ENDOCRINE

① Classification of Thyroid Neoplasms

I. Benign → Follicular adenoma.
Hyalinizing trabecular tumour.
Hurthle cell adenoma.

II. Malignant → 1. papillary thyroid carcinoma. → ~~papillary carcinoma~~.
(PTC)
2. Follicular thyroid carcinoma.
3. Medullary thyroid carcinoma.
4. Anaplastic thyroid carcinoma.
5. Hurthle cell carcinoma.
6. .

(if for more marks - draw diagram)
(if for small marks)

② pathogenesis of malignant thyroid Neoplasms.

Two main origins of thyroid cancers.

- follicular cell derived cancers → papillary ca, follicular ca, Anaplastic ca.
  - due to.
  - gain of function mutations in
    - MAP kinase pathway
    - PI3K/AKT pathway.
  - ← genetic
- Non-follicular (C-cell) derived cancers → medullary ca thyroid.
  - due.
  - germline RET protooncogene mutations.
  - ← genetic

Environmental factors
① Ionizing radiations:
② deficiency of dietary Iodine.

Papillary thyroid Carcinoma

- Most common primary thyroid ca (85%)
- age 20 - 50
- H/o exposure to ionizing radiations ✓

Genetic factors

papillary ca.
↓
activation of MAP Kinase pathway.
↓ by or ↓ by

- RET/PTC fusion gene.
- BRAF point mutations

Clinical features

- asymptomatic thyroid nodules.
- sometimes presenting symptom might only be lymph node enlargement.

IHC: thyroglobulin
pancytokeratin
TTF1
PAX8.

MORPHOLOGY

GROSS {image in corner} single / multiple focus lesions.

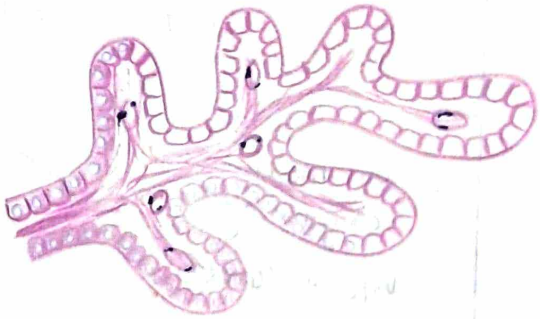
- usually infiltrative
- with ~~infiltrative~~ ill defined borders.
- white to tan, hard tx.
- granular texture

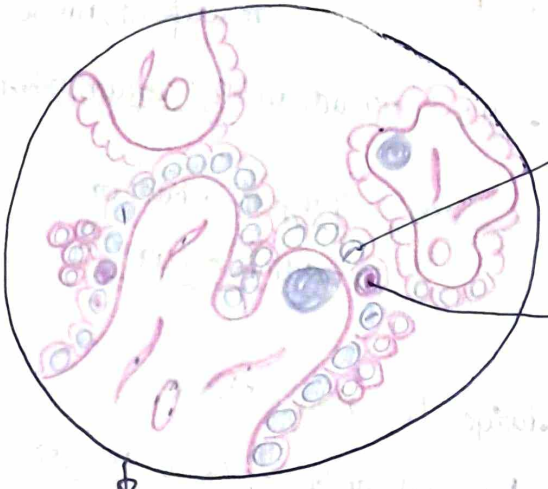
Cut surface → grossly visible papillary structures

gritty - due to calcification & psammoma bodies.

- areas of fibrosis, calcification, cystic spaces etc..

MICROSCOPY





- papillae with fibrovascular core.
- overlapping.
- ground glass appearance of nuclei
- nuclear pseudoinclusions.

- Complex branching papillae with fibrovascular core.

papillae are covered by single / multiple layer of cuboidal / columnar epithelial cells.

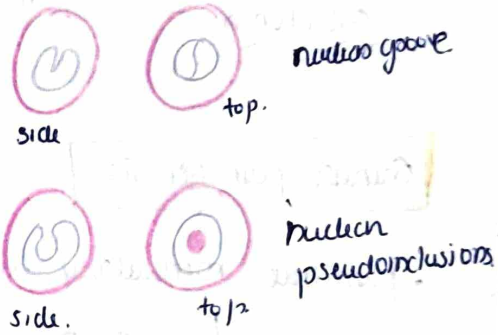
Nuclear features

- important for diagnosis. even in absence of papillary architecture.
- Ground glass / orphan Annie nucle. : due to finely dispersed chromatin.
- Intranuclear groove
- Intranuclear inclusions.

invagination of cytoplasm into nucleus → gives appearance of pseudo inclusions or nuclear groove.

- psammoma bodies - concentrically calcified structures.
  - diagnostic of papillary Ca.
  (absent in medullary, follicular etc).

✓ invagination of cytoplasm into nucleus. ↓ appears as.



Histological variants of Papillary Ca.

1. Follicular variant
2. Tall & columnar cell variant
3. Diffuse sclerosing variant
4. papillary microcarcinoma.

MEDULLARY CARCINOMA THYROID

- they are neuroendocrine tumours derived from
  → parafollicular cells / C-cell.
- they secrete Calcitonin → useful in diagnosis.

