fluid and see it under the microscope, but that not sufficient to differentiate between adenoma and carcinoma

if you still remember we said that to differentiate between adenoma and carcinoma you must take a section from the tumor to see the capsule

well-defined, intact capsule >> adenoma

invasion to capsule >> carcinoma

Carcinomas

Carcinomas of the thyroid are relatively uncommon, accounting for about 1.5% of all cancers

- Papillary carcinoma (85% of cases)
- Follicular carcinoma (5% to 15% of cases)
- Anaplastic (undifferentiated) carcinoma (less than 5% of cases)
- Medullary carcinoma (5% of cases)

**Papillary carcinoma**

As mentioned earlier, papillary carcinomas represent the most common form of thyroid cancer. These tumors may occur at any age (mainly in young patients), and they account for the vast majority of thyroid carcinomas associated with previous exposure to ionizing radiation (history of radiation in the neck)

- It's a non-functional tumor >> means that if we do thyroid hormone test we will find that thyroid hormone normal or euthyroid (having a normally functioning thyroid gland)

- most of tumor have genetic mutation also
- Activation of the MAP kinase pathway

Rearrangements of RET (RET/PTC) ..BRAF

* to diagnosis papillary carcinoma
  -- we can find Papillae (which it a small rounded protuberance on a part or of the body)
  -- nuclear features: clearing of nucleus >> we call it orphan annie nuclei
  -- lymphatic permeation >> metastasis to LN << But prognosis still good

-- indolent lesions, with 10-year survival rates in excess of 95%

**Follicular thyroid carcinomas:**

* Follicular carcinomas account for 5% to 15% of primary thyroid cancers. They are more common in women, and manifest at an older age than that typical for papillary carcinomas, with a peak incidence between the ages of 40 and 60 years.

  Follicular carcinoma

* Its more frequent in areas with dietary iodine deficiency

  so mainly the most common reason of follicular carcinoma ''iodine deficency''

* usually patient with follicular carcinoma comes with solarity cold nodules
and as we said before, cold nodules = nonfunctional tumor means that if we do thyroid function test will be normal or euthyroid

*most of carcinoma has genetic mutation here that
mutations in the PI-3K/AKT signaling pathway:
RAS and PIK3CA
PTEN
PAX8/PPARG fusion genes  (the doctore just read it !!)

**mainly follicular carcinoma has 2 types
-mimimally invasive: invasion just on the capsule
-widely invasive: invasion to thyroid and extracelluar tissue
mainly we have invasion in the carcinoma but the site of invasion determine if it was mimimally or widely

-hematogenous dissemination means that the cancer spread by blood to another tissue like lung, liver, bone
-treatment will be by surgical excision, radioactive iodine

Anaplastic Carcinoma

Anaplastic carcinomas are undifferentiated tumors of the thyroid follicular epithelium, accounting for less than 5% of thyroid tumors. They are aggressive, with a mortality rate approaching 100%. Patients with anaplastic carcinoma are older than those with other types of thyroid cancer, with a mean age of 65 years

from where it comes???

-its undifferentiated carcinoma so it comes from old tumor (it comes from old well differentiated carcinoma like papillary or follicular
>>and thats tumor become undifferentiated to Anaplastic carcinoma)

undifferentiated means that the cell does not appear normal or even not appear like other cancers, the cells appear giant and spindle

Medullary Carcinoma

-from all the tumor we have talked about it, its the only one which we consider it as neuroendocrine tumor >>not from epithelial cells
-arise from parafollicular cell ""cell which surround the follicles ""

*mainly 2 types
-Sporadically
-familial cases (30%), inherited cases ---- MEN syndrome 2A, 2B, familial medullary thyroid carcinoma

*Usually it is RET mutation

*single or multiple nodules ???

-mainly single, but in the case of familial it will be multicentric

-So multicentric C cell hyperplasia just in the Familial cases not sporadic

* presentation of mass and hypersecretion of peptide hormone

*histological section from medullary carcinoma shows that

-Amyloid deposite derevied from altered calcitonin molecules
Parathyroid gland

**The parathyroid glands are four, superior and inferior pairs**

* two types of cells - chief or and oxyphil cells>>they secrete parathyroid hormone

**PTH acts on osteoclasts, and the epithelial cells of the renal tubule, to increase plasma calcium by promoting bone resorption and increasing renal calcium absorption, and it will lower phosphate level in the blood* (remember this very well, we will talk about it)

**the regulation of parathyroid hormones not comes from pituitary gland, it comes from calcium level of the blood

--less calcium in the blood >> PTH>> increase resorption from the bones >> calcium level retain to normal

***Diseases of parathyroid gland

""HYPERPARATHYROIDISM"" increase the activity of PTG

TYPES 3

- Primary : primary cause from parathyroid gland
- Secondary : sec to another causes mainly from renal failure
- Tertiary : long standing secondary hyperparathyroidism

**Primary Hyperparathyroidism: from parathyroid**

Adenoma—85% to 95% -

Primary hyperplasia (diffuse or nodular)—5% to 10% -

Parathyroid carcinoma—1% -

-majority of cases will be sporadic>> Cyclin D1(parathyroid neoplasia gene), MEN1

-Familial ------ MEN1, MEN2A, Familial hypocalciuric

*in familial hypocalciuric: after releasing of PTH, the calcium level will elevated >> and by negative feedback of the thyroid and inhibit PTH by binding to its receptors in PTG (that’s normally)

BUT in familial hypocalciuric the calcium can not bind to its receptors, so PTH will be continue to stimulating

-the patient comes with hypercalcemia like symptoms

***parathyroid adenomas

-- the most common one of the primary Hyperparathyroidism

--- parathyroid adenomas are almost invariably confined to single glands (more than one gland >> becomes parathyroid hyperplasia)

The weight of adenoma (0.5—5 Grams) why we talk about weight here???

