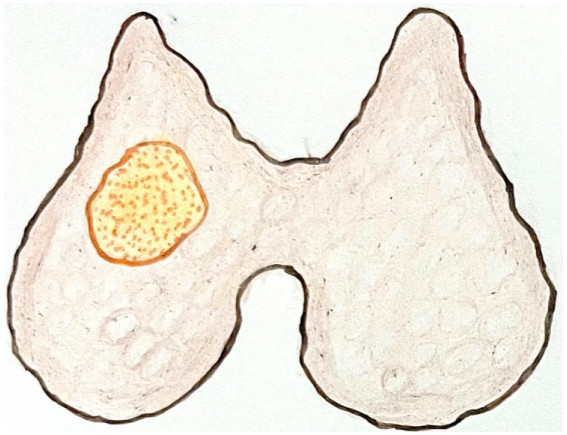
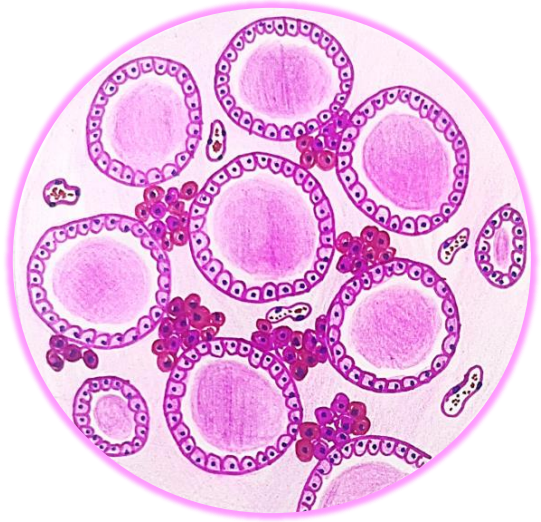
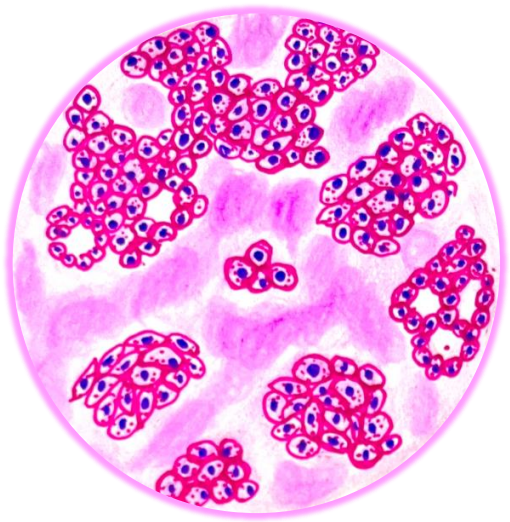
MEDULLARY CARCINOMA - THYROID







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MEDULLARY CARCINOMA

- Malignant neuroendocrine tumor of thyroid gland composed of cells showing parafollicular C-cell differentiation
- Tumor cells like C cells secrete calcitonin which is calcium regulator causing decrease in serum calcium levels by inhibiting renal tubular reabsorption of calcium and osteoclastic activty
- Synonym –
  - C-cell carcinoma
  - Parafollicular cell carcinoma
  - Solid carcinoma with amyloid stroma

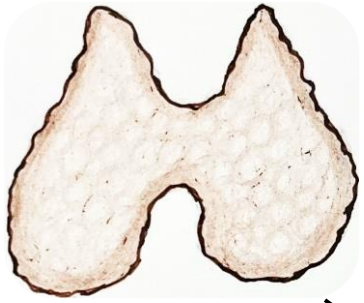
MEDULLARY CARCINOMA

Epidemiology

- Accounts for <2-3% of all thyroid malignancies
- Sex – female predominance
- Age
  - Sporadic (70%) – 5th or 6th decades of life
  - Hereditary (30%) – younger age group

MEDULLARY CARCINOMA

ETIOLOGY

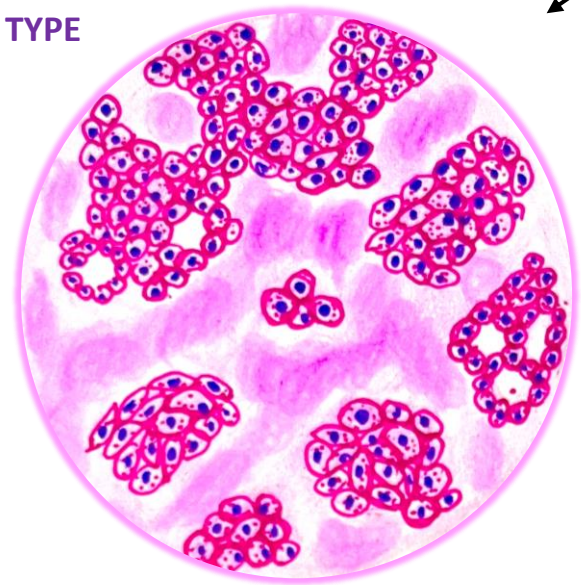


Point mutations of RET protooncogene

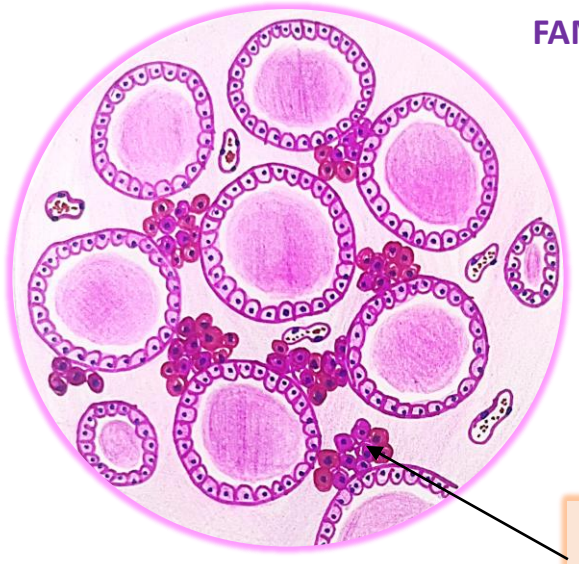
No relationship between external ionizing radiation of head and neck