Genetic pathogenesis.

- familial medullary carcinoma.
  → occurs in
  MEN 2 syndrome. multiple endocrine Neoplasia Syc.
  → associated with RET mutation.

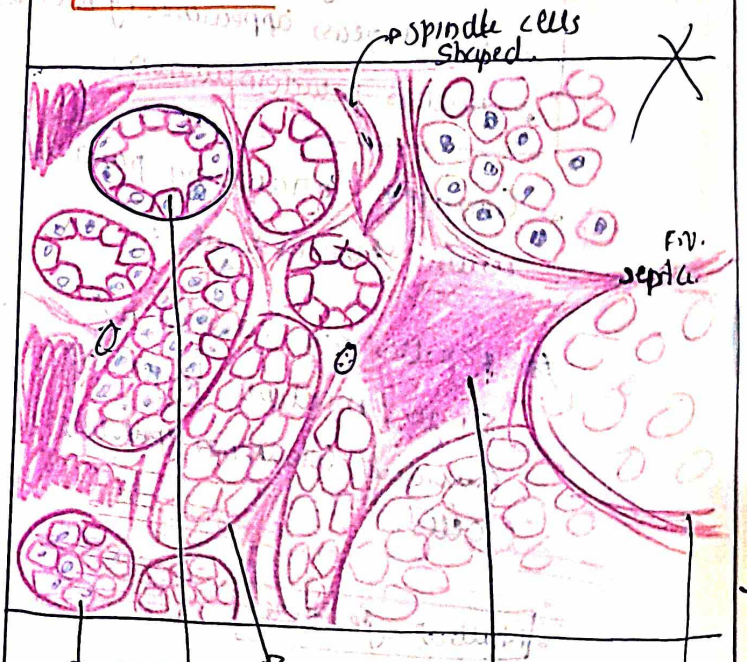
Normally. protooncogene RET → codes for → Tyrosine kinase receptor.

germline/sporadic mutations → Oncogene RET. → Constitutive activation of Tyrosine kinase receptor. → cell proliferation.

MORPHOLOGY

- solitary – sporadic
- multifocal, bilateral – familial
- often paradoxically circumscribed
- firm, greyish-white or reddish brown Tx.
- large Tx may show hemorrhage & Central necrosis.

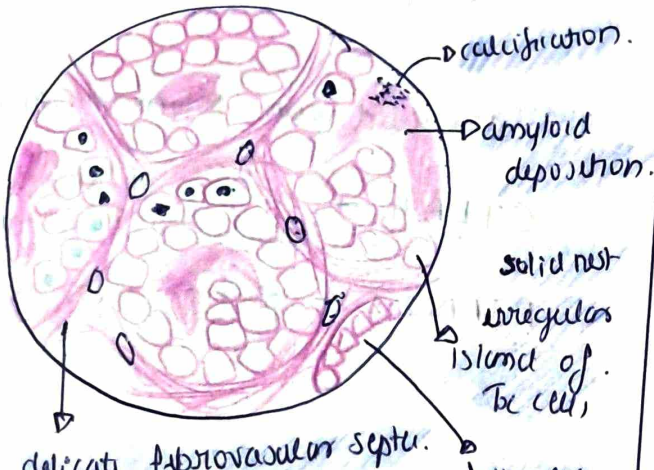
MICROSCOPY



- tumour cells : polygonal to spindle shaped cells.
- arrangement : nest
  trabecular.
  follicles.
- traversed by delicate fibrovascular septa.
- Prominent vasculature

familial cases : C-cell hyperplasia

- amyloid deposits in stroma - due to calcitonin production



- ~~neuroendocrine cells with~~
- ~~salt & pepper chromatin.~~

→ positive staining in IHC ✓
- essential for diagnosis ✓

IHC → calcitonin. within cell cytoplasm & amyloid.

- ~~Cytokeratin (+) neuroendocrine marker (+)~~

Electron mc.

- membrane bound electron-dense granules in cytoplasm of tumour cells.

familial vs sporadic.

table - SC.

IHC → calcitonin.
Carcinoembryonic Antigen (CEA)
→ Chromogranin A
synaptophysin

Follicular Carcinoma.

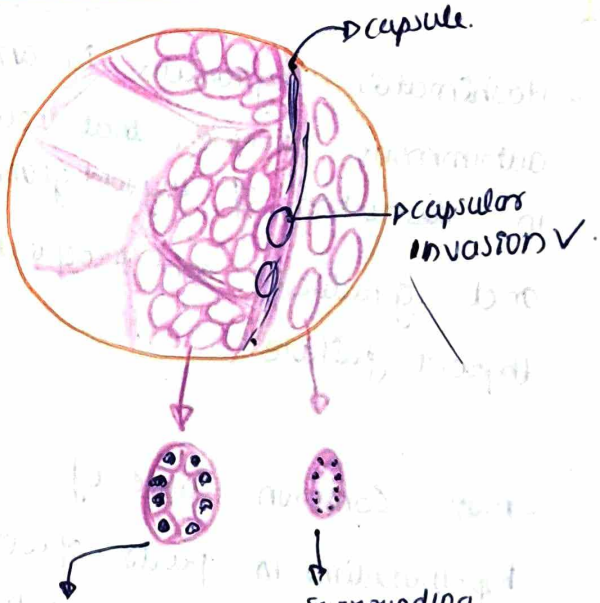
GROSS

- Single nodules
- well circumscribed / widely infiltrative.

Cut section
- tan, pink, may be translucent. {due to colloids}
- foci of haemorrhage.

degenerative changes like → central fibrosis & calcification.

MICROSCOPY



Thyroiditis

- group of disorders characterised by Inflammation of thyroid gland.

Types of Thyroiditis.

1. Hashimoto's thyroiditis.
2. Granulomatous thyroiditis.
3. Subacute lymphocytic thyroiditis.

Hashimotos thyroiditis / Chronic Lymphocytic thyroiditis.

- Hashimato's thyroiditis is an autoimmune disease that results in destruction of thyroid gland and gradual and progressive thyroid failure.

- most common cause of hypothyroidism in parts of world where Iodine levels are sufficient.

Clinical presentation

- painless enlargement
- diffuse & symmetric enlargement
- associated hypothyroidism.

Etiology

- It has a strong genetic component.

- associated with polymorphism in.

CTLA4 – cytotoxic T lymphocyte associated Antigen-4

PTPN22 – protein tyrosine phosphat 22.

Pathogenesis

Figure

failure of self tolerance.

↓

Induction of thyroid autoimmunity

↓

destruction of thyrocyte by 3 ways

↓

hypothyroidism.

Thyroid epithelium.

↓

Breakdown in self tolerance.

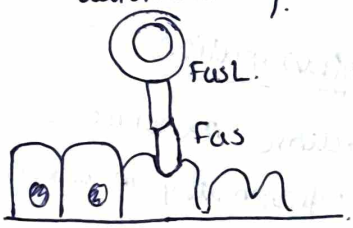
↓

Induces thyroid autoimmunity & causes destruction of thyrocytes.

CD8+ cytotoxic Tcell.

↓

T-cell mediated autoimmunity.



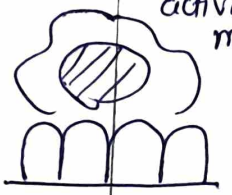
① CD8+ cytotoxic Tcell mediated cell death ✓

CD4+ TH1 cells.

↓

IFN-γ.

↓



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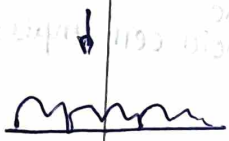
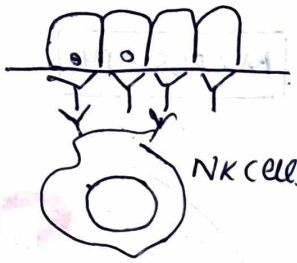


Thyrocyte injury.

② cytokine mediated cell-death. ✓

↓

antithyroid antibodies.



Antibody dependent cell mediated cytotoxicity.

③ ADCC. ✓

- Autoantibodies
  - anti-thyroglobulin.
  - anti-Thyroid peroxidase
  - anti-TSH receptor.

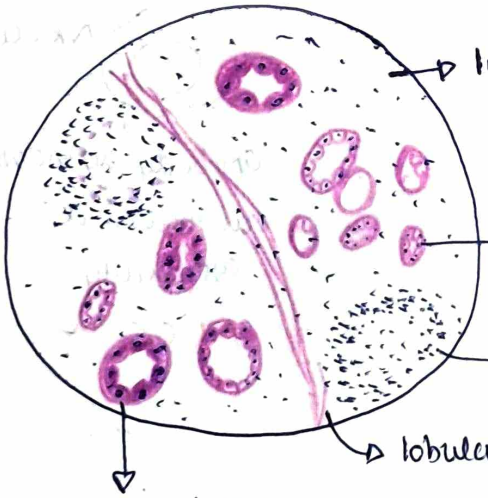
MORPHOLOGY

GROSS : Diffuse & Symmetric enlargement of thyroid gland.

- firm, nodular gland
- capsule – intact – gland is well demarcated from adjacent structures.

Cut surface: pale yellow-tan.
Slightly nodular.

MICROSCOPY



① Inflammation
- dense mononuclear inflammatory infiltrates.
- lymphoid follicles with prominent germinal centres.

② epithelial changes
- atrophy of thyroid follicles
- Hurthle cell metaplasia

③ fibrosis.

Hurthle cell metaplasia.

- It is metaplastic response of follicular epithelium to injury.

↓

Hurthle cell / askanazy | oxyphil | oncocytes.
cells

↓

- abundant eosinophilic, granular cytoplasm & lines some of the follicles
- ultrastructurally they have → prominent mitochondria.