--because from weight we can differentiate from adenoma and carcinoma "" note that carcinoma more than 10 g""

--adenoma must be in a single parathyroid gland , cuz in more than one it become parathyroid hyperplasia
Adipose tissue is inconspicuous within adenomas.

NORMALLY we able to see adipose tissue in parathyroid gland, but in adenoma we can not able to see that adipose tissue.

--rim of compressed, non-neoplastic parathyroid tissue, generally separated by a fibrous capsule.

**Parathyroid hyperplasia:**

--Multiglandular process "not in single gland

--weight of all glands rarely exceeds 1.0 g

**Parathyroid carcinomas:**

--exceed 10 g in weight

--invasion of surrounding tissues and metastasis (when we talk about any carcinoma >> always there will be invasion and met)

Morphologic changes in other organs: due to hypercalcemia (Focus on the red)

--osteitis fibrosa cystica: Bone resorption is accompanied by increased osteoblastic activity and the formation of new bone trabeculae,. In more severe cases the cortex is grossly thinned and the marrow contains increased amounts of fibrous tissue accompanied by foci of hemorrhage and cysts

--brown tumors: Aggregates of osteoclasts, reactive giant cells 
and hemorrhagic debris occasionally form masses that may be mistaken for neoplasms

--Nephrolithiasis: stones in the kidney

--Nephrocalcinosis: calcification in the kidney

--Metastatic calcification: calcification to any part of the body

clinical feateurs

The most common manifestation of primary hyperparathyroidism is an increase in serum ionized calcium.

we have more than one reason for hypercalcemia ,, but if you see level of PTH high << the hypercalcemia most likely to become from primary hyperparathyroidism >> adenoma

for the other reasons that cause hypercalcemia >> we will find normal level of PTH even low

--primary hyperparathyroidism is the most common cause of clinically silent hypercalcemia --- PTH is high, hypophosphatemia (we said that more PTH >>MORE ca++ >> less phosphate)

-clinical silent means that the patient come to the clinic just to check ,,not from any symptoms and suddenly he find high level of calcium

so the most common cause for this silent clinically >> adenoma
the most common cause of clinically apparent hypercalcemia in adults is paraneoplastic syndromes (small cell lung carcinoma as paraneoplastic syndromes), associated with malignancy and bone metastases.

<table>
<thead>
<tr>
<th>Cause of Hypercalcemia</th>
<th>Decreased PTH</th>
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<tbody>
<tr>
<td>Hyperparathyroidism</td>
<td>Hypercalcemia of malignancy, osteolytic metastases, PTHrP-related protein-mediated</td>
</tr>
<tr>
<td>Primary adenoma &gt; hyperplasia*</td>
<td>Vitamin D toxicity, vitamin D excess, immobilization, drugs (thiazide diuretics)</td>
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<tr>
<td>Secondary</td>
<td>Granulomatous diseases (sarcoidosis)</td>
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Table 19-4: Causes of Hypercalcemia

*Primary hyperparathyroidism is the most common cause of hypercalcemia overall. Malignancy is the most common cause of asymptomatic hypercalcemia. Primary hyperparathyroidism and malignancy together account for nearly 90% of cases of hypercalcemia.

Not that: hypercalcemia comes from high level of parathyroid hormone due to **Hyperparathyroidism**

**Features of primary hyperparathyroidism mainly come from hypercalcemia**

--Painful bones (fractures), renal stones, abdominal groans, and psychic moans

--Gastrointestinal disturbances: constipation, nausea, peptic ulcers, pancreatitis, and gallstones

--Central nervous system alterations: depression, lethargy, and seizures

--Neuromuscular abnormalities: weakness and hypotonia

--Polyuria and secondary polydipsia

**Secondary Hyperparathyroidism**

- Renal failure is by far the most common cause of secondary hyperparathyroidism

- We said before >> function of the PTH --- rise ca++ level in plasma and excreted phosphate from the body

- SO PTH elevate blood ca++ and depress blood phosphate

- In renal failure patient can not excreted phosphate from the body On the other hand pateint with renal failure can not reabsorped ca++ >> hypocalcemia

- So pateint with renal failure express hyperphosphatemia and hypocalcemia

- The body will observe that there is hyperphosphatemia >> PTH will release to supress that high level

- When PTH release > ca++ elevated to become normal again (we said that in renal failure >> hypocalcemia, so PTH will elevate ca++)

**The parathyroid glands in secondary hyperparathyroidism are hyperplastic non adenoma**

- As we said before hyperplastic means that (in more than one parathyroid gland)

**Tertiary hyperparathyroidism >> long standing sec hyperparathyroidism**

- PTH elevated without regulation comes from ca++, autonomous nodule >> will find it in tertiary hyperathyroidism

The last thing in this lec 😊
--the most common cause of hypoparathyroidism >> Surgically induced hypoparathyroidism (thyroidectomy)

--when a surgeon do thyroidectomy ,its easy Inadvertently to remove parathyroid (cuz its embedded in thyroid gland), so that will lead to hypoparathyrodism

--Congenital absence of PTG : mainly from digeorge syndrome

--for u to know DiGeorge Syndrome (DGS) is a primary immunodeficiency, often but not always, characterized by cellular (T-cell) deficiency, characteristic facies, congenital heart disease and hypocalcemia. DGS is caused by abnormal formation of certain tissues during fetal development

--Autoimmune hypoparathyroidism

**Hypocalcemia:the main symptoms of hypoparathyroidism

--increased neuromuscular irritability (tingling, muscle spasms, facial grimacing, and sustained carpopedal spasm or tetany)

--Cardiac arrhythmias

--increased intracranial pressures and seizures

Our lecture has ended

Thank you