Pheochromocytoma

Pheochromocytoma

- Tumors of the adrenal gland.
- Neoplasms composed of chromaffin cells, which **tumor cells synthesize and release catecholamines** and some may produce peptide hormones.
- These tumors are the rare cause of surgically correctable **hypertension**.
- Mutations in genes-RET, NF1, VHL and three succinate dehydrogenase complex subunit genes, i.e. SDHB, SDHC, and SDHD.

Rule of 10s

- 10% of pheochromocytomas are **extra-adrenal-**occur in organs of Zuckerkandl and the carotid body.
- Extra-adrenal pheochromocytomas are called as **paragangliomas.**
- 10% of sporadic adrenal pheochromocytomas are **bilateral**.
- 10% of adrenal pheochromocytomas **metastasize** and are **malignant (malignancy is more common in extra-adrenal paragangliomas, and tumors developing due to germline mutations)**.
- 10% not associated with hypertension.

Morphology

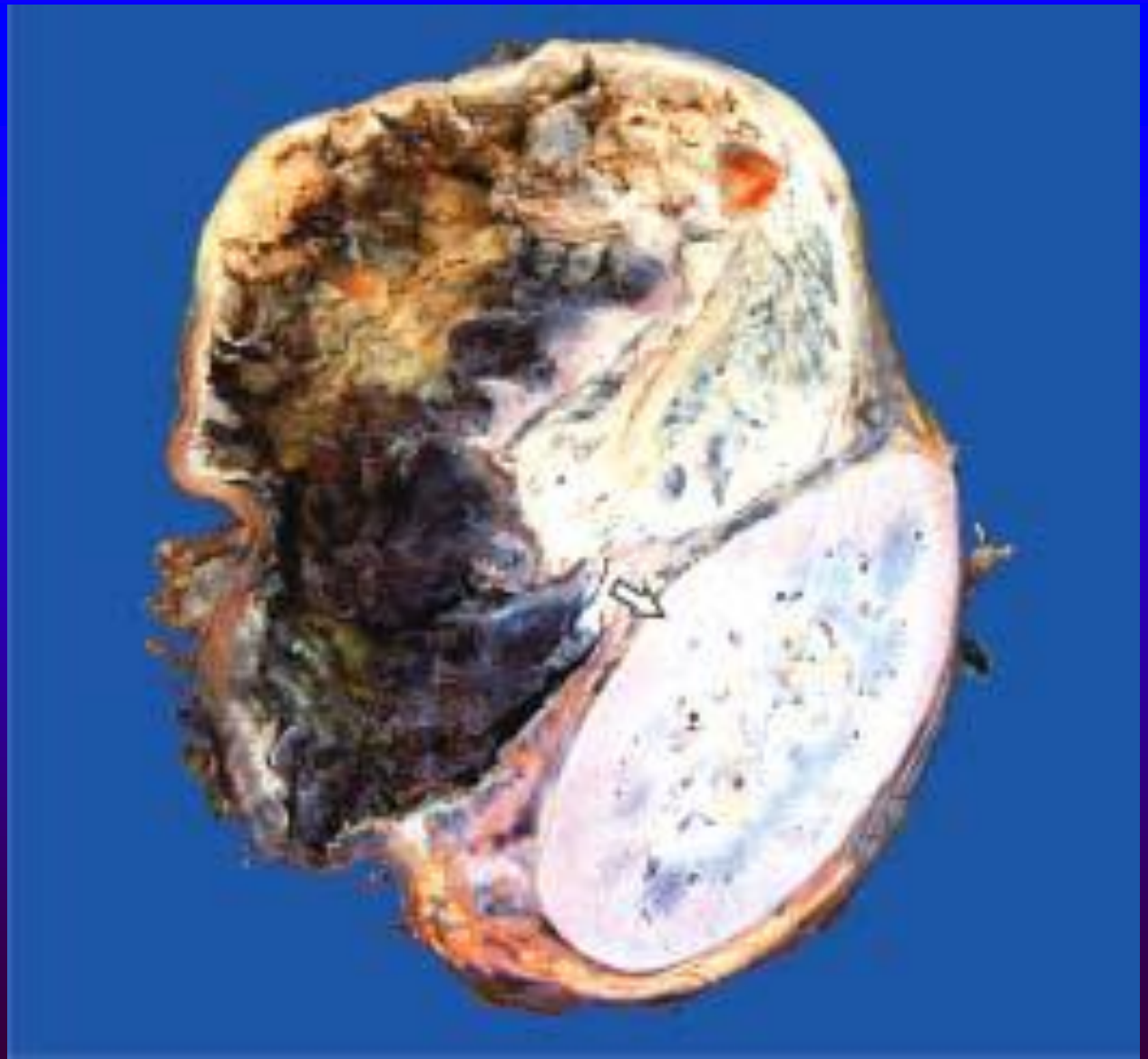
Gross:

- **Size: Varies** and may range from small, circumscribed lesions confined to the adrenal to large hemorrhagic masses.
- Larger tumors are **well-demarcated** and **may** produce a **lobular pattern.**

Cut surface:

- Small have **yellow tan.**
- **Well defined lesions** that compress the adjacent adrenal glands large lesion show areas of **hemorrhage, necrosis, and cystic changes.**

Gross:



Chromaffin reaction:

- When the **fresh tumor tissue is incubated in potassium dichromate solution** it turns the **tumor dark brown in color** due to oxidation of stored catecholamines.
- This is termed positive **chromaffin reaction**.

Microscopy

Zellballen pattern:

- The tumor consists of **polygonal to spindle-shaped chromaffin cells or chief cells**, clustered with the sustentacular cells **into small nests or alveoli (Zellballen)** separated by a **rich vascular network.**

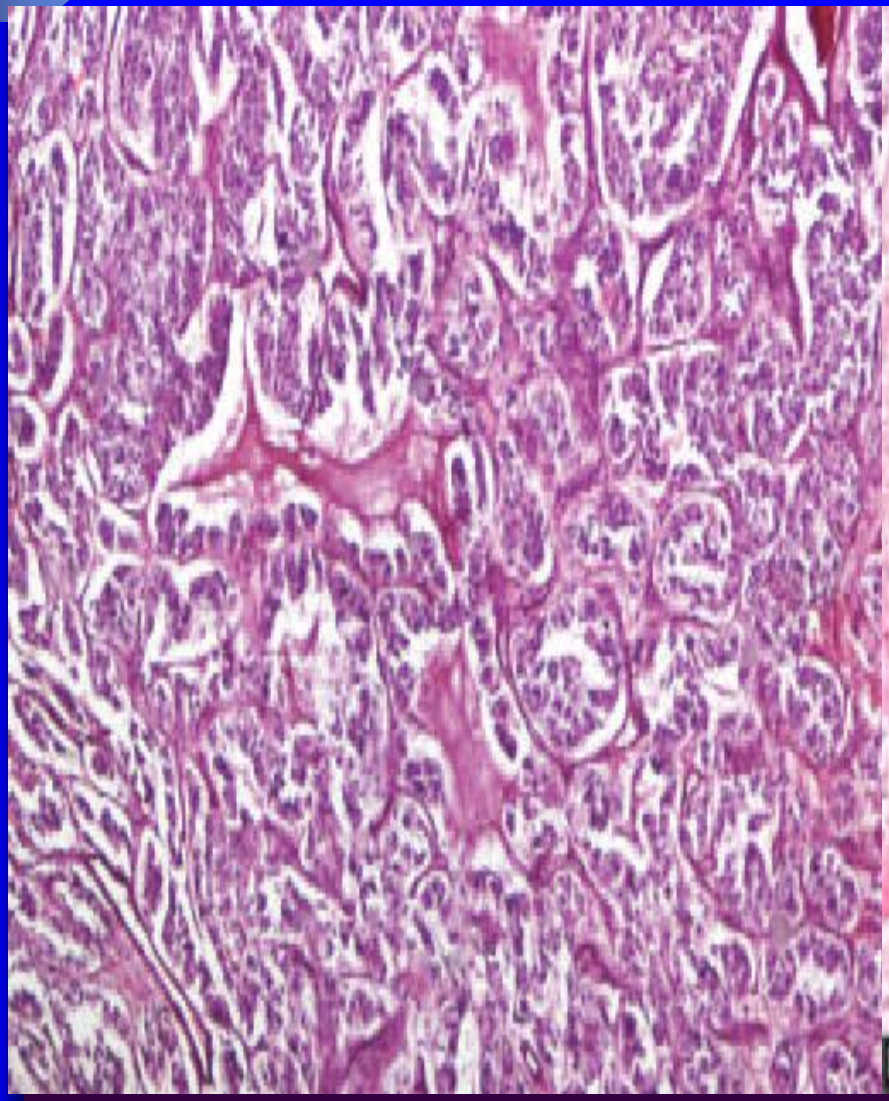
Cytoplasm:

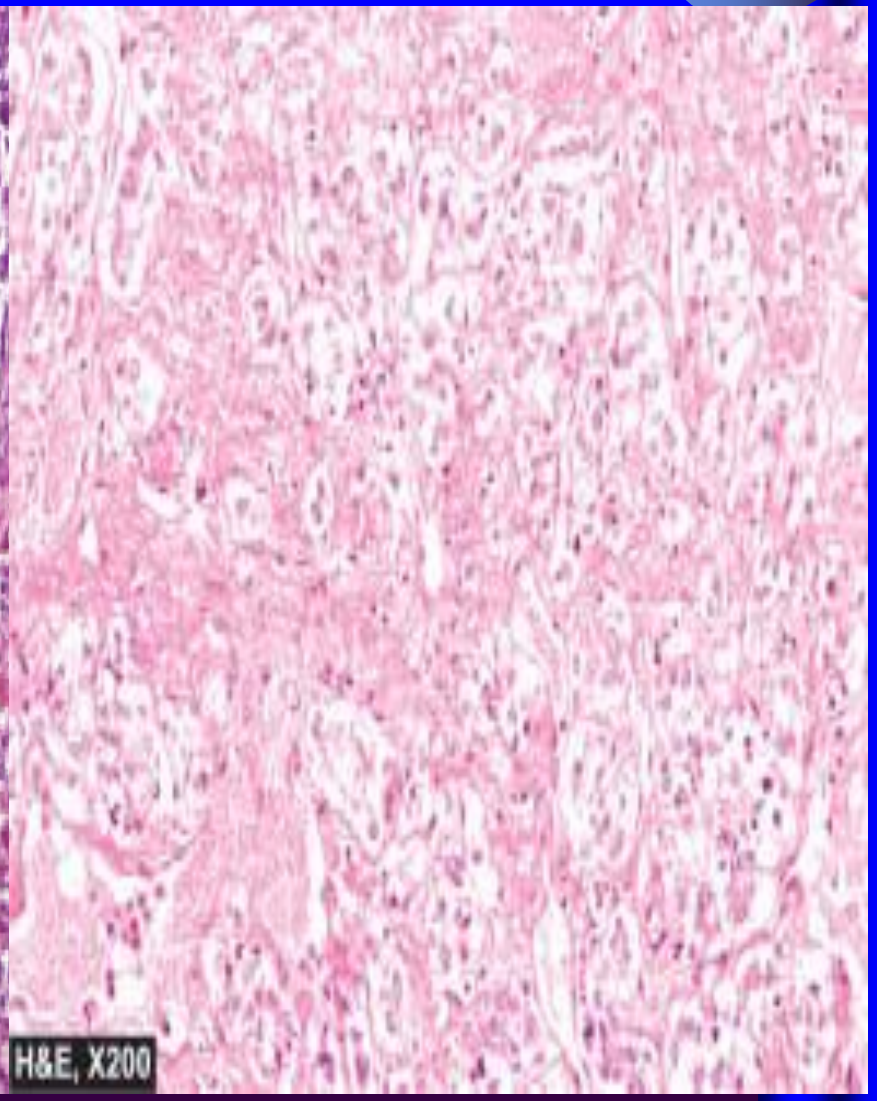
- It has a **finely granular appearance due to** the presence of granules containing **catecholamines.**

Nuclei:

- Round to oval, with a stippled **"salt and pepper"** chromatin(neuroendocrine tumors).

Microscopy





Electron microscopy:

- It shows **membrane-bound, electron-dense secretory granules**.

Immunohistochemistry:

- **Neuroendocrine markers (chromogranin and synaptophysin)** are positive in the chief cells.

Criteria for Malignancy:

- Based on the presence of **metastases.**
- Histologic features associated with an **aggressive behavior and increased risk of metastasis** include:
  - **Numbers of mitoses**
  - **Confluent tumor necrosis**
  - **Spindle cell morphology**
- **Capsular and vascular invasion may be found in benign lesions.**

Clinical features

- Hypertension in 90% of patients.
- **Paroxysmal episodes(2/3rd):** It is characterized by abrupt, precipitous elevation in blood pressure, associated with tachycardia, palpitations, headache, sweating, tremor, and a sense of apprehension.
- **Isolated paroxysmal episodes:** Less common.
- **Chronic**, sustained elevation in blood pressure punctuated by paroxysms.
- The elevations of blood pressure are induced by the sudden release of catecholamines.
- This may precipitate congestive heart failure, pulmonary edema, myocardial infarction, ventricular fibrillation, and cerebrovascular accidents.

Complications

- **Catecholamine cardiomyopathy.**
- Catecholamine-induced myocardial instability.
- Ventricular arrhythmias.

Laboratory Diagnosis

- It is based on demonstration of **increased urinary excretion of free catecholamines and their metabolites**, such as vanillyl-mandelic acid and metanephrines.
- Isolated benign pheochromocytomas are treated with surgical excision.
- With multifocal lesions, long term medical treatment for hypertension may be required.