- Autosomal dominant pattern of inheritance
- Gain of function mutations of RET protooncogene
- Associated with syndromes like
  - MEN type 2which includes MEN 2A and MEN 2B
  - Von-Hippel Lindau syndrome
  - Neurofibromatosis

SPORADIC TYPE



FAMILIAL TYPE



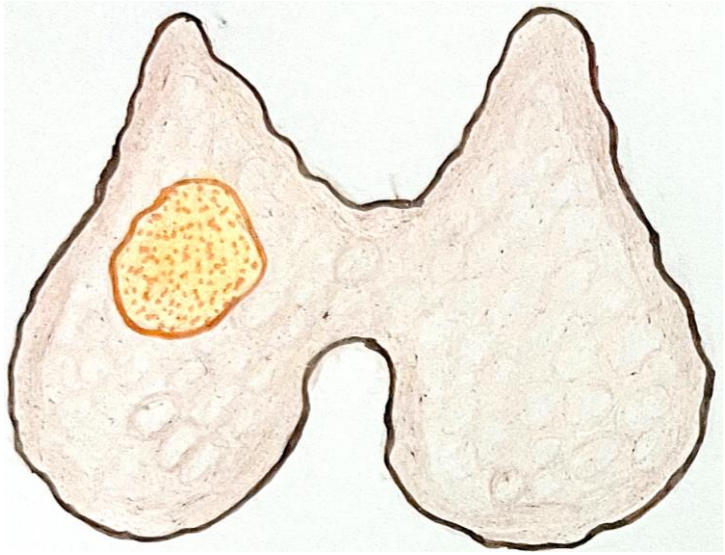
C cell hyperplasia (precursor lesions)

Medullary carcinoma

MEDULLARY CARCINOMA

Localization

- Located at the junction of upper and midportion of thyroid lobes, corresponding to areas which in which C cells are normally concentrated



MEDULLARY CARCINOMA

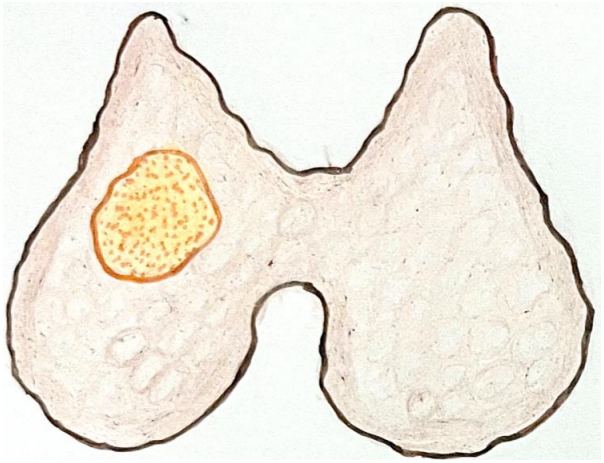
Clinical features

- Sporadic tumors –
  - Present as painless thyroid mass which appears cold on scanning
  - 70% of cases – present with palpable thyroid nodule and cervical node metastasis
  - 10% - have distant metastasis
- Direct extension of local growth of tumor – upper airway obstruction and dysphagia
- Presents with diarrhea and flushing due to high levels of calcitonin
- Some tumors produce ACTH – develops Cushing syndrome

MEDULLARY CARCINOMA

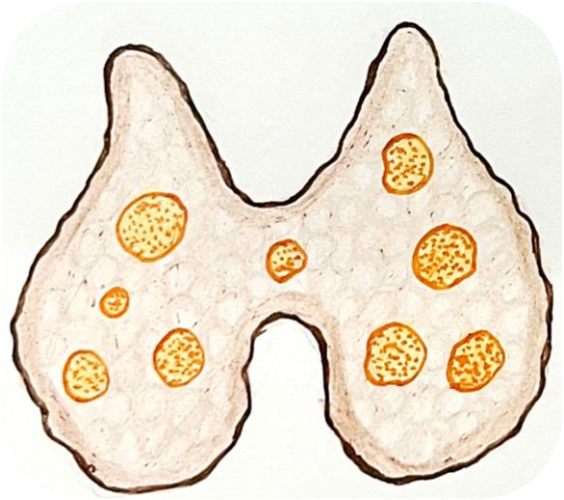
Morphology
Gross

Sporadic MTC



Typically presents as a single sharply circumscribed but unencapsulated greyish tan to yellow mass of variable consistency

