CA LUNG:

Lung cancer is the most frequent And common cause of cancer.
- Malignant tumor which arises from the Resp epithelium present on the bronchi, bronchiole or Alveoli

CLASSIFICATION:

- Epithelial tumor - benign & malignant. → Papillomas, Adenomas.
- Mesenchymal tumor.
- Lymphohistocytic tumor
- Tumor of ectopic origin.
- Lung neuroendocrine neoplasm — Small cell lung carcinoma, Large cell neuroendocrine carcinoma, Carcinoid.

ETIOLOGY:

Tobacco - smoking — carcinogen.

→ 80% lung cancer occurs in Active smokers.

→ The strongest association of smoking with squamous cell & small cell cancer

→ Cigarette smoking is Also associated with pancreas, uterine, cervix, kidney, UB

→ MAJOR CARCINOGEN IN SMOKE - Polycyclic Aromatic hydrocarbons (benzo∝pyrene,), Radioactive element (Arsenic, nickel).

→ Occupational Hazards, Radon → ↑ lung cancer
↳ Asbestos, silicosis

→ Air pollution → Uranium mines

PATHOGENESIS:

Classified into — Non-small cell lung carcinoma (NSCLC) (80%)
— Small cell lung carcinoma (20%)

with distinct, genetic, epigenetic, molecular Alteration

1. NON-SMALL CELL LUNG CARCINOMA (NSCLC)

↳ Includes - Adenocarcinoma, Squamous cell carcinoma, large cell carcinoma.

1.) ADENOCARCINOMA: → non-smokers.

→ Associated with genetic mutation

✓ Gain of function mutation in gene

EGFR Mutation (Epidermal Growth factor Receptor)

↓

Activation lead to uncontrolled cell proliferation

✓ Mutation in KRAS - poor prognosis

✓ Activating Rearrangement of ALK gene:

fusion of EML4-ALK lead to Activation of ALK gene

- Mutation of BRAF
- Other ROS1, MET Amplification, RET fusion.

2) SQUAMOUS CELL CARCINOMA (SCC)

SCC is strongly linked with smoking & arises from the bronchial epithelium.

→ Inactivation of tumor suppressor gene Alterations:

→ loss of functional mutation
↳ Chromosome deletion involving tumor suppressor loci involving 3p, 9p, 17p

- TP53 mutations — 60-90% of SCC → Apoptosis evasion
- CDKN2A mutation — 65% of SS
  ↳ Unchecked cell cycle progression
- FGFR1 Amplification

II SMALL CELL CARCINOMA → MOLECULAR PATHOGENESIS
Associated with smoking.

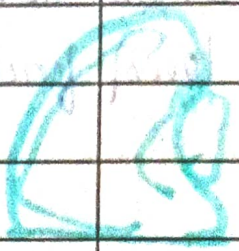
- TP53 Mutation ~10% cases → loss of tumor suppressor And genomic Instability.
- Mutation of RB gene (Always mutated gene in SCLC)
  ↳ Cause unRestricted cell cycle progression
- MYC Amplification → Rapid proliferation & tumor Aggressiveness
- NOTCH Inactivation → promote tumor stem-like properties
- BCL2 Overexpression

HISTOLOGIC TYPE:

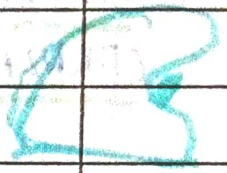
- Small cell lung cancer (20%)
- Non small cell lung cancer (80%)
  ↳ Adenocarcinoma
  ↳ Squamous cell carcinoma
  ↳ Large cell carcinoma.

MORPHOLOGY OF LUNG CANCER:

Location of Lung Cancer: — peripheral
                          — hilar Region.



⇒ central (hilar) ~ 75% arise from bronchus.
Include → SCC. Squamous cell carcinoma



⇒ Peripheral — Arise from peripheral bronchiole
Include — Adenocarcinoma,

ADENOCARCINOMA — Minimally invasive ~~Adenocarcinoma~~
                 — Invasive Adenocarcinoma
(most common in ~~women And~~ non smokers)

MORPHOLOGY:
Location → Peripherally located
App → irregular mass.
Cut section → Appear grayish-white

MICRO Growth pattern: lepidic, Acinar, papillary, solid, micropapillary
Immunohistochemistry = +ve for thyroid transcription factor 1 (TTF-1)

SQUAMOUS CELL CARCINOMA: — >men, cigarette smoking
Location → from major bronchi
• Peribronchial growth: ulcerated lesion is Bronchi penetrate the wall of involved bronchus Along the peribronchial growth.

· Intra parenchymal growth : → tumor grow cauliflower like mass

· Exophytic growth - project into the lumen of the bronchi → obstruct.
color : Gray white
cut : Area of hemorrhage or necrosis.

MICROSCOPY:
Keratinization : Epithelial keratin pearls.
Intercellular bridge - seen as slender gap b/w Ad cells.
well differentiated - appear small Round nest of highly eosinophilic Aggregates of keratin surrounded by onion skin layer of squamous cells.

SMALL CELL LUNG CARCINOMA :
- Highly malignant.

MORPHOLOGY:
GROSS : appear as large purplish mass in major bronchi (central region)
cut section : soft, friable, white, extensive hemorrhage

MICRO (light)
Size & shape : Round, oval or spindle-shaped small cell (oat cell)
- 3 times less than size of small lymphocyte
- cells are fragile & show fragmentation of crush artifacts.

- Cytoplasm : scanty, faintly, ill defined cell Bordes.
- Nucleus : hyperchromatic, finely granular chromatin.

Mitotic count: ↑

Necrosis : The blood vessel wall may stain blue due to the deposition of DNA called (Azzopardi effect)

Growth pattern : sheet or clusters.

Immunohistochemistry : Chromogranin, synaptophysin & / CD56.

EM → tumor cell show membrane bound neurosecretory granules.

COMPLICATION:

→ Obstruction : Partial / Total
→ Suppuration
→ compression or invasion of SVC.

Compress
→ Esophagus - Dysphagia
→ chest wall → Destruction of Rib

SPREAD OF TUMOR:

⇒ Direct spread : invade the wall of bronchus, extend into pleural surface

A tumor at the Apex of lung invade neural structures → Resulting in Pancoast syndrome

⇒ Lymphatic spread : initially hilar nodes
later superclavicular nodes (Virchow's node)

Hematogenous spread.

Common site of metastasis are Adrenal, liver, bone of back

PARANEOPLASTIC SYNDROME:

- Cushing syndrome → Gynecomastic
- Carcinoid syndrome → Acanthosis nigricans.
- Hyponatremia. → Leukemoid Rx.
- Hypercalcemia

IHC marker - Chromogranin, Synaptophysin, EPSA.