Hereditary MTC



Typically bilateral and multicentric

Size - < 0.1cm in diameter to large tumors which replace the entire thyroid lobe

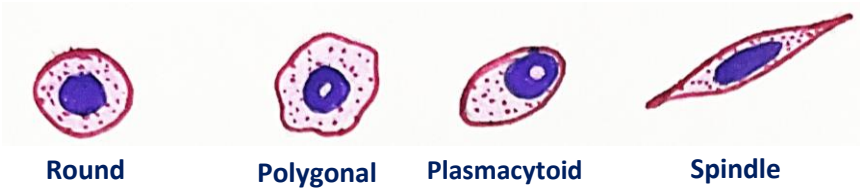
Tumors m/s <1cm in diameter have been called medullary thyroid microcarcinoma

MEDULLARY CARCINOMA

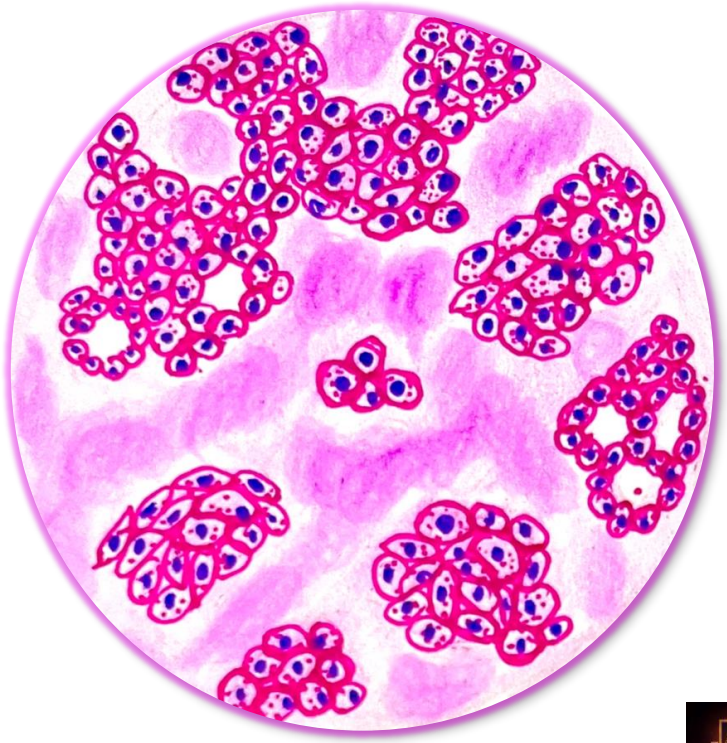
Morphology

Microscopy

Classical tumor –



- Solid, lobular, trabecular, insular or cribriform pattern
- Individual tumor cells –
  - Variably sized and can be round, polygonal, plasmacytoid or spindle shaped with frequent admixtures of these type
  - Nuclei are generally round with coarsely clumped chromatin with small nucleoli and occasional pseudoinclusions are present
  - Cytoplasm is eosinophilic to amphophilic and appears finely granular (EM – calcitonin in granules)
- Nuclear pleomorphism low to moderate
- Mitotic activity – relatively low

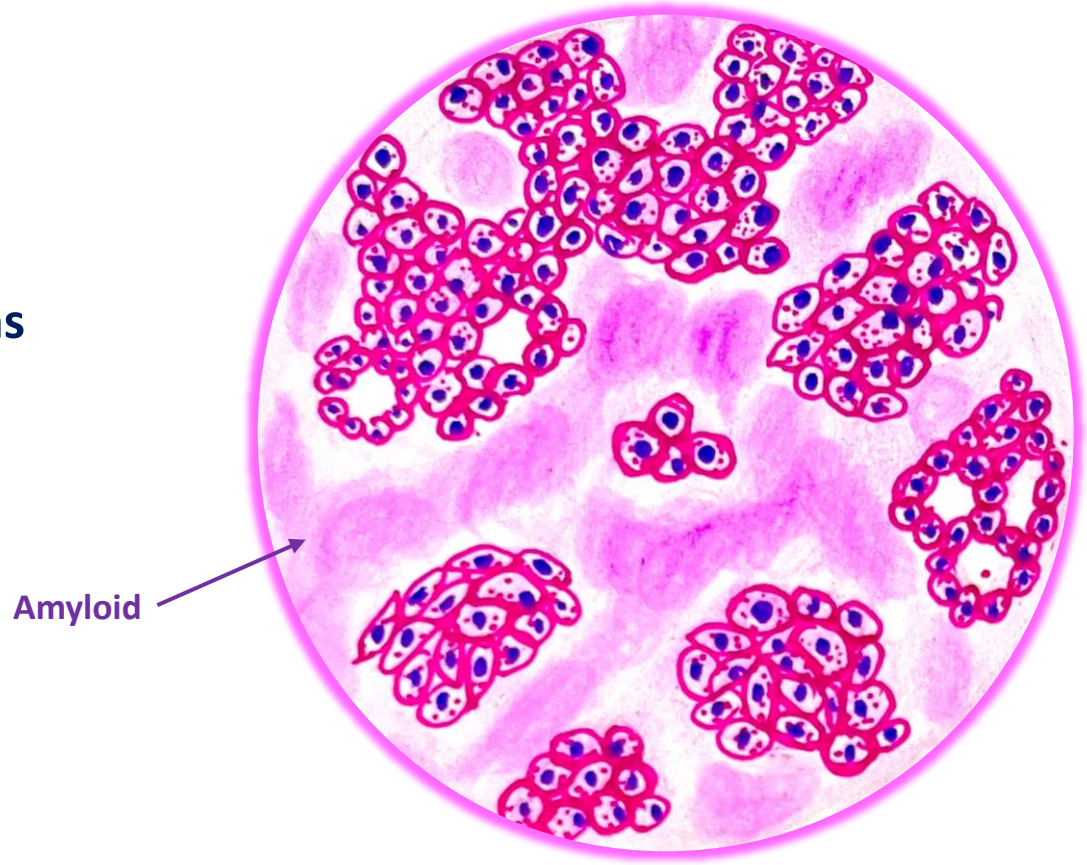


MEDULLARY CARCINOMA

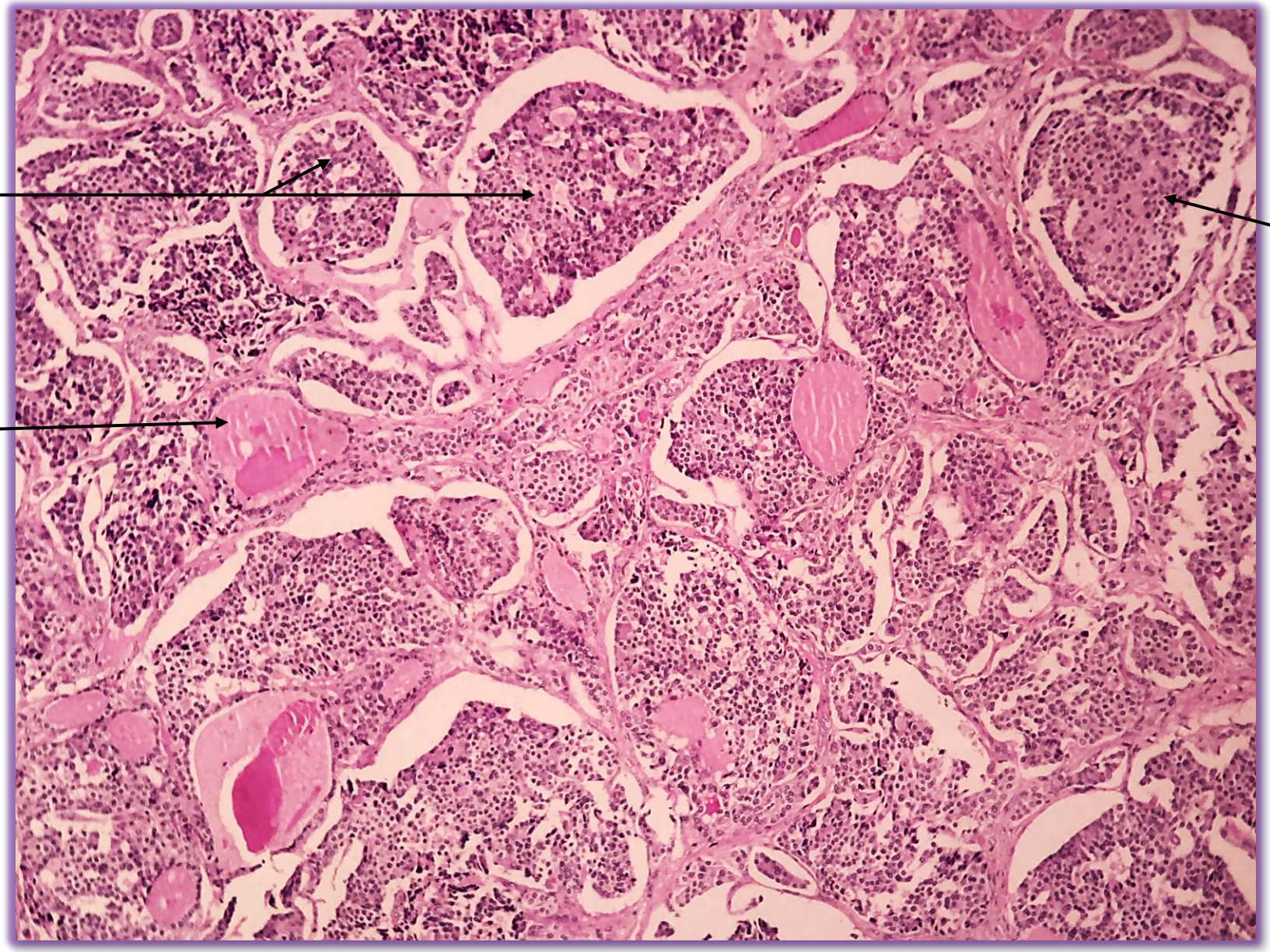
Morphology

Microscopy

- Stroma – amyloid deposit (90% of cases) which contains full length calcitonin as their major constituents
- Hereditary MTC is similar to sporadic MTC morphologically except for their bilaterality, multicentricity and association with primary C-cell hyperplasia

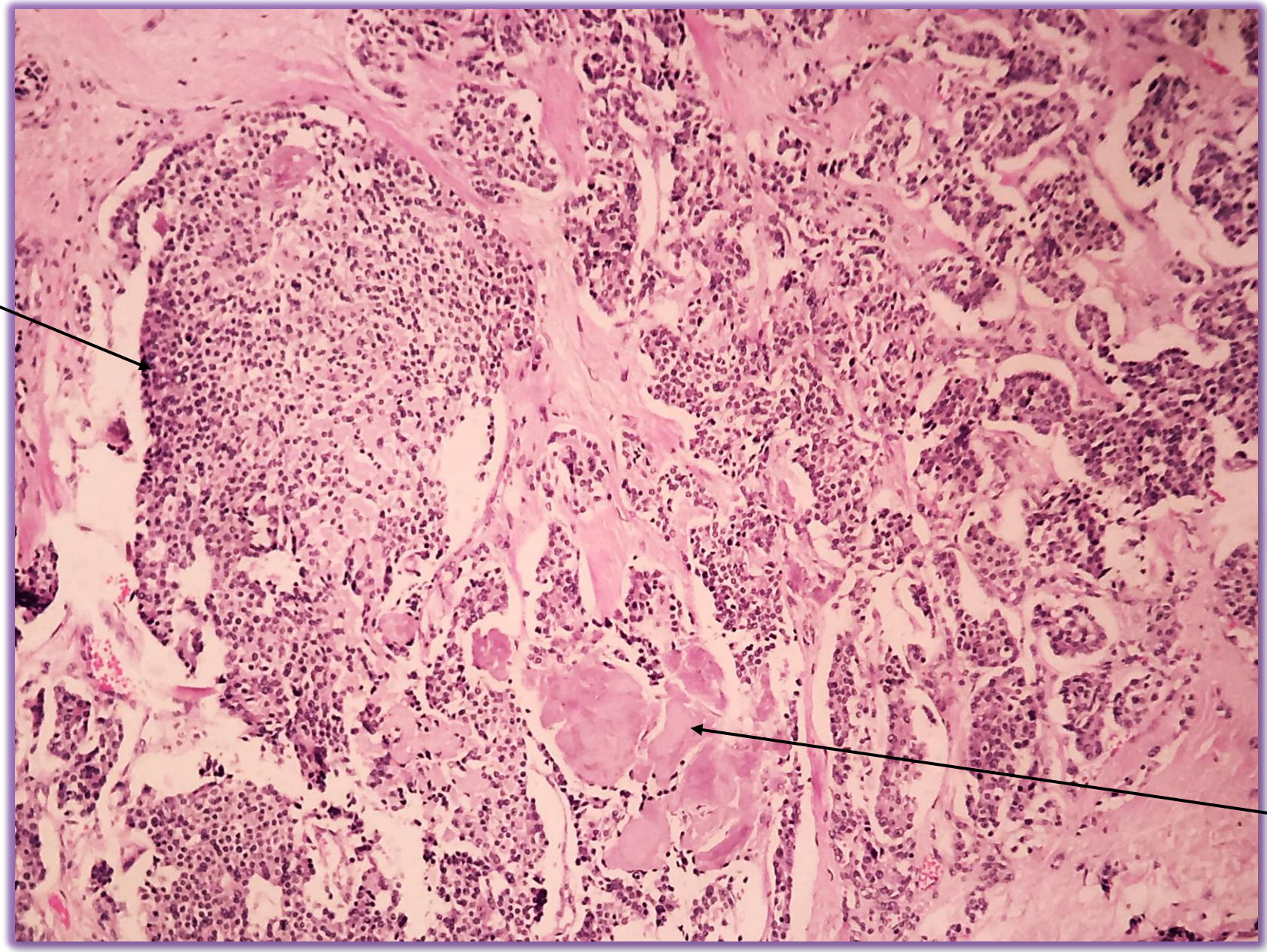


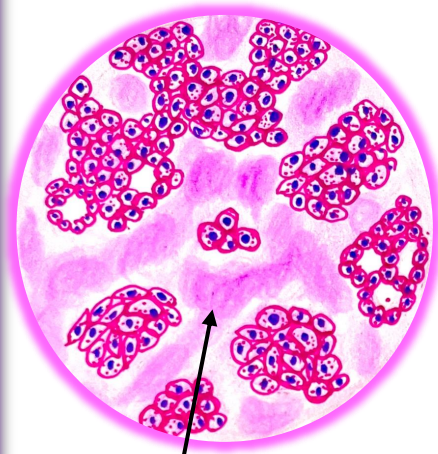
MEDULLARY CARCINOMA



MEDULLARY CARCINOMA

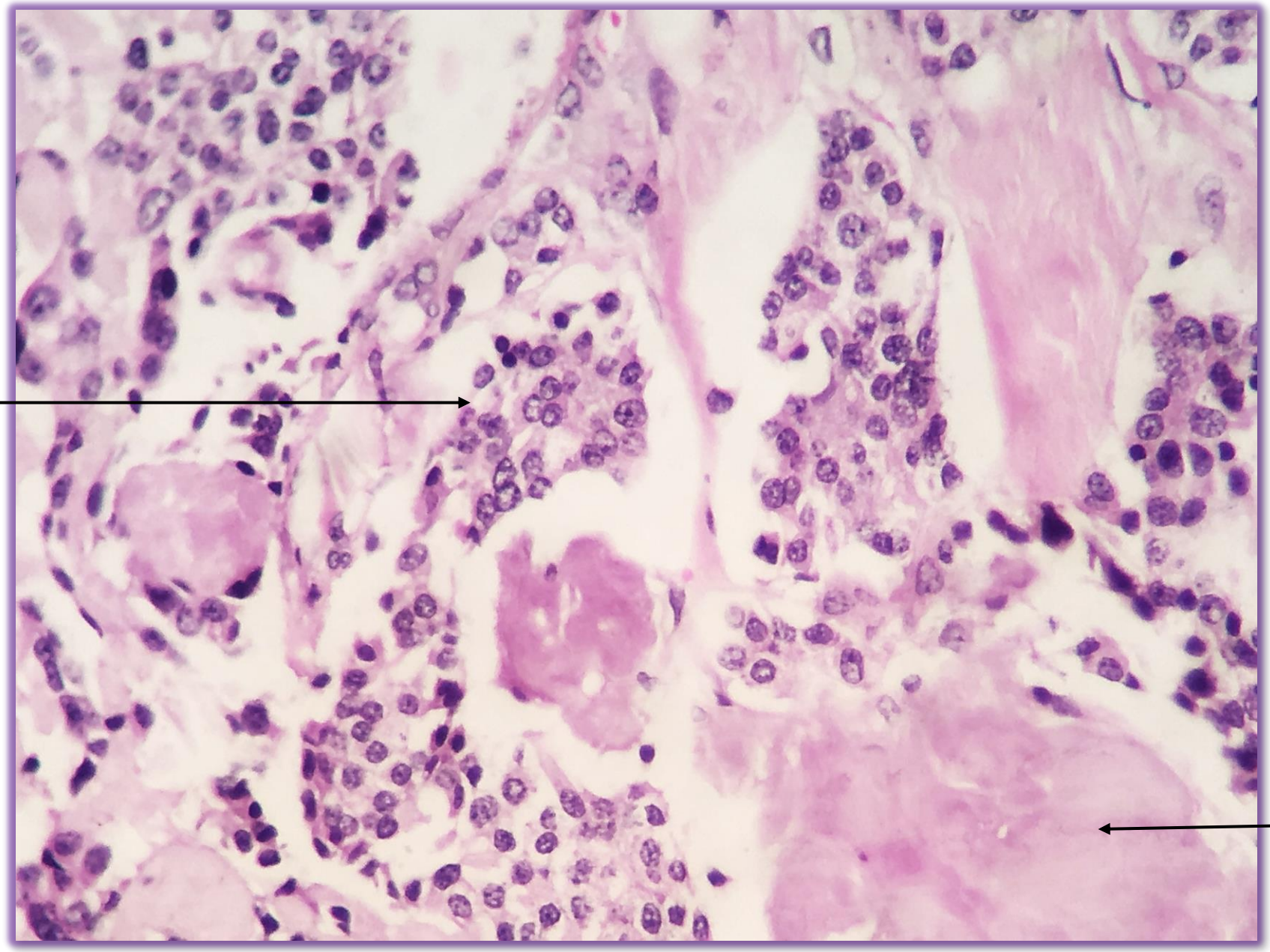
Tumor cells
arranged in lobules



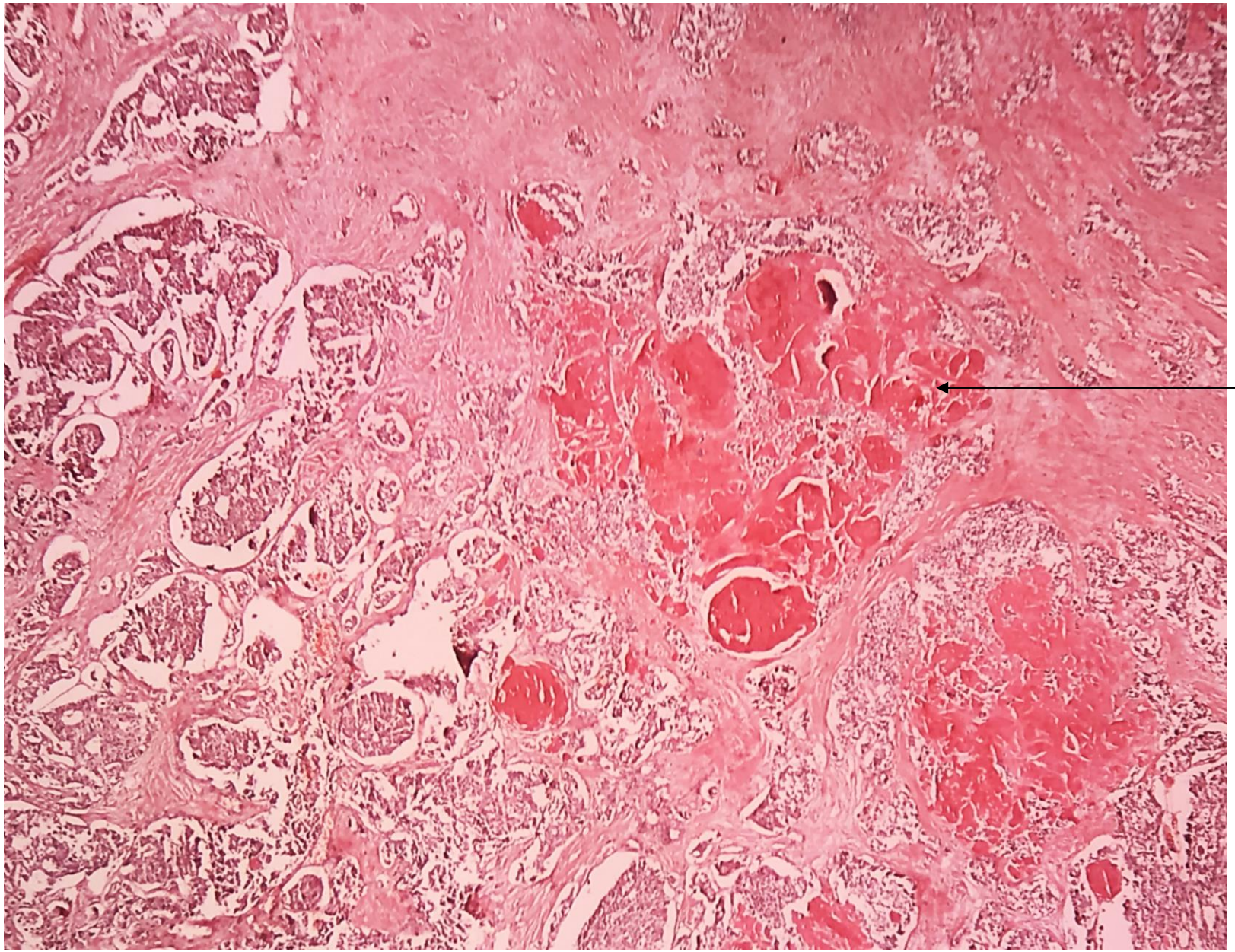


Amyloid deposition
in stroma

MEDULLARY CARCINOMA



MEDULLARY CARCINOMA

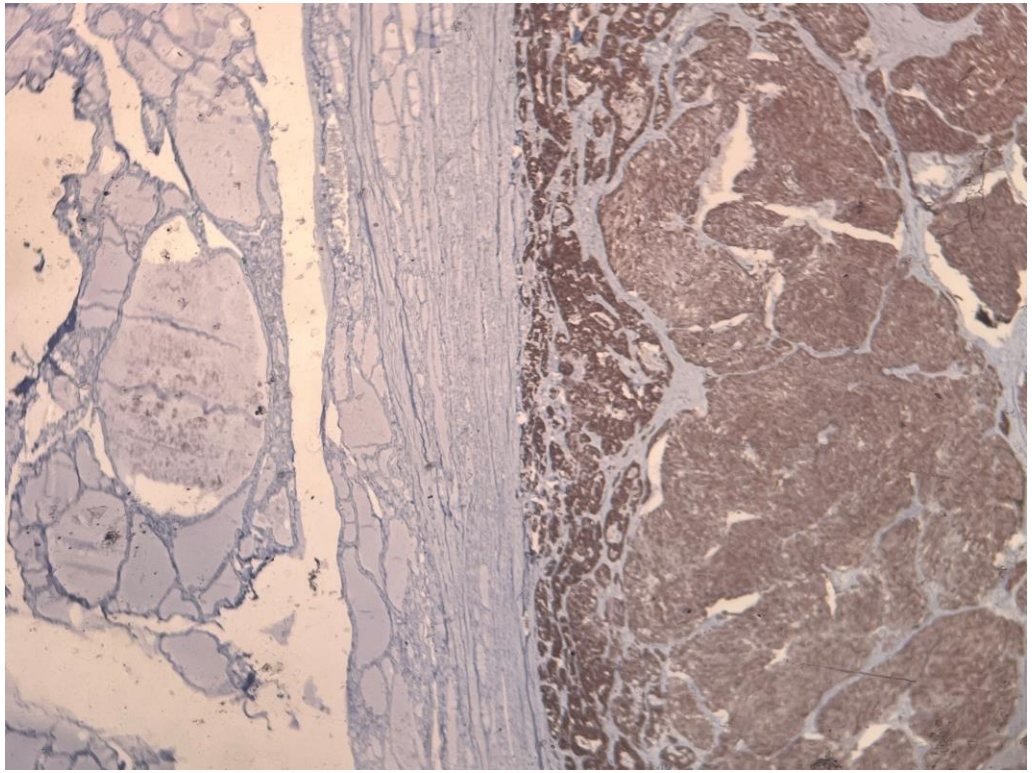


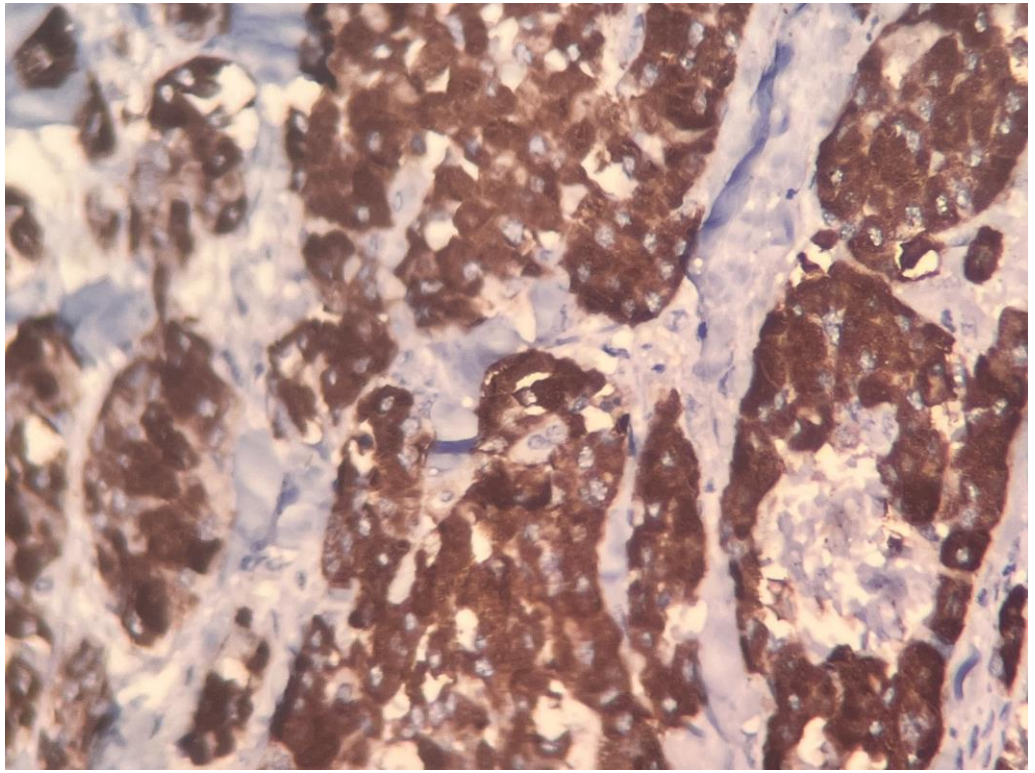
Congored staining of Amyloid

MEDULLARY CARCINOMA

Immunohistochemistry

- Tumor cells are positive
  - for calcitonin – related peptide
  - Neuroendocrine markers including synaptophysin and chromogranin





MEDULLARY CARCINOMA

Immunohistochemistry

Tumor cells are positive

- **TTF -1 – less intensity than seen in follicular cell neoplasm**
- **Thyroglobulin – negative**
- **CEA – Positive in vast majority of cases**

MEDULLARY CARCINOMA

Variants

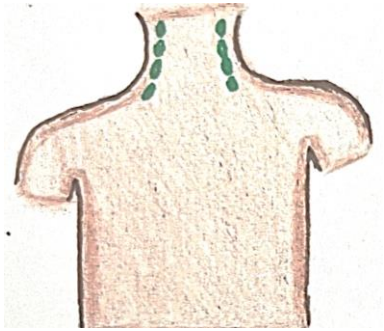
- No significant impact on prognosis but identification is important to prevent confusion with other tumor type

- Variants are
  - Papillary variant
  - Follicular (tubular/glandular variant)
  - Spindle cell variant
  - Giant cell variant
  - Clear cell variant
  - Oncocytic variant
  - Melanotic variant
  - Squamous variant
  - Amphicrine variant – cells contain both mucin and calcitonin
  - Paraganglioma-like variant
  - Angiosarcoma like variant
  - Small cell variant – more aggressive

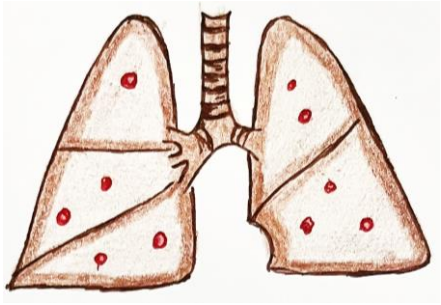
MEDULLARY CARCINOMA

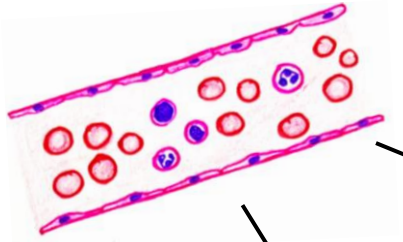
Mode of spread

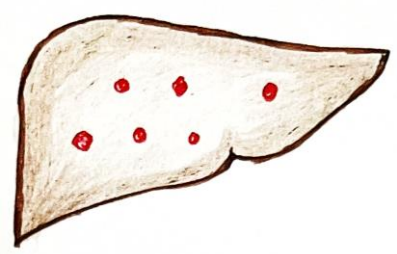
Lymph nodes (75% of tumors)

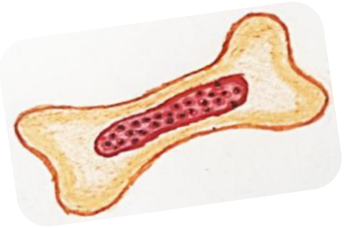


Hematogenous spread









Other organs

- **Adrenal glands**
- **Pituitary gland**
- **Breast**

MEDULLARY CARCINOMA

- Poor prognostic factors
  - Older than 50 years
  - Lymphnode metastasis and Distant spread
  - Patients with other endocrine tumors due to MEN II-B syndrome
  - Tumor with RET mutation
  - Residual disease or recurrence

MEDULLARY CARCINOMA

Treatment

- **Surgery – total thyroidectomy with bilateral neck dissection and**
- **Radiation therapy**

SUMMARY

MEDULLARY CARCINOMA

Parafollicular C cell tumor (neuroendocrine tumor)

2% - 3% of thyroid malignancies
Common in females

SPORADIC (70%)

- 5th and 6th decade
- Mutations of RET gene

Gross – solitary

FAMILIAL (30%)

- Younger age group
- Autosomal dominant
- RET mutations
- Associated syndromes
  - MEN type 2
  - Neurofibromatosis
  - Von-Hippel Lindau syndrome

Gross – multicentric and bilateral

Microscopy :

- Round, polygonal, spindle, plasmacytoid tumor cells
- Solid, lobular, insular, cribriform pattern
- Stroma shows amyloid containing calcitonin

Mode of spread

- Lymph nodes (75%)
- Hematogenous spread
  - Lung
  - Bone
  - Liver
  - Adrenal
  - Pituitary
  - breast

Poor prognostic factors

- Age - old
- Metastasis
- RET mutation
- Other tumors -MENIIb
- Residual disease or recurrence


Thank